

Pesticide Formulations

ACS SYMPOSIUM SERIES **371**

Pesticide Formulations

Innovations and Developments

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Developed from a symposium sponsored
by the Division
of Agrochemicals
at the 194th Meeting
of the American Chemical Society,
New Orleans, Louisiana,
August 30-September 4, 1987



American Chemical Society, Washington, DC 1988



Library of Congress Cataloging-in-Publication Data

Pesticide formulations.

Barrington Cross, editor. Herbert B. Scher, editor.

Developed from a symposium sponsored by the Division of Agrochemicals at the 194th Meeting of the American Chemical Society, New Orleans, Louisiana, August 30–September 4, 1987.

p. cm.—(ACS Symposium Series, 0097–6156; 371).
Includes bibliographies and indexes.

ISBN 0–8412–1483–2

I. Pesticides—Formulations—Congresses.

I. Cross, Barrington, 1935– . II. Scher, Herbert B., 1937– . III. American Chemical Society. Division of Agrochemicals. IV. Series

TP248.P47P485 1988
668'.65

88–10419

CIP

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PRINTED IN THE UNITED STATES OF AMERICA

American Chemical Society
Library
1155 16th St., N.W.
Washington, D.C. 20036

In Pesticide Formulations; Cross, B., et al.;

ACS Symposium Series; American Chemical Society: Washington, DC, 1988.

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Foreword

The ACS SYMPOSIUM SERIES was founded in 1974 to provide a medium for publishing symposia quickly in book form. The format of the Series parallels that of the continuing ADVANCES IN CHEMISTRY SERIES except that, in order to save time, the papers are not typeset but are reproduced as they are submitted by the authors in camera-ready form. Papers are reviewed under the supervision of the Editors with the assistance of the Series Advisory Board and are selected to maintain the integrity of the symposia; however, verbatim reproductions of previously published papers are not accepted. Both reviews and reports of research are acceptable, because symposia may embrace both types of presentation.

Preface

OPTIMIZING PESTICIDAL ACTIVITY THROUGH FORMULATION is the major theme of this book. This volume complements the 1984 book *Advances in Pesticide Formulation Technology*, ACS Symposium Series 254, edited by Herbert B. Scher, which addressed controlled release, flowables, and computer applications to formulation technology.

The current book covers three major topics and has a general section dealing with diverse topics. The first section deals with the effects of surfactants on pesticide wetting, penetration, and transport in plants. Authors trace the transport of pesticides in plants. They present models for these processes and new methods for determining permeation effects of surfactants.

Although the major theme of the book is the optimization of pesticidal activity through formulation, the second section discusses toxicity reduction through formulation.

The third section is devoted to emulsion technology; these chapters survey techniques to select surfactants. Cohesive energy density parameters are discussed as a means of selecting solvents. Solvent-phase interactions in microemulsions and the mode of action of structure agents in suspension concentrates are reviewed.

The last section covers topics on the controlled release of herbicides, insecticides, and natural products, in addition to granulation techniques and the effects of droplet size on distribution and efficacy.

This book provides much needed information on the current trends in pesticidal formulation for researchers working in industry, universities, or government agencies. As such, it should provide a valuable status review of pesticidal formulation for scientists involved in the development of formulations as well as those who use them. The agrochemical community at large should find this book a useful source of information.

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December 1987

Chapter 1

Innovations and Developments in Pesticide Formulations

An Overview

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Pesticide formulators are concerned with development of physically and chemically stable pesticide compositions which can be applied uniformly by the user and which result in effective and efficient pest control. The various types of pesticide formulations and the factors which affect formulation choice have been well documented (1). Pesticide formulation ingredients include biologically active agents, clays, solvent diluents, surfactants and polymers.

New concepts and developments in the use of surfactants and polymers in pesticide formulations form the basis for the collection of papers in this book. Even though most surfactants and polymers are biologically inert when applied to plants or insects, these same chemicals can profoundly affect the biological activity of the pesticide when used as part of a pesticide formulation.

Surfactants play many roles in pesticide formulations (2), serving as:

- 1) Emulsifiers for Emulsifiable Concentrates and Micro-emulsions and Wetting and Dispersing Agents for Wettable Powders, Water Dispersible Granules and Flowables.
- 2) Spray Tank Additives to aid droplet adhesion and wetting of foliage.
- 3) Spray Tank Additives to enhance performance of pesticides by increasing uptake into the plant.

Polymers also play many roles in pesticide formulations, including:

- 1) Protective Colloids in concentrated emulsions and dispersions (3).
- 2) Suspending Agents in concentrated emulsions and dispersions (1, 4).

0097-6156/88/0371-0001\$06.00/0

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- 3) Binders for extruded and agglomerated granule formulations.
- 4) Barriers in controlled release formulations (5).

This book is divided into four sections. The first section (Effects of Surfactants on Pesticide Wetting, Penetration and Transport in Plants) and the second section (Toxicity Reduction Through Formulation) are related in that the pesticides must penetrate through a complex natural barrier. In the case of plants the barrier is called the cuticle and the formulator attempts to maximize pesticide penetration through the cuticle in order to maximize pesticide effectiveness. In the case of skin the barrier is called the stratum corneum (6) and the formulator attempts to minimize pesticide penetration through the skin in order to minimize dermal toxicity. Both types of barriers are complex in that they have hydrophilic and lipophilic components. The plant cuticle has a layered structure. The outer surface of the cuticle is composed of wax. Under the wax is the cutin layer which is a crosslinked matrix of hydroxy-fatty acids forming a three dimensional polyester network infiltrated with waxes. Below the cutin is a hydrophilic layer composed of pectin and cellulose. The skin stratum corneum is composed of hydrophilic Keratin (protein) and lipids (fatty acids).

The formulation factors which affect pesticide penetration through both the cuticle and stratum corneum are:

- . Oil/Water Partition Coefficient of Pesticide
- . Formulation Type
 - . Physical properties of pesticide (solid or liquid)
 - . Presence of organic solvents
 - . Presence of barriers in controlled release formulations
- . Type and Concentration of Surfactants

The third section (Emulsion Technology) concentrates on the use of surfactants and polymers in the formation of pesticide emulsions and microemulsions and the fourth section (General Topics - Advances in Pesticide Formulations) concentrates on the use of polymers in the production of controlled release pesticide formulations.

Introductory remarks for each Section follow, along with a discussion of how the papers relate to the general subject matter and to each other.

Effects of Surfactants on Pesticide Wetting, Penetration and Transport in Plants

This first section of the book focuses on the effects of surfactants on pesticide spray droplet size distribution, adhesion, spreading

and wetting, penetration and transport (7, 8). The type and concentration of surfactant has a large effect on both the surface tension at the air/water interface and the contact angle at the water/plant interface. The surface tension affects the spray droplet size distribution which in turn affects both the efficiency of transport to the plant surface (drift losses) and the sticking efficiency on the plant surface (reflection losses). The product of the surface tension and the cosine of the contact angle (9) affects adhesion which in turn affects sticking efficiency on the plant surface. The product of the surface tension and the cosine of the contact angle also affects spreading and wetting which in turn affects plant coverage and runoff. The type and concentration of surfactant also has a large effect on pesticide permeation through the plant cuticle and pesticide transport within the plant. The surfactant can move into the cuticle, cause swelling and hence increase permeability. However, the surfactant effect on increasing permeability of the plant to the pesticide can often be offset by decreasing pesticide transport within the plant.

Pesticide Toxicity Reduction Through Formulation

Insights into the physicochemical factors that control percutaneous absorption are given in the paper by Ridout and Guy. These authors suggest a practical and inexpensive means of assessing the relative risk from dermal exposure for a structurally related series of chemicals. Their method involves correlating lipid-water partition coefficients with permeabilities through a model membrane composed of the same lipid.

The formulation type chosen for a particular pesticide is often dictated by a combination of the physical properties of the pesticide and the economics of the marketplace. However Hudson and Tarwater suggest that within the physical property and economic constraints there is still opportunity for reduction of pesticide toxicity through formulation and packaging choices.

The paper by Morgan, Rodson and Scher demonstrates a technique for reduction of toxicity of insecticides which involves combining the effects of a microcapsule wall barrier with a surfactant monolayer barrier created at the water/skin interface.

Emulsion Technology

The ease of emulsion formation and wetting of a surface is influenced by the rate of surfactant migration to the interface and the extent to which the interfacial tension is reduced by the surfactant at the interface. In the paper by Berger, Hsu, Jimenez, Wasan and Chung the maximum bubble pressure technique is used to measure the dynamic surface tension for a series of nonionic and anionic spray tank adjuvants and it is shown that there is a good correlation between rapid surface tension lowering and rapid wetting using the Draves wetting test.

Theory involving the use of the cohesive energy density concept can be useful in the initial phase of choosing emulsifiers for a pesticide emulsifiable concentrate formulation. The paper by Meusbürger shows how one goes about calculating the cohesive energy

for the organic pesticide phase (Group Contribution Method) and for an aqueous phase containing electrolyte.

The paper by Graff, Bock and Robbins shows the effect of solvent structure on the phase behavior of solvent in water micro-emulsions. They demonstrate that alkyl chain branching, allyl chain cyclization and the presence and position of hydrophilic functional groups in the solvents profoundly influence the observed phase behavior. The authors also suggest that the emulsion stability of macroemulsions should also be influenced by the same trends recognized for the phase behavior in microemulsions.

In the paper entitled "Mechanism of Action of Hydroxyethyl-cellulose as Structure Agent for Suspension Concentrate Formulations" Wedlock concludes that the mechanism involves controlled flocculation by bridging. These same type of mechanistic studies should also be conducted for the stabilization of concentrated emulsion formulations since it is likely that different mechanisms of stabilization (protective colloid action and immobilization of emulsion particles by creation of a structure with a yield value) are involved.

General Topics - Advances in Pesticide Formulations

Controlled release pesticide formulations (10) can be categorized (4) as follows.

- 1) Polymer Membrane - Pesticide Reservoir Systems
- 2) Matrix Systems Containing Physically Trapped Pesticides
- 3) Polymer Systems Containing Covalently Bound Pesticides
- 4) Coated Pesticide Granule Systems

The first category includes microcapsule systems. The paper by Morgan, Rodson and Scher in the second section (Pesticide Toxicity Reduction Through Formulation) deals with a microcapsule system.

The paper by Lohmann and D'Hondt fits into the third category where alkali-catalyzed hydrolysis, photolysis or cation exchange were employed to trigger the cleavage of susceptible chemical bonds connecting the active agents with the macromolecular carrier.

The paper by Van Voris, Cataldo, Cowan, Gordon, Cline, Burton and Skeins demonstrates the use of inert matrices (2nd category) such as polyvinylchloride and polypropylene to control the release of herbicides and the paper by Connick demonstrates the use of a biodegradable alginate matrix (2nd category) to control the release of biological control agents.

The paper by Lin describes the use of fluidized bed technology to produce water dispersible granules and water soluble granules. However fluidized bed technology can also be used to produce coated pesticide granules (4th category).

The paper by Hall discusses the effects of spray particle size distribution on the efficiency of pesticide transfer from the spray equipment to the plant. Water soluble polymers are

often used to modify the properties of the spray solution in order to control drift or effect a controlled release response. This paper could have just as easily fit into the first section (Effects of Surfactants on Pesticide Wetting, Penetration and Transport in Plants) of the book.

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RECEIVED December 28, 1987

Chapter 2

Factors Affecting Foliar Penetration and Translocation of Pesticides

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Foliar uptake of 12 radio-labelled agrochemicals, following microsprayer application, has been measured in maize, rape, strawberry, and sugar beet with and without a non-ionic surfactant. Uptake rates during the first 24 h after application were up to 50 times greater than those during the second and third 24 h periods and they were always greater in waxy (strawberry and rape) than non-waxy (sugar beet) leaves. Highest uptake rates were measured for highly lipophilic compounds [$\log P$ (partition coefficient) >3] applied with surfactant but rates of translocation within the treated leaves for these compounds were low. Lowest uptake rates were found for water soluble compounds. Greatest rates of uptake and translocation were observed for compounds of median lipophilicity [$\log P$ 1-2; $\log S$ (molar water solubility) -1.5 - -3.5] both with and without surfactant. Addition of surfactant enhanced uptake of active ingredient up to 27-fold but had little effect on translocation. For compounds of similar water solubility, \log (% uptake) increased linearly with $\log P$ reaching a maximum at $\log P \sim 1$ in strawberry, sugar beet and rape leaves. For compounds of similar $\log P$, \log (% uptake) into rape, strawberry and sugar beet in the presence of surfactant was linearly correlated with $\log S$.

Interest in the efficient delivery of foliar applied pesticides as a means of optimising biological performance has led to considerable advances in spray technology with major improvements in product formulation [1] and the development of new types of application equipment. Thus, sprays, formulated as emulsion concentrates, suspension concentrates, wettable powders, water dispersible granules and oil or water solutions, can be applied to leaves in widely differing volume rates ($1-500 \text{ l ha}^{-1}$), droplet sizes ($100-500 \mu\text{m}$) and application rates ($0.05 - 10 \text{ Kg ha}^{-1}$) [2]. However, relatively little attention has been given to systematic studies of the factors controlling the redistribution of pesticides and spray formulants into and through the outermost layers of the leaf and in consequence these complex interactions are poorly understood.

0097-6156/88/0371-0008\$06.00/0

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Published reports of pesticide uptake patterns have yielded conflicting results, several authors [3-5] demonstrating relationships with lipophilicity and water solubility of the active ingredient (a.i.), others [6] finding weak correlations with molecular properties. The latter may have resulted from the high variability in the cuticular properties of field-grown plants.

The factors governing the uptake of surfactants and other adjuvants seem equally complex involving multiple rate-determining processes [7]. Although relatively little of the parent surfactant is translocated from the original site of application [8] the formation of metabolites by certain plant species within a few hours of leaf treatment [9] indicates that many adjuvants diffuse rapidly across the cuticle.

Interpretation of the uptake patterns of foliar applied pesticides is often difficult due to the close correlation between partition coefficient (P) and water solubility (S). In an attempt to resolve this difficulty we have identified 26 chemicals (including 22 pesticides) which can be arranged into 8 groups in which one of these properties is essentially held constant whilst the other varies over 2-3 orders of magnitude. In this paper we present an initial report of the uptake and translocation profiles of a representative range of these chemicals applied to the leaves of four plant species with widely differing cuticular properties [4]. We report the effects of addition of a non-ionic surfactant on these profiles and demonstrate correlations between uptake and the physicochemical properties of the active ingredient.

Materials and Methods

Plant materials

Plants of *Zea mays* cv. LG 11, rape *Brassica napus* cv. Rafal, sugar beet *Beta vulgaris* cv. Nomo and strawberry *Fragaria ananassa* cv. Red Gauntlet were grown in pots (10 cm) of John Innes compost maintained in controlled environment cabinets. Environmental conditions during the day (16 h) were 20°C, rh 70%, radiant energy rate: 300 $\mu\text{mol m}^{-2} \text{sec}^{-1}$ and night: 16°C, rh 80%.

Spray Application and Analysis

Sprays containing ^{14}C -radio-labelled tracers were prepared as solutions (1 g l⁻¹) in aqueous methanol (1:1v/v) with and without Ethylan TU (NP8) surfactant (nonylphenol ethoxylate; average 8 moles ethylene oxide). The labelled tracers were ring labelled with the exception of chlortoluron $^{14}\text{C}=0$, isoproturon $^{14}\text{CH}(\text{CH}_3)_2$ and NAA $^{14}\text{CH}_2\text{COOH}$. For a preliminary formulation study, suspension concentrates (s.c.) were prepared by blending 2 mg of the ^{14}C -labelled chemical with 2% NP8 surfactant (100 μl) using a 1 ml glass tissue grinder. The s.c. (particle size 2-5 μm) was diluted with water (1.9 ml) immediately prior to application to leaves of the four plant species. The use of the microsprayer [10] which dispensed monosized droplets (330-350 μm diam.) at controlled rates (5-10 droplets sec⁻¹) and velocity (3-4 m sec⁻¹) ensured that the leaf coverage, droplet spreading and droplet drying rates were comparable to those of field applied sprays. A water soluble tracer Uvitex 2B incorporated at low concentration (0.5 g l⁻¹) provided immediate confirmation that droplets had been applied uniformly to the target area [for rape,

^{*} aqueous methanol (7:3 v/v) used for lipophilic compounds with log S < 10⁻⁴.

Table 1 Water solubility and partition coefficient for selected chemicals used in uptake study

Compound	Log S molar	Log P
Group 1		
Uracil (UR)	-1.6	-1.1
Maleic hydrazide (MH)	-1.3	-0.8
Phenylurea (PU)	-1.4	0.8
Metalaxyl (ME)	-1.6	1.6
Group 2		
Naphthaleneacetic acid (NAA)	-2.6	1.9
Chlortoluron (CT)	-3.5	1.9
Isoproturon (ISO)	-3.6	2.2
Atrazine (AT)	-3.8	2.0
Simazine (SI)	-4.6	1.8
Group 3		
Chloroxuron (CX)	-4.8	3.2
Bitertanol (BT)	-4.8	4.2
Diclofop-methyl (DCM)	-5.2	4.3

strawberry and sugar beet a central mid-vein area (2 cm diam.); for maize a 20 x 6 mm segment of leaf avoiding the mid-vein] and that multiple impactions were minimal (5-10%). Tests performed immediately after droplet drying (1-2 min) showed, without exception, that the bulk of the a.i. (>98%) was recovered from the target area using 1 ml aqueous methanol (1:1 v/v) followed by 1 ml methanol. Accordingly, these solvents were used for the recovery of surface residues from a disc (2.4 cm diam.) including the target area (for maize a 24 x 8 mm segment), removed from the leaf 24, 48 and 72 h after droplet application. After removal of the surface deposits, compounds retained in the epicuticular wax layer were recovered by washing the disc with chloroform (1 ml). The annulus of tissue (1 cm wide) surrounding the target area was also removed for radio-analysis from rape, strawberry and sugar beet leaves (for maize the area included a 2 cm length of leaf above, below and adjacent to the treated surface). Radioactivity in the surface wash, wax extract, washed treated tissue and the area surrounding the treated tissue were determined by radiocombustion analysis and liquid scintillation counting [4]. Each experiment was replicated 4 times. Uptake is defined as the proportion of applied chemical not recovered in the methanol wash. Translocation is defined as the proportion of applied chemical recovered in the area surrounding the treated tissue. In separate experiments, compounds which showed significant rates of uptake were applied to leaves, and labelled products were recovered in a methanol surface wash and methanol homogenate 72 h after application. These extracts were analysed by radio t.l.c. using a Raytest Rita 68000 analyser.

Published octanol/water partition coefficients were confirmed by the shake flask method and by HPLC using aqueous methanol (4:1 v/v) as mobile solvent and a C₁₈ reverse phase column [11]. Water solubilities are expressed in molar units (Table 1). Procedures used to study dried spray deposits by fluorescence microscopy, scanning electron microscopy (SEM) and autoradiography have been described in detail elsewhere [12].

ResultsPreliminary Formulation Studies

For pesticide evaluation, chemicals are often applied as solutions in aqueous methanol or acetone but it has been suggested that the use of these solvents may affect uptake behaviour. Therefore, at the start of this investigation we compared uptake rates of two compounds naphthalene acetic acid (NAA) and atrazine, which have markedly different water solubilities, formulated with surfactant both as an s.c. and a solution in aqueous methanol. Uptake of the two chemicals into rape leaves over a 72 h post-treatment period followed an almost identical pattern (Table 2). Spread factors and interfacial areas for both formulations were also similar, with a.i. and surfactant being largely concentrated within a broad annulus at the periphery of the dried deposit. The uptake patterns were similar also when the two formulations were applied to maize and strawberry leaves. Uptake of either chemical into sugar beet leaves was consistently greater from aqueous methanol solution. Since the droplets dried within 20-30 seconds following application this increase can be attributed to differences in the spreading properties of the formulations rather than to solvent-mediated cuticular penetration. Aqueous methanol was used therefore, to apply compounds in solution both with and without surfactant. In separate experiments to determine the effect of increasing surfactant concentration on uptake no increase in NAA uptake into rape or sugar beet leaves was observed at concentrations above 1 g l^{-1} (Table 3). On the other hand, droplet shatter and reduced uptake were noted for rape leaves using the lower concentration (0.3 g l^{-1}).

Table 2 Uptake (% applied ^{14}C) of atrazine and NAA, formulated as solutions and suspension concentrates, into rape and sugar beet leaves (means and s.e. of means)

Species and chemical	Time after application (h)		
	24	48	72
Rape			
Atrazine solution	34 (2.6)	44 (5.6)	41 (4.0)
" suspension [†]	35 (0.9)	38 (5.0)	49 (4.2)
NAA solution	94 (0.8)	95 (1.6)	96 (0.5)
" suspension*	79 (4.5)	73 (3.1)	86 (1.1)
Sugar beet			
Atrazine solution	25 (4.6)	27 (1.1)	27 (1.0)
" suspension [†]	11 (1.3)	13 (0.9)	15 (1.3)
NAA solution	31 (3.0)	52 (5.7)	53 (1.0)
" suspension*	29 (4.1)	36 (7.0)	45 (4.5)

[†] water solubility 30 mg l^{-1}

* water solubility 420 mg l^{-1}

Table 3 Effect of surfactant concentration on the uptake (% applied ^{14}C) of NAA into rape and sugar beet leaves (means and s.e. of means)

Species	Surfactant concentration (g l^{-1})		
	0.3	1	3
Rape	60*(10.3)	94 (0.8)	93 (3.8)
Sugar beet	25 (6.8)	22 (2.8)	25 (2.6)

* some droplet shatter

Factors Affecting Foliar Uptake

Variability between species The uptake patterns shown in Figure 1 for the polar maleic hydrazide and lipophilic diclofop-methyl, applied to leaves in the presence of surfactant, were typical of the species-to-species variation found for most compounds tested. Uptake rates for all compounds were consistently greater for the waxy leaves of strawberry and rape than for maize and sugar beet. These species differences were evident even though uptake rates differed as much as 20-fold between the different chemicals. The overall patterns were

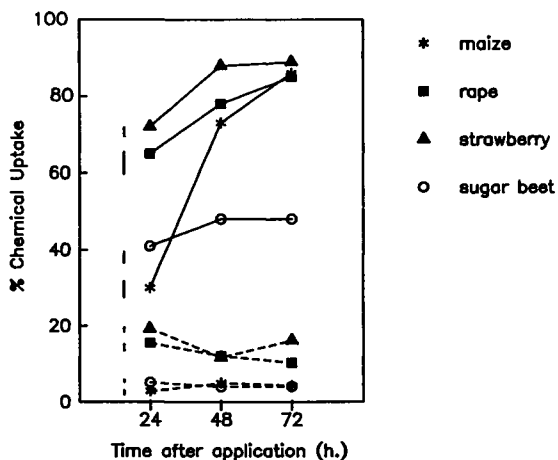


Figure 1 Uptake of maleic hydrazide (---) and diclofop-methyl (—) into leaves of selected species. Vertical bars are s.e. of treatment means.

also similar, with uptake rate declining rapidly within 24 h following droplet application. For instance, the uptake of maleic hydrazide into strawberry leaves was completed within 24 h of application whilst the average uptake rate for diclofop-methyl during this initial period was 6- and 30-fold greater respectively than during each of the succeeding 24 h periods. One of the few exceptions to this uptake pattern was found with diclofop-methyl uptake into maize leaves, in which average rates during successive 24 h periods were 1.2, 1.8 and 0.5% applied dose/h.

Effect of Surfactant The uptake profiles with and without surfactant measured 72 h after droplet application for compounds ranging from polar maleic hydrazide to the highly lipophilic bitertanol (Table 1) are shown in Figure 2a and b. Uptake was enhanced in most cases by the addition of surfactant although there was some variation with the physico-chemical properties of the compound. For example, uptake was generally very low (4-11%) for water soluble chemicals ($\log P < 0$) and addition of surfactant had little effect on uptake rates (Table 4).

Table 4 Ratios between the with and without surfactant values of total uptake and translocation of compounds into rape and sugar beet leaves 72 h after application

	MH	UR	ME	Compound [†]		CT	CX	BT
				PU	AT			
Rape								
Uptake	1.4	1.2	1.2	2.0	1.5	3.6	15.0	27.0
Translocation	2.0	1.0	1.0	4.2	1.6	2.5	6.0	3.0
Sugar beet								
Uptake	0.8	1.5	0.9	3.9	2.3	1.6	3.2	5.0
Translocation	1.0	1.0	0.7	4.7	2.0	1.2	1.5	1.0

[†] Compound code from Table 1

In the case of maleic hydrazide applied to sugar beet leaves uptake was slightly reduced in the presence of surfactant. By comparison, uptake of highly lipophilic chemicals increased markedly in the presence of surfactant. The effect was particularly noticeable for waxy leaves; uptake of chloroxuron and bitertanol into rape increasing 15- and 27-fold, respectively, as compared with 3- and 5-fold into 'non-waxy' sugar beet leaves. Highly variable effects of surfactant were observed for chemicals of intermediate lipophilicity ($\log P$ 0.5-2.5) due in part to the wide differences in uptake attained in the absence of surfactant (14-72% applied dose). For example, uptake of metalaxyl in the absence of surfactant was high in both waxy (74%) and non-waxy (58%) leaves, and little affected by surfactant (1.2- and 1.0-fold respectively). Because of the formation of degradation products of metalaxyl on maize leaf surfaces (see below) results on the uptake of metalaxyl into this species should be treated with some caution. In contrast, uptake of chlortoluron into rape leaves and phenylurea into sugar beet increased almost 4-fold in the presence of surfactant.

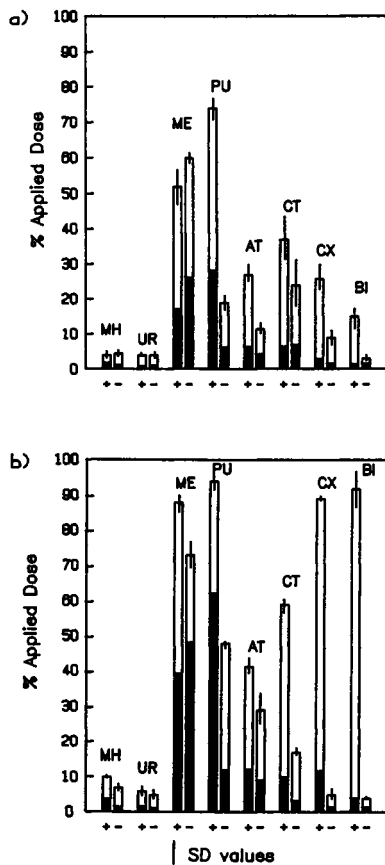


Figure 2. Uptake and translocation profiles (% applied ^{14}C) 72 h after droplet application for selected chemicals applied with (+) and without (-) surfactant to leaves of a) sugar beet and b) rape. \square = total uptake \blacksquare = total translocation.

Variability of uptake with Partition Coefficient Relationships between foliar uptake and partition coefficient were investigated using the compounds listed in group 1 (Table 1). Molar water solubilities for these chemicals differed less than 2-fold whereas partition coefficient ranged over about 3 orders of magnitude. Almost identical relationships were found between uptake in the presence of surfactant and log P for the two waxy leaved species strawberry and rape whilst results for sugar beet were similar (Fig. 3a). Regression analysis indicated that quadratic curves accounted for >94% of the variance in the data for these species, equations for the lines being:

$$\begin{aligned}\log (\% \text{ uptake}) &= 1.7 + 0.6 \log P - 0.26 \log P^2 \text{ (rape)} \\ \log (\% \text{ uptake}) &= 1.8 + 0.51 \log P - 0.28 \log P^2 \text{ (strawberry) and} \\ \log (\% \text{ uptake}) &= 1.5 + 0.6 \log P - 0.30 \log P^2 \text{ (sugar beet)}\end{aligned}$$

In the absence of surfactant uptake for these three species increased linearly with log P for the four compounds examined; a quadratic curve accounted for <5% of additional variability compared to the linear equation. In contrast to the other species, uptake with maize was linearly related to log P in the presence of surfactant ($\log \text{ uptake} = 0.89 + 0.36 \log P$) but appeared to follow a parabolic curve in the absence of surfactant: $\log (\text{uptake}) = 0.19 + 0.16 \log P + 0.36 \log P^2$. The apparent minimum at $\log P = -0.2$ in the absence of surfactant is probably a statistical artefact arising from the wide spread in the data points.

Variability of uptake with water solubility The relationship between uptake and water solubility was studied for the compounds listed in group 2 (Table 1). The partition coefficients of the five chemicals differed less than 2-fold whereas water solubility ranged over 2 orders of magnitude. A linear correlation between log S and uptake was obtained for rape and sugar beet leaves in the presence of surfactant (Figure 3b). Regression equations for the best fit between log (% uptake) (y) and log S (x) were very similar for these species viz. rape $y = 6.7 + 0.8x$, sugar beet $y = 6.3 + 0.86x$ accounting for 92% and 86% of the variability respectively. Log uptake also increased linearly with log S for strawberry both with and without surfactant. However, whilst the equation for the best fit line without surfactant ($y = 6.9 + 0.95x$) accounted for 74% of the variability, there was no significant relationship for uptake in the presence of surfactant. There was no significant relationship between solubility and uptake into maize both with and without surfactant and for rape and sugar beet without surfactant.

Factors affecting translocation

The high rates of translocation for metalaxyl in rape, strawberry and sugar beet leaves may be due in part to the formation of polar metabolites. Translocation patterns in the four species for the selected compounds were almost identical showing a parabolic dependence on water solubility and lipophilicity both in the presence and absence of surfactant (Figure 2). In rape, increase in the ratio between translocation with and without surfactant paralleled the increase in uptake but this trend was less marked for sugar beet leaves (Table 4). In general, movement of a.i. out of the target tissues increased with increased uptake. However, when expressed as a percentage of a.i. in the plant, translocation was often higher in the absence of surfactant (Table 5).

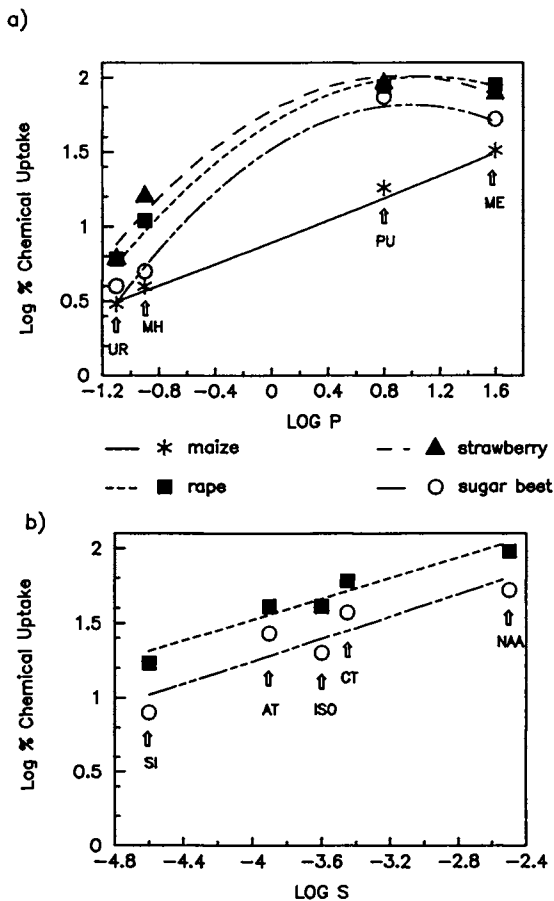


Figure 3 Log (% uptake) for selected chemicals a) v Log P s.e. of means maize 0.07, rape 0.06, strawberry 0.07, sugar beet 0.06; b) v log S s.e. of means rape 0.05, sugar beet 0.04.

Table 5 Effect of surfactant (NP8) on foliar translocation (expressed as %total uptake) 72 h after application

Chemical	Rape		Sugar beet	
	+NP8	-NP8	+NP8	-NP8
Maleic hydrazide	34.3	18.8	35.0	30.0
Uracil	25.9	20.0	15.0	20.0
Metalaxyl	45.5	65.5	32.2	42.8
Phenylurea	55.4	43.7	38.2	38.2
Atrazine	30.2	30.3	23.3	35.4
Chlortoluron	16.7	21.4	16.7	23.8
Chloroxuron	13.0	30.0	11.4	15.9
Bitertanol	4.3	25.0	7.7	30.0

Form and Distribution of Spray Deposits

Addition of surfactant to the spray formulation altered the spreading and drying properties of the impacting droplet which was subsequently reflected in the form and distribution of the dried deposit. Almost without exception spray droplets containing surfactant dried down to form an annulus at the periphery of the dried deposit whereas uniform deposits were obtained in the absence of surfactant, particularly for chemicals of median lipophilicity (log P 0.5 - 2.5). The droplet spread factor (ratio between diameter of dried deposit and in-flight droplet diameter) was greater with surfactant (1.8-2.8) than that without (1.2-1.7). This is illustrated by the data for phenylurea (Table 6). The formation of annuli in the presence of surfactant meant that the actual contact area of the compounds with the leaf increased by less than that indicated by the spread factor. Thus, in the presence of surfactant the contact area comprised 62-76% of the overall area within the outer periphery of the annulus compared with 100% for deposits of spray applied without surfactant. The ratio (coverage ratio) between the deposit contact area (μm^2) and droplet in-flight diameter (μm) is a useful indicator of droplet coverage. The coverage ratio data for phenylurea (Table 6) indicates that the increase in deposit contact area resulting from addition of surfactant varies from 2.2-fold (maize) to only 1.06-fold for sugar beet and is typical of the pattern found for the other compounds.

The physical form of the deposits examined with the SEM 24 h after droplet application varied with the polarity of the a.i. Water soluble compounds such as maleic hydrazide, uracil and phenylurea crystallised as large needles (5-20 μm) both with and without surfactant. Compounds of median lipophilicity and water solubility such as metalaxyl and NAA were difficult to visualise presumably due to the high uptake rates (60-95%). Compounds of median lipophilicity and relatively low water solubility such as chlortoluron, atrazine and simazine formed large amorphous deposits with arrangements of fine crystals 1-3 μm projecting from the deposit surface. Highly lipophilic chemicals including chloroxuron, bitertanol and diclofop-methyl dried as amorphous deposits with and without surfactant.

Table 6 Effect of surfactant on droplet spread, form of "dried" deposit and leaf coverage for phenylurea sprays applied to maize, rape, strawberry and sugar beet leaves

Parameter	Maize	Rape	Species Strawberry	Sugar beet
Deposit form				
+NP8	ann.	ann.	ann.	ann.
-NP8	unif.	unif.	unif.	unif.
Spread factor				
+NP8	2.6	2.0	2.2	1.9
-NP8	1.5	1.5	1.3	1.7
Deposit Contact area (% deposit area)				
+NP8	62	62	65	76
- NP8	100	100	100	100
Coverage ratio (μm)				
+NP8	1170	496	788	695
-NP8	521	353	344	654

ann. = annular distribution; unif. = uniform distribution

Degradation and Metabolism of selected chemicals

Since low rates of uptake were measured for uracil, maleic hydrazide and simazine these compounds were not included in the degradation studies. Radio tlc also showed that bitertanol was stable in plant tissue over the 72 h treatment period. The proportion of parent compound recovered in the surface wash and tissue homogenates of leaves 72 h after treatment with the remainder of the compounds is shown in Table 7. The proportions of the label recovered in the wash and tissue homogenate differed from that shown in Figures 2a and b. This was attributed partly to the higher surface concentrations of applied chemical required for detailed metabolism studies and partly to irreversible sorption to the leaf tissue. Breakdown of parent compound was studied mainly in relation to the translocation data since in most cases uptake was largely completed within 24 h of droplet application. High proportions of labelled a.i. were recovered from leaves sprayed with solutions of atrazine, phenyl urea and chlortoluron whilst formation of conjugates accounted for low recoveries of NAA in sugar beet and maize leaves. In contrast, metalaxyl and chloroxuron were extensively degraded whilst diclofop-methyl was metabolised to the free acid and a more polar metabolite in rape and strawberry leaves.

Recovery of metalaxyl in the surface wash from maize leaf was low (<10%) even though less than 20% of the applied label penetrated the cuticle. Extensive losses of radiolabel from ^{14}C -metalaxyl deposits applied to glass slides and freeze-dried leaf discs have been previously reported [13]. Our investigations however, showed negligible loss of ^{14}C -label from leaves of any of the species and therefore the results obtained for maize leaf must be ascribed to the formation of the labelled polar degradation products which were detected by radio-tlc.

Table 7 Proportion (% applied dose) of parent compound recovered 72 h after application in the surface wash and methanol macerates of leaves of four species sprayed with selected chemicals with surfactants

Chemical	Maize	Rape	Species	
			Strawberry	Sugar beet
Atrazine				
wash	90	56	47	52
macerate	3	39	24	37
Metalaxyl				
wash	8	11	2	10
macerate	<1	13	38	19
Phenylurea				
wash	58	70	35	71
macerate	1	10	20	6
NAA				
wash	38	5	4	22
macerate	5	80	83	43
Chlortoluron				
wash	87	57	3	47
macerate	5	8	42	9
Chloroxuron				
wash	25	5	3	50
macerate	6	7	8	15
Diclofop-methyl				
wash	80	26	39	78
macerate	11	<1	11	10

Discussion

Although further work is required to complete these studies the data currently available are sufficient to show the general patterns of uptake and the changes resulting from the addition to the spray formulation of a non-ionic surfactant. It is evident that uptake rates during the initial 24 h after droplet application greatly exceed rates thereafter, such that in many cases uptake is largely complete within this period. The greater penetration into waxy than "non-waxy" plants irrespective of the properties of the a.i. is consistent with the proposal that diffusion through the lipoidal cuticle is the primary stage in the uptake of all foliar applied systemic chemicals. Similar species effects have been observed in uptake studies with radiolabelled surfactants applied to a range of waxy and 'non-waxy' leaves [8]. Although uptake of all chemicals increased in the presence of the non-ionic NP8 surfactant, the increase was greater (4-5-fold) for lipophilic than for polar chemicals. However, translocation was not proportionately increased in the presence of NP8, indeed in several cases translocation (as % uptake) decreased. Since the diameter of the deposits which dry as an annulus in the presence of surfactant is greater than that of the uniform deposits formed in the absence of surfactant, addition of surfactant does not lead to reduced leaf cover as previously suggested [4]. On the contrary, contact area increased up to 2.5-fold in the presence of surfactant.

Our results support the suggestion [13] that uptake is optimal for compounds of median lipophilicity. Although wide distinctions have been drawn in this and in previous surveys between polar and lipophilic chemicals, it should be recognised that a considerable number of pesticides are of median polarity ($\log P$ 1 - 2.0; $\log S$ -2 - 3.5). In consequence, a high proportion of the pesticide (5-50%) will be in solution in the diluted spray formulation. In the presence of a hygroscopic surfactant the "dried" deposit seems likely to consist of a water-surfactant gel [5] which will retain much of the a.i. in relatively high concentration in a partially hydrated form and maintain intimate contact between the deposit and the leaf surface. These conditions should lead to optimal diffusion rates for individual chemicals. In contrast, diffusion rates into the lipoidal cuticle will be low for polar compounds whilst highly lipophilic chemicals will bind tightly to the cutin matrix. Rates of uptake substantially higher than those of the water soluble compounds included in the present investigations have been reported for cationic herbicides [9,14-16] and growth regulators [13,17]. Stevens [13] attributed the relatively high rates of uptake of chlormequat chloride into strawberry and rape leaves to the concentration gradient resulting from binding of the cations to exchange sites within the cuticle.

The consistently greater uptake of lipophilic than of water soluble chemicals suggests that if polar routes exist through the cuticle they are relatively inefficient. Substantial cuticular permeability to polar compounds conflicts with the established role of the cuticle in maintaining leaf turgor by providing a highly efficient barrier to the passage of water. Alternative mechanisms are therefore required to account for the effective performance of water soluble chemicals such as glyphosate, paraquat and maleic hydrazide. One explanation might be that water soluble compounds are rapidly re-solubilised in conditions of high humidity or by dew. In the presence of a hygroscopic surfactant re-wetted water soluble compounds could spread extensively entering the leaf via preferential sites of uptake such as the veination or leaf axil. In our laboratory re-wetted deposits spread up to 1000-fold during one exposure (8 h) to simulated dew.

Acknowledgments

We wish to thank Dr N.H. Anderson for help with the pesticide selection and valuable discussion ; Mrs A. Williams and Mr J. Blair for able assistance with the experimental work and Mrs S. Brooks and Ms R. Butler for assistance with the production of the figures. ¹⁴C chemicals were supplied by Bayer, Ciba-Geigy, Hoechst and Uniroyal. Long Ashton is funded through the Agricultural and Food Research Council.

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RECEIVED January 22, 1988

Chapter 3

In Vitro Test for Effects of Surfactants and Formulations on Permeability of Plant Cuticles

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The effects of surfactants on water permeability of isolated astomatous cuticles from Citrus leaves were measured. Rates of water loss across cuticles were determined gravimetrically prior to and after application of surfactants using coverages ranging from 0.015 to 25 g/m². Sodium dodecylsulfate did not affect water permeability. Polyoxyethylene p-t-octylphenol and polyoxyethylene nonylphenol in the HLB range of 4 to 16 increased water permeability by up to 2.1 fold. Polyoxyethylene alkylether in the HLB range of 5 to 13 increased water permeability by seven- to eightfold. The cationic surfactant dodecyltrimethylammonium chloride (HLB 18.5) increased water permeability very effectively by up to twentytwofold.

Most formulations of pesticides contain surfactants as emulsifiers and as wetting agents. In addition, surfactants may affect the biological activity of the active ingredient of a formulation (1). This effect is not well understood (2). Better wetting and greater retention may be responsible in part, but effects on permeability of cuticles have also been considered to explain improved herbicidal activity in the presence of surfactants (3, 4).

Generally, permeation of a solute molecule across a cuticular membrane depends on the concentration of that molecule in the membrane (which is a function of the concentration gradient in the adjacent solutions and the partition coefficient) and its mobility (5,6). When analysing the effects of surfactants on penetration of active ingredients it is therefore necessary to investigate both the effects of surfactants on the concentration and on mobility of the solute in the cuticle. To date, systematic studies of this type do not appear to have been conducted.

Plant cuticles are lipid membranes. They have a high sorption capacity for lipophilic solutes. Cutin is the main sorbent (7, 8). Transport resistance is due to soluble lipids associated with the cutin (9, 10, Kerler, F.; Schönherr, J. Arch. Environ. Contam. Toxicol., in press). The permeability of cuticles increases with

0097-6156/88/0371-0022\$06.00/0

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increasing lipid solubility of the solutes. For solutes having the same size (molar volume) permeability is proportional to the cuticle/water partition coefficient (11).

Equilibrium distribution of a solute between the cuticle and an aqueous solution is greatly affected by surfactants when present in concentrations above the critical micelle concentration (cmc) (11). Lipophilic solutes tend to be solubilized in the micelles and cuticle/water partition coefficients decrease rapidly with increasing surfactant concentration. As a consequence, the concentration of a solute in the cuticle is much lower in presence of surfactants in the aqueous solutions and the flow across the cuticle is slowed in proportion. Surfactant concentration increases during droplet drying. Active ingredients that did not enter the cuticle during droplet drying will eventually be dissolved in pure hydrated surfactant or formulation.

In this simplest case, surfactants reduce rates of penetration, because they reduce the driving force, i.e. the concentration gradient of the solute in the cuticle. It is important to realize that transport properties of the cuticle (that is the mobility of the solute in the cuticle) are not affected by the surfactant. If permeability coefficients or permeances were calculated using the correct driving force, namely the concentration gradient of the solute in the cuticle, rather than the concentration gradient in the adjacent bulk solutions, the coefficients would be independent of the concentration of the surfactants. Of course, permeation of polar solutes, which are not solubilized in surfactant micelles, will not be slowed, because their concentration gradient in the cuticle will be unaffected by the presence of surfactants in solution.

If permeability coefficients for solutes depend on the concentration of surfactants, even though they were calculated using the concentration gradient in the cuticle, it must be concluded that transport properties of the cuticles were changed by the surfactants. The barrier limiting transport across cuticles consists of soluble lipids associated with the cutin (cuticular waxes). If permeability is increased by surfactants, it is likely that structure and/or composition of soluble cuticular lipids have been altered.

These considerations show that surfactants can have two opposing effects on the flow of a chemical across the cuticle: (1) They slow it by decreasing the driving force and (2) they may increase permeability by altering the properties of the wax barrier. Both effects act simultaneously and they depend on surfactant concentration and lipophilicity of solutes. In simple experiments they cannot be separated and depending on experimental conditions and type of solute, surfactants may enhance, depress or have no effect on herbicide activity (1). It follows, that effects of surfactants on permeation can only be understood if the above effects are studied separately. The test we are presenting here measures effects of surfactants on the transport properties of the barrier. The partition coefficient effect is absent, because water permeability is studied. The driving force of water across cuticles (the gradient of water activity) is practically unaffected by the presence of surfactants.

Soluble cuticular lipids are the limiting barrier for water

just as for solutes and a good correlation between water permeability and solute permeability of cuticles has been reported (Schönherr, J.; Riederer, M. Rev. Environ. Contam. Toxicol., in press). It is, therefore, meaningful to study the effects of surfactants on transport properties of cuticles by measuring the effects of surfactants on water permeability.

Materials and Methods

The stomatous adaxial leaf cuticles from healthy and vigorously growing Citrus aurantium L. trees were used. In one experiment the stomatous cuticles from commercially supplied green pepper fruits (Capsicum annum L.) were used. The cuticles were isolated enzymatically (12), air dried and stored in the refrigerator (4°C) for further use. These isolated cuticles will be referred to as cuticular membranes (QM). Mature leaves were taken from trees grown in growth chambers (16 h light at 500 to 800 $\mu\text{E m}^{-2} \text{s}^{-1}$ PAR, 25°C, 50 % relative humidity; 15°C and 90 % relative humidity during the dark period). Leaves were never treated with any pesticide to avoid contact with surfactants and/or formulations prior to experimentation.

Table I. Surfactants used for experimentation

Trade name	chemical name	EO	HLB
BRLJ 52	POE cetyl ether	1	5.2
BRLJ 30	POE lauryl ether	3	9.8
BRLJ 56	POE cetyl ether	9	12.9
BRLJ 58	POE cetyl ether	20	15.8
BRLJ 35	POE lauryl ether	20	16.9
RENEX 36	POE tridecyl ether	6	11.6
TRITON X-15	POE p-t-octylphenol	1	3.6
TRITON X-35	POE p-t-octylphenol	3	7.8
TRITON X-45	POE p-t-octylphenol	5	10.4
TRITON X-100	POE p-t-octylphenol	9-10	13.5
TRITON N-57	POE nonylphenol	5	10.0
TRITON N-101	POE nonylphenol	9-10	13.5
	Na-dodecylsulfate	-	40.0
	Dodecyltrimethyl-ammonium chloride	-	18.5

Surfactants were purchased from Serva (Heidelberg, FRG) and were used without further purification. They are listed in Table I. The ethylene oxide contents (EO) are averages. The hydrophile lipophile balance (HLB) figures were taken from the literature (13, 14).

The test procedure is very simple. Water permeability of each cuticular membrane is measured gravimetrically (15) prior to and after application of predetermined amounts of surfactant. The transpiration chambers depicted in Figure 1 were used. They are made of brass and are fitted with a rubber O-ring to attain a good seal. Each chamber is filled with 0.5 ml deionized water and a QM is positioned on top of it, the morphological inner side facing the

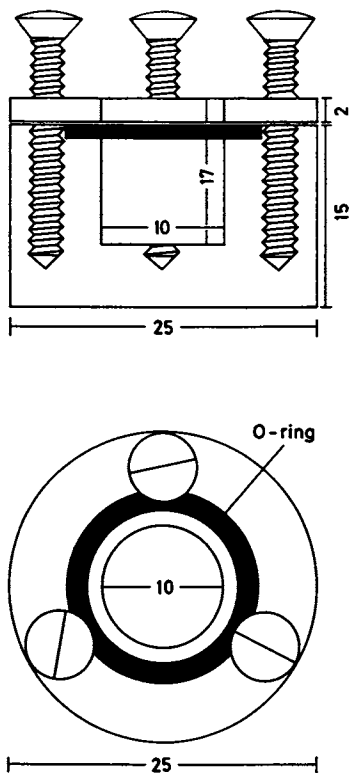


Figure 1: Drawing of a brass chamber used in the test.

water. The brass ring is coated lightly with high vacuum silicon grease on the surface facing the CM (to minimize creeping of surfactant solution between cuticle and metal ring) and is secured with 3 screws. These chambers are then inverted and placed in a desiccator half filled with dried silica gel. To prevent damaging the cuticular membranes a coarse metal screen was positioned between the silica gel and chambers. The desiccators were kept at 24.5 to 25.5 °C and the water loss from the chambers was followed by periodically weighing them until about 10 to 20 mg of water had been lost.

Surfactants were dissolved in deionized water and 50 µl of these test solutions were applied to the outer surfaces of the cuticles after placing the chambers up right. The desiccators were closed and after the water had evaporated, the chambers were inverted again and weighing was resumed as before. A Satorius 1702 MP8 electronic balance (0.1 mg accuracy) online with an Olivetti M24-SP computer was used. At the end of an experiment the rates of water loss prior to and after treatment with surfactant were determined by linear regression analysis. The effect of the treatment was judged from the ratio of the slopes after and before treatment. The ratio is unity in case of an ineffective surfactant and it is greater than unity if water permeability was increased. For each surfactant and coverage 12 to 15 membranes were used as replicates. Data are reported as means together with a 95 % confidence interval ($p = 95 \%$).

During the second weighing period, the outer surfaces of the CM were coated with a thin layer of surfactant, rather than with an aqueous solution of the surfactant. This was intended to simulate the situation in the field, after the water of the spray has evaporated. Initially, all surfactants were tested using a relatively high coverage (mass per area of 5 to 25 g/m²) of surfactant in order to screen out the most effective ones. Later some of the surfactants were tested using a wide range of surface coverages (0.015 to 25 g/m²).

During the drying of the test solutions the surfactant contained in the droplets were not deposited quantitatively on the surfaces of the cuticles as explained below. The yield of deposition was determined using (phenyl-3H(N))-labelled Triton X-100 (NEN, specific activity 48.1 MBq/mg). A 50 µl droplet containing labelled Triton X-100 was placed on each of 30 CM mounted as usual on top of the chambers. After the droplets had dried in the desiccator the area of the cuticles exposed to the solutions was excised and the radioactivity was determined by liquid scintillation counting. Recovery was 46.2 % (standard deviation 8.5 %) and 53.4 % (standard deviation 14.8 %) for theoretical coverages of 5 and 10 g/m², respectively. The average recovery for both coverages was 49 % (standard deviation 11 %). The effective surface coverages were calculated from the theoretical values assuming that only 49 % were deposited on the surfaces of the cuticular membranes. The remaining 51 % of radioactivity were probably deposited on the surfaces of the top metal rings used to prevent spreading of the droplets. Some may also have been lost due to lateral diffusion between ring and cuticle. Since all test solutions were applied at concentrations far above the cmc and since the concentration effect on recovery was small it was assumed

that wetting of and sorption on the metal rings (and thus recovery) would be the same (within experimental error) for all surfactants and concentrations.

Results

In Figure 2 typical results obtained with a control (A) and with a treated cuticular membrane (B) are shown. The control membrane was treated with 50 μ l water, whereas the CM in Figure 2 B was treated with an aqueous Renex 36 solution at a concentration equivalent to 5 g/m^2 . Slopes 1 and 2 of the control membrane do not differ significantly, as the 95 % confidence intervals of the slopes overlap. In experiments with fewer data points than shown in Figure 2 confidence intervals are larger, such that slope ratios ranging from 0.7 to 1.3 are statistically not significantly different from unity. Treatment with Renex 36 resulted in a 7.4 fold increase in water permeability, which is statistically highly significant ($p > 99.9 \%$).

Surfactants from the Triton series had a very small effect on water permeability of Citrus CM (Figure 3), even at the rather high surface coverage of 15.5 g/m^2 . The effects of Triton surfactants on water permeability ranged from 1.6 to 2.1 and there were no significant ($p = 95\%$) differences between different types of Triton surfactants. The effect of the surface coverage on water permeability was studied using Triton N-101 and Triton X-35 and was found to be rather small (Figure 4).

A very high increase in water permeability by about a factor of seven was observed with Brij 52, Brij 30 and Brij 56, while the other two members of the series with HLB values around 16 to 17 had very little effect (Figure 3). Note that the surface coverage was only 5 g/m^2 , which is about 1/3 that used with the Triton series.

Renex 36 increased water permeability very effectively. A small, but statistically significant increase in water permeability was observed even at very low coverages of 15 mg/m^2 (Figure 4).

An effect comparable to that observed with Renex 36 and the more effective members of the Brij series was found for the cationic surfactant dodecyltrimethylammonium chloride, whereas the anionic surfactant sodium dodecylsulfate was ineffective and even reduced water permeability at higher surface coverages (Figure 4).

The effect of Renex 36 on water permeability of green pepper fruit CM was much smaller than the effect observed with Citrus CM. At a coverage of 1.5 g/m^2 water permeability of pepper CM was only increased by a factor of 1.4 (confidence interval 1.3-1.5), whereas with Citrus a 3.5 fold increase was observed at the same coverage (Figure 4).

Renex 36 increased water permeability of Citrus polymer matrix membranes (CM from which soluble lipids were removed with chloroform). At a surface coverage of 2.4 g/m^2 an increase by a factor of 2.0 (confidence interval 1.8 - 2.1) was observed. At this coverage the water permeability of CM would have been increased by a factor of about 4.2 (Figure 4).

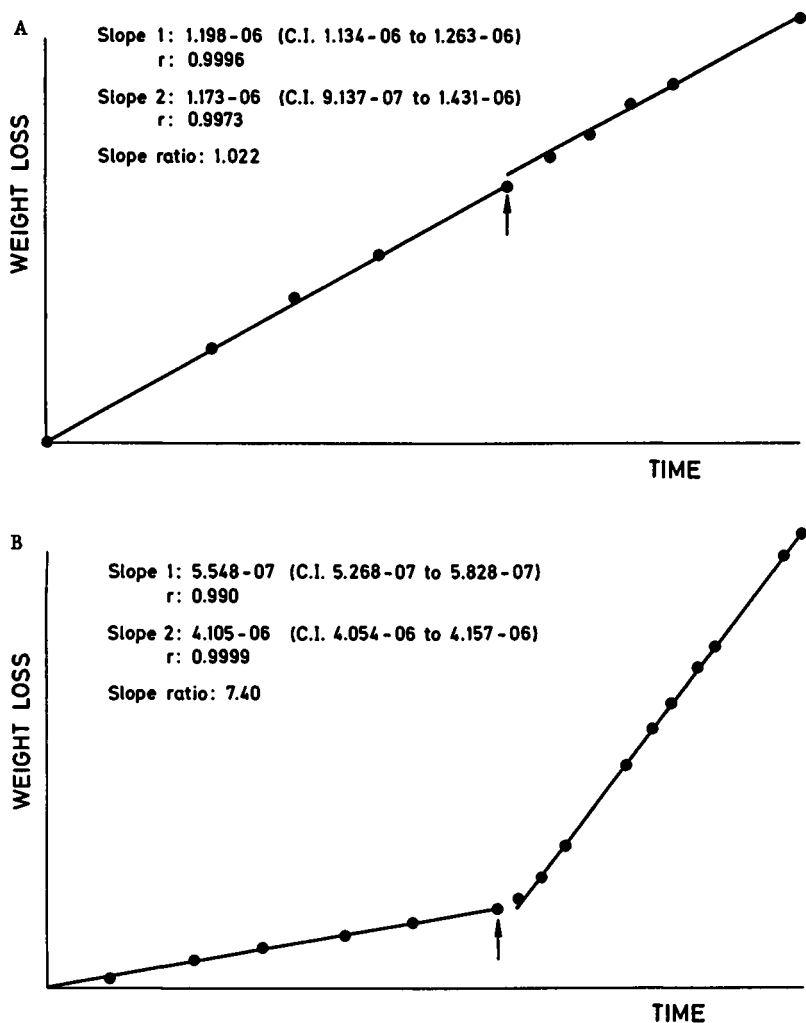


Figure 2: Typical examples of computer printouts (redrawn) from a control experiment (A) and a cuticle treated with Renex 36 (B). Arrows indicate time of treatment. The slopes have the dimension g/min.

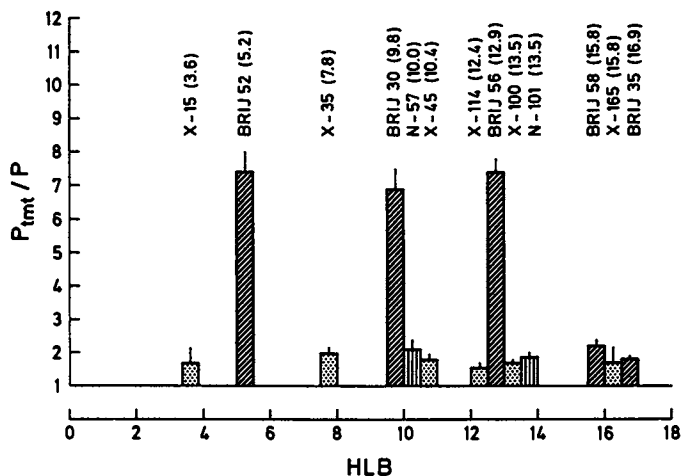


Figure 3: The effects of Triton (X or N) and Brij surfactants on water permeability of *Citrus* cuticular membranes. The coverage was 15.5 g m^{-2} and 5 g m^{-2} for the Triton and Brij surfactants, respectively. HLB values are given in parentheses. The effect is given as the ratio of the permeances (P) after and prior to treatment. Bars represent half a confidence interval ($p = 95 \%$).

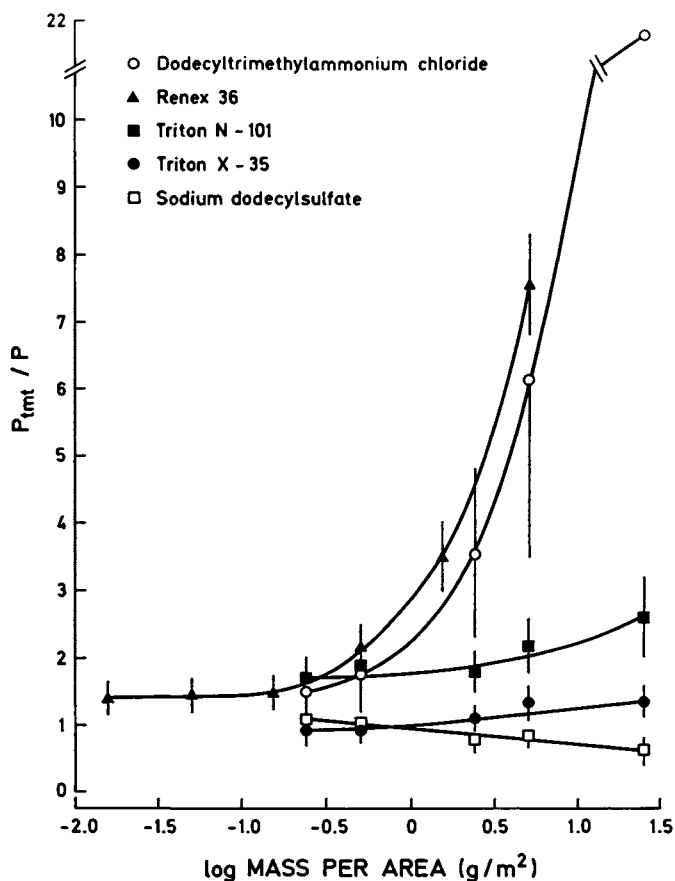


Figure 4: The effect of coverage (mass per area) of selected surfactants on water permeability of *Citrus* cuticular membranes. Bars represent the confidence intervals ($p = 95\%$). The effect is given as the ratio of the permeances (P) after and prior to treatment.

Discussion

The gravimetric method of measuring water permeability is simple and inexpensive. The test is very sensitive, because it uses the method of paired observations. Each membrane serves as control and as treatment and biological variability of water permeability of CM is thus eliminated. Furthermore, there was no correlation between the effect of a surfactant and the water permeability of the CM before treatment. The sensitivity of the test can be adjusted a priori to the needs of the experimenter by using the appropriate number of data points. There is a limit to this, however, because the total water loss from a chamber during the experiment should not exceed 50 mg. The loss of water is accompanied by a decrease in pressure in the chamber. The CM assumes a concave curvature and could rupture.

When the gravimetric method was introduced (15), chambers made of plexiglass were used. These had a small but finite water permeability, such that total water loss from the chambers was the sum of two parallel flows, namely across the cuticles and across the walls of the chambers. The walls of the brass chambers are impermeable to water and the permeance of a membrane is easily calculated from the slope (g/min), the membrane area ($7.85 \times 10^{-5} \text{ m}^2$) and the driving force. The gradient of water activity is practically unity, because the activity of pure water in the chamber is 1 and the activity over dried silica gel is practically zero. The permeance (P) is therefore

$$P = \text{slope}/(\text{area} \times \text{driving force}) \quad (1)$$

This permeance has the dimension $\text{g}/\text{min m}^2$ which can be converted to the usual units (m/s) by dividing by the specific gravity of liquid water and by 60 to obtain seconds instead of minutes. Since area and driving force are the same before and after treatment, they cancel and the effect of a surfactant on permeance (i.e. the ratio of the permeance of the CM treated with surfactant over the permeance prior to treatment; P_{tmt}/P) is numerically identical to the ratio of the slopes after and before treatment (Figures 3 and 4).

There is no clear-cut dependence of water permeability on either HLB or surfactant structure. Maximum effects were found in the HLB range 5 to 13 (Brij 52, Brij 30, Brij 56, Renex 36). The nonionic surfactants with HLB values above 13 have little effect, but the cationic surfactant dodecyltrimethylammonium chloride which has a HLB of 18.5 very effectively increases water permeability. The anionic surfactant sodium dodecylsulfate (HLB about 40) did not increase water permeability.

The test was designed to measure the effects of surfactants on water permeability of cuticles rather than to reveal the cause(s) of effectiveness or ineffectiveness. At this point, we can only speculate.

The barrier that is rate limiting in both transport of water and solutes across cuticles is made up of soluble cuticular lipids, probably in association with cutin (10, 11, 16). Extracting soluble cuticular lipids with chloroform increases permeability of Citrus CM much more than that of pepper fruit CM (16). Water permeability

of Citrus QM is much more affected by Renex 36 than permeability of pepper fruit QM indicating that surfactants interact with the soluble cuticular lipids, leading to an increased mobility of water in the cuticle.

Surfactants also interact with the cutin, because water permeability of polymer matrix membranes (free of soluble cuticular lipids) was also increased by Renex 36, even though to a lower extent than permeability of QM.

There are basically two ways, how water permeability of cuticles could be increased by surfactants. They could swell the polymer matrix and they may solubilize cuticular waxes. Swelling of the polymer matrix would increase the water content of cuticles. As a consequence of swelling, the diffusion coefficient of water in the cuticle might be increased. Both effects could explain the increase in water permeability of polymer matrix membranes. Swelling of the polymer matrix of cuticular membranes could lead to defects between wax crystallites and thus increase permeability. Surfactants may also partially solubilize cuticular waxes. These hypotheses are currently under investigation.

Fairly high coverages have been used in most of our screening tests. The Citrus QM used had a mass per area of about 2.5 g/m^2 and the soluble cuticular lipids amount to only about 0.1 g/m^2 , which is 4 % by weight (17). Only Renex 36 was tested at coverages equivalent to the amounts of soluble cuticular lipids (Figure 4). All other surfactants were tested using coverages in excess of the amounts of soluble cuticular lipids. This appears to be necessary for large effects on water permeability.

Sodium dodecylsulfate actually decreased water permeability when applied at high surface coverages. This surfactant is in the solid state at 25°C . At a coverage of 25 g/m^2 the layer of surfactant on top of the QM was 10 times thicker than the cuticle itself and it probably acted as resistance in series.

Even though it is not clear how surfactants increase water permeability of cuticles, it is a fact that some of them significantly do so. Since soluble cuticular lipids are the main barrier not only for water, but also for solutes, solute permeability is most likely increased by surfactants that increase water permeability (Schönherr, J.; Riederer, M. Rev. Environ. Contam. Toxicol. in press). However, as pointed out earlier, with lipophilic solutes this effect will be confounded with the effect of surfactants on the partition coefficient. Both effects act in opposite direction. The partitioning effect will decrease permeability, whereas an increase in mobility of solutes in the cuticle will increase the permeability. In an experiment comparing the uptake of a pesticide with and without a surfactant (or a formulation) the two effects could cancel and it would be concluded that the surfactant had no effect on the cuticle.

The advantage of our test is, that when measuring water permeability the partitioning effect is absent and the effect of surfactants on mobility of water (and solutes) can be measured unobscured by other effects. The test may also be used for mixtures of surfactants, complete formulations containing solvents or for other adjuvants.

Surfactants that increase water permeability of cuticles, will probably also increase permeability for surfactants. Since

surfactants are toxic to cells (18) they can increase toxicity of herbicides applied to the foliage.

Acknowledgment

This work was supported by a grant from the Deutsche Forschungsgemeinschaft.

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RECEIVED December 28, 1987

Chapter 4

Studies on Octylphenoxy Surfactants

Effects of Concentration and Mixtures on 2-(1-Naphthyl)acetic Acid Sorption by Tomato Fruit Cuticles

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Effects of polyethoxy (EO) derivatives of octylphenol (OP) with 5 (OP+5EO), 7.5 (OP+7.5EO), 9.5 (OP+9.5EO) and 40 (OP+40EO) ethyleneoxy groups on sorption of 2-(1-naphthyl)acetic acid (NAA) by cuticles enzymatically isolated from mature tomato (Lycopersicon esculentum Mill. cv. Sprinter) fruit were studied at pH 3.2 and 25°C. Below the critical micelle concentration (CMC), surfactants had little effect on sorption by cuticular membranes (CM) and dewaxed CM (DCM). Above the CMC, sorption decreased with an increase in surfactant concentration, except for OP+5EO and OP+7.5EO where sorption by CM, but not DCM, increased at concentrations (0.1%) just above the CMC. Surfactant mixtures (1:1) of OP+9.5EO and OP+40EO, OP+7.5EO and OP+40EO, and OP+5EO and OP+7.5EO all yielded NAA sorption values significantly lower than control or component surfactant treatments.

Surfactants are commonly used in agrochemical formulations to improve the characteristics of the spray solution and to increase absorption of the active ingredient (1-3). However, there is evidence suggesting that surfactants do not always enhance foliar absorption of an applied compound (4-6). A better understanding of surfactant/active ingredient/plant surface interactions may provide insight into the mechanism(s) of surfactant action, thereby leading to more effective use of surfactants and improved agrochemical formulations.

The cuticle covering plant surfaces is the initial (7) and primary (8) barrier to the penetration of foliar-applied chemicals. Utilization of cuticles isolated from the underlying cells allows for explicit examination of surfactant/active ingredient/cuticle

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NOTE: This is the sixth in a series of studies on octylphenoxy surfactants.

0097-6156/88/0371-0034\$06.00/0
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interactions. Although earlier studies (9, 10) have documented significant surfactant effects, an adequate data base is lacking. To this end, we have focused on the effects of selected polyethoxylated derivatives of octylphenol (OP) on 2-(1-naphthyl)acetic acid (NAA) sorption by plant cuticles. Sorption was selected for study because it is an important component of membrane (cuticle) permeability (11) and can be viewed as an early phase in the foliar penetration process.

Experimental

Plant Material/Cuticle Isolation. Locally field-grown mature tomato (*Lycopersicon esculentum* Mill. cv. Sprinter) fruit free of visual defects were selected for reasons previously discussed (12). Discs, 20 mm in diameter, were punched from the fruit and incubated at $35 \pm 1^\circ\text{C}$ in an aqueous mixture of pectinase (4%, w/v; ICN Nutritional Biochemicals), cellulase (0.4%, w/v; Sigma) and NaN_3 (1 mM) in 50 mM sodium citrate buffer at pH 4.0 (13). After two days and two changes of enzyme solution, the cuticle was separated from the cell walls of the epidermis. Adhering cellular debris was removed with a jet of distilled water and the cuticles were air-dried and stored at 23°C until used. Cuticles isolated by this procedure will be referred to as cuticular membranes (CM). CM extracted for 3 d with at least 10 changes of chloroform:methanol (1:1, v/v) at 50°C to remove the epicuticular and cuticular waxes, i.e. soluble cuticular lipids (SCL), will be termed DCM.

Radioisotope. Radioactive 2-(1-naphthyl[1- ^{14}C])acetic acid (sp. act. $2.3 \text{ GBq mmol}^{-1}$; Amersham) with a purity of 98%, as determined by radio-TLC, was used in this study.

Surfactants. 4-(1,1,3,3-tetramethyl)butylphenol (OP) condensed with either 5 (OP+5EO), 7.5 (OP+7.5EO), 9.5 (OP+9.5EO) or 40 (OP+40EO) moles ethylene oxide (EO) was used. Trade names (registered trademarks, Rohm and Haas Co.) for these four nonionic surfactants are Triton X-45, Triton X-114, Triton X-100 and Triton X-405, respectively. Selected properties of these surfactants relevant to foliar penetration have been reported (14).

The octylphenoxy surfactants were representative of commercial preparations. The EO number listed is an average value, with the ethoxymer mole ratio distributions following a Poisson distribution (15). No attempt was made to chemically purify any of the surfactants. The CMC values for OP+5EO, OP+7.5EO, OP+9.5EO and OP+40EO were 0.005, 0.012, 0.019 and 0.16% (w/v), respectively. Concentrations used were on a w/v basis.

Measurement of Sorption. Sorption was measured for the systems CM/buffer and DCM/buffer using the procedure of Riederer and Schönherr (16). Sodium citrate buffer (20 mM) at pH 3.2, containing 1 mM NaN_3 to prevent bacterial and fungal growth, was used in all experiments. The pK_a of NAA is 4.2.

Random samples (20 to 50) of CM or DCM discs were selected and sliced into small (approx. 1 mm x 10 mm) strips (preliminary results showed no significant effect of strip size). Weighed sub-

samples (approx. 5 mg) were placed into 5 ml glass vials and 1.5 ml of ^{14}C -labeled NAA (300-500 nM) buffered solution was pipetted into each vial. Vials were closed with teflon-lined screw caps and shaken horizontally in a water bath at $25 \pm 0.5^\circ\text{C}$.

At designated time intervals, 100 μl aliquots were removed and radioactivity determined by liquid scintillation spectrometry (LKB-Wallac LSC, Model 1211). Scintillation cocktail was composed of 1,4-dioxane (10 ml), containing 100 g naphthalene and 5 g diphenyloxazole (PPO) liter $^{-1}$. All samples were counted to a 2σ error of approximately 1.0% and corrected for background. Since quenching was constant throughout the course of these experiments, all calculations were performed with CPM values. The amount of ^{14}C -labeled NAA sorbed by the CM or DCM was determined by subtracting the quantity of ^{14}C -NAA in the dosing (bulk) solution from the amount originally present (17).

Radioassay of the bulk solution in control vials, containing only ^{14}C -NAA treatment solution (no CM or DCM), indicated there was negligible loss in ^{14}C -NAA over the experimental periods for the following treatments: buffer-only control, OP+7.5EO, OP+9.5EO, OP+40EO and the various surfactant mixtures used. These results were for all concentrations examined. Therefore, the assumption was made that the total amount of ^{14}C -NAA lost from the bulk solution was sorbed (or associated) by CM or DCM.

For the ^{14}C -NAA treatment solutions containing OP+5EO, there was a consistent 3 to 5% decrease in ^{14}C -NAA in the bulk solution in control vials. This decrease in ^{14}C -NAA from the bulk solution of control vials may be associated with low OP+5EO water solubility and/or OP+5EO adsorbing to glass walls of the vials. Equilibrium in the control vials was reached rapidly (unpublished results), demonstrating that vial leakage was not a factor. The assumption was made that the loss in ^{14}C -NAA observed in OP+5EO control vials would not be affected by the presence of cuticle. Therefore, a correction factor was developed on this basis and used in calculating the quantity sorbed. If this loss was not independent of the presence of the CM or DCM, our sorption values would be slightly underestimated.

Statistics. All measurements were made using five replications per treatment. For the time-course measurements, the same five replicates were repeatedly sampled. The results are presented as means with their respective 95% confidence intervals (Figures 1-6) or coefficients of variation (Table I).

Results and Discussion

Sorption of NAA by tomato fruit CM and DCM was markedly affected by the OP derivatives. Factors having the greatest effect on surfactant interaction with the NAA/CM or DCM systems were: surfactant concentration, EO chain length and presence of mixed micelles.

Concentration Effects: Pre-CMC. Surfactant concentrations below the CMC had little or no effect on NAA sorption by tomato CM and DCM, compared to controls, for OP+5EO, OP+7.5EO (Figures 1 and 2,

respectively), OP+9.5EO (Figure 4) and OP+40EO (Figures 3, 4, 5). Levy et al. (18) suggested that polysorbate 80 may form a surfactant monomer/drug complex which increased rates of drug absorption. The observation that NAA sorption was independent of surfactant concentrations below the CMC (Figures 1, 2, 3) suggests that a surfactant monomer/NAA complex was not formed in our system. The slight increase in NAA sorption at concentrations below the CMC may be related to improved wetting of the tomato CM and DCM by the sorbate solution, thereby increasing the accessibility of sorbing sites within the cutin matrix. Thus, our data support the hypothesis that octylphenoxy surfactant monomers and NAA molecules interacted with CM or DCM independently of one another. Withington and Collett (19) also concluded that transfer of salicylic acid across cellophane membranes occurred independent of surfactant monomers.

Concentration Effects: Post-CMC. At surfactant concentrations above the CMC, significant concentration-dependent enhancement or depression of NAA sorption was observed (Figures 1, 2, 3). Both OP+5EO and OP+7.5EO caused significant increases in NAA sorption by CM at 0.1% (Figures 1, 2), while OP+40EO did not (Figure 3). This enhancement of NAA sorption was only observed over a relatively narrow concentration range and when the SCL were present. With a further increase in surfactant concentration (above 0.1%) NAA sorption by CM was dramatically suppressed to where at 4% and higher no sorption was detectable (Table I).

Table I. Sorption of NAA by Tomato Fruit Cuticular Membrane, as Affected by OP+5EO Concentration

Surfactant Concn (%, w/v)	Amount Sorbed $\mu\text{mol}\cdot\text{kg}^{-1}$
0	59 (2) ^a
0.5	65 (8)
1.0	23 (12)
2.0	6 (20)
4.0	0 ^b
8.0	0 ^b

^aDetermined at equilibrium (48 h), pH 3.2 and 25°C. Mean of five replications with coefficient of variation in parenthesis.

^bNone detected.

These results (Figures 1, 2; Table I) suggest that OP+5EO and OP+7.5EO micelles influenced NAA sorption by CM. However, the nature of the response (enhancement or depression) was dependent on surfactant concentration. For OP+40EO, NAA sorption by CM was inversely related to post-CMC surfactant concentration (Figure 3). These results were similar to those obtained with OP+9.5EO and CM (unpublished data).

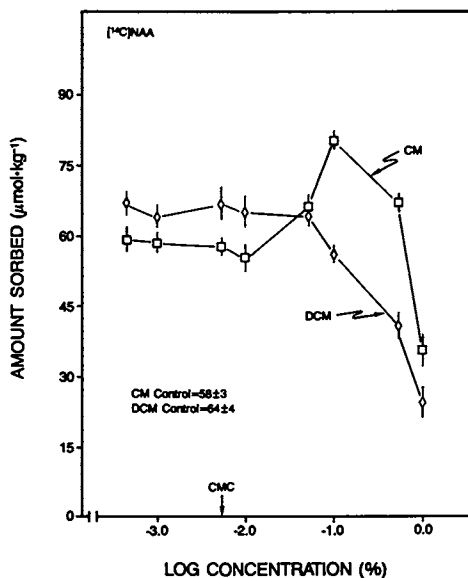


Figure 1. Effect of selected OP+5EO concentrations on sorption of NAA by tomato fruit cuticular membranes (CM) and dewaxed cuticular membranes (DCM).

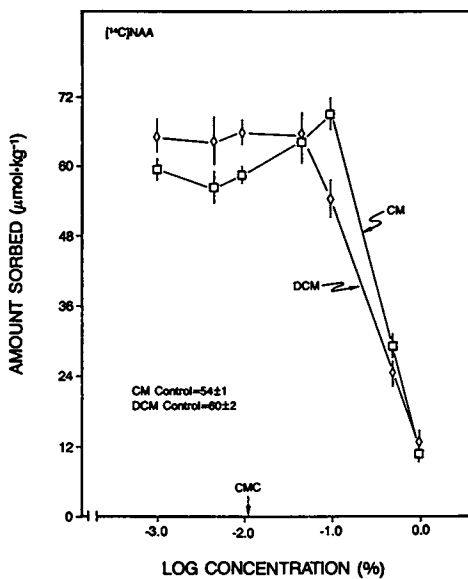


Figure 2. Effect of selected OP+7.5EO concentrations on sorption of NAA by tomato fruit cuticular membranes (CM) and dewaxed cuticular membranes (DCM).

The effects of OP+5EO and OP+7.5EO on sorption of NAA by DCM were qualitatively similar to the effects obtained with OP+9.5EO (unpublished data) and OP+40EO (Figure 3). That is, no significant effect of surfactant concentration below the CMC, but above the CMC, NAA sorption was inversely related to surfactant concentration. These data provide strong evidence that the OP+5EO and OP+7.5EO surfactants interact with the SCL, resulting in increased NAA sorption by CM.

There may be two explanations for the suppression of NAA sorption observed in our study. Firstly, the surfactant may physically block sorption sites and secondly, micelles may compete with the CM or DCM for NAA thereby reducing the amount of NAA available for sorption (20). Based on data obtained in our studies (unpublished data), NAA partitioning into micelles was the more likely mechanism responsible for decreased NAA sorption by tomato CM and DCM at post-CMC concentrations. However, adsorption of OP+9.5EO by cuticles was shown to occur at high concentrations (21). Therefore, one cannot preclude the possibility that at high surfactant concentrations physical blocking of NAA sorption sites also occurred.

The mechanism of enhanced NAA sorption by OP+5EO and OP+7.5EO over a relatively narrow concentration range is not clear. Octylphenoxy surfactants are mixtures of various ethoxymers (15, 22). The enhancement of NAA sorption with OP+5EO and OP+7.5EO at 0.1% may reflect a specific ethoxymers mole distribution pattern which enables higher NAA sorption (or association) by CM to occur. The specific ethoxymers distribution at 0.1% may have led to a softening or swelling of the CM, leading to increased accessibility of NAA sorption sites. Since there was no specific increase in the sorption of OP+5EO by CM at 0.1%, as compared to 0.5 or 1.0% (21), it is unlikely that this enhancement was related to NAA associated with the surfactant (e.g. in micelles) sorbed by the CM. It is clear that the SCL of the CM play an important role, since no surfactant-enhancement of NAA sorption was observed when they were removed (DCM). Elucidation of the mechanism(s) responsible for the enhancement effects remains to be documented. Further, it should be noted that OP+5EO and OP+7.5EO enhancement of NAA sorption has been observed also with CM isolated from pepper fruit and *Ficus* leaves (Shafer, W. E.; Bukovac, M. J.; Fader, R. G. Proc. Adjuvants and Agrochemicals, Vol. 1, CRC Press, in press).

EO Chain Length Effects. At 0.1%, enhanced NAA sorption by CM was greatest with OP+5EO, slightly less with OP+7.5EO, and absent with OP+40EO (Figures 1, 2, 3). In a related study (unpublished data), it was determined that the enhancement effect was lost when the average EO chain length was 9.5EO or greater. With an EO chain length of 9.5EO or greater with CM, or for any octylphenoxy surfactant studied with DCM, NAA sorption was, in general, directly related to EO chain length. This response was similar for plant cuticles from several genera and also held for a surfactant series where the hydrophobe was a linear alcohol (Shafer, W. E.; Bukovac, M. J.; Fader, R. G. Proc. Adjuvants and Agrochemicals, Vol. 1, CRC Press, in press). These results clearly demonstrate that small shifts in the ethoxymers mole distribution can profoundly affect NAA sorption.

Mixed Surfactant Effects. Results obtained with selected octylphenoxy surfactant mixtures provide interesting data regarding surfactant/NAA/CM interactions (Figures 4, 5, and 6). Addition of OP+4EO (0.1%) to OP+9.5EO or OP+7.5EO (0.1%) resulted in a significant decrease in NAA sorption (Figures 4 and 5, respectively). Considering these experiments, three factors should be noted: (a) OP+4EO was present at a concentration below its CMC, (b) OP+7.5EO resulted in significantly higher NAA sorption at 0.1% in the absence of OP+4EO and (c) total surfactant concentration in the mixtures was 0.2%. Thus, differences in EO chain length of octylphenoxy surfactants had a profound impact on NAA sorption by CM, and, in all cases, mixtures resulted in less NAA sorption than component surfactants.

Perhaps the most intriguing mixture effect was observed with OP+5EO and OP+7.5EO (Figure 6). Both surfactants, at 0.1%, yielded high (60 to 70 $\mu\text{mol}\cdot\text{kg}^{-1}$) NAA sorption values. However, when OP+5EO and OP+7.5EO were combined at equal concentrations (total surfactant concentration of 0.1 or 0.2%), the NAA-enhancement effect was lost. The mixture treatments yielded sorption values (29 to 39 $\mu\text{mol}\cdot\text{kg}^{-1}$) significantly lower than sorption values obtained with controls (45 $\mu\text{mol}\cdot\text{kg}^{-1}$). It should be mentioned that for the two concentrations examined, both surfactants were above their CMC.

Two explanations for the mixture effects may be proposed: (a) the total number of micelles increased on mixing, thereby increasing the total quantity of NAA partitioning into micelles and/or (b) mixed micelles were formed with greater NAA solubilizing capacity. However, since a direct micellar/CM (or specifically SCL) interaction has already been established, perhaps the focus should be on decreased micellar/SCL interactions, rather than increased micellar/NAA interactions. These suggestions do not preclude the possibility that some other mechanism(s) may be involved.

Our results with surfactant mixtures suggest that the blending of different surfactants for various purposes (1) should be carried out with the recognition that some negative consequences may occur.

Conclusions

Based on the data obtained herein, the following conclusions regarding octylphenoxy surfactant/NAA/cuticle interactions can be made.

1. A surfactant monomer/NAA complex was not involved in NAA sorption by CM or DCM.
2. Surfactant micelles competed with the CM/DCM for NAA molecules, thereby decreasing NAA sorption.
3. OP+5EO and OP+7.5EO surfactant micelles at 0.1% interacted with the SCL, leading to a significant increase in NAA sorption by, or association with, the CM.
4. Mixed surfactant systems (total concentration greater than CMCs) resulted in decreased NAA sorption by CM.

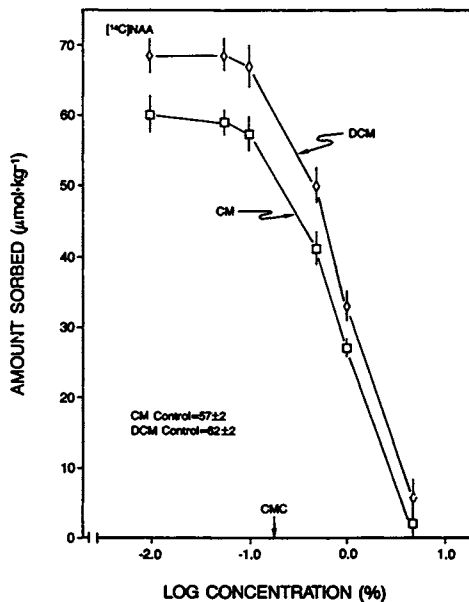


Figure 3. Effect of selected OP+40EO concentrations on sorption of NAA by tomato fruit cuticular membranes (CM) and dewaxed cuticular membranes (DCM).

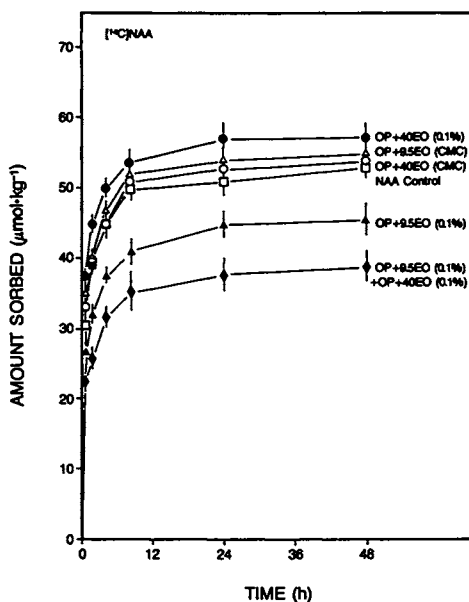


Figure 4. Effect of selected OP+9.5EO and OP+40EO concentrations and an OP+9.5EO/OP+40EO (0.1/0.1%) mixture on time-course of NAA sorption by tomato fruit cuticular membranes.

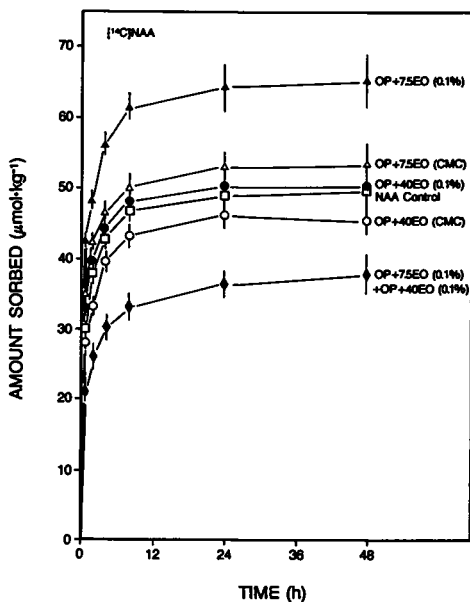


Figure 5. Effect of selected OP+7.5EO and OP+40EO concentrations and an OP+7.5EO/OP+40EO (0.1/0.1%) mixture on time-course of NAA sorption by tomato fruit cuticular membranes.

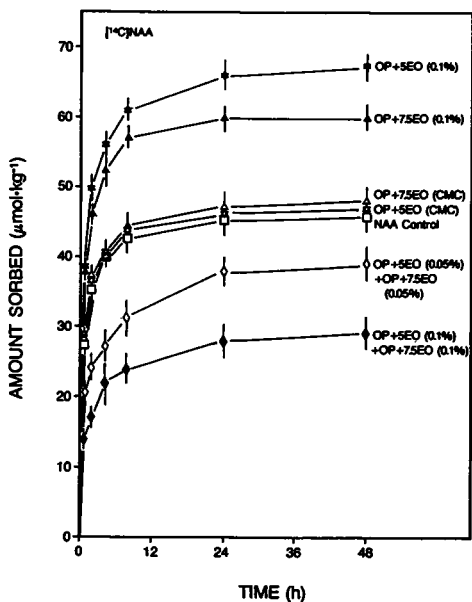


Figure 6. Effect of selected OP+5EO and OP+7.5EO concentrations and OP+5EO/OP+7.5EO (0.05/0.05%, 0.1/0.1%) mixtures on time-course of NAA sorption by tomato fruit cuticular membranes.

Acknowledgments

This paper (Journal Article No. 12489, Michigan Agricultural Experiment Station) is based on work supported, in part, by U.S. Department of Agriculture under Agreement No. CWU 3607-20300-004-01s and by a grant from the Shell Development Co., Modesto, CA 95352. The authors thank Dr. A. Y. S. Yang, E. I. DuPont, Wilmington, DE for stimulating discussions.

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RECEIVED December 28, 1987

Chapter 5

Mode of Action of a Nonionic and a Cationic Surfactant in Relation to Glyphosate

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Addition of Ethomeen T/25 (polyoxyethylene (15) tallow amine) at different concentrations enhanced the glyphosate toxicity to seedlings of winter-wheat. The nonionic Renex 688 (polyoxyethylene (8) nonylphenol) showed a relatively poor capacity to enhance glyphosate toxicity. Absorption of ^{14}C -glyphosate is inhibited by Renex 688 and enhanced by Ethomeen T/25, which explains the observed difference in influence on glyphosate toxicity.

Scanning electron microscopy revealed that the epicuticular waxes seem rather unimpaired after application of the surfactants. The two surfactants penetrate into the cuticle. Application of Ethomeen T/25 resulted in the appearance of necrotic lesions whereas Renex 688 gave much less injury. The results are discussed in relation to the physical-chemical properties of Renex 688 and Ethomeen T/25.

Addition of relatively high (0.1% (w/v)) concentrations of surfactant may give increased phytotoxicity of glyphosate (8,12). The cationic polyoxyethylene amine surfactants appear to be the most appropriate compounds for combination with glyphosate (12). Because the influence of surfactants on glyphosate toxicity is not completely understood (4,8), this study was started to develop a better understanding of the mode of action of surfactants. Insight in the underlying mechanisms may lead to the use of surfactants based on rational arguments.

0097-6156/88/0371-0044\$06.00/0

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The experiments in this study have been carried out with the nonionic Renex 688 (polyoxyethylene (8) nonylphenol), the cationic Ethomeen T/25 (polyoxyethylene (15) tallow amine) and technical grade glyphosate which have been applied to winter wheat grown under controlled environmental conditions. The difference between Ethomeen T/25 and Renex 688 in their capacity to enhance glyphosate activity has been investigated by measuring the relation between surfactant concentration and glyphosate toxicity. As increased glyphosate toxicity may result from an increased deposition, the relation between surfactant concentration and deposition was measured by fluorimetry.

After passage of the cuticle glyphosate is thought to penetrate into the symplast (3). The cuticle, the cell wall and the plasmalemma may be penetration limiting factors for a water soluble anionic compound like glyphosate as the cuticle and the plasmalemma are lipophilic and negatively charged. The cell wall is permeable to water soluble compounds but also negatively charged. Addition of surfactants may result in increased absorption of glyphosate (4,7). It is not obvious whether increased permeability of the cuticle or facilitated entry into the symplast is the main factor for this phenomena. Scarce data on this matter (8,11) give an indication that the facilitated entry into the symplast may be the most relevant factor.

In this study the absorption of ^{14}C -glyphosate is measured at different concentrations of surfactant. Scanning electron microscopy has been used to investigate the capacity of the surfactants to dissolve epicuticular waxes. Penetration of surfactants into the mesophyll must be preceded by diffusion throughout the cuticle. The absorption of Renex 688 and Ethomeen T/25 into the cuticle has been measured by using a colorimetric method for determination. The influence of both surfactants on the permeability of the plasmalemma has been investigated by measuring the leakage of electrolytes from potato discs after incubation in surfactant containing medium. A rough estimation for penetration of surfactants into the tissue was obtained by observation of the appearance of necrotic lesions.

Materials and Methods

Plant Material. Winter wheat (cv. Arminda) was grown in 11 cm-diam. plastic pots (6 plants/pot) filled with a mixture of sand and humic potting soil (1:2). The pots were subirrigated with $\frac{1}{2}$ -strength Steiner's nutrient solution (9). The plants were grown in a growth chamber under the following conditions: 16 h light, 18/12 °C (day/night) temperature and 70% relative humidity. Light was provided by high pressure mercury lamps and incandescent lamps to give 65 W/m² at leaf level.

Phytotoxicity of glyphosate. The plants were treated at the 3-leaf stage. Sprays were applied with a laboratory sprayer fitted with three nozzles (Birchmeier Helico Sapphire 1.2 mm provided with a whirling pin 2F-0,6 mm perforated) to give a volume of 440 l/ha. Three weeks after treatment the parts above the ground were harvested by cutting at 1 cm above the ground and the fresh weight was measured.

Glyphosate activity is expressed as percentage of the fresh weight of plants treated with demineralized water. Glyphosate solutions were prepared from technical grade glyphosate (isopropylamine salt). The application rate of the salt was equivalent to 0.095 kg glyphosate/ha. The surfactants were included in the spray solution on a percentage (w/v) basis. Renex 688 (polyoxyethylene (8) nonylphenol) and Ethomeen T/25 (polyoxyethylene (15) tallow amine) were used in this study. Treatments were replicated four times in a randomized complete block design in all experiments.

Deposition and surface tension measurements. Deposition of spray solutions (containing surfactants at appropriate concentrations) was quantified by spectrofluorimetry according to Richardson (6). Fifteen minutes after spray application the dye was washed off the plants. The absolute deposition is expressed as the volume of spray solution retained per gram dry weight (ul/g). The relative deposition of the solutions is expressed as percentage of the deposition of demineralized water. Treatments were replicated four times in a randomized complete block design in all experiments.

The static surface tension was measured according to the ring method. Three measurements were taken for each solution.

Absorption of ^{14}C -glyphosate. After emergence the wheat seedlings were thinned to one seedling per pot. Applications were made at the 3-leaf stage. Methyl labelled ^{14}C -glyphosate (Amersham, specific activity 2.2 GBq/mmol) was converted to the monoisopropylamine salt by the addition of isopropylamine in a 1:1 molecular ratio. Non-labelled technical grade glyphosate (monoisopropylamine salt), surfactants (on a weight to volume basis) and demineralized H_2O were added to the ^{14}C -glyphosate such that, the concentration of glyphosate (labelled plus non-labelled) amounts to 1.3 mM which is the concentration used in the spray solutions. The glyphosate solution was applied alone or in combination with Renex 688 and Ethomeen T/25 as four 1- μl droplets (0.83 kBq) to a discrete area on the adaxial side of the second leaf. The discrete area was marked by using waterproof drawing ink. All applications were made using a Burkard Microapplicator PAX 100 fitted with a 50 μl syringe and PFTE coated needle. Each treatment was replicated three times in a randomized complete block design. At indicated times the treated leaf was removed and washed with 5 ml water. This procedure removed 100% of the glyphosate immediately after droplet application. A 1-ml aliquot from the wash was added to 10 ml hydroluma (Lumac/3 M). Radioactivity was quantified using standard liquid scintillation spectrometry techniques.

Absorption of surfactants. Applications were made at the 3-leaf stage. Surfactant solutions (0.5% (w/v)) were applied as 10 1- μl droplets (50 μg) to a discrete area on the adaxial side of the second leaf using the microapplicator as described with the application of ^{14}C -glyphosate. At indicated times the deposit was removed by gently wiping the treated area with a small pellet of cotton-wool moistened with water. The pellet was extracted with 6 ml chloroform. The amounts of surfactant were measured by using a colorimetric method (1). Uniform plants were selected and each treatment was replicated

three times. The colorimetric method used showed a relatively low sensitivity for Renex 688. Deposits smaller than 10 μg could not be measured accurately. Therefore the absorption of Renex 688 with deposits in this range is expressed as "higher than 80%" (>80%).

Scanning electron microscopy (SEM). Conditions of application in relation to the plants were as described for the absorption studies. Surfactant solutions at appropriate concentrations were applied as one 1- μl droplet.

Twenty-four hours after application the leaf sections were removed from the plant and immediately frozen in nitrogen slush and freeze-dried. Then the leaf sections were mounted on aluminium SEM stubs, sputtered with gold-palladium and examined in the scanning electron microscope at an accelerating potential of 15 kV.

Leakage of electrolytes. Potato discs (cv. Bintje) were cut (diam. 11 mm, thickness 2 mm) and washed twice with 20 ml water. Then 5 discs were transferred to a 100 ml flask with 20 ml bathing medium containing surfactant solutions at appropriate concentrations. The flasks were gently shaken during one hour at 20 °C under natural illumination. Then the conductivity was measured and corrected for response caused by the bathing media themselves. The conductivity was expressed as percentage of the value obtained after incubation in demineralized water. The incubations were replicated three times in one experiment.

Estimation of injury. Conditions of application in relation to the plants were the same as described for the absorption studies. Surfactant solutions at appropriate concentrations were applied as three 1- μl droplets. Seventy-two hours after application the injury was estimated by visual observation of the appearance of necrotic lesions.

Results and Discussion

Glyphosate phytotoxicity. The low application rate of glyphosate gave a small reduction in fresh weight (Figure 1). Ethomeen T/25 and Renex 688 enhanced the glyphosate toxicity. At all concentrations applied Ethomeen T/25 gave a higher reduction than Renex 688. Addition of Ethomeen T/25 gave a rapid reduction in fresh weight. With Renex 688 the phytotoxicity does not change when the surfactant concentration increased from 0.001% (w/v) to 0.01% (w/v). The results with Ethomeen T/25 agree with the observation that addition of MON 0818 (polyoxyethylene tallow amine) at different concentrations enhanced the glyphosate toxicity to seedlings of common milkweed and hemp dogbane (12). The relatively pore capacity of Renex 688 to enhance glyphosate phytotoxicity agrees to a certain extent with the observation that a similar surfactant (formulated as Agral 90) does not influence the glyphosate toxicity to several species (5). Application of the surfactants themselves at 1.0% (w/v) did not result in reduction of fresh weight.

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Deposition. With the discussion on the deposition data the assumptions have been made that the behaviour of the fluorescent dye is the same as that of glyphosate and that the presence of glyphosate (1.3 mM) does not change the data obtained with surfactant solutions.

Both surfactants increase the deposition on the difficult to wet wheat seedlings (Figure 2). At a surfactant concentration of 1% (w/v) a 5 to 6 times enhanced deposition could be observed. The relation between concentration and deposition is similar for Ethomeen T/25 and Renex 688 with Renex 688 giving a somewhat higher deposition. As a difference in deposition does not seem to cause the observed difference in phytotoxicity (Figure 1), difference in entry of glyphosate into the plant must give the difference in phytotoxicity. By taking the point at which the surface tension did not further decrease (data not shown) the critical micelle concentrations (CMC) of the surfactants can be estimated. The CMC amounts to 0.003% (w/v) for Renex 688 and 0.01% (w/v) for Ethomeen T/25. This implies that the continuously increasing deposition at relatively high concentrations of surfactant can not be explained by decreased static surface tension. It was suggested by Taylor (10) that relatively high concentrations of surfactant are necessary as the concentration of surfactant affects the speed at which the surface tension of the drop is changed during the time the drop moves from the nozzle towards the plant.

Absorption of ^{14}C -glyphosate. The absorption data of glyphosate alone and glyphosate with Ethomeen T/25 at 0.05% (w/v) and 0.5% (w/v) show that most radioactivity has been absorbed within 6 h after application (Table I).

Table I. Absorption^a of ^{14}C -Glyphosate

Treatment	% of applied Dose		
	6h	24h	48h
Glyphosate	21.5 ± 3.1	20.6 ± 4.2	31.6 ± 7.4
Glyphosate + Renex 688 0.05%	2.5 ± 0.9	- ^b	9.0 ± 1.9
Glyphosate + Renex 688 0.5 %	11.8 ± 2.4	17.8 ± 1.5	23.1 ± 2.6
Glyphosate + Ethomeen T/25 0.05%	49.2 ± 1.8	54.1 ± 5.0	67.6 ± 3.3
Glyphosate + Ethomeen T/25 0.5 %	46.5 ± 3.6	60.1 ± 2.2	61.7 ± 3.8

^a Means ± SE calculated from 2 experiments with each 3 replicates

^b - = no absorption

Ethomeen T/25 at 0.05% (w/v) and 0.5% (w/v) enhances the absorption whereas Renex 688 at 0.05% (w/v) and 0.5% (w/v) gives a decreased absorption. This observation confirms the conclusion derived from the phytotoxicity and the deposition data with respect to a possible limited entry of glyphosate in the presence of Renex 688. A more than twofold increased glyphosate absorption as the result of addition of a polyoxyethylene tallow amine (MON 0818) was also observed with field bindweed (7). An inhibitory effect on glyphosate absorption was

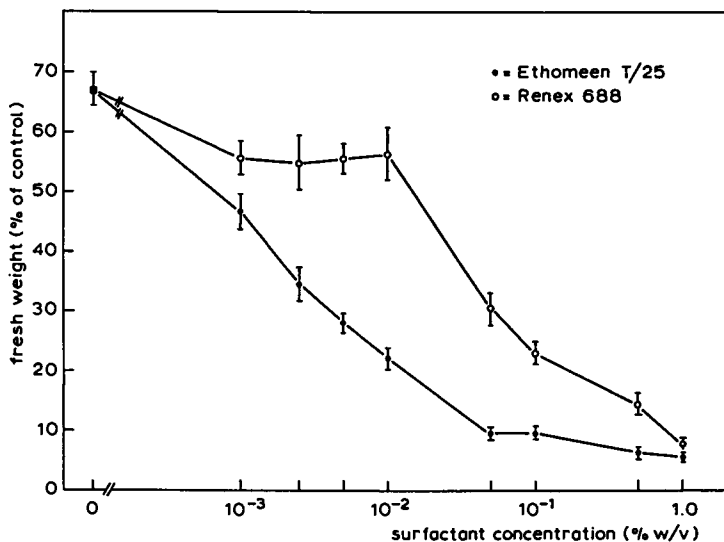


Figure 1. Effect of surfactant concentration on glyphosate toxicity expressed as % of the control's fresh weight. Values are means \pm SE calculated from 4 experiments with each 4 replicates. The control's fresh weight (mean value per experiment) ranged from 32 to 46 g per pot.

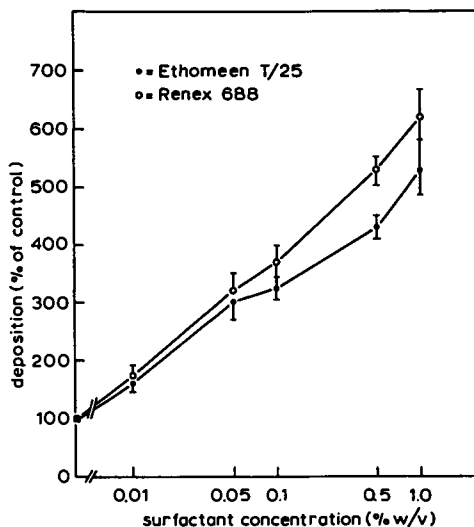


Figure 2. Effect of surfactant concentration on deposition. Deposition is expressed as % of the control sprayed with water. Values are means \pm SE calculated from 3 experiments with each 4 replicates. Deposition of the control (mean value per experiment) ranged from 41 to 54 ul/g dry weight.

demonstrated with Renex 36 (polyoxyethylene 6- tridecyl ether) after application to barley seedlings (4). Based on enhanced leakage of electrolytes from barley segments the suggestion was made that disruption of membrane integrity may lead to reduced absorption (4). Our observation that lowering of the concentration of Renex 688 from 0.5% (w/v) to 0.05% (w/v) results in a higher inhibition of glyphosate absorption seems to conflict with this suggestion.

Table II. Absorption^a of Surfactants

		% of applied Dose		
		6h	24h	48h
Renex 688	0.5% (w/v)	62.8 ± 7.8	> 80 ^b	> 80 ^b
Ethomeen T/25	0.5% (w/v)	38.4 ± 7.2	56.0 ± 5.4	73.2 ± 3.5

^aMeans ± SE calculated from 3 experiments with each 3 replicates

^bSee section Materials and Methods

Absorption of surfactants. Renex 688 and Ethomeen T/25 penetrate into the cuticle (Table II). With both surfactants more than a half of the deposit is absorbed within 6 hours after application. The course of uptake and the percentages of uptake agree along rough lines with the results obtained after application of ¹⁴C-polyoxyethylene tallow amine (MON 0818) to field bindweed (8) and polyoxyethylene (8.5) nonylphenol to wheat (2). The values for absorption of Renex 688 exceed those for Ethomeen T/25. Hydration of both surfactants at 95% RH (data not shown) revealed that hydrated Renex 688 exists as a gel whereas hydrated Ethomeen T/25 shows a soft solid form. These differences in uptake and physical form support the conclusion of Anderson and Girling (2) that the uptake of surfactants is at least partly related to their physical form. The rapid penetration of Renex 688 into the cuticle does not provide an obvious explanation for the observed inhibition of glyphosate absorption.

The movement of Ethomeen T/25 into the cuticle implies that increased cuticle permeability, injury to underlying cells and/or complexation with glyphosate may lead to the observed increase in absorption (Table I).

Scanning electron microscopy. Scanning electron micrographs (Figure 3) show that the crystalline epicuticular waxes seem rather unimpaired 24 h after application of surfactants. After application of Ethomeen T/25 at 0.05% (w/v) and 0.5% (w/v) a layer of surfactant covering the epicuticular waxes can be observed. Folds are visible (Figure 3F) which may be the result of small air pockets within the deposit which burst during drying. Application of Renex 688 at 0.05% (w/v) and 0.5% (w/v) results in a much thinner deposit. This result confirms the rapid penetration of Renex 688 (Table II). The results with Ethomeen T/25 concur with scanning electron micrographs obtained after application of polyoxyethylene tallow amine (MON 0818) to field bindweed (8). A deposit of surfactant was observed and there was no

evidence for disruption of epicuticular waxes. These results do not form a proof but indicate that enhanced absorption of glyphosate in the presence of Ethomeen T/25 is not a result from dissolved cuticular waxes. With Ethomeen T/25 at 0.5% (Figure 3E) and to a smaller extent at 0.05% (w/v) a shrinking of underlying epidermal cells could be observed which indicates disruption of the plasmalemma by Ethomeen T/25 within 24 h after application. Application of Renex 688 did not result in shrinking of cells. This observation and the observed penetration of Renex 688 into the cuticle (Table II) lead to the conclusion that Renex 688 does not diffuse away from the underside of the cuticle or Renex 688 is less disruptive than Ethomeen T/25 to the plasmalemma.

Leakage of electrolytes. Measurement of electrolyte leakage from leaf discs pretreated with surfactant or after incubation in surfactant containing medium may be affected by the cuticle as a barrier for penetration of surfactants into the tissue. For that reason potato discs were used in this study. Ethomeen T/25 and Renex 688 enhanced the leakage of electrolytes (Table III). A relatively large increase of the leakage can be observed at a relatively low concentration of surfactant (0.005% (w/v)). The leakage with Ethomeen T/25 exceeds the leakage with Renex 688 at all concentrations but the values are of the same of order of magnitude.

Table III. Leakage^a of Electrolytes from Potato Discs

Surfactant	Conductivity as % of Control		
	Concentration of Surfactant		
	0.005% (w/v)	0.05% (w/v)	0.05% (w/v)
Renex 688	343	454	517
Ethomeen T/25	506	846	1050

^aMean values from a representative experiment with 3 replicates

The membrane disrupting property of Renex 688 and the absence of shrunk epidermal cells as was observed with scanning electron microscopy support the idea that Renex 688 penetrates rapidly into the cuticle but does not or only to a small extent diffuse from the cuticle to the apoplast.

Injury caused by surfactants. Application of Ethomeen T/25 at 0.05% (w/v) and 0.5% (w/v) gave necrotic lesions (observed 72 hours after application). At 0.5% (w/v) this injury was more severe than at 0.05% (w/v). Renex 688 did not give injury symptoms at 0.05% (w/v) but at 0.5% (w/v) some small necrotic lesions could be observed. This result supports the view that Renex 688 is retained by the cuticle. Nevertheless at the relatively high concentration of 0.5% (w/v) penetration of Renex 688 occurs which may partly explain the enhanced glyphosate absorption compared with absorption at 0.05% (w/v) (Table I).

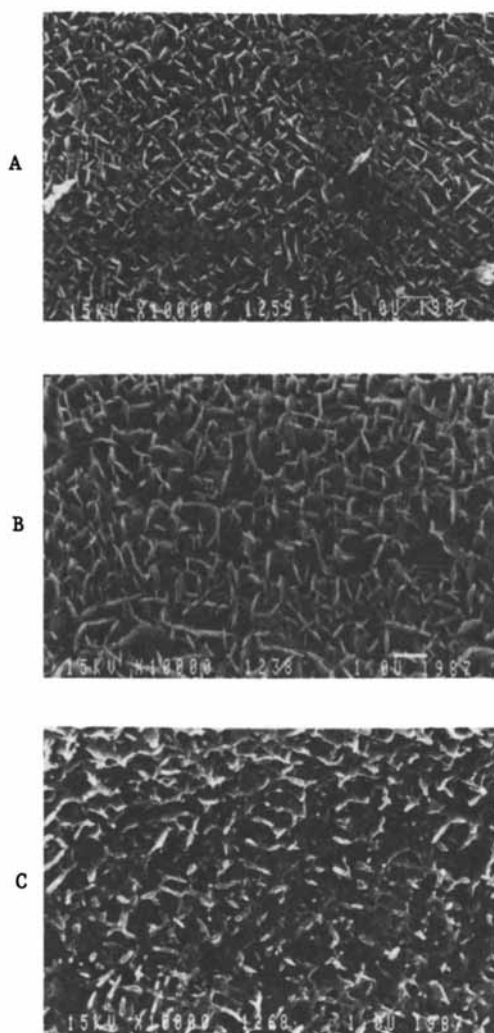


Figure 3. Scanning electron micrographs of the adaxial side of winter wheat; A) Untreated, x 10 000; B) Renex 688 0.05% (w/v), x 10 000; C) Renex 688 0.5% (w/v), x 10 000.

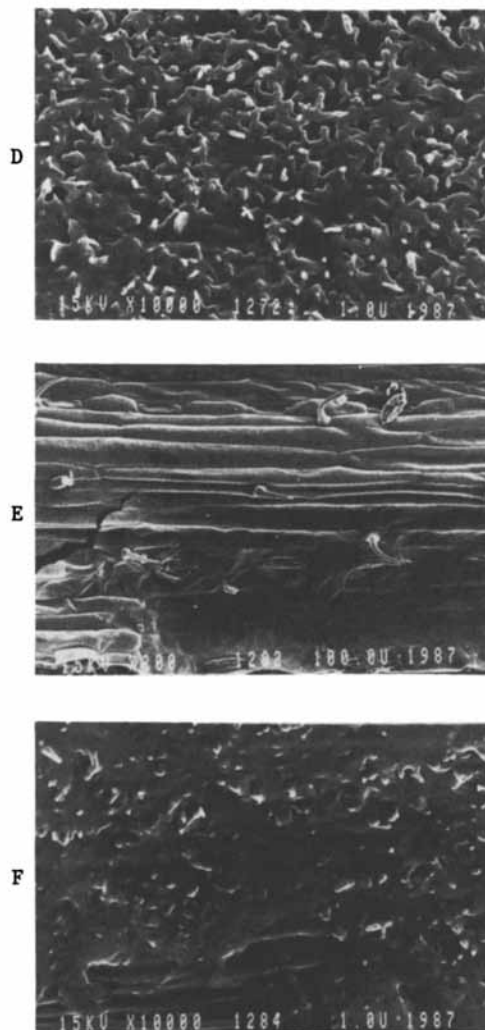


Figure 3. Continued D) Ethomeen T/25 0.05% (w/v), x 10 000; E) Ethomeen T/25 0.5% (w/v), x 200; F) Ethomeen T/25 0.5% (w/v), x 10 000.

Table IV. Summarized Data from this and two other Studies (4,7)

Surfactant	HLB	Ionic form ^d	Species	Enhanced Glyphosate absorption	Injury
Ethomeen T/25 ^a	19.3	C	wheat	+	+
Renex 688 ^a	12.3	N	wheat	-	±
Tween 20 ^b	16.7	N	barley	+	
Renex 36 ^b	11.5	N	barley	-	-
Tween 20 ^c	16.7	N	field	-	±
MON 0818 ^c		C	bindweed	+	+

^athis study; ^bO'Donovan JT a.o. (1985); ^cSherrick SL a.o. (1986);
^dC= cationic, N = nonionic.

Conclusions

The absorption of glyphosate is inhibited by Renex 688 and enhanced by Ethomeen T/25. Both surfactants are absorbed by the cuticle. The results of this study indicate that the partition of these surfactants between the lipophilic cuticle and the apoplast favours a position of Renex 688 in the cuticle whereas Ethomeen T/25 diffuses to a larger extent than Renex 688 into the apoplast. This suggestion agrees with the lipophilic character of Renex 688 and the high water solubility of the cationic Ethomeen T/25.

The presence of Renex 688 in the cuticle may cause the observed inhibition of glyphosate absorption when Renex 688 is applied at 0.05% (w/v). However the cause of the partial neutralization of this inhibition with Renex 688 at 0.5% (w/v) is not clear.

The penetration of Ethomeen T/25 into the underlying tissue may lead to increased permeability of the cell wall and the plasmalemma to glyphosate. The possibility of correlation between enhanced absorption of glyphosate and penetration of surfactants into the tissue is also supported by two other studies (4,7) on this matter (Table IV).

Acknowledgments

The authors acknowledge AKZO Chemie for providing Ethomeen T/25, ICI-Holland for providing Renex 688 and B.V. Luxan for providing technical grade glyphosate.

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RECEIVED December 28, 1987

Chapter 6

Formulation, Structure, and Physical Properties

Factors Affecting the Rate of Penetration of Yellow Foxtail Cuticle by a Series of Aryloxyphenoxypropionate Herbicides

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The cuticular penetration behavior in yellow foxtail as measured by a penetration rate constant (k_{pen}) for six aryloxyphenoxypropionates was found to be dependent primarily on the structural class (pyridinyloxy, quin-oxalinyloxy and phenoxy) and secondarily on formulation. Correlations of k_{pen} with the physical properties melting point, log P, vapor pressure and water solubility were examined and determined to be unreliable because separation of the penetration behavior of the six compounds into structural classes reduced the number of compounds available for such correlations. The rate constant, k_{pen} , was extracted by mathematically modeling the distribution of the ^{14}C -aryloxyphenoxypropionate herbicides in the relevant environmental and plant compartments over a 24- to 48-hour period. For each herbicide, the two formulations used were 0.1% Ortho X-77 in 50% acetone/water with (+COC) and without (-COC) 0.3% Agri-dex crop oil concentrate.

The transport of a foliarly applied herbicide through the plant cuticle is the first process affecting the overall efficacy of the chemical. In this study the factors influencing foliar absorption of a series of similar herbicidal compounds in simple formulations will be examined. This work will provide insight into the relationships among chemical, plant cuticle and adjuvant that control cuticular penetration. This information will aid more sophisticated formulation efforts and herbicide discovery research.

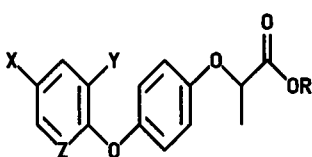
The suitability of the aryloxyphenoxypropionate family of herbicides for this study lies in 1) the diversity of structures (three classes) within this family (six compounds) showing herbicidal activity (Table I) and 2) the importance of this new group of chemicals in the post-emergent grass control market.

The objective of this work was to examine how structure, physical properties and/or the nature of the adjuvant affect cuticular penetration in yellow foxtail as measured by a cuticular

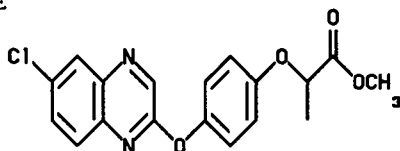
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Table I. Structures of the Aryloxyphenoxypropionate Herbicides



COMPOUND	X	Y	Z	R
<u>Pyridinyloxy:</u>				
Haloxifop	CF ₃	Cl	N	H
Haloxifop-ME ^a	CF ₃	Cl	N	CH ₃
Haloxifop-EE	CF ₃	Cl	N	CH ₂ CH ₂ OCH ₂ CH ₃
Fluazifop-BE	CF ₃	H	N	CH ₂ CH ₂ CH ₂ CH ₃
<u>Phenoxy:</u>				
Diclofop-ME	Cl	Cl	CH	CH ₃
<u>Quinoxalinyloxy:</u>				
Quizalofop-ME				



^aSee Legend of Symbols for the abbreviations used.

penetration rate constant, k_{pen} . The available aryloxyphenoxypropionates include pyridinyloxy, quinoxalinyloxy and phenoxy. The physical properties of the aryloxyphenoxypropionates which potentially could correlate with k_{pen} are water solubility, vapor pressure, melting point and log P, which is a measure of the hydrophobicity of the chemical. The range in these physical parameters for the aryloxyphenoxypropionate series is sufficient (Table II) to detect any correlations if they exist.

In these experiments the amount of herbicide distributed on the plant surface, beneath the plant cuticle, and in the air was monitored at 7-9 time points over a 24- to 48-hour period. The value of k_{pen} was then extracted from the compound-distribution-versus-time data using a reasonable kinetic model and mathematical modeling. Extracting a parameter directly related to the time course of penetration, i.e. k_{pen} , rather than using a penetration value determined at one time point gives a more realistic view of penetration rates. The one-time-point method levels the penetration value of fast penetrators to the same number which is related to the experimental time period chosen rather than to any physical or chemical property of the system. If strong correlations exist between k_{pen} and structure or physical properties, etc. then they should be derivable from the six compounds used in this study.

Table II. Physical Constants for the Aryloxyphenoxypropionate Herbicides^a

COMPOUND	Log P ^b	Water Solubility, ppm	Vapor Pressure, mm Hg	Melting Point, °C
Haloxyfop ^c	4.316	43.4	<1E-8	106
Haloxyfop-ME ^c	4.642	9.3	6.5E-7	56
Haloxyfop-EE ^d	5.149	2.7	<1E-8	57
Fluazifop-BE ^e	5.761	2 ^f	4.1E-7 ^g	5
Quizalofop-ME ^h	4.529	0.3 ^g		92
Diclofop-ME ^h	5.521	3 ⁱ	6.9E-7	40
Range:	1.4	43	>100	101

^aWater solubility and vapor pressure measured at 25°C except were noted.

^bMedChem Software, Release 3.42, August 1986, Medicinal Chemistry Project, Pomona College, Claremont, CA.

^cSwann, R. L., McKendry, L. H., Markley, L. D. Hertel, J. A., The Dow Chemical Company, unpublished data.

^dSwann, R. L., The Dow Chemical Company, unpublished data.

^eSee Reference 1.

^fAmbient temperature.

^g20°C.

^hSee Reference 2. Water solubility and melting point data are for the ethyl ester.

ⁱ22°C.

Experimental Section

Yellow Foxtail Growth and Treatment. Yellow foxtail plants (*Seteria glauca* (L.) Beauv.) were grown under greenhouse conditions in soil/vermiculite (1/1) until the plants reached the 2- to 3-leaf stage. The plants were moved to the plant chambers at least 12 h before the application of the formulated ¹⁴C-labeled aryloxyphenoxypropionate. Six to nine sets of plants, three plants per set, were treated with the formulated herbicide. The formulation was applied at a rate of 0.017 μmol/5 μL/plant which is equivalent to 0.31 kg/ha in a spray volume of 280 L/ha. The 5 μL of formulated compound was applied to the first true leaf of the yellow foxtail plant in 0.5 μL drops.

Plant Chambers. The chambers used for containment of the yellow foxtail plants during treatment with the aryloxyphenoxypropionate herbicides were modeled after a design originally presented by Nash et al.(3) The chambers allowed isolation of the plants and their atmosphere in a temperature-controlled room. A complete description of the modifications used here was given recently by McCall et al.(4) In summary, the air in the chambers was drawn through polyurethane foam plugs at a flow rate of approximately 0.8 km/h to

trap any chemical volatilized from the plant surface. The temperature of the room was controlled at 20(±2)°C with a 14-h light period. Light was provided by a 1000-W General Electric Duraglow Luminaire metal halide lamp located directly above the plant chamber.

Aryloxyphenoxypropionates and Their Formulations. The specific activities of the ¹⁴C-phenyl-labeled aryloxyphenoxypropionates (specific activities in mCi/mmol) were haloxyfop (11.2 and 16.7), haloxyfop-ME (11.7 and 20.0), haloxyfop-EE (11.2), fluazifop-BE (10.3), quizalofop-ME (9.65), and diclofop-ME (9.34). The radiochemical purity of the ¹⁴C-aryloxyphenoxypropionate compounds was greater than 98% as determined by high-performance liquid chromatography (HPLC). The base formulation was 50% acetone in water with 0.1(v/v)% Ortho X-77, and was designated -COC. All of the aryloxyphenoxypropionates were soluble in this formulation. The base formulation with 0.3(v/v)% Agri-Dex crop oil concentrate (COC) was also examined and designated +COC. Ortho X-77 is a mixture of alkylaryl polyoxyethylenes, glycols, free fatty acids and isopropanol. Agri-Dex crop oil concentrate contains 17% nonionic surfactant in a crop oil base.

Sample Collection and Analysis. At or about 0, 1, 2, 4, 8, 12, 24, 32 and 48 hours after application of the formulated herbicide, the amounts of ¹⁴C-labeled compound volatilized and trapped in the foam plugs (AIR compartment), remaining on the treated leaf surface (SRF compartment) and entering the plant (PEN compartment) were determined.

AIR. First, the recovery efficiency of the polyurethane foam plugs in the plant chamber with only three foam plugs was determined for the most volatile compound, haloxyfop-ME. Nine foam plugs were used in the original design (4). A known quantity of ¹⁴C-labeled chemical was deposited on a glass slide and allowed to evaporate in the plant chambers under the conditions of the plant experiments for at least 24 hours. A recovery of >99% of the applied haloxyfop-ME was obtained. The decrease from nine to three foam plugs for trapping any volatilized chemical resulted in an improved limit of detection for the AIR measurement, since the volume of solvent required was reduced from two liters to one half liter. The volatilized ¹⁴C compound was extracted from the plugs by rinsing each of the three plugs three times with about 70 mL of acetone. The acetone washes were combined and brought to a final volume of 500 mL. A 2-mL aliquot was counted in 18 mL of Aquasol on a Packard Tri-Carb Liquid Scintillation Counter, Model 4530 or Model 2000CA. The spectral index of external standard method with automatic efficiency control was used to correct for counting inefficiencies.

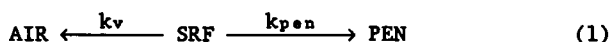
SRF. After collection of the foam plugs the plants in one set were severed at the soil surface. The resulting shoots were rinsed by swirling in two successive 10-mL aliquots of methanol (10 s/rinse) to remove any chemical remaining on the treated-leaf surface. These brief rinses are not expected to solubilize the cuticle. Bucholtz and Hess (5) showed that a methanol rinse of less than one min removed less than 1% of subcuticular ¹⁴C activity in

cabbage seedlings. A 0.1-mL aliquot of each rinse in 10-mL of Aquasol was analyzed by liquid scintillation counting (LSC) as for the plug rinses.

PEN. The amount of compound that entered the plant was determined by combustion of the rinsed shoot and the root-plus-soil fraction. The rinsed shoot and the root-plus-soil fraction were either refrigerated and combusted the next day or frozen and combusted within several weeks. A Harvey Biological Oxidizer (Model OX-400 or OX-100) interfaced to a Packard Tri-Carb Sample Oxidizer (Model B306 or 306, respectively) was used for the combustions. The released ^{14}C was collected in 7 mL of CarboSorb and diluted with 13 mL of Permafluor V for LSC. After initial experiments showed that <2% of the applied radioactivity translocated to the roots, the root-plus-soil fraction was no longer collected.

Reapplication Experiments. Yellow foxtail plants were treated with haloxyfop in the +COC formulation at a rate of $0.0062 \mu\text{mol}/5 \mu\text{L}/\text{plant}$. Sample collection proceeded for six hours. Then a second application of either the original haloxyfop +COC formulation or a formulation blank was made on the same area of the leaf used for the first application. Sample collection proceeded for another six hours.

Kinetic Model Analysis. The simplest model for foliar absorption of a volatile compound is given in equation 1, where AIR is the amount



of the ^{14}C -labeled compound volatilized, SRF is the amount of the ^{14}C -labeled compound remaining on the treated-leaf surface, PEN is the amount of ^{14}C -labeled compound found inside the plant, k_v is the rate constant for volatilization and k_{pen} is the rate constant for penetration of the plant cuticle by the applied ^{14}C -labeled chemical. This model was termed simple penetration (SP) since only one rate constant was required to describe the penetration behavior. The rate constant k_{pen} is given by equation 2 where A is the area of the applied herbicide spot on the leaf surface, V is the volume of the applied spot, D is the diffusion constant for the compound

$$k_{pen} = \frac{A}{V(\Delta x)} \times DK \quad (2)$$

penetrating the cuticle of effective thickness Δx and K is the partition coefficient for the transfer of the solute from the applied spot to the cuticle (11). The $A/V(\Delta x)$ factor in equation 2 is an experimental technique factor whereas DK depends on the properties of the compound of interest. According to this simple analysis the penetration rate constant should be first order and directly related to the structural and/or physical properties of the penetrating chemical. Previously, McCall et al. (4) showed that k_v was first order under these conditions.

The method of fitting the model to the experimental data involved writing the differential equations for the model (equations

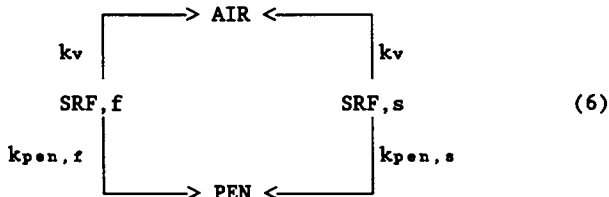
$$d[\text{AIR}]/dt = k_v[\text{SRF}] \quad (3)$$

$$d[\text{SRF}]/dt = -(k_v + k_{pen})[\text{SRF}] \quad (4)$$

$$d[\text{PEN}]/dt = k_{pen}[\text{SRF}] \quad (5)$$

3-5) and solving the set of differential equations with SIMUSOLV* modeling and simulation software developed at The Dow Chemical Co.

Under some conditions the simple penetration model could not satisfactorily fit the experimental data. A model that included a fast-penetrating compartment, SRF,f, and a slow-penetrating compartment, SRF,s, with corresponding $k_{pen,f}$ and $k_{pen,s}$ was necessary (equation 6). This model was termed biphasic penetration



(BP) since the concentration-versus-time plots showed biphasic kinetics, i.e. two rate constants were necessary to describe the penetration behavior.

Results

-COC. The %-of-applied-radioactivity versus time plots for quizalofop-ME and diclofop-ME in the -COC formulation are shown in Figure 1 and for the pyridinyloxy class in Figures 2 and 3. Figure 1 shows that the penetration behavior of quizalofop-ME and diclofop-ME was described by one rate constant and was fit by the SP model. For the pyridinyloxy class, penetration (Figures 2 and 3) slowed markedly after 1-8 hours. For a satisfactory fit of the calculated response to the experimental points, two rate constants were required to describe cuticular penetration as provided by the BP model.

+COC. The %-of-applied-radioactivity versus time plots for the pyridinyloxy class are shown in Figures 4 and 5. The penetration behaviors of haloxyfop-ME, haloxyfop-EE and fluazifop-BE in the +COC formulation were governed by one rate constant as provided by the SP model. Haloxyfop still showed biphasic penetration; however, the fast phase was extended to about nine hours with COC from one hour without COC.

Summary of the Models and the Rate Constants. Table III lists the kinetic model which best fits the experimental data for the six compounds examined. The rate constants extracted from the data with the SP model and the BP model are collected in Tables IV and V,

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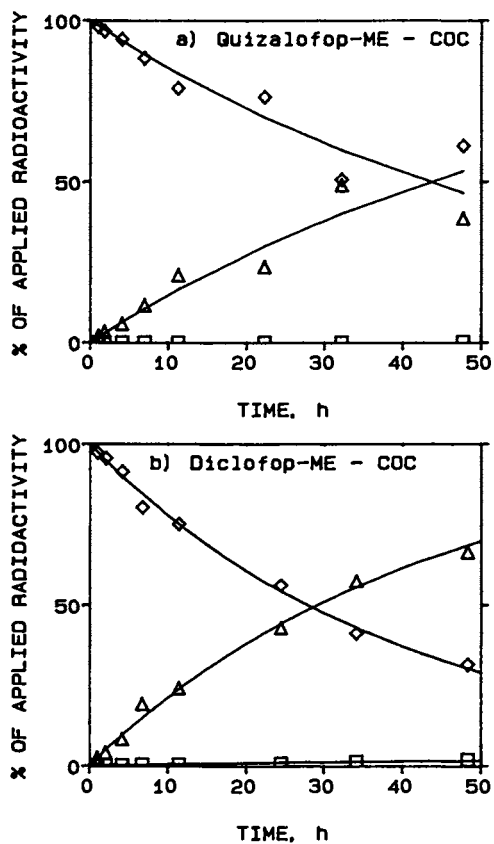


Figure 1. Aryloxyphenoxypropionates in -COC formulation. \diamond SRF; Δ , PEN; \square , AIR; —, fit with simple penetration model.

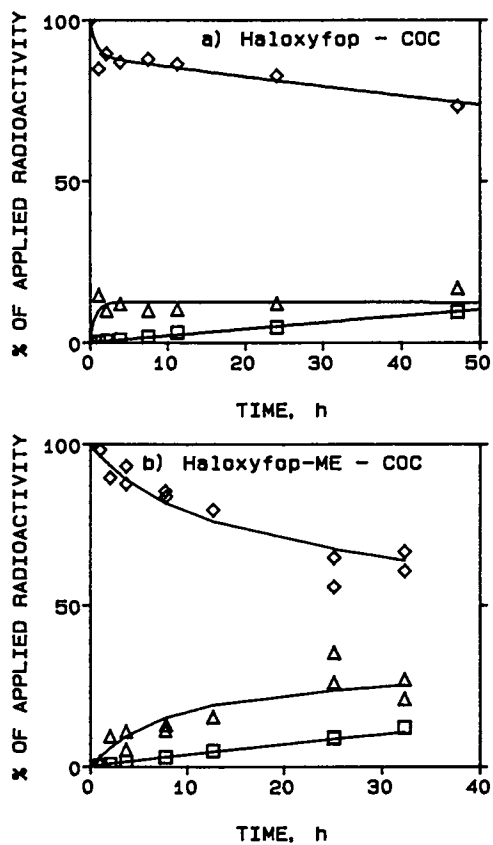


Figure 2. Pyridinyloxyphenoxypropionates in -COC formulation. \diamond , SRF; Δ , PEN; \square , AIR; —, fit with biphasic penetration model.

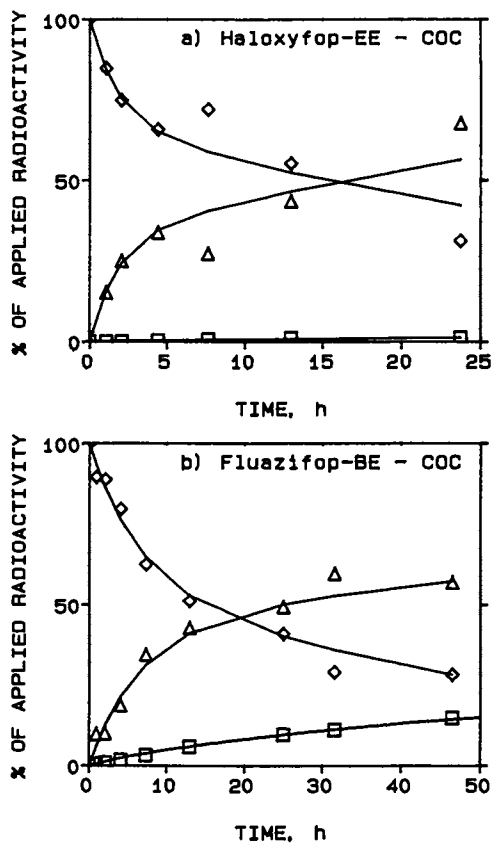


Figure 3. Pyridinyloxyphenoxypropionates in -COC formulation. \diamond , SRF; Δ , PEN; \square , AIR; —, fit with biphasic penetration model.

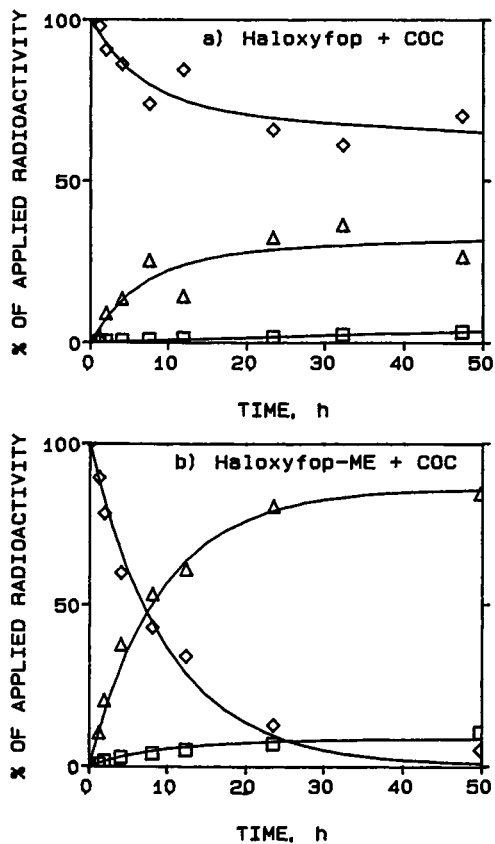


Figure 4. Pyridinyloxyphenoxypropionates in +COC formulation. \diamond , SRF; Δ , PEN; \square , AIR; —, a) fit with biphasic penetration model and b) fit with simple penetration model.

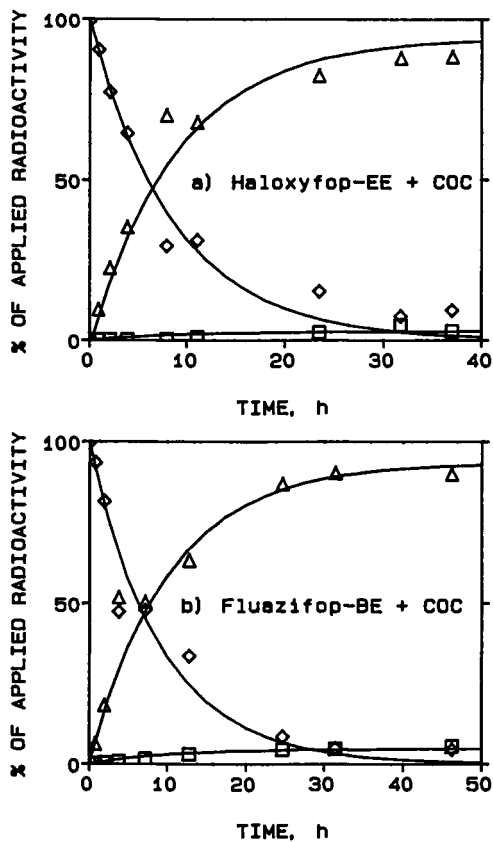


Figure 5. Pyridinyloxyphenoxypropionates in +COC formulation.
 ◇, SRF; △, PEN; □, AIR; —, fit with simple penetration model.

Table III. Penetration Model Summary

COMPOUND	-COC	+COC
<u>Pyridinyloxy:</u>		
Haloxypop	BP ^a	BP
Haloxypop-ME	BP	SP ^b
Haloxypop-EE	BP	SP
Fluazifop-BE	BP	SP
<u>Quinoxalinyloxy:</u>		
Quizalofop-ME	SP	SP
<u>Phenoxy:</u>		
Diclofop-ME	SP	SP

^aBP = biphasic penetration model^bSP = simple penetration modelTable IV. Summary of the Rate Constants for the Simple Penetration Model^a

COMPOUND	k _v , -COC	k _v , +COC	k _{pen} , -COC	k _{pen} , +COC
Haloxypop	0.003	0.001	BP ^b	BP
Haloxypop-ME	0.004	0.008	BP	0.09
Haloxypop-EE	0.0006	0.0008	BP	0.11
Fluazifop-BE	0.006	0.004	BP	0.092
Quizalofop-ME	N.M. ^c	N.M.	0.016	0.16
Diclofop-ME	0.0005	0.0009	0.024	0.19

^aUnits are h⁻¹.^bBP = biphasic penetration model^cN.M. = not measurableTable V. Summary of the Rate Constants for the Biphasic Penetration Model^a

COMPOUND	k _{pen,f}	k _{pen,s}	SRF, f ^b	SRF, s ^b
Haloxypop	1.3	0.001	11	89
(Haloxypop	0.15	0.003	33	67) ^c
Haloxypop-ME	0.16	0.0003	19	81
Haloxypop-EE	0.11	0.001	24	76
Fluazifop-BE	0.15	0.009	42	58

^aUnits for the rate constants are h⁻¹. Data are from -COC formulation.^bSRF, f = % of compound in fast-penetrating compartment

SRF, s = % of compound in slow-penetrating compartment

^cData are from the +COC formulation.

respectively. For some of the compounds the experiments were repeated to determine the reproducibility of the experimental method. A relative standard deviation (RSD) of 20-40% was obtained for SRF,f and k_v when the experiments were performed throughout the year and for k_{pen} when the experiments were performed from fall to spring; however, k_{pen} showed a 2- to 8-fold increase when experiments from the summer were considered.

Discussion

Reliability of k_{pen} , k_v and SRF,f. For k_{pen} to be related directly to the ability of the applied chemical to penetrate the cuticle, the experimental technique factor, $A/\Delta x$, in equation 2 must be held constant over the time period for collection of the ^{14}C -distribution-versus-time data for all the compounds. That time period was about 11 months. This requires reproducibility in applying the formulated compound and in providing the same growth conditions for the plants. The RSD for k_{pen} over the fall-to-spring period indicates the necessary experimental reproducibility was achieved. The noticeable increase in k_{pen} variability for the summer experiments indicates growth conditions and/or experimental technique changed. The same individual applied the formulated compounds with the same procedure throughout the study; however, during the summer months the greenhouse roof at Dow is whitewashed. This treatment reduces the amount of natural sunlight reaching the plants. A study of the permeability of cuticles developed under different temperatures and light intensities showed that the correlation between the flux through a cuticle and the permeability of the cuticle is a function of partition coefficient, cuticle thickness and cuticle wax content (6). A difference in light intensity could be responsible for the variability in k_{pen} over the summer months. Because of this anomaly k_{pen} comparisons were made only with data collected in the fall to spring months.

The volatilization rate constant, k_v , and the percent of the applied compound found in the fast-penetrating compartment, SRF,f, showed no anomalous behavior for the summer experiments. These parameters would not be sensitive to the growth conditions if they were caused by surface phenomena. Temperature control is probably the most important factor in their reproducibility. The values of k_v and SRF,f obtained over the entire data collection period were used since the RSD values were satisfactory over that period.

Simple Penetration Versus Biphase Penetration. The model summary presented in Table III shows the importance of structure and adjuvant in controlling the penetration mechanism. Cuticular penetration by the pyridinyloxy class without COC was markedly impeded after an initial fast penetration stage. With the exception of haloxyfop the addition of COC to the formulation simplified the penetration kinetics in the pyridinyloxy class. The quinoxalinyloxy (quizalofop-ME) and phenoxy (diclofop-ME) classes acted as one group as far as model behavior and adjuvant effects are concerned. Quizalofop-ME and diclofop-ME both showed about a ten-fold increase in k_{pen} when COC was added to the formulation.

Explanations for Biphasic Kinetics. Several possible explanations for biphasic kinetics with the pyridinyloxy class without COC will be examined.

1. The pyridinyloxy compounds precipitate during the evaporation of the solvent from the formulation. This explanation could account for the short period of fast penetration (1 h) with haloxyfop without COC; however, it does not explain the penetration behavior of the other pyridinyloxy compounds with longer periods of fast penetration (6-8 h) and a melting point range of 5-57°C. Thus, fluazifop-BE with a melting point of 5°C is a liquid at the temperature of the experiment (20°C), however, the fluazifop-BE-without-COC data were fit better by the BP model than the SP model. Thus, precipitation of the herbicidal compound on the treated-leaf surface is not a complete explanation for the penetration behavior of the pyridinyloxy acid and esters.

2. Pyridinyloxyphenoxypropionate transport through the cuticle is blocked by "sorption" of the polar pyridinyloxy- acid and esters at active sites in the cuticle. The cuticle proper contains an assortment of functional groups, e.g. alcohol, aldehyde, ketone, ester, and epoxide (7). Enzymatically isolated plant cuticles were shown to have polyelectrolyte properties with an isoelectric point of approximately 3 (8). Interaction of the diffusing chemical and the cuticular matrix is possible and has been demonstrated (9). To test the cuticular "sorption" hypothesis, reapplication experiments were performed. Figure 6 illustrates the results of these experiments with haloxyfop +COC which also follows BP penetration kinetics. Reapplication of the formulation blank does not re-establish the initial conditions of biphasic penetration behavior. See dashed lines after the reapplication of the formulation blank in Figure 6. These results indicate that the initial solubilization conditions for haloxyfop +COC could not be re-established on the treated-leaf surface within the period of time before the evaporation of the solvent from the re-applied formulation. The surface haloxyfop was present in such a state that the available COC could not "pull" it into the cuticle. Possibly zwitterionic haloxyfop acid exists in ion pairs or as micelles with itself when not solubilized by solvent and surfactant. Reapplication of formulated herbicide does lead to another step function in the penetration of haloxyfop. See the solid lines after the reapplication of haloxyfop in Figure 6. The size of the second penetration step is almost as large as that for the initial penetration step. Therefore hindrance of transport through the cuticle by "blocked channels" is not observed.

3. The break to slow penetration is caused by the loss of an agent required to assist cuticular penetration. The transition between fast and slow penetration occurred at about 6-8 hours for all the pyridinyloxy esters with the exception of haloxyfop-EE. This suggests that a factor external to the nature of the penetrating species is controlling the fast-phase penetration behavior of the pyridinyloxy esters. The three components of the -COC formulation were acetone, water and Ortho X-77. Acetone and water evaporate long before the 6-8 h transition in penetration behavior. It appears that Ortho X-77 must be participating in the uptake of the pyridinyloxy esters.

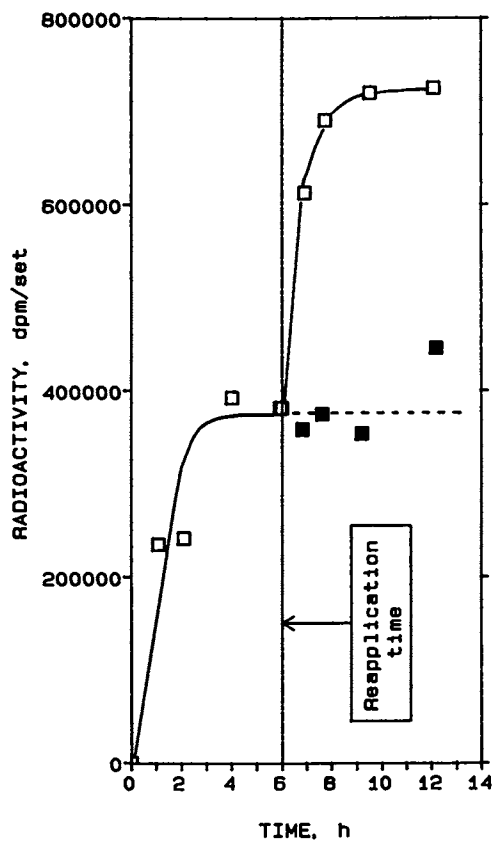


Figure 6. Haloxyfop in +COC formulation (□) with reapplication of either haloxyfop in +COC formulation (□) or only +COC formulation (■) at six hours.

The importance of the penetration behavior of nonionic surfactants in determining the foliar absorption of agrochemicals was recently examined by Silcox and Holloway (10). They found that the kinetics of uptake of a given chemical could be markedly altered by varying the structure of the surfactant. The nonionic surfactant 1-dodecanol octaethoxylate on bean leaves was absorbed rapidly to the extent of about 80% of that applied within the first 8- to 16-hours then penetration slowed significantly. When both 1-dodecanol octaethoxylate and difenzoquat were applied to bean leaves, the uptake of difenzoquat initially proceeded rapidly than slowed markedly at about the same time as for the surfactant alone. In contrast, with a uniformly slow penetrating surfactant, such as octylphenol ethoxylate, the uptake of difenzoquat proceeded at the same rate as the surfactant alone for the first 48 hours following simple penetration kinetics. In addition, Silcox and Holloway found that the foliar uptake of a given surfactant could be altered significantly by varying the chemical from positively-charged to negatively-charged. Except for the time frame, the penetration behavior of the 1-dodecanol octaethoxylate/difenzoquat system is the same as that observed with the Ortho X-77/pyridinyloxy ester system. Thus, with our Ortho X-77/pyridinyloxy ester system penetration of the plant cuticle must be assisted by Ortho X-77. The uptake of the pyridinyloxy ester then slows after 6- to 8-hours because either a) the uptake of Ortho X-77 is fast enough to leave "bare" pyridinyloxy compound on the surface unable to penetrate rapidly unassisted or b) the uptake of Ortho X-77 is biphasic and penetration assistance offered by this surfactant is also biphasic.

Quizalofop-ME and diclofop-ME in the -COC formulation did not exhibit breaks in their penetration behavior at 6-8 hours or any time up to 48 hours. Either their uptake is not assisted by Ortho X-77 or the quinoxalinyloxy/phenoxy ester group alters the penetration behavior of the Ortho X-77 to slow it to a uniform penetrating system. The lack of uptake assistance is felt to be the better argument since the quinoxalinyloxy/phenoxy ester group includes neutral, hydrophobic compounds which should be quite compatible with the cuticle.

The quinoxalinyloxy and phenoxy classes do not have the polar terminal pyridine ring. The polar nature of the pyridine ring for the pyridinyloxy esters and the zwitterion character for haloxyfop must be the properties that require the assistance of a surfactant to facilitate the movement of the pyridinyloxy compounds through the cuticle.

The lack of biphasic penetration behavior with the pyridinyloxy esters in the +COC formulation suggests that COC penetrates at least as slowly as the esters. Thus, with COC, pyridinyloxy ester penetration is assisted over the entire time required for complete movement of the ester into the plant. The ten-fold increase in k_{pen} with COC versus without COC observed in the quinoxalinyloxy/phenoxy esters was not observed for the pyridinyloxy esters. In the case of the pyridinyloxy esters COC still enhances penetration by keeping the applied pyridinyloxy ester in the fast penetrating compartment changing the penetration behavior from biphasic to simple.

A previous study of the foliar absorption behavior of the haloxyfop acid and esters with and without COC in the XRM-4570 formulation, which contains an alkylbenzenesulfonate surfactant and an alkylphenol ethoxylate emulsifier in a xylene range solvent, found simple penetration kinetics over a 13 to 30°C temperature range (McCall, P. J. Weed Sci., submitted for publication). The more complex formulation completely circumvented the biphasic penetration behavior for the haloxyfop series.

Correlations of k_v , k_{pen} and SRF, f with Aryloxyphenoxypropionate Physical Properties. A comparison of k_v , -COC and k_v , +COC (Table IV) shows a two-fold or less difference for the six compounds (with the exception of haloxyfop). Decreases in volatilization losses in the +COC formulation are related to increased k_{pen} rather than to large decreases in k_v , +COC. For those compounds following simple penetration kinetics (SP model) inspection of Table IV reveals that the value of k_{pen} depends chiefly on adjuvant and on structural class with the pyridinyloxy compounds serving as one class and the quinoxalinyloxy/phenoxy compounds as the other. With the reduction of the six compounds into two data sets there are too few representatives in either class to evaluate any rate constant/physical property correlation. For those compounds following biphasic penetration kinetics, $k_{pen,r}$ again was very similar for all the pyridinyloxy esters (Table V).

The value of SRF, f, the % of pyridinyloxy ester in the fast penetrating compartment, does vary over the pyridinyloxy ester class. The plots of SRF, f with melting point, log P and water solubility show a correlation between SRF, f and melting point (Figure 7) and SRF, f and log P (Figure 8); however, the plot of SRF, f against water solubility (Figure 9) suggests the correlation behaviors of the esters fall into two classes--fluazifop-BE and the haloxyfop series. Confidence in these possible correlations is low because of the low number of members in the pyridinyloxy ester class.

Conclusions

The most important factors in controlling the foliar absorption of the aryloxyphenoxypropionate family of herbicides are the nature of the adjuvant (with or without COC) and the structural class of the compound (pyridinyloxy, quinoxalinyloxy or phenoxy). For simple formulations structural class is the dominating factor in deciding penetration behavior. The structural class determines if simple (one k_{pen} value) or biphasic (two k_{pen} values) penetration is observed and what the magnitude of the change in penetration rate is between -COC and +COC formulations. For the quinoxalinyloxy/phenoxy classes simple penetration is observed both with and without COC with a $k_{pen,+COC}/k_{pen,-COC}$ ratio of about ten. For the pyridinyloxy class biphasic penetration is observed without COC with only 11-42% of the applied acid or ester in the fast penetrating compartment. Except for pyridinyloxy acid, the addition of COC to the formulation eliminates the slow penetrating species but does not give increased k_{pen} values as was the case with the quinoxalinyloxy/phenoxy class.

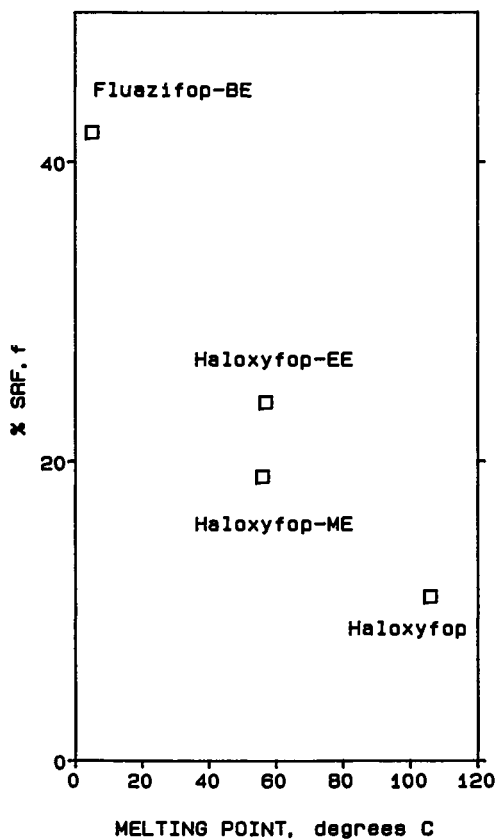


Figure 7. A plot of the % of applied radioactivity in the fast-penetrating compartment, SRF, f, of the biphasic penetration model versus the melting point of the pyridinyloxyphenoxypropionates.

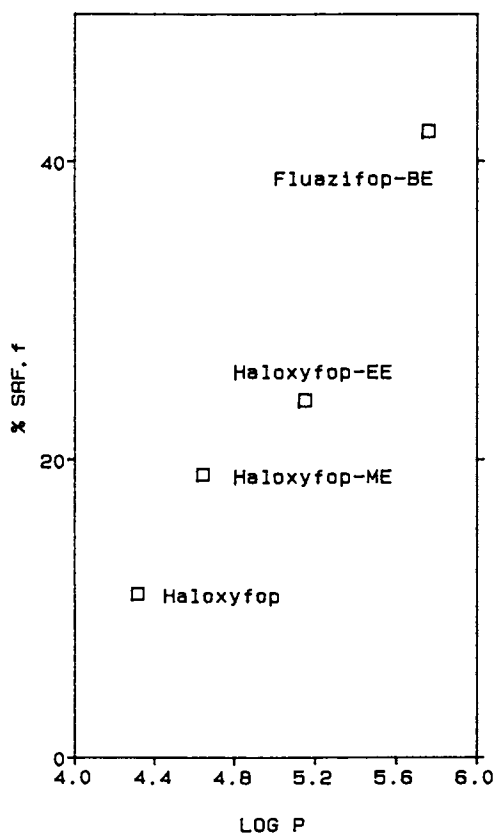


Figure 8. A plot of the % of applied radioactivity in the fast-penetrating compartment, SRF, f, of the biphasic penetration model versus log P for the pyridinyloxyphenoxypropionates.

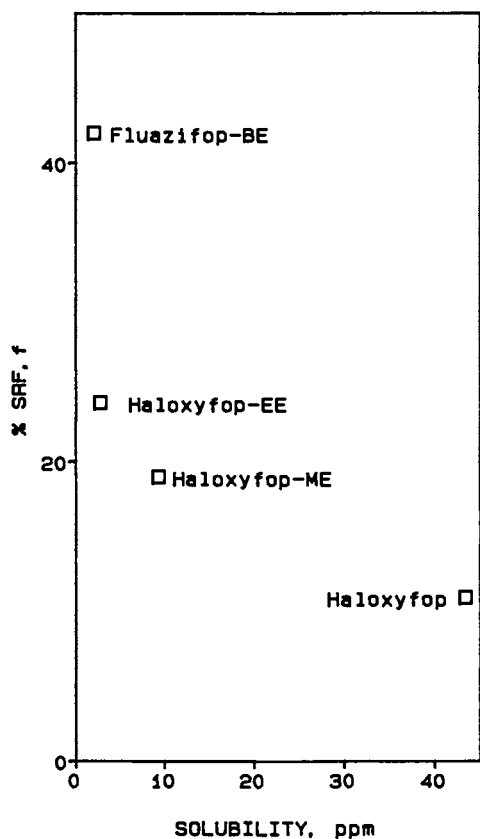


Figure 9. A plot of the % of applied radioactivity in the fast-penetrating compartment, SRF, f , of the biphasic penetration model versus the water solubility of the pyridinyloxyphenoxypropionates.

It is suggested that the biphasic penetration behavior of the pyridinyloxy esters without COC is due to the rapid (relative to k_{pen}) penetration of Ortho X-77 in the formulation which leaves the "bare", polar pyridinyloxy ester behind on the treated-leaf surface. These polar esters require the assistance of the surfactant and/or COC to penetrate the plant cuticle satisfactorily.

Since the penetration behavior of the aryloxyphenoxypropionates fell into structural classes with two to four members, correlation of the parameters k_v , k_{pen} and SRF, f with any physical properties could not be done with confidence.

Acknowledgments

The authors wish to thank Jeffrey L. Jensen and Eric J. Martin for productive discussions concerning this work.

Legend of Symbols

ME - methyl ester
EE - ethoxyethyl ester
BE - n-butyl ester

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RECEIVED December 28, 1987

Chapter 7

Effects of Surfactants on Droplet Spreading and Drying Rates in Relation to Foliar Uptake

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Various non-ionic organosilicone and organic surfactant solutions were compared by means of droplet contact angle, spread area and drying time measurements. Several organosilicone surfactant solutions had leaf wetting and spreading capabilities far superior to the organic surfactant solutions. Surfactants were characterised further by their influence on the uptake of ¹⁴C-2-deoxyglucose into bean, eucalypt and Citrus foliage. Obvious plant species differences exist that could not be completely overcome by the surfactants tested. Similar rates of foliar uptake of the deoxyglucose were found with selected organosilicone and organic surfactants. The organosilicone solution properties were such that both cuticular penetration and stomatal flooding were possible. This may be of value in the field with "difficult" plant species or adverse spraying conditions.

The factors enhancing or constraining foliar uptake of herbicides have been investigated and reviewed many times (1-5), with much emphasis on the nature of the leaf surface and the effects of spray additives (6-9). There has also been a recognition that some spray formulation properties may be self-conflicting, e.g. retention and coverage (7); rapid uptake and phytotoxicity (10, 11); uptake and translocation (12). The incorporation of a suitable surfactant into a spray formulation is generally essential. However, the large number of candidate surfactants and their varied behaviour has not made their evaluation easy. Of the physical tests available, only the wetting, contact angle and spreading coefficient values of surfactant solution droplets on leaf or

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0097-6156/88/0371-0077\$06.00/0
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artificial surfaces have been deemed useful (13, 14). Pesticide uptake studies have not provided sufficiently consistent data to enable useful correlations to be made between penetration rates and the various physical and chemical properties of surfactants (2, 15). However, there are clearer trends with the various plant factors which influence pesticide uptake, such as cuticle thickness and leaf morphology (16-18). In the case of "difficult" plants, with irregular or pubescent surfaces or thick cuticles, the addition of suitable surfactants to spray solutions is essential so that the droplets can contact the true leaf surface (i.e. the epidermis) and allow penetration of the active ingredient through the cuticle. Such spray formulations need to have low surface tensions, but because most solutions have surface tensions rarely below 30 mN m^{-1} , they fail to be fully effective. Such was the situation with the sprays used for the control of gorse (*Ulex europaeus*), a thorny, woody shrub of the legume family. Extensive screening of candidate surfactants by physical methods, and uptake of ^{14}C -labelled herbicides into the plant, led to the choice of an organosilicone block co-polymer surfactant as the most suitable adjuvant for several commercial herbicides (19).

Improved gorse control in the field was also demonstrated but the reason for this enhanced herbicidal activity on addition of Silwet L-77 surfactant was not known. Gorse is too difficult a plant to use for fundamental studies, therefore other species (bean, eucalypt and Citrus) were used instead. To avoid physiological interactions caused by the active ingredient e.g. contact phytotoxicity, a non-phytotoxic radiolabelled compound was used for the foliar uptake studies. The compound chosen had to be water soluble (no further formulation needed); non-ionic (no possibility of interaction with ionic surfactants); metabolically stable and available at sufficiently high specific activity for low concentration use.

This present work describes the effects of three organosilicone surfactants on droplet contact angle, spreading and drying rates, and compares them to two organic surfactants. These aqueous solutions were also tested on leaves of several plant species to determine their influence on the uptake of an "inert" radiolabelled compound (2-deoxyglucose).

Materials and Methods

Plant material. Bean plants (*Vicia faba* var. Evergreen) were grown from seed in a 3:1 peat:pumice mixture in a glasshouse. Eucalyptus plants (*Eucalyptus botryoides*) were grown from seed outdoors then at approx. one year of age potted into 10 l of sandy-loam soil. Plants were used approx. four months later when they were 1-1.4 m tall with 5-10 side branches. Mandarin plants (*Citrus nobilis* var. Unshin, Silverhill strain) were obtained from a commercial nursery when they were approx. two years old. The scions shared a common parent source and were grafted onto a trifoliolate rootstock. All plants were brought into the growth room for preconditioning prior to treatment.

In all experiments the leaves used were fully expanded and mature; with bean, the youngest, fully-developed bi-lobed leaves were treated. Unless specified otherwise all treatments were to

the adaxial leaf surfaces and in the growth room. Conditions : 8 h photoperiod; 20°/15°C day/night temperature; 70% relative humidity; light intensity 300-340 $\mu\text{mol}\cdot\text{s}^{-1}\text{m}^{-2}$.

Surfactants. Initially a wide range of Union Carbide Silwet organosilicone surfactants was screened. The three chosen for further study were Silwet L-77, L-7607 and Y-6652 (all silicone polyalkyleneoxide copolymer variants). Organic surfactants used for comparison purposes were Triton X-45 (Rohm and Haas; octylphenyloxyethylene product) and Agral (ICI; nonylphenyloxyethylene product, either 90% or 30% active ingredient).

Contact angle. Leaf wax was obtained from leaves of field-grown plants by washing with chloroform (20 s). Solutions were dried, filtered and concentrated. Portions of the wax were redissolved in chloroform (10 mg/ml) and a modified tlc applicator was used to apply 20 μl onto microscope glass slides to give an even coating of wax equivalent to 39 $\mu\text{g}/\text{cm}^2$.

Droplets (3 μl) of each test solution were applied with a microsyringe to the waxed surface of each slide and the droplet's image was projected; the height and diameter were measured and the contact angle (CA) calculated (20). All determinations were made at 20°C and 55-65% rh with a minimum of 20 replications.

Droplet spread areas. Spread areas (SA) were measured on wax films on glass slides and on leaf surfaces using solutions containing surfactant (0.5% v/v) and Blankophore-P fluorescent dye (1% w/v; Bayer). Droplet sizes were 0.5 μl ; all treatments (maximum of 10 replicates) were carried out at 20°C and 55-65% rh under dim illumination to prevent any photo-degradation of the fluorescent indicator. When the droplets were dry, the spread areas were visualised under uv light (360 nm) and measured with an Optimax Image Analyser.

Droplet drying. A Li-Cor 6000 portable photosynthesis porometer was used to measure droplet drying rates. The porometer included a Varsala humidity sensor and a chamber temperature thermistor, producing a continual readout for percentage rh, temperature and time.

Citrus and eucalypt leaves were chosen for uniformity of growth and absence of surface blemishes. They were detached from the shoots and left at 20°C, 55-65% rh under dim illumination to equilibrate for 30 min. Each leaf was used for only a single determination (6 replicates). Droplets (4 x 0.5 μl) were applied either to wax films on microscope slides or to adaxial leaf surfaces. These were then placed inside the porometer chamber and readings of percentage rh and temperature taken at regular intervals. Vapour pressures were calculated (21) and a line-fitting computer program was used to determine the actual time at which the drops were dry.

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C-2-deoxyglucose uptake. The 2-deoxy-D-[U-¹⁴C] glucose (¹⁴C-DOG; Amersham, UK) solutions (approx. 5 to 15 ng/ μl) with surfactants (0.05% to 0.5%) were applied as four 0.5 μl droplets to

equivalent regions of selected leaves on intact plants in the growth room. At the end of the treatment period (6 h to 48 h) the treated leaf was excised and the treated leaf surface washed with at least 10 ml methanol:water (10:90 ratio for beans; 40:60 ratio for eucalypt and Citrus) to remove residual unabsorbed ^{14}C -DOG. Aliquots (1 ml) of the washings were analysed for radioactivity (in 10 ml scintillant solution; 2:1 toluene:Triton X-100 plus 5.5 g/l Permablend). The washed leaves were freeze-dried, ground, and portions oxidised using a Micromat BF5010. All samples were radioassayed in a Packard 4430 scintillation counter (10 ml scintillant solution :15% MeOH/toluene with 5.5 g/l Permablend; plus 0.5 ml phenethylamine). Percentage uptake into the leaf was calculated from the radioactivity recovered.

Statistical treatments. Standard errors (SE) were calculated and least significant differences (LSD) were determined where appropriate. The non-linear regressions (shown in Fig. 2) were determined by an optimisation procedure using GENSTAT. The regression equation for wax film results was found to be $\hat{y} = 319.917x - 0.39086$ ($R^2 = 0.86$); for leaf surface data $\hat{y} = 460.743x - 0.47715$ ($R^2 = 0.82$). In each case y is time (seconds) and x is area (mm^2).

Results

Contact angle measurements were used as an initial screening of surfactant solutions at different concentrations. Each solution showed similar behaviour on wax films regardless of the plant source (Figure 1). Overall they could be grouped into three categories. These were: solutions that caused total wetting (like Silwet L-77); those that gave adequate wetting (like Triton X-45 or Silwet L-7607); and those that had high CA values indicating poor wetting (values of 80° or more, not illustrated).

Spread areas are presented in Table I. The organic surfactant solutions had similar (and low) SA values on both wax films and leaf surfaces. In contrast Silwet solution SA values were generally greater on leaves than on wax films. The largest difference was seen with eucalypt. When viewed under the SEM, bean leaves had little epicuticular wax; Citrus had larger quantities but with an even surface, while eucalypt had a dense coating of wax platelets.

The drying times of droplets of the same solution were tested on Citrus leaf and wax film surfaces. The results (Table II) show that the solutions with the largest SA values also dried the fastest (90 vs 299 secs for Silwet L-77 and water on wax films) and the same trends were observed on leaf surfaces (127 vs 322 secs for Silwet L-77 and water). Drying times on leaf surfaces were longer in all cases except for Silwet Y-6652 for unknown reasons.

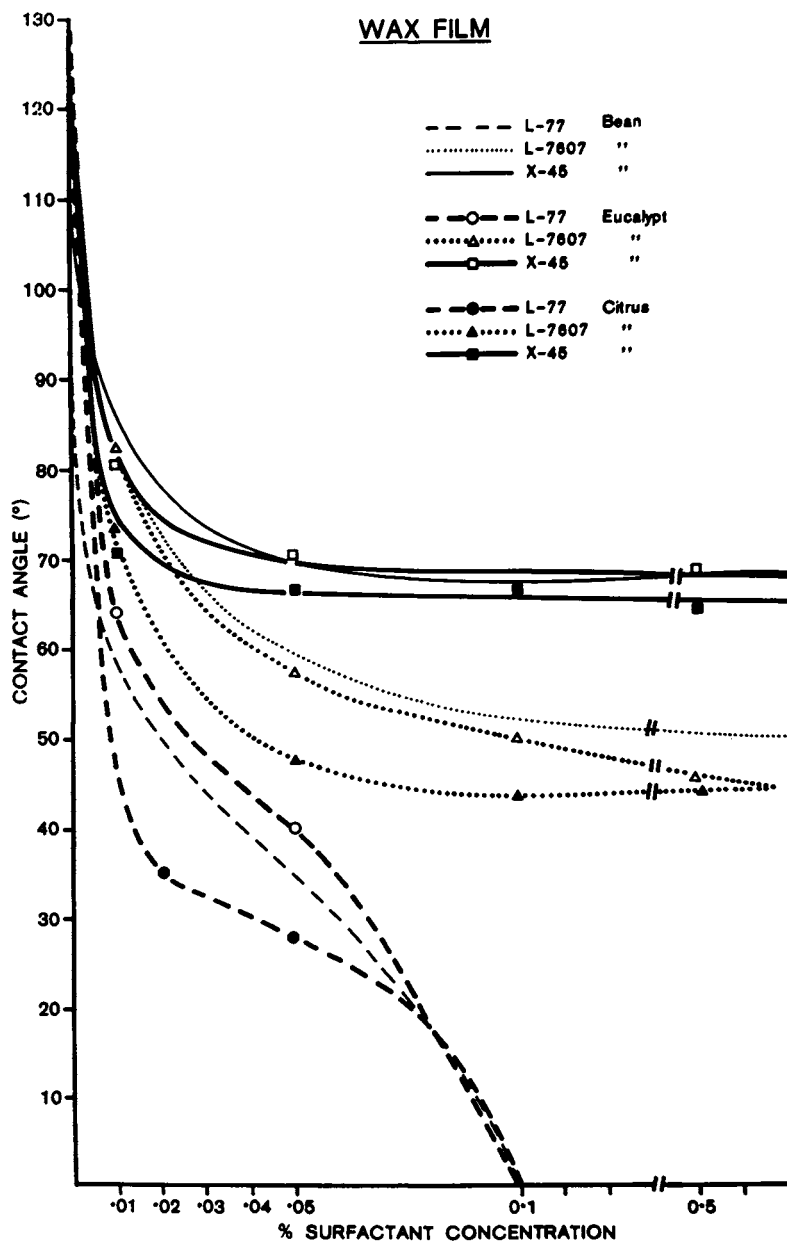


Figure 1. Contact angle variation of surfactant solutions (3.0 μ l droplets) on bean, eucalypt and Citrus wax films

TABLE I. Comparison of droplet (0.5 μ l) spread area (in mm^2)
on wax films and leaf surfaces

Species	BEAN		EUCALYPT		CITRUS	
	Film	Leaf	Film	Leaf	Film	Leaf
Solution						
Water	1.0(0.1)	2.8(0.2)	1.4(0.1)	1.6(0.1)	1.3(0.1)	1.8(0.1)
0.5% Agral*	2.6(0.1)	3.1(0.2)	2.1(0.1)	2.7(0.1)	3.0(0.1)	3.3(0.1)
0.5% Triton X-45	3.0(0.1)	4.3(0.1)	2.5(0.1)	3.7(0.1)	3.1(0.1)	4.1(0.1)
0.5% Silwet L-7607	3.6(0.1)	3.9(0.3)	2.9(0.1)	16.6(0.3)	4.1(0.1)	5.8(0.4)
0.5% Silwet Y-6652	25.4(2.3)	23.4(5.2)	11.7(0.2)	19.4(0.3)	7.6(0.2)	8.6(0.1)
0.5% Silwet L-77	89.2(3.7)	79.6(11.7)	16.5(0.6)	146.9(1.9)	12.2(0.7)	50.8(4.5)

SE in brackets

*Agral 90 for bean; Agral LN (30% active) for eucalypt and Citrus

TABLE II. Droplet (0.5 μ l) drying times on Citrus leaf and wax film surfaces

Solution	Drying time (seconds)	
	Film	Leaf
Water	299(7.5)	322(23.7)
0.5% Agral LN	232(5.8)	305(11.5)
0.5% Triton X-45	215(8.0)	261(9.5)
0.5% Silwet L-7607	187(6.4)	202(11.5)
0.5% Silwet Y-6652	134(4.9)	119(2.4)
0.5% Silwet L-77	90(2.7)	127(4.1)

SE in brackets

The percentage uptake of ^{14}C -DOG into leaves of the three species over a 48 h period varied markedly (Table III). There was nearly complete uptake into bean from all solutions (even water alone), variable uptake into eucalypt, and much reduced uptake overall into Citrus foliage. Though only the data for 0.5% surfactant solutions are shown in Table III, the same relative behaviour was noted for all the surfactants over the range of concentrations from 0.05% to 0.5%. Reduced uptake was evident with lower surfactant concentrations (data not presented).

TABLE III. Uptake of ^{14}C -DOG into foliage over a 48 h period

Solution	uptake (%)		
	Bean	Eucalypt*	Citrus
Water	98.7(0.1)	25.6(0.7)	16(1.4)
+ 0.5% Agral 90	99.4(0.1)	98.4(0.1)	31(3.2)
+ 0.5% Triton X-45	99.5(0.1)	90.5(4.0)	32(4.7)
+ 0.5% Silwet L-7607	99.5(0.2)	90.8(1.6)	41(5.5)
+ 0.5% Silwet Y-6652	99.7(0.1)	60.4(5.8)	N/A
+ 0.5% Silwet L-77	99.9(0.1)	37.4(2.5)	30(2.6)

SE in brackets; Eucalypt LSD (0.05)=6.8; Citrus LSD (0.05)=12.3

N/A = not available

*Determined from 100(total applied-leaf residue/total applied)

The influence of the surfactant solutions was tested further on bean foliage over a reduced time period (6 h) and showed that the relative behaviour of the solutions was the same (Table IV). Under equivalent growing conditions highest uptake was shown from Silwet L-7607, Triton X-45 and Agral 90 surfactant solutions, with lesser amounts from Silwet L-77 and Silwet Y-6652 solutions. At other times Silwet L-7607 effects were inferior to those of Silwet L-77 (as shown in column 3).

TABLE IV. Uptake of ^{14}C -DOG into bean foliage over a 6 h period

Solution	uptake (%)		
	(1)*	(2)	(3)
Water	12.0(0.5)	4.0(0.7)	18.5(3.2)
0.5% Agral 90	62.9(5.6)	N/A	48.7(1.5)
0.5% Triton X-45	61.3(3.7)	N/A	61.4(4.5)
0.5% Silwet L-7607	78.2(2.2)	57.6(6.2)	56.6(3.1)
0.5% Silwet Y-6652	33.8(5.6)	N/A	43.6(5.5)
0.5% Silwet L-77	44.4(5.2)	30.0(6.3)	77.2(2.7)

SE in brackets; (1) LSD (0.05)=11.15; (2) LSD (0.05)=11.7; (3) LSD (0.05)=11.02

N/A = not available

*Determined from 100(total applied-leaf residue/total applied) (1) and (2) treatments in growth room; (3) treatment in growth cabinet

The possibility existed that uptake into leaves of low surface tension solutions, such as Silwet L-77 and Silwet Y-6652, could also be through flooding into open stomata. In eucalypt the adaxial surface is astomatous, the abaxial surface has many stomata. Application of surfactant solution droplets to upper (adaxial) and lower (abaxial) eucalypt leaf surfaces gave the results shown in Table V.

TABLE V. Uptake of ^{14}C -DOG into eucalypt leaf from adaxial and abaxial surfaces (over 48 h) treated with Silwet L-77 solutions

Solution	uptake (%)	
	Adaxial	Abaxial
Water	17.2(0.4)	N/A
0.05% Silwet L-77	43.5(2.5)	41.1(1.5)
0.1% Silwet L-77	36.1(8.3)	47.3(4.2)
0.5% Silwet L-77	34.7(0.2)	43.2(2.2)

SE in brackets: 0.05% L-77, LSD (0.05)=6.38; 0.1% L-77, (LSD 0.05)=17.07; 0.5% L-77, LSD (0.05)=6.2

There was an indication that Silwet L-77 solutions enhanced uptake when applied to abaxial surfaces. The test was repeated but over a much shorter period of time (2 minutes) before the applied solution droplets were washed off. An Agral 90 solution treatment was included for comparison (Table VI).

TABLE VI. Uptake of ^{14}C -DOG into eucalypt leaf from adaxial and abaxial surfaces (after 2 min) treated with Agral 90 and Silwet L-77 solutions

Solution	uptake (%)	
	Adaxial	Abaxial
0.5% Silwet L-77	4.7(0.4)	18.6(3.1)
0.5% Agral 90	0.5(2.3)	1.4(2.3)

SE in brackets. No uptake from any solution with 0.3% or lower surfactant concentration

*Determined from 100(total applied-leaf residue/total applied)

Only the 0.5% Silwet L-77 solution showed substantial uptake from the abaxial surface. None of the Agral solutions (at 0.05% to 0.5% conc. range) nor Silwet L-77 at 0.3% or less gave accelerated uptake (data not presented). This result suggests that there can be rapid flooding of leaf stomata by surfactant solutions and confirms visual observations of stomatal penetration by Silwet L-77 solutions (unpublished observations).

Discussion

There are a number of non-ionic organosilicone surfactants which can reduce solution surface tension very substantially and it is surprising that this capability has not been exploited further, as the performance of several such surfactants had been demonstrated over a decade earlier (22, 23). However, in place of the field testing methods used to evaluate them then, measurements of formulation droplet behaviour were deemed to be a more practical method in this wider-ranging, screening program.

The four laboratory techniques described in this paper have been used for this purpose on a wide range of organic and organosilicone surfactants. Contact angle (CA) measurement is a simple means of ranking surfactants in order of their solution wetting capability. It was known that surface roughness would reduce droplet contact angle (24), so the initial screening of surfactants was for those having CA values substantially less than 80° on smooth wax films. This resulted in the selection of several organosilicones which had excellent wetting properties (Figure 1). However, droplet spread and behaviour on plant surfaces are more relevant to agronomic situations. The magnitude of these effects cannot be measured nor predicted by CA determinations. The data in Table I show that the three species chosen exhibited a wide range of leaf surface/surfactant interactive effects. Comparing the effects on wax films and leaf surfaces, addition of surfactant gave minimal increase in SA on bean leaves (having a very sparse epicuticular wax); significantly larger increases (4-fold) were found with Citrus leaves (which have a continuous covering of smooth wax); and much larger increases with eucalypt (9-fold; the leaf surfaces having a "micro-rough" covering of dense wax platelets). It is obvious that the more irregular the surface, the greater is the degree of spreading, as was shown in particular by the organosilicones.

The expectation that greater SA values would lead to faster droplet drying was confirmed (Tables I and II). A good correlation was also derived between spread area and drying time on wax films (Figure 2) for surfactant solutions that do not have very large enhancement of SA values on leaf surfaces. In the case of Silwet L-77 and Silwet Y-6652 where there was proportionately greater spread area on the leaf surface, drying times were longer than expected. It is known that these surfactants are hygroscopic and this property may be part of the reason for this behaviour (26).

Greatest spreading occurred on eucalypt leaves, hence shortest droplet drying times and lowest uptake could be expected. This was not the case as shown by the uptake for ¹⁴C-DOG in Table III. Lowest uptake (for all treatments) was by Citrus; highest by bean, indicating that other plant or leaf characteristics e.g. cuticle

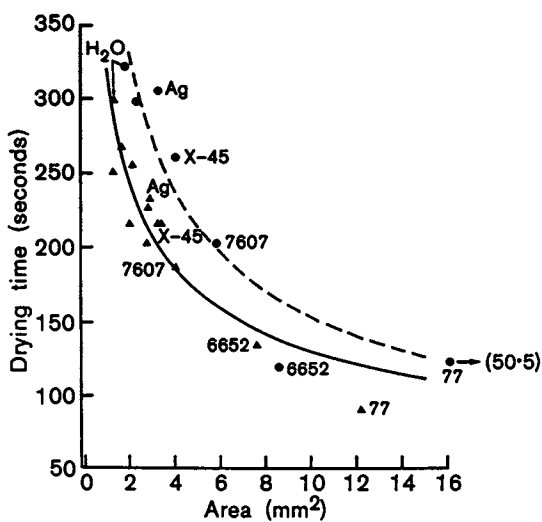


Figure 2. Relationship between droplet (0.5 μ l) drying time and spread area on Citrus leaf (---) and wax film (—)

thickness were more dominant. Nor could greater amounts of ^{14}C -DOG/deposit area be the sole controlling factor. A comparison of droplet spread areas, SA values relative to water, dose of DOG applied and percentage uptake for eucalypt leaves is given in Table VII. Highest "dose" was with the pure water solution but this gave the lowest uptake. However, within the surfactant solution series there appeared to be a trend that the larger the dose or amount/unit leaf area the larger the uptake. These results are in agreement with previous findings (11, 25) that uptake may or may not depend on the concentration of surfactant and/or active used.

TABLE VII. Comparison of surfactant properties and influence on uptake of ^{14}C -DOG into eucalypt leaves (48 h)

Solution	Spread area* (mm ²)	Spread area ratio	^{14}C -DOG (ng/cm ²)	% uptake
Water	1.6	1	245.0	25.6
0.5% Agral 90	2.7	1.7	110.3	98.4
0.5% Triton X-45	3.7	2.3	38.9	90.5
0.5% Silwet L-7607	16.6	10.4	8.1	90.8
0.5% Silwet Y-6652	19.4	12.1	7.3	60.4
0.5% Silwet L-77	146.9	91.8	2.0	37.4

* for 0.5 μl droplet

In the case of previous studies with gorse (19), Silwet L-77 surfactant (at 0.5% v/v) was best at enhancing uptake of glyphosate applied at "field" rates. In the present study, using "tracer" or "research" rates of herbicidally inactive ^{14}C -DOG, there was superior uptake at the same surfactant concentration by Silwet L-7607, Agral 90 and Triton X-45 into eucalypt leaves. On bean, there was a similar trend, but at times Silwet L-77 was superior to these three surfactants (Table IV), suggesting that either plant or growing conditions can strongly influence foliar uptake.

One of the recognised problems with formulations is that of contact phytotoxicity by the spray droplets, which may limit the uptake and translocation of the active chemical (27-29). This may be due to either the toxicity of the adjuvant itself or to too rapid an uptake of the herbicidal component. In the present trials the use of a non-herbicidal, radiolabelled chemical at low concentration prevented the latter possibility. It can also be argued that large spread areas would minimise the potential phytotoxicity from either surfactant or herbicide since the amount/unit leaf area would be less (by a factor of 10 at least in the case of some of the Silwet products) and would reduce the likelihood of cellular damage.

The low surface tension of the Silwet solutions should also permit stomatal flooding. A substantial amount of information exists to support such a capability either on theoretical grounds (30) or by experimentation and observation (4, 31, 32). However, in none of the previous studies is there a report of stomatal flooding from small droplets applied to a leaf surface. In the present studies bean leaves placed on the surface of 0.5% Silwet L-77 solutions were infiltrated within seconds. Similar behaviour

could be observed under the microscope with flooding of individual stomata when droplets were applied to the bean leaf surface. Studies with ^{14}C -DOG and eucalypt leaves attempted to quantify this effect. A short-term (2 min.) uptake experiment (Table VI) demonstrated convincingly that there was enhanced uptake from the abaxial treatment. Thus, on the evidence available, 10-15% of radiolabelled material was taken up via the stomata. If larger proportions were to be taken up into stomata from higher volume applications, then this could be a significant contribution to making the spray solution "rainfast" in field situations. Such behaviour could be of considerable significance in situations where "ideal" spraying conditions do not exist.

These characteristics can also explain the observed enhanced field efficacy when Silwet L-77 is added to certain herbicides. Namely, it could be due to a combination of (1) the ability of the spray solution to reach the true leaf surface; (b) further redistribution to stem, petiole etc. which may be more readily penetrated; and (c) uptake via stomata.

Conclusions

The Silwet organosilicone surfactants are a further class of non-ionic surfactants for use with pesticidal formulations in aqueous spray applications. Addition of low concentrations of these surfactants gives solutions good wetting and spreading properties on leaf surfaces. This in turn enhances droplet drying. Several members of the Silwet organosilicone surfactant family have been characterised by these properties as well as by their influence on the uptake of ^{14}C -2-deoxyglucose into different plants. Obvious species differences exist as shown by the uptake of this compound, which cannot be overcome entirely by the surfactants tested to date. The Silwet solution characteristics are such that it is possible to obtain stomatal penetration and this may have implications for spray "rainfastness" properties in field situations.

Acknowledgments

We wish to thank S. Bodle, T. Faulds, C. Faulds, M. Godfrey and J. Hobbs for assistance with plant materials and growth room facilities; S.O. Hong with statistics; ICI and Rohm and Haas in New Zealand for supplying samples of their surfactants; Union Carbide (USA) for samples of their surfactants and financial support to DC and FE.

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RECEIVED December 28, 1987

Chapter 8

Absorption and Translocation of Herbicides

Effect of Environment, Adjuvants, and Inorganic Salts

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Absorption and translocation of herbicides can be significantly increased when adjuvants are added to foliar applied spray mixtures. The level of increased control from adjuvants is usually affected by the environmental conditions at the time of herbicide application. In most cases, herbicide absorption and translocation are greatest under environmental conditions which are most favorable for growth of the treated plant. Adjuvants added to treatment solutions often increase absorption and translocation of foliar applied herbicides, especially when plants are under stress at time of treatment. Inorganic salts in spray solutions also affect absorption, translocation and subsequent toxicity of herbicides. Many inorganic salts with monovalent (+1) cations increase herbicide activity while some salts with divalent (+2) and trivalent (+3) cations inhibit herbicide activity.

Activator adjuvants are almost always added to spray mixtures of herbicides applied to plant foliage (1). They serve to enhance the level of weed control obtained with herbicides. Adjuvants enhance biological activity of herbicides by a) increasing herbicide penetration, b) maximizing efficacy through increased phytotoxicity or selectivity, and/or c) improving spray application or retention (2). Herbicide absorption and translocation are increased by activator adjuvants which include surfactants, wetting agents, penetrants, and oils (3).

The usefulness of surfactants for aiding in wetting, spreading, and sticking of spray solutions to leaf surfaces has been noted since the turn of the century (4). A report published in 1890 on the use of surfactants showed that an arsenical insecticide which normally had no effect on plants caused injury to plants when soap was added to the spray solution (5). However, little attention was given to the importance of foliar penetration before the introduction of organic herbicides (4). The use of

0097-6156/88/0371-0090\$06.00/0

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surfactant to enhance herbicidal activity was reported in early research with 2,4-D [(2,4-dichlorophenoxy)acetic acid] (6). A later development involved extending the use of diuron [N'-(3,4-dichlorophenyl)-N,N-dimethylurea] from being only a soil applied herbicide to becoming also a selective foliar applied herbicide. This was accomplished by the addition of an activator surfactant to the spray solution (7).

As the benefits of including surfactants in mixtures of foliar applied herbicides became widely established, researchers began to recognize that other factors were also interacting to influence the effectiveness of herbicides at the time of application (8) (9). Relative humidity was shown to affect the absorption of 2,4-D (8) and both temperature and relative humidity influenced the absorption and translocation of dalapon (2,2-dichloropropanoic acid) (9). As early as 1942, Harris and Hyslop (10) found that phytotoxicity of the sodium salt of DNOC (4,6-dinitro-*o*-cresol) could be increased by the addition of the inorganic salt, ammonium sulfate, to the spray solution. Turner and Loader (11) used ammonium sulfate to increase the phytotoxicity of picloram (4-amino-3,5,6-trichloro-2-pyridinecarboxylic acid). Szabo and Buchholz (12) found that other inorganic salts could increase phytotoxicity of herbicides. These researchers increased leaf penetration of the triethanolamine salt of 2,4-D by adding ammonium nitrate and disodium phosphate to the spray solution. We have conducted studies to determine further the effects of environment, adjuvants and inorganic salts on absorption and translocation of a number of herbicides in various weed and crop species.

Surfactants

In studies where surfactant was a treatment variable, herbicide absorption and translocation were increased by the addition of a surfactant to the spray solution (13-16). The addition of the surfactant, nonoxynol [a-(p-nonylphenyl)-w-hydroxypoly(oxyethylene)] (9 to 10 POE), to the treatment solution frequently increased the translocation of radiolabeled ¹⁴C-glyphosate [N-(phosphonomethyl)glycine] applied to the leaves of cotton (Gossypium hirsutum) (13). The addition of nonoxynol also increased the penetration and translocation of dalapon in johnsongrass (Sorghum halepense) as determined by the increased control of the regrowth of shoots clipped at the soil level 24 h after treatment (14).

¹⁴C Absorption and translocation of the radiolabeled herbicide, mefluidide

{N-[2,4-dimethyl-5-[[trifluoromethyl)sulfonyl]amino]phenyl]acetamide methylcarbamodithioic acid} was increased by the addition of nonoxynol or ethomeen 0/15 (oleyl tertiary amino ethylene oxide condensate) at 0.5% (v/v) (15). Herbicide absorption was increased when either surfactant was added to the herbicide solution and applied to soybeans (Glycine max) (Table I) and johnsongrass (Table II); whereas, nonoxynol was the most effective surfactant when the two surfactants were compared on common cocklebur (Xanthium pensylvanicum) (Table III).

¹⁴C Wills and McWhorter (16) showed that the absorption of fluazifop {(±)-2-[4-[[5-(trifluoromethyl)-2-pyridinyl]

Table I. Movement of ^{14}C -mefluidide in Soybeans 72 h after Application to a 2.5-cm² Area on the Center Leaflet of the Second Trifoliolate of Plants 24 cm Tall

Air Temp. (°C)	RH (%)	Adjuvant	Percent of applied ^{14}C Activity ^a		
			Absorbed	Remaining in Treated Leaf	Translocated From Trt. Lf.
22	40	None	14 g	10 f	4 f
		Nonoxynol	62 cd	41 bc	21 d
		Ethomeen	38 e	32 cd	6 f
	100	None	22 f	17 ef	5 f
		Nonoxynol	80 ab	36 cd	44 a
		Ethomeen	69 bc	55 ab	14 e
32	40	None	50 de	28 de	22 d
		Nonoxynol	70 bc	41 bc	29 c
		Ethomeen	86 a	64 a	21 d
	100	None	52 d	12 f	40 ab
		Nonoxynol	69 bc	34 cd	35 bc
		Ethomeen	78 ab	48 b	30 c

^aNumbers within a column not followed by the same letter are significantly different at the 5% level as determined by Duncan's multiple range test.

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oxy]phenoxy]propanoic acid) by bermudagrass (*Cynodon dactylon*) was not affected to the same extent by the addition of either nonoxynol or oil-surfactant (17% polyoxyethylene sorbitan fatty acid ester in 83% mineral oil) (Table IV). Absorption of ^{14}C -fluazifop was significantly increased by the addition of the oil-surfactant while the results were inconclusive from the use of nonoxynol. Van Valkenburg (17) noted that there is an optimum herbicide-surfactant balance for each herbicide and plant species being treated, and this could account for the varied levels of herbicide absorption and translocation obtained by the use of different surfactants in our studies.

Temperature

In general, an increased temperature up to 35°C resulted in increased herbicide absorption and translocation (13-16, 18-21). When ^{14}C -2,4,5-T [(2,4,5-trichlorophenoxy)acetic acid] was applied to the leaves of winged elm (*Ulmus alata*) at 3-week intervals throughout the growing season, analysis of the data indicated that daily temperature in the range of 24 to 40°C enhanced absorption and translocation of the radiolabel when compared to applications made at daily temperature in the range of 11 to 34°C (18). Studies in environmentally controlled growth chambers showed similar temperature effects (13-16, 19-21). Absorption of ^{14}C -acifluorfen {5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrobenzoic acid} applied to showy crotalaria (*Crotalaria spectabilis*) was approximately four-fold greater at 27 and 35°C than at 18°C

Table II. Movement of ^{14}C -mefluidide in Johnsongrass 72 h after Application to a 2.5-cm^2 Area on the Third Leaf of Plants 70 cm Tall

Air Temp. (°C)	RH (%)	Adjuvant	Percent of applied ^{14}C Activity ^a		
			Absorbed	Remaining in Treated Leaf	Translocated From Trt. Lf.
22	40	None	7 i	4 e	3 g
		Nonoxynol	19 h	9 cd	10 fg
		Ethomeen	30 g	12 bcd	18 f
	100	None	45 ef	9 cde	36 de
		Nonoxynol	49 de	11 bcd	38 d
		Ethomeen	56 d	10 cd	46 c
32	40	None	14 hi	8 de	6 g
		Nonoxynol	52 de	13 bc	39 cd
		Ethomeen	37 fg	10 cd	27 e
	100	None	70 c	15 ab	55 b
		Nonoxynol	91 a	9 cd	82 a
		Ethomeen	81 b	18 a	63 b

^aNumbers within a column not followed by the same letter are significantly different at the 5% level as determined by Duncan's multiple range test.

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temperature (19). When ^{14}C -sethoxydim {2-[1-(ethoxyimino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one} was applied to leaves of bermudagrass, absorption was the greatest (70%) at 35°C and least (33%) at 18°C (Table V) (20). Translocation was similarly affected with 17% of the applied radioactivity being translocated at 35°C and only 8% being translocated at 18°C. When ^{14}C -glyphosate was applied to cotton leaves, absorption was 43 and 36% at 32° and 22°C, respectively (13). Translocation of glyphosate was not affected by differences in air temperature at the time of treatment.

There was a 1.2- to 3-fold increase in the absorption and translocation of ^{14}C -fluazifop in bermudagrass maintained at 35°C as compared to bermudagrass maintained at 18°C air temperature during the first 48 h after application (Table IV) (16). There was approximately a 2-fold increase in absorption of ^{14}C -mefluidide in soybeans, common cocklebur, and johnsongrass as temperature was increased from 22 to 35° and a similar increase in translocation in soybeans and johnsongrass only, between the two temperatures (Tables I, II, III) (15).

Absorption of ^{14}C -glyphosate in johnsongrass nearly doubled and translocation was increased as temperature increased from 24 to 35°C (Table VI) (21). However, in soybeans, both absorption and translocation of ^{14}C -glyphosate significantly decreased as temperature increased from 24 to 35°C (Table VII). Furthermore, when dalapon was applied without surfactant to johnsongrass, both penetration and translocation of the herbicide decreased as temperature was increased from 16 to 38°C (14).

Table III. Movement of ^{14}C -mefluidide in Common Cocklebur 72 h after Application to a 2.5-cm^2 Area on the Second Alternate Leaf of Plants 22 cm Tall

Air Temp. (°C)	RH (%)	Adjuvant	Percent of applied ^{14}C Activity ^a		
			Absorbed	Remaining in Treated Leaf	Translocated From Trt. Lf.
22	40	None	10 f	6 d	4 f
		Nonoxynol	37 c	17 bc	20 c
		Ethomeen	25 de	11 cd	14 de
	100	None	31 cd	13 cd	18 cd
		Nonoxynol	56 b	18 bc	38 b
		Ethomeen	54 b	16 c	38 b
32	40	None	22 e	11 cd	13 de
		Nonoxynol	35 c	16 c	23 c
		Ethomeen	28 de	14 c	10 ef
	100	None	56 b	38 a	18 cd
		Nonoxynol	78 a	23 b	55 a
		Ethomeen	55 b	38 a	17 cde

^aNumbers within a column not followed by the same letter are significantly different at the 5% level as determined by Duncan's multiple range test.

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Relative Humidity

Absorption and translocation of herbicides were increased by increases in relative humidity (RH) during the first 24 to 96 h after application (13, 14, 15, 16, 19, 21). There was consistently greater movement of ^{14}C -radiolabeled herbicides into and within plants when treatments were applied at 95 to 100% RH than at 35 to 45% RH. Absorption of ^{14}C -acifluorfen into showy crotalaria was 3 to 4 times greater at 100 than at 40% RH (19). Absorption and translocation were influenced by RH when glyphosate was applied to cotton (13). Absorption and translocation of ^{14}C -glyphosate increased 3 to 6 fold at 100% RH, compared to that at 40% RH. The effect of RH on the movement of ^{14}C -fluazifop into and throughout bermudagrass was not as great as with other herbicide-plant combinations, but in general absorption and translocation was greater at 100 than at 40% RH (Table IV) (16).

Where ^{14}C -mefluidide was applied to johnsongrass, common cocklebur, and soybeans, absorption and translocation increased 5 to 6 fold in johnsongrass, about 3 fold in common cocklebur and less than 2 fold in soybeans as RH increased from 40 to 100% (Tables II, III, and I, respectively) (15). Translocation was often greater when ^{14}C -glyphosate was applied to johnsongrass and soybeans at 100 than at 45% RH (21).

Soil Moisture

Both absorption and translocation of herbicides were often increased when soil moisture was maintained at or near field

Table IV. Effect of Environment on the Distribution of ^{14}C -fluazifop in Bermudagrass 48 h after Treatment

Air Temp. ($^{\circ}\text{C}$)	RH (%)	Adjuvant	Percent of applied ^{14}C Activity ^a		
			Absorbed	Remaining in Treated Leaf	Translocated From Trt. Lf.
18	40	None	17 i	10 h	7 gh
		Nonoxynol	10 i	8 h	2 h
		Oil-Surfactant	62 fg	41 d	21 cdefg
	100	None	28 h	14 gh	14 efgh
		Nonoxynol	18 i	8 h	10 fgh
		Oil-Surfactant	67 ef	43 cd	24 bcde
35	40	None	63 fg	29 e	32 bc
		Nonoxynol	74 de	12 h	62 a
		Oil-Surfactant	92 abc	77 a	15 defgh
	100	None	87 bc	27 e	60 a
		Nonoxynol	95 ab	25 efg	70 a
		Oil-Surfactant	98 a	54 bc	45 b

^aNumbers within a column not followed by the same letter are significantly different at the 5% level as determined by Duncan's multiple range test.

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Table V. Effect of Environment on the Distribution of ^{14}C -Sethoxydim in Common Bermudagrass 12 h After Application to a Single Leaf Midway Along Shoots of Plants 15 to 20 cm Tall

Air Temp. ($^{\circ}\text{C}$)	RH (%)	Percent of applied ^{14}C Activity ^a		
		Absorbed	Remaining in Treated Leaf	Translocated From Trt. Lf.
18	40	33 a	27 c	6 c
	100	43 a	35 c	8 c
35	40	56 b	39 b	17 b
	100	70 c	40 b	30 a

^aNumbers within a column not followed by the same letter are significantly different at the 5% level as determined by Duncan's multiple range test.

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Table VI. Effects of Air Temperature, Relative Humidity and Soil Moisture on the Movement of ^{14}C -Glyphosate in Johnsongrass 72 h After Application. The ^{14}C -Glyphosate was Applied to a 2.5-cm² Area on the Third Leaf of Plants 70 cm Tall

Air Temp. (°C)	RH (%)	Soil Moisture (%)	Percent of applied ^{14}C Activity ^a		
			Absorbed	Remaining in Treated Leaf	Translocated From Trt. Lf.
24	45	12	23 e	16 f	7 f
		20	37 d	20 ef	17 de
	100	12	34 d	14 f	20 cd
		20	40 d	16 f	24 bc
35	45	12	43 cd	24 de	19 d
		20	64 b	50 a	14 e
	100	12	62 b	29 cd	33 a
		20	74 a	36 b	38 a

^aNumbers within a column not followed by the same letter are significantly different at the 5% level as determined by Duncan's multiple range test.

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capacity at the time of treatment (14, 21, 22) (Tables VI, VII). Absorption and translocation of ^{14}C -glyphosate in johnsongrass and soybeans was frequently increased with high soil moisture as compared to low soil moisture (21). Dalapon translocated in johnsongrass better when soil moisture was near field capacity than near the wilting point (14). The distribution of ^{14}C -bentazon [3-(1-methylethyl)-(1H)-2,1,3-benzothiadiazin-4(3H)-one2,2-dioxide] was consistently better in common cocklebur plants and was often greater in soybeans at high than at low soil moisture (22).

Inorganic Salts

Absorption and translocation of glyphosate and MSMA (monosodium salt of methanearsonic acid) were determined in purple nutsedge (*Cyperus rotundus*) by treating the shoots and removing them by clipping 24 h after treatment (Tables VIII, IX) (23). Percent reduction in leaf regrowth (as compared to untreated plants) was used to indicate herbicide translocation. Glyphosate was applied in spray mixtures with 0.1 M concentrations of 29 different inorganic salts that included the cations Na^+ , K^+ , NH_4^+ , Ca^{++} , Zn^{++} , and Fe^{++} and the anions Cl^- , NO_3^- , SO_4^{--} , CO_3^{--} and PO_4^{--} . MSMA was applied in combination with 12 of these inorganic salts including the same cations but with only the Cl^- and PO_4^{--} anions.

Control of leaf regrowth by glyphosate was increased 15 to 36% by KHCO_3 , KH_2PO_4 , NaHCO_3 , NaH_2PO_4 , NaHSO_4 and all the ammonium salts in this study (Table VII). There was no significant effect on glyphosate toxicity by the addition of NaNO_3 , NaCl , KNO_3 , KCl or KHSO_4 . Addition of $\text{Ca}(\text{NO}_3)_2$ resulted in reduced weed control; however, no other calcium salt caused a reduction in weed control when compared to the untreated plants. $\text{Zn}_3(\text{PO}_4)_2$ and FePO_4 did not

Table VII. Effects of Air Temperature, Relative Humidity and Soil Moisture on the Movement of ^{14}C -Glyphosate in Soybeans 72 h After Application to the Center Leaflet of the Second Trifoliolate of Plants 24 cm Tall

Air Temp. (°C)	RH (%)	Soil Moisture (%)	Percent of applied ^{14}C Activity ^a		
			Absorbed	Remaining in Treated Leaf	Translocated From Trt. Lf.
24	45	12	18 b	6 bc	12 b
		20	22 a	7 ab	15 ab
	100	12	23 a	8 a	15 ab
		20	23 a	5 c	18 a
35	45	12	7 d	6 bc	1 f
		20	10 cd	7 ab	3 ef
	100	12	11 c	6 bc	5 def
		20	17 b	8 a	9 c

^aNumbers within a column not followed by the same number are significantly different at the 5% level as determined by Duncan's multiple range test.

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affect glyphosate toxicity, but other salts of zinc and iron significantly reduced glyphosate toxicity.

Control of purple nutsedge with MSMA was increased 13 to 40% by the addition of $\text{NH}_4\text{H}_2\text{PO}_4$, NH_4Cl , NaH_2PO_4 , NaCl , KH_2PO_4 , CaHOP_4 , and $\text{Zn}_3(\text{PO}_4)_2$ (Table IX). KCl and FePO_4 did not affect the toxicity of MSMA. Control was reduced 12 to 32% below that with MSMA alone by the addition of CaCl_2 , ZnCl_2 , and FeCl_3 to the spray solution.

The salts of monovalent cations usually increased toxicity of both glyphosate and MSMA. The salts of the divalent and trivalent cations Zn^{++} and Fe^{+++} often reduced herbicide toxicity. The salts of the divalent Ca^{++} had little or no effect on herbicide efficiency. The effect of different anions on herbicide activity was often influenced by the associated cation. Little or no correlation was found between spray solution pH and the effect of the individual salts on herbicide toxicity.

Interactions Between Environment and Additives

In general, factors which individually increased herbicide absorption and translocation caused even further increases in these functions when combined. In all the examples in this report, high relative humidity (95 to 100%) resulted in the greatest herbicide absorption and translocation (13-16, 19-21). In most of our studies, high relative humidity combined with high temperature (32 to 38°C) caused even greater herbicide movement. Exceptions included glyphosate (21) and mefluidide (15) on soybeans and dalapon (14) on johnsongrass. These herbicides were more effective with high relative humidity at lower temperatures (24, 22, and 16°C).

Table VIII. Effect of Foliar Applications of Various Inorganic Salts Applied in Combination with Glyphosate at 0.25 kg in 150 L of Water/Ha on Regrowth of Purple Nutsedge Leaves

Inorganic salt		pH of glyphosate salt mixture	Control of leaf regrowth ^a
Chemical name	Formula (0.1 M)		(%)
Potassium bicarbonate	KHCO_3	7.6	73 j
Ammonium bisulfate	NH_4HSO_4	1.6	71 ij
Potassium phosphate monobasic	KH_2PO_4	4.5	68 ij
Ammonium phosphate monobasic	$\text{NH}_4\text{H}_2\text{PO}_4$	4.5	67 ij
Sodium bicarbonate	NaHCO_3	7.6	67 ij
Ammonium chloride	NH_4Cl	4.5	61 hij
Sodium biphosphate	$\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$	4.5	60 hi
Ammonium nitrate	NH_4NO_3	4.4	59 ghi
Ammonium bicarbonate	NH_4HCO_3	7.5	58 ghi
Sodium bisulfate	$\text{NaHSO}_4 \cdot \text{H}_2\text{O}$	1.6	52 fgh
Potassium nitrate	KNO_3	4.5	47 efg
Potassium bisulfate	KHSO_4	1.6	47 efg
Calcium phosphate dibasic	CaHPO_4	5.6	44 def
Sodium nitrate	NaNO_3	4.5	43 def
Sodium chloride	NaCl	4.5	43 def
Potassium chloride	KCl	4.5	41 def
Calcium sulfate	$\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$	5.0	37 cde
Glyphosate alone		4.4	37 cde
Calcium chloride	$\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$	4.1	34 bcd
Calcium carbonate	CaCO_3	6.4	26 bc
Zinc phosphate	$\text{Zn}_3(\text{PO}_4)_2$	4.5	26 bc
Ferric phosphate	$\text{FePO}_4 \cdot 2\text{H}_2\text{O}$	4.5	25 bc
Calcium nitrate	$\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$	4.0	24 b
Zinc nitrate	$\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$	4.5	6 a
Ferric nitrate	$\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$	1.7	4 a
Ferric chloride	$\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$	1.8	4 a
Zinc sulfate	$\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$	1.6	0 a
Zinc chloride	ZnCl_2	4.6	0 a
Zinc carbonate	ZnCO_3	7.6	0 a
Untreated (control)			0 a
Ferric sulfate	$\text{Fe}_2(\text{SO}_4)_3$	3.1	-1 a

^aNumbers within a column followed by the same letter are not significantly different at the 5% level.

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Table IX. Effect of Foliar Applications of Various Inorganic Salts in Combination with MSMA (1 kg/ha) Plus Nonoxynol Surfactant (0.25%, w/v) Applied in 150 L of Water/Ha on the Regrowth of Purple Nutsedge Leaves

Inorganic salt		pH of	Control
Chemical name	Formula	salt mixture	of leaf regrowth ^a
	(0.1 M)		(%)
Sodium biphosphate	$\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$	5.5	79 g
Potassium phosphate monobasic	KH_2PO_4	5.7	78 g
Ammonium phosphate monobasic	$\text{NH}_4\text{H}_2\text{PO}_4$	5.7	77 g
Ammonium chloride	NH_4Cl	5.9	73 g
Zinc phosphate	$\text{Zn}_3(\text{PO}_4)_2$	6.1	57 f
Sodium chloride	NaCl	5.9	52 ef
Calcium phosphate dibasic	CaHPO_4	6.4	52 ef
Potassium chloride	KCl	5.9	46 de
Ferric phosphate	$\text{FePO}_4 \cdot 2\text{H}_2\text{O}$	5.7	41 d
MSMA plus surfactant alone		5.9	39 d
Calcium chloride	CaCl_2	5.4	27 c
Zinc chloride	ZnCl_2	4.2	12 b
Ferric chloride	$\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$	2.4	7 ab
Untreated (control)			0 a

^aNumbers within a column not followed by the same letter are significantly different at the 5% level as determined by Duncan's multiple range test.

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The addition of surfactant often increased both absorption and translocation at each environmental condition in our studies. Where the most effective relative humidity was combined with the most effective temperature, the addition of a surfactant usually caused further increases. In these studies, the addition of surfactant more frequently increased herbicide absorption than translocation (Tables I, II, III, IV).

The addition of monovalent inorganic salts in combination with selected surfactants increased both absorption and translocation. McWhorter and Jordan (14) found that the addition of KH_2PO_4 plus nonoxynol surfactant increased the penetration and translocation of dalapon over that with the addition of the surfactant alone while the addition of KH_2PO_4 alone had no significant effect on the movement of dalapon. Recently, Wills and McWhorter (24) found that the addition of $(\text{NH}_4)_2\text{SO}_4$ or KH_2PO_4 and surfactant [oxysorbic (20 POE) (polyoxyethylene sorbitan monolaurate)] increased the efficacy of the herbicides imazaquin and imazethapyr when compared to the addition of surfactant or either salt alone to the herbicide solutions.

Effect of Surfactants on Herbicide Translocation.

Surfactants, within themselves, do not possess biological activity. They are involved primarily with solubility relationships between herbicides and plant structures. Surfactants affect the activity of herbicides in the penetration of the outer

lipid layer and stomates of plant foliage (25-30) and in translocation within the aqueous system of the plant (17). There is an optimum lipid/aqueous solubility level for each herbicide-plant system where the greatest amount of herbicide is absorbed and translocated throughout a plant. Surfactant-herbicide combinations which are too aqueous soluble will not readily penetrate the outer lipid layer of plant foliage. Conversely, combinations which are too lipid soluble will readily combine with the outer lipid layer but will not be easily released into the aqueous translocating medium of the plant (31).

Griffin (32) developed an empirical numbering system to characterize surfactants according to their hydrophilic-lipophilic balance (H.L.B.). He assigned a value of 1 to the most lipophilic (oleic acid) and 20 to the most hydrophilic (potassium oleate) surfactant. A surfactant with the optimum H.L.B. for a particular herbicide-plant combination will alter the solubility relationships to obtain the maximum herbicide translocation (33).

Further information is available on the effect of surfactant on herbicide translocation. Ashton and Crafts (34) include the effects of surfactants in their book on herbicide mode of action. Bayer and Lumb (35) discuss the interactions of herbicides and surfactants among plant surfaces. Freed and Morris (36) cover surfactant efficacy along with herbicide-environment interactions. Holly (37) discusses herbicide selectivity in reaction to formulations. Parr and Norman (38) have reviewed the use of surfactants in plant systems.

Results of the studies discussed herein have shown that optimum conditions for obtaining the greatest response of herbicides on weeds vary with different herbicide-weed species combinations. More detailed studies are needed to determine the most efficient methods of using individual herbicides with regard to combinations of adjuvants used under different environmental conditions.

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RECEIVED January 22, 1988

Chapter 9

Influence of Adjuvants on the Postemergence Phytotoxicity of Haloxyfop Methyl Herbicide on *Setaria* spp.

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Greenhouse bioassay studies with haloxyfop methyl (methyl 2-[4-((3-[3-chloro-5-(trifluoromethyl)-2-pyridinyl)oxy]phenoxy)propionate) indicated that the postemergent herbicidal response to *Setaria faberi* (3-4 leaf) and *Setaria lutescens* (3-4 leaf) was a function of both the nature of the adjuvant and its concentration in the spray solution. Crop oil concentrate (COC) gave greater activity enhancement than did the various vegetable oils and was effective at concentrations of 0.2-0.25 volume percent in a spray volume of 187 liters. Nonionic emulsifiers added to the spray solution of haloxyfop methyl varied in their phytotoxicity potential. Application of certain ones caused tissue necrosis and reduced ¹⁴C transport from treated leaves of *Setaria faberi*. Nonionic emulsifiers, in general, were not as effective as oils, particularly when bentazon was co-applied with haloxyfop methyl. Radiolabeled studies on *Setaria faberi* showed COC enhanced ¹⁴C transport from the treated leaf and minimized the antagonism associated with bentazon in tank mixes.

Haloxyfop methyl, the active ingredient in VERDICT herbicide, is a postemergence herbicide that provides selective control of a wide range of annual and perennial grasses in soybeans [*Glycine max* (L.) Merr] and other dicotyledenous crops(1-3). Foliar absorption of haloxyfop methyl is essentially complete within 48 hours(4) Haloxyfop methyl is rapidly hydrolyzed to haloxyfop in treated leaves and then translocated to the meristematic regions within the plant(4). In addition to excellent postemergence activity, it possesses good preemergence activity even when applied at postemergence rates. The preemergence activity is exhibited through root uptake of haloxyfop from the soil(5).

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For the uptake of foliar applied herbicides, the cuticle represents the barrier to penetration(6). There are numerous reports of the beneficial effect that adjuvants have on foliar herbicides(7,18). The effect of an adjuvant or surfactant on cuticle penetration may be related to its ability to partition into the cuticular wax.

Greenhouse and field research on haloxyfop methyl as well as other postemergence germinicides indicate that phytotoxicity may be influenced by adjuvants(2,3,8-12). Hartzler and Foy(2) observed that the addition of adjuvants to the spray solution of sethoxydim increased herbicide phytotoxicity when applied at rates below 0.14 kg/ha. There was no difference in phytotoxicity among the adjuvants. Field research by Nalawaja et al(12) indicated that petroleum oil additives enhanced the phytotoxicity of fluazifop butyl, haloxyfop methyl, and diclofop methyl more than crop origin oils. However, sethoxydim was equally enhanced by crop origin and petroleum oils containing 1% v/v ATPLUS 300F emulsifier. Horng and Ilnicki (10) reported better barnyardgrass [*Echinochloa crus galli* (L.) Beauv.] control with sethoxydim in the presence of two surfactants than with a phytoblend oil at 1% (v/v). Chernicky et al(8) reported a 10 to 12% increase in sethoxydim phytotoxicity on a series of annual grasses in the presence of a COC and nonionic surfactant. Porter and Harvey(3) reported an enhancement of fluazifop butyl phytotoxicity to wild proso millet [*Panicum miliaceum* (L)] using a COC versus a nonionic surfactant under dry climatic conditions. Buhler and Burnside(11) reported COC increased fluazifop butyl, haloxyfop methyl, and sethoxydim activity to annual grasses. Anderson(2) reported no advantage of a COC over a nonionic surfactant at 0.5% (v/v) with fluazifop butyl or haloxyfop methyl on annual grasses. Whereas with sethoxydim, he found the COC to be more effective at 0.5% (v/v). He found no concentration effect for COC on any of the herbicides over the range of 0.5 to 2.0% (v/v).

In order to obtain broadspectrum weed control of grasses and broadleaves, it is common practice in agriculture to tank mix two or more herbicides. A reduction in grass activity has been observed in combinations of the new postemergence grass herbicides with bentazon(13,16). Antagonism can also exist between two broadleaf herbicides(17). Reduction of absorption and/or translocation of the grass herbicide by bentazon has been suggested as the basis for a number of the observed herbicide antagonisms(14-16). The role the adjuvant may play in this antagonism is not well known nor has it been intensely investigated(13). For instance, Rhodes and Coble(13) reported that increases in sethoxydim rate reduced the severity of the antagonism by bentazon in some cases, while the addition of oil concentrate had no effect. Sorenson et al(17) reported that COC tended to reduce the bentazon/acifluorfen interaction toward several broadleaves.

The objectives of this research were: 1) to investigate the effect of adjuvant type and concentration on haloxyfop methyl phytotoxicity to yellow foxtail [*Setaria lutescens* (L)]; 2) to determine the influence of bentazon on haloxyfop methyl phytotoxicity and how this interaction is influenced by the type

and concentration of adjuvant; and 3) to quantify the effect of adjuvants and bentazon on ^{14}C haloxyfop methyl uptake/translocation in giant foxtail [*Setaria faberi* (L)].

Materials and Methods

Adjuvant Study. A series of petroleum and vegetable oil-based adjuvants and nonionic surfactants were screened in the greenhouse to evaluate their potential to enhance haloxyfop methyl phytotoxicity to yellow foxtail. A list of adjuvants, their composition, and corresponding manufacturer are shown in Table I.

Experiments were conducted during 1985. Yellow foxtail seed was planted in drainable, polyethylene pots (5 x 5 x 8 cm) containing Jiffy mix. Established seedlings were thinned to 0.1 to 0.2 plants cm^2 , a moderate population. Prior to spraying, all pots were surface watered as needed. The greenhouse was maintained at $25 \pm 5^\circ\text{C}$. Supplemental lighting maintained a photoperiod of 16 hours of $550 \mu\text{E}\cdot\text{m}^{-2}\cdot\text{s}^{-1}$ photosynthetically active radiation. Plants were grown to the 3-4 leaf stage (requiring approximately 14 days) before herbicide treatment. Experiments were arranged in a randomized complete block design with at least three replications. Visual ratings (0 equals no kill and 10 represents total kill) were taken 28 days after treatment. Plants were selected for uniformity and treated with foliar applications of commercially formulated haloxyfop methyl (VERDICT herbicide) and bentazon (BASAGRAN). All treatments were applied in a spray chamber with an automated track sprayer operating at 4.8 km/hr calibrated to deliver a total spray volume of 187 L/ha at 276 kPa pressure. A T-JET flat fan nozzle orifice was operating 46 cm above the grass. The soil surface was covered with a vermiculite absorbent prior to treatment to prevent soil activity of the individual herbicides. It was removed after spray treatments were dried. Plants were watered with one-half strength Hoagland's solution by subirrigation as needed. Application rates were selected based on preliminary experiments. A formulation blank of haloxyfop methyl was prepared and applied at 140 g a.e./ha concentration for the zero dose of the active. All adjuvants were added as percent (v/v) of the total spray solution (TSV). City water was used, having a calcium hardness of approximately 80 ppm w.

GR₈₀ values were computed using linear regression analysis with a 95% confidence level. The GR₈₀ value is the amount of active ingredient needed, expressed as g a.e./ha of the parent acid (acid equivalent -- a.e.), to control 80% of the weed species.

^{14}C Methodology. Three-four leaf stage seedlings of giant and yellow foxtail were used for all ^{14}C studies. Plants were grown in a vermiculite and Jiffy mix blend (50:50) in drainable, polyethylene pots (5 x 5 x 8 cm) under the same nutritional schedule, temperature, and light conditions as described for greenhouse bioassays. Experiments were conducted in an environmental chamber at $550 \mu\text{E}\cdot\text{m}^{-2}\cdot\text{s}^{-1}$ at 28°C after incubating the plants in the chamber for 24 hours. Application of haloxyfop methyl-ph-UL- ^{14}C , specific activity 19.98 mCi/mmol, in its commercial formulation was made to second leaves with a

Table I. Adjuvant Compositions and Manufacturers

Adjuvant	Manufacturer	Composition
Crop oil concentrate (COC) Atplus 411F	ICI Americas Inc.	83-85% paraffin oil and 15-17% nonionic emulsifier
Crop oil (CO) Sunspray 11E	Sun Oil Co.	97% paraffin oil and 3% nonionic emulsifier
Soybean oil concentrate Atlas CD-352	Atkemix, Inc.	Same as crop oil concentrate but with soybean oil
Canola oil concentrate Atlas CD-351	Atkemix, Inc.	Same as crop oil concentrate but with canola oil
Ortho X-77 spreader	Chevron	Alkylaryloxy-ethylene glycols free fatty
Polyglycol 59-13 surfactant	Dow Chemical	Tridecyl alcohol ethoxylate
T-Det N-9.5 surfactant	Thompson-Hayward	Nonyl phenol ethoxylate, 9.5 moles EO
T-Det C-30 surfactant	Thompson-Hayward	Castor oil ethoxylate, 30 moles EO
X2-5152 surfactant	Dow Corning	Ethoxylated siloxane
X2-5177 surfactant	Dow Corning	Ethoxylated siloxane

microsyringe at the rate of 140 g a.e./ha in 187 L of tap water. Treatment combinations included bentazon (840 g a.e./ha), COC (2.3 L/ha), and bentazon plus COC. At each sampling period, four replications of each treatment were harvested. Treated leaves were removed and washed in acetonitrile for ten seconds to collect unabsorbed ^{14}C activity. The rinsed leaves were combusted in a tissue oxidizer to determine uptake (minus transport) into the treated leaf. Plants were cut at the soil line, roots carefully removed from the potting medium and then combusted to determine ^{14}C basipetal transport. Recoveries of ^{14}C activity were expressed as a percent of applied to plants at zero time.

Results and Discussion

Greenhouse Bioassay. The nonionic surfactants and oil adjuvants were applied at 0.25% (v/v) and 1.25% (v/v), respectively. In the absence of bentazon, all of the adjuvants provided comparable control, $\text{GR}_{80} < 35$ g a.e./ha (data not shown). These results are in good agreement with the field results of Anderson(2) where he found equal enhancement of haloxyfop methyl activity with a COC or nonionic surfactant on giant foxtail, wild proso millet, and corn.

When bentazon at 840 g/ha was co-applied with haloxyfop methyl, the adjuvant type strongly influenced yellow foxtail phytotoxicity (Table II). The petroleum oils provided the greatest enhancement of phytotoxicity. Polyglycol 59-13 was the least effective ($\text{GR}_{80} = 84$ g a.e./ha) but provided better control than haloxyfop methyl alone ($\text{GR}_{80} > 140$ g a.e./ha). Among the nonionic surfactants, Ortho X-77 was the most effective ($\text{GR}_{80} = 38$ g a.e./ha). The emulsified petroleum based oils provided better control than did the emulsified vegetable oils. The antagonistic influence of bentazon on the grass activity of haloxyfop ($\text{GR}_{80} > 140$ g a.e./ha with bentazon versus 53 g a.e./ha without bentazon) was minimized by the use of emulsified petroleum oils (< 35 g a.e./ha in the presence or absence of bentazon). Nonionic surfactants varied in their ability to minimize bentazon antagonism and were generally less effective than the emulsified petroleum oil.

Adjuvant dose response of four adjuvants was investigated with haloxyfop methyl co-applied with bentazon (Table III). Crop oil (CO), COC, and soybean oil concentrate were evaluated at 0.25, 0.625, and 1.25% (v/v) in the total spray solution. Dow Corning X2-5152 was investigated at 0.1, 0.175, and 0.25% (v/v). Of the concentrations investigated, the phytotoxicity of haloxyfop methyl to yellow foxtail was not influenced by the concentration of the organosilicone X2-5152, soybean oil, or COC. With CO the activity of haloxyfop methyl decreased as the CO concentration decreased. Anderson(2) reported that the concentration of COC had little or no effect on haloxyfop methyl grass control in the field which confirms the greenhouse results shown here.

Jansen(19) reported that nonionic silicone surfactants often provided greater enhancement in grass activity than did a standard organic surfactant, polyoxyethylenes(20) sorbitan monooleate [TWEEN 20], particularly for herbicides with very low water solubility. Under the antagonistic influence of bentazon, yellow foxtail

Table II. GR₅₀ Estimates for Haloxyfop Methyl When Co-Applied with Bentazon (840 g a.e./ha) on Setaria lutescens

Adjuvant	Concentration (v/v) in 187 L/ha	
	Spray Volume	4 WAT GR ₅₀ (g a.e./ha)
None	0	> 140
ATPLUS 411F	1.25	38
SUNSPRAY 11E	1.25	23
Soybean oil concentrate	1.25	53
Canola oil concentrate	1.25	40
POLYGLYCOL 59-13 emulsifier	0.25	84
T-DET C-30 surfactant	0.25	72
T-DET N-9.5 surfactant	0.25	53
ORTHO X-77 spreader	0.25	38
Dow Corning X2-5152	0.25	58
Dow Corning X2-5177	0.25	43

Table III. Adjuvant Dose Response for Haloxyfop Methyl When Co-Applied with Bentazon (840 g a.e./Ha) on Setaria lutescens

Adjuvant	% Adjuvant (v/v) in 187 L/ha Spray Volume	--4 WAT GR ₅₀ (g a.e./ha)--		
		95% Lower Limit	Predicted	95% Upper Limit
Crop oil concentrate	0.25	35	45	59
ATPLUS 411F	0.75	30	45	79
	1.25	28	43	66
Soybean oil concentrate	0.25	44	52	64
ATLAS CD-352	0.75	45	52	63
	1.25	41	48	58
Crop oil	0.25	43	50	61
SUNSPRAY 11E	0.75	4	27	39
	1.25	13	21	27
Silicone surfactant	0.10	50	56	66
Dow Corning X2-5152	0.175	49	59	79
	0.25	50	55	63
Control (check)	0		> 140	

response to haloxyfop methyl was not enhanced relative to the organic surfactants. This particular study, however, did not establish a threshold concentration for enhancement by the nonionic surfactant. The data would suggest that it is less than 0.1% (v/v). Jansen(18,19) pointed out that although the maximum reduction in surface tension occurs at a surfactant concentration corresponding to the critical micelle concentration of 0.01 to 0.1% (v/v), surfactants generally exhibit their greatest biological effects at concentrations exceeding this level. Jansen(18) found the threshold concentration for enhancement by silicone glycol was 0.01% (v/v) in susceptible species and 0.1% (v/v) in a resistant specie.

¹⁴C Uptake and Transport Studies. The effect of COC on uptake of ¹⁴C activity by *Setaria* spp. was studied. Leaves of *Setaria faberi* and *Setaria lutescens* were treated with aqueous suspensions of ¹⁴C haloxyfop methyl (140 g a.e./ha) with and without COC. After suitable incubation periods, treated leaves were rinsed and combusted to determine nonextractable recoveries, reflecting uptake (Figure 1). Crop oil concentrate markedly enhanced the rate of uptake of ¹⁴C activity and by 24 hours resulted in a 45% to 50% increase in uptake. Differences in uptake behavior due to plant species were not apparent.

In another experiment, the effect of COC and bentazon on uptake and transport of ¹⁴C activity from applications of ¹⁴C haloxyfop methyl was studied in giant foxtail. Applications of haloxyfop methyl at 140 g a.e./ha alone and in combination with COC, bentazon, and COC plus bentazon were made and recoveries taken through 24 hours. Results of uptake and basipetal transport are summarized in Figures 2 and 3, respectively. COC enhanced leaf uptake of ¹⁴C activity from applications of haloxyfop methyl with or without bentazon. Without COC bentazon decreased penetration of ¹⁴C activity (Figure 2). Bentazon was highly antagonistic to basipetal transport of ¹⁴C activity (Figure 3); however, by 24 hours COC was effective in alleviating its antagonistic response.

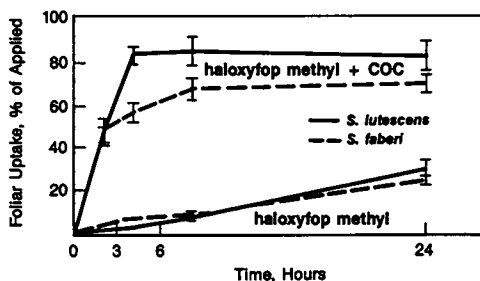


Figure 1

The Effect of COC (2.3 L/ha) on Uptake of ¹⁴C Activity from Grass Species Treated with Haloxyfop Methyl (140 g a.e./ha)

Work reported by Gerwick and Noveroske(15) indicated that bentazon decreased both absorption and transport of haloxyfop methyl in *Setaria lutescens*, suggesting that the basis for antagonism resides in an effect on penetration. Results summarized above for *Setaria faberi* in Figures 2 and 3 are in agreement with these findings and, in addition, indicate a lag effect exists in the ability of COC to alleviate the antagonism of ^{14}C transport caused by bentazon.

Haloxyfop methyl tank mixes with COC appear an effective means of maximizing transport for control of noxious weed problems caused by *Setaria* spp. and promoting tank mix compatibility with bentazon.

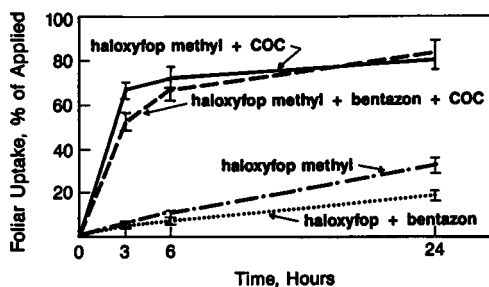


Figure 2

The Effect of Bentazon (840 g a.e./ha) and COC (2.3 L/ha) on Leaves of *Setaria faberi* Treated with Haloxyfop Methyl (140 g a.e./ha)

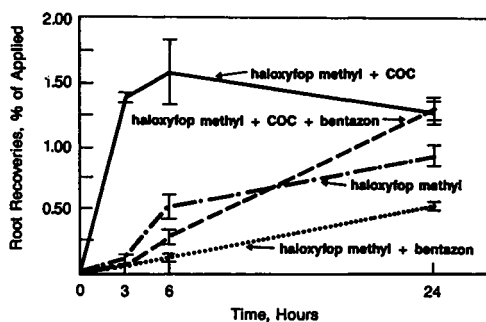


Figure 3

The Effect of Bentazon (840 g a.e./ha) and COC (2.3 L/ha) on Basipetal Transport of ^{14}C Activity from the Leaves of *Setaria faberi* Treated with Haloxyfop Methyl (140 g a.e./ha)

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RECEIVED January 27, 1988

Chapter 10

Structure-Penetration Relationships in Percutaneous Absorption

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Insight into the physicochemical factors that control percutaneous absorption (PA) is necessary for prediction of the dermal penetration characteristics of environmental and industrial toxins that contact the skin. Penetration data for series of barbiturates, nicotines, phenols, steroids and a selection of other compounds were obtained from our laboratory and from the literature; experiments using (a) excised skin (hairless mouse or human cadaver) and (b) artificial membranes (dimethylpolysiloxane or model lipid systems representative of those present in the stratum corneum) were considered. The rank order of resistance to penetration provided by the model systems matched that of excised skin. The transport data were correlated with several corresponding organic-aqueous partition coefficients (K). In most cases, membrane permeability increased with increasing K. However, exceptions were found and the degree of correlation was dependent upon the organic phase of the partitioning system and/or the physicochemical nature of the penetrants studied. Although K(octanol-aqueous) has been widely employed in the past, other lipids such as isopropyl myristate or tetradecane may provide more relevant media for the assessment of penetrant lipophilicity in structure-PA correlations.

Human skin is a multilayered heterogeneous organ composed of two main tissue layers, the dermis and epidermis, supported on a layer of subcutaneous fat (Figure 1). The dermis consists of a matrix of dense collagenous, elastic connective tissue imbedded in mucopolysaccharide. It has an average thickness of 3-5 mm and forms the bulk of the skin (1). The main functions of the dermis are to support and bind the epidermis and to impart strength and elasticity to the skin. Many structures are distributed throughout, and supported by, the dermis, including the vascular and nerve supplies,

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hair follicles and sebaceous and sweat glands. The avascular epidermis is the most superficial skin layer and is formed of several layers of rapidly proliferating cells (keratinocytes) which ascend from the basal layer at the epidermal-dermal junction. The thickness varies; the average being 40-50 μm over most of the body surface (2). As the cells migrate upwards they generate fibrous proteins and specific lipids and transform from living cells into a dead, keratinised zone that is ten to fifteen cell layers deep. It is generally accepted that this outermost skin layer, the stratum corneum, and more specifically the intercellular lipid matrix within, is the rate limiting barrier to the transport of most molecules across the skin (3). Most simply, therefore, skin provides a bilaminate membrane barrier to transport consisting of the thin, but highly resistant and lipophilic stratum corneum and the more substantial, aqueous gel-like viable tissue (the living epidermis and viable tissue) (4).

The long term objective of this research is to predict the kinetics and extent of percutaneous penetration *in vivo* from the physicochemical and pharmacokinetic properties of the chemical in question. From this knowledge, one should for example, be able to determine the risk of toxicity arising from dermal exposure to pesticide formulations. As a first step, penetration data for series of barbiturates, nicotines, phenols, steroids and a selection of other compounds were obtained from our laboratory and from the literature; experiments using (a) excised skin (hairless mouse or human cadaver) and (b) artificial membranes (dimethylpolysiloxane or model lipid systems) were considered. Principal attention was focussed upon the utility of various organic-aqueous partition coefficients (K) as rank order indicators of transdermal flux and upon the predictability of the different model systems investigated.

Systems Studies

[1] The rotating diffusion cell (RDC) has been widely used to study the transport of various penetrants from aqueous solution through artificial lipid membranes (5-6). The model membrane consists of a 0.2 μm cellulose nitrate membrane filter saturated with the chosen lipid. In the RDC, stagnant diffusion layers of thickness Z_D are created on either side of the lipid membrane. The cell can be rotated at different speeds (W) and, once pseudo-steady state conditions have been established, theory predicts that Z_D is proportional to $W^{-1/2}$ (5). Permeability coefficients (P) are measured as a function of $W^{-1/2}$ and extrapolation of the resultant linear relationship to infinite rotation speed (where Z_D is zero) yields the intrinsic total membrane permeability to solute (P'). P' is a composite permeability coefficient that accounts for permeation across the membrane and the two aqueous-organic interfaces.

The utility of the RDC as a system in which to set up such an *in vitro* model for percutaneous absorption has been studied previously using an isopropyl myristate (IPM) membrane as the stratum corneum model (5-6). Most recently, Hadgraft and Ridout (1987) have measured the permeability characteristics of an IPM membrane to eight model penetrants and contrasted these with steady-state permeation through excised full-thickness human cadaver

skin (7). The model chemicals were selected so as to reflect the diverse physicochemical properties that a penetrant might possess. They were an analogous series of barbiturates (amylobarbitone [A], barbitone [B], butobarbitone [U] and phenobarbitone [P]), two bases (isoquinoline [I] and nicotine [N]), hydrocortisone [H] and salicylic acid [S]. The mean values of P' for each penetrant crossing the lipid membrane were determined in at least five separate experiments. Figure 2 compares the biological barrier with the IPM membrane using $K(\text{IPM-aqueous}) [K_i]$ as the index of lipophilicity. If the membrane is considered homogeneous and it is assumed that the diffusion coefficients across the membrane are invariant compared to K , with respect to the low molecular weight solutes studied, then P should be a linear function of K ; the RDC data fits this relationship well. However, although the skin data shows a similar trend, the permeation of nicotine is relatively high, a fact which the model fails to predict. In addition, the overall permeability of the model membrane is 100-fold higher than that of skin.

Tetradecane (TD) has been suggested as being a more representative model of stratum corneum lipids (6). The permeability of a TD membrane to the same eight penetrants was measured and the correlation with human skin reassessed using $K(\text{TD-aqueous}) [K_t]$ as the lipophilicity index (Hadgraft, J.; Ridout, G. *Int. J. Pharm.*, in press). Figure 3 shows that TD does predict the increased permeation of nicotine and that the magnitude of permeability for this membrane is only 100-fold higher than the skin. TD provides, therefore, a better model than IPM for this set of compounds. In Figure 4 the two sets of RDC data are shown on a common scale of K . Although the upper limit of K is similar for both lipids, the range of K_i is much condensed in the hydrophilic region compared with K_t . It follows that, IPM has a greater capacity for uptake of hydrophilic chemicals than TD. Figure 5 shows the three sets of permeability data plotted as a function of penetrant $K(\text{octanol-aqueous}) [K_o]$, the traditionally used index of lipophilicity. The essentially linear relationships between permeability and lipophilicity observed using both K_i and K_t are less apparent, suggesting that octanol is a poorer representative for stratum corneum than IPM or TD. The range of K_o covers 2 log units (similar to K_i); however, there is an overall shift to the lipophilic end of the scale. With the exception of the barbiturate series, the rank order of K is significantly different for each lipid used.

Guy and co-workers (Houk, J.; Guy, R. H. *Chem. Rev.*, in press; Ridout, G.; Houk, J.; Palmieri, J. A.; Aliabadi, D.; Guy, R. H., unpublished data) have also employed the RDC with IPM and TD membranes to study the penetration characteristics of series of nicotines, phenols and steroids. Figures 6 and 7 show the relationship between P' and the corresponding K for IPM and TD membranes, respectively. The data also includes those of Hadgraft and Ridout, described above. In both cases, a parabolic dependency of P' upon K was found, suggesting that as degree of lipophilicity increases from a value of between 1 and 2, the rate-controlling step in permeation shifts from membrane diffusion to interfacial transport. As previously, the range of K for IPM is compressed and shifted to the lipophilic end of the scale.

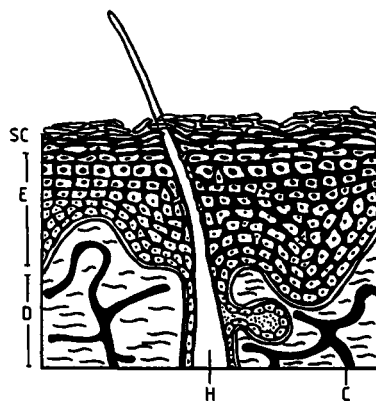


Figure 1. Schematic representation of human skin. Key: D = dermis; E = epidermis; SC = stratum corneum; C = capillary bed; H = hair follicle.

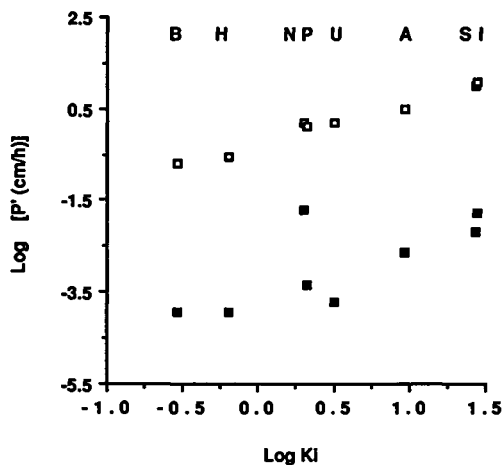


Figure 2. Permeability coefficients of a diverse set of compounds through an IPM membrane (□) and excised human skin (■) plotted as a function of penetrant K_1 . Key: A = amylobarbitone; B = barbitone; P = phenobarbitone; U = butobarbitone; H = hydrocortisone; I = isoquinoline; N = nicotine; S = salicylic acid.

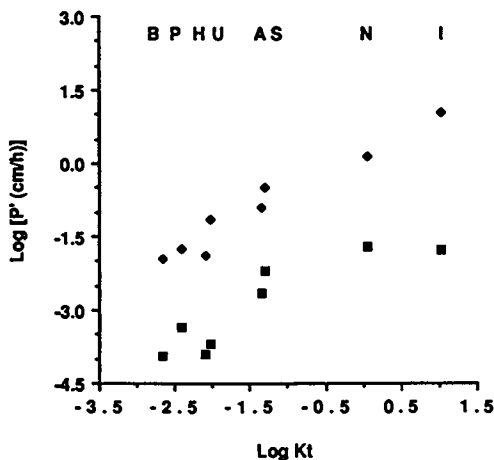


Figure 3. Permeability coefficients of a diverse set of compounds through an IPM membrane (◆) and excised human skin (■) plotted as a function of penetrant K_t . Compound identities as Figure 2.

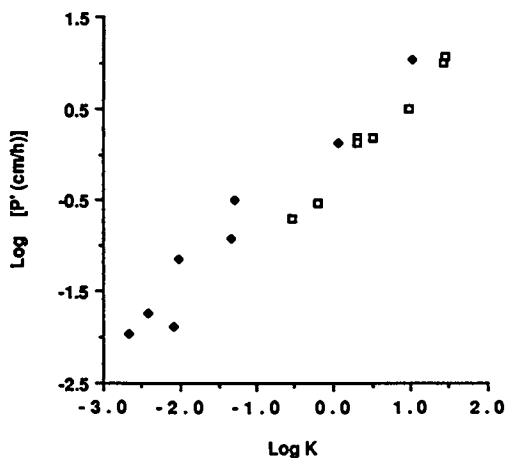


Figure 4. Permeability coefficients of a diverse set of compounds through both IPM (□) and TD (◆) membranes plotted as a function of penetrant K .

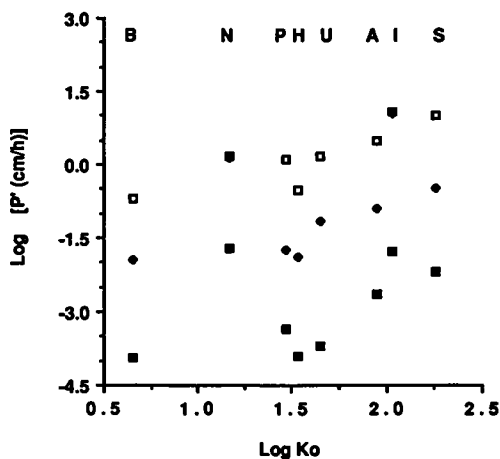


Figure 5. Permeability coefficients of a diverse set of compounds through both IPM (□) and TD (◆) membranes and excised human skin (■) plotted as a function of penetrant K_0 .

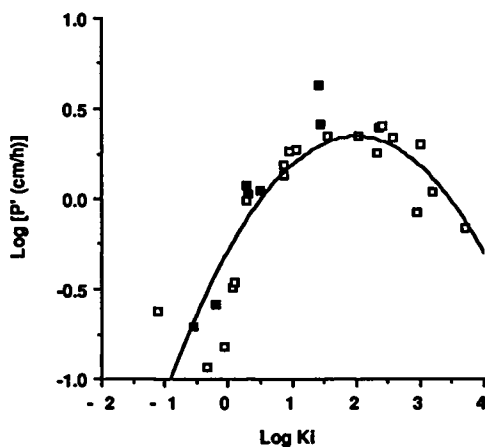


Figure 6. Permeability coefficients of nicotinates, phenols and steroids (□) and a diverse set of compounds (■) through an IPM membrane plotted as a function of penetrant K_1 .

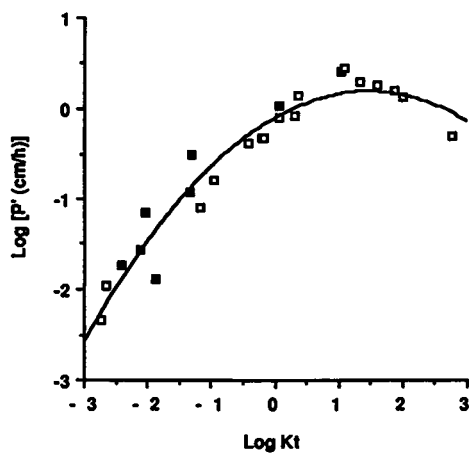


Figure 7. Permeability coefficients of nicotines, phenols and steroids (□) and a diverse set of compounds (■) through a TD membrane plotted as a function of penetrant K_t .

[2] The in vitro permeability of hairless mouse skin (8) and human epidermis (9) to series of phenols has been studied. Figure 8 compares this data with that obtained by Houk and Guy, described above. K_o was used as the lipophilicity scale as neither K_i nor K_t was available for all the compounds studied. As previously, it is evident that the artificial TD membrane can provide a reasonable model of human skin, the permeability being 10-fold lower than that of the IPM membrane. The permeability of murine skin is compared with that of human skin for six of the phenols in Figure 9. It is evident from the limited data available, that murine skin provides a barrier which is less than an order of magnitude smaller than that of human skin.

[3] Dimethylpolysiloxane (Silastic) membranes have also been used to model chemical transport across skin. The permeability of dimethylpolysiloxane to a series of phenols (10) and to homologous series of alkyl para-aminobenzoates (11) as a function of $K(\text{hexane-aqueous}) [K_{\text{hex}}]$ is shown in Figure 10. The penetrants studied were phenol (PH), dinitrophenol (DN), 2-nitrophenol (2N) and 4-nitrophenol (4N); and the methyl (ME), ethyl (ET), propyl (PR), butyl (BU) and pentyl (PE) aminobenzoates. Once again, linear relationship was found. It appears that, K_{hex} (like K_t) offers a reasonable index for membrane lipophilicity.

[4] The permeabilities of several steroids through excised human epidermis and the corresponding $K(\text{stratum corneum-aqueous}) [K_{\text{sc}}]$ were reported by Scheuplein (12). Figure 11 shows the resultant linear relationship between P and K_{sc} ($r^2 = 0.86$). When P was plotted against K_o , on the other hand, the correlation was less impressive, $r^2 = 0.69$. Scheuplein also determined $K(\text{amyl caproate-aqueous}) [K_{\text{ac}}]$ and $K(\text{hexadecane-aqueous}) [K_{\text{hdec}}]$ for each of the steroids. Of these, amyl caproate provided a similar index of lipophilicity to K_{sc} (Figure 12, $r^2 = 0.87$), as compared to either K_{hdec} ($r^2 = 0.75$) or K_o . However, it should be noted that the slope of $\log P$ versus $\log K_{\text{sc}}$ was approximately twice that observed when the model lipid partition coefficients were used. Therefore, although these simple systems are useful rank order predictors, their quantitative utility requires further careful consideration.

Summary

Although K_o has been widely employed in the past, other lipids such as esters (amyl caproate, isopropyl myristate) or alkanes (hexane, tetradecane) may provide more relevant media for the assessment of penetrant lipophilicity in structure-PA correlations. The rotating diffusion cell, with appropriate lipid membranes, and hairless mouse skin, under carefully controlled conditions, can offer reasonable models for skin penetration studies.

A practical, and inexpensive, means of assessing the relative risk of toxicity arising from dermal exposure is suggested by the results described in this paper. For a structurally related series of chemicals, measurement of (a) a simple lipid-water partition coefficient and (b) selected permeabilities through a model membrane composed of the lipid, can accurately rank order transport rates across the skin. Such an approach should permit, therefore,

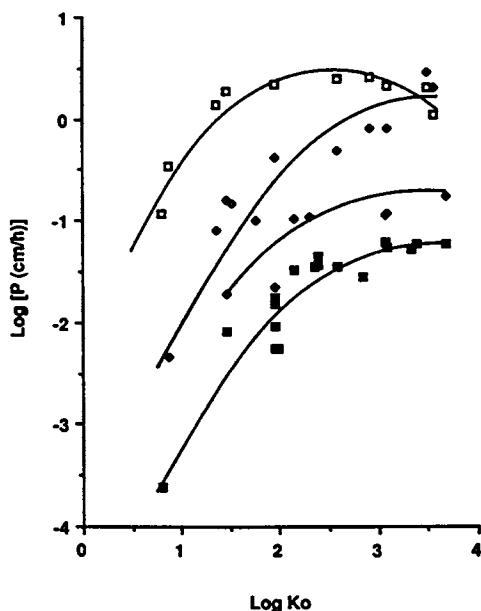


Figure 8. Comparison between the permeability coefficients of phenols through excised human (\square) and mouse skin (\diamond) and IPM (\blacksquare) and TD (\blacklozenge) membranes.

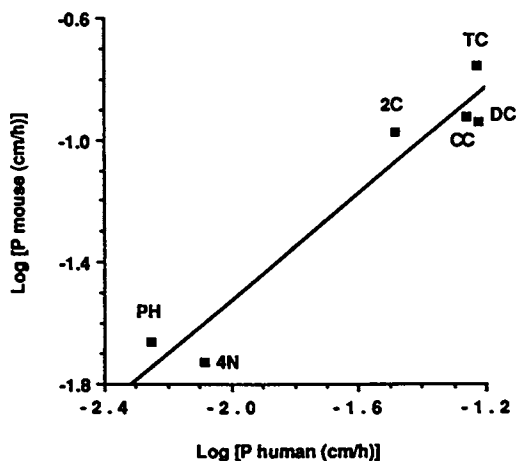


Figure 9. Comparison between the permeability coefficients of chlorocresol (CC), 2-chlorophenol (2C), dichlorophenol [DC], 4-nitrophenol (4N), phenol (PH) and trichlorophenol (TC) through excised human and mouse skin.

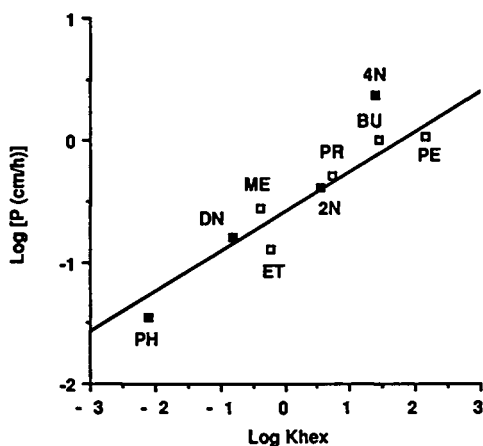


Figure 10. Permeability coefficients of alkyl para-aminobenzoates at 25°C (\square) and phenols at 37°C (\blacksquare) through a dimethylpolysiloxane membrane as a function of K_{hex} .

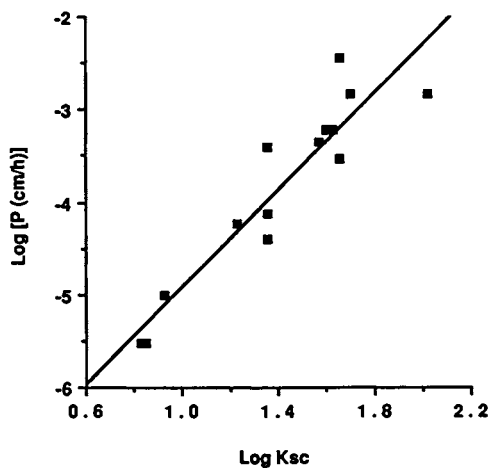


Figure 11. Permeability coefficients of a series steroids through excised human epidermis as a function of K_{sc} (linear regression line drawn through the data).

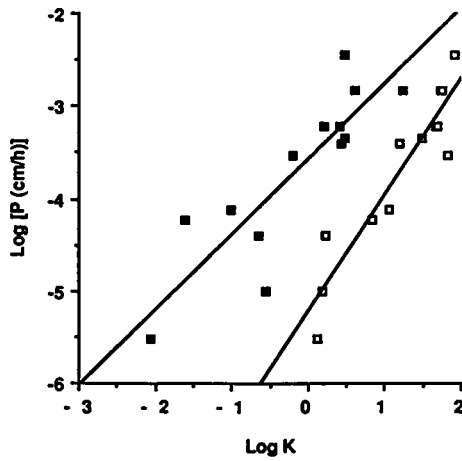


Figure 12. Permeability coefficients of a series steroids through excised human epidermis as a function of K_{ac} (\square) and K_{hdec} (\blacksquare).

selection of a chemical which demonstrates high potency for its proposed utilization (e.g., as a pesticide), but presents a low risk with respect to worker toxicity resulting from dermal exposure.

Acknowledgments

Financial support was provided by grants from NIOSH, NIGMS, EPA, SERC and the UC Toxic Substances Program. We thank Joy Houk, Darius Aliabadi, and James Palmieri for sharing with us their unpublished data, and Professor J. Hadgraft for helpful comment.

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RECEIVED January 22, 1988

Chapter 11

Reduction of Pesticide Toxicity by Choices of Formulation

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While the toxicity of the active ingredient of a pesticide is a property which cannot be changed, the acute toxicity effects of the formulation (for example, dermal or ocular toxicity, or exposure of the mixer-loader) are strongly influenced by the way in which the active ingredient is formulated. Alternate formulation types often have different FIFRA ratings. An emulsifiable concentrate usually causes more severe ocular toxicity than does an aqueous suspension of the same active ingredient. The preliminary toxicology profile of a new active ingredient can be utilized in deciding which formulation types to develop. For example, if a new active shows severe dermal irritation, the development of an emulsifiable concentrate should be avoided. Exposure of the mixer-loader is strongly influenced by the formulation type. While pesticide formulations are influenced by both the physical-chemical properties of the active ingredient and the economic pressures of the marketplace, there are formulation choices which will increase the safety of pesticide formulations.

The Formulation Science of Agrichemicals is a challenging and scientifically rigorous research area that is constrained by a) increasing economic pressures due to the general state of the farm economy; and b) governmental regulations that are designed to obtain the greatest safety profile possible for our products. Safety concerns related to pesticide products have been further highlighted by recent EPA actions including their policy on frequently used inert ingredients in pesticide products (Inert Ingredients in Pesticide Products; Policy Statement: Federal

0097-6156/88/0371-0124\$06.00/0

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Register, April 22, 1987, Pages 13305-13309). Those inert ingredients of toxicological concern should then be avoided for safety reasons.

This then is our challenge: develop effective pesticide products that have high safety profiles without substantially increasing the cost to the consumer. This research and development must be done under rigorous scientific standards.

The formulation chemist's work is further complicated by not having the luxury to select the active compounds with which new formulations must be developed. The choice of active ingredients is usually the result of extensive laboratory and greenhouse screening as well as field research.

Therefore, for the purpose of this presentation the physical and chemical properties of the active ingredients will not be considered. Comments relative to the choices of formulation ingredients will be based on providing increased safety of the final product, usually to mixer-loader-applicators, as well as to chemists, formulators, processors, etc. Some attention will be given to safety towards wildlife as well.

Let us first spend a moment reviewing the general formulation types, their inherent properties, and their market popularities.

Sprayable Formulations

Pesticide manufacturers produce more products of this group than any other. This group includes emulsifiable concentrates (E.C.), aqueous suspensions (A.S.) or flowables (F), wettable powders (WP), water dispersible granules (WDG) or dry flowables (DF), and solutions (S). The physical and chemical properties of the active ingredient often dictate the type of formulation that may be practical for a particular product. Liquid formulations have been desirable because they disperse well in water and can be handled easily (pumping, measuring, etc.). Emulsifiable concentrates and solutions have been particularly well accepted because of their reduced agitation requirements after dispersion in water. Aqueous suspensions also offer some of these advantages, but may require more vigorous agitation for suspension than emulsifiable concentrates, particularly after the mixture is allowed to stand.

Solid formulations such as wettable powders and dry flowables are also dispersed in water before spraying. Obviously, a wettable powder is capable of producing significant amounts of dust, particularly under windy conditions, and may present a concern to the mixer-loader. A well designed dry flowable is essentially dust-free and has become increasingly more attractive over the last few years. Both of these formulation types have yielded products containing high concentrations of active ingredient (80 to 90 percent) and can be economically attractive.

Nonsprayable Formulations

These are products such as granules, dusts, briquettes, pellets, etc., which are applied directly without dilution in water.

Granules currently have major applications in a variety of market segments, while the other dry products are used for more specialized applications.

Toxicity Considerations

Throughout this discussion, I will be referring to the rat acute oral toxicity, rabbit dermal toxicity and irritation, rabbit ocular irritation, and rat inhalation toxicity of various formulation types based on their FIFRA categories, as outlined in the Federal Insecticide, Fungicide, and Rodenticide Act (Labeling Requirements For Pesticides and Devices, Proposed Rule: Federal Register, September 26, 1984, Pages 37960-37995). I am sure that many of you are familiar with this system, but I would like to review it briefly. Table I contains the types of hazard studies, FIFRA categories, and appropriate signal words for precautionary labelling statements on product labels.

Table I. FIFRA Toxicity Criteria and Categories

Acute Hazard Studies	FIFRA Categories			
	Category I	Category II	Category III	Category IV
Rat Oral LD ₅₀ -mg/kg	0 - 50	>50 - 500	>500 - 5000	>5000
Rabbit Dermal LD ₅₀ -mg/kg	0 - 200	>200 - 2000	>2000 - 5000	>5000
Rat Inhalation LC ₅₀ 4 hr exposure-mg/l	0 - 0.05	>0.05 - 0.5	>0.5 - 5	>5
Rabbit Ocular Irritation	Corrosive or irreversible eye damage: >21 days	Irritation clearing in 8 - 21 days	Irritation clearing in 7 days or less	Irritation <24 hr
Rabbit Dermal Irritation	Corrosive: Tissue destruction	Severe irritation at 72 hr	Moderate irritation at 72 hr	Mild or slight irritation
Signal Word	DANGER	WARNING	CAUTION	CAUTION

Source: Labeling Requirements For Pesticides and Devices, Proposed Rule: Federal Register, September 26, 1984, Pages 37960-37995.

Products must be labeled with the signal word delineating the highest hazard of the various categories. A product with a high hazard category (FIFRA I, which carries a DANGER label) obviously presents increased hazards to the user and in certain cases may be regulated by EPA as a "Restricted Use Pesticide".

As mentioned earlier, liquid formulations, such as emulsifiable concentrates and aqueous suspensions (suspension concentrates or flowables), have been particularly attractive to the end user. However, emulsifiable concentrates generally are

more irritating to the eyes and skin than aqueous suspensions of the same active ingredient, probably because of the organic solvents and surfactants in E.C. formulations. Experience with neat or undiluted solvents is limited, but heavy aromatic naphtha or xylene-range solvents are known to produce very slight eye irritation. More polar solvents such as cyclohexanone or glycol ethers have demonstrated moderate levels of ocular irritation. Vegetable oils such as corn and soybean oils are reported to produce low orders of ocular irritation. Unfortunately, they have not demonstrated the necessary solvency in most cases to permit their economical use.

Sometimes the safety of an E.C. may be increased either by decreasing the amount of emulsifier in the system or by complete modification of the surfactant system. Emulsifiers normally are selected to give the best emulsion stability in a variety of water hardnesses, temperatures, and perhaps in liquid fertilizers, but we have frequently observed that fine, stable emulsions produce more ocular irritation than less elegant emulsions containing lower surfactant levels. The actual mechanism of increased ocular irritation may be potentiation of the inherent toxicity of the active ingredient by increasing its surface area in the smaller emulsified droplets, increased absorption due to an increase in the lipid solubility of the active ingredient, or disruption of lipid membrane barriers in the cornea. Emulsifier levels usually range from 3 to 5 percent, but in certain situations where additional foliar wetting is required, or where the properties of the active or solvent system dictate, higher levels may be used. These higher levels often result in severe dermal irritation or corrosive ocular effects, which in turn result in FIFRA I classifications and DANGER product labels. Table II shows the resulting classifications for a particular fungicide in various formulations. In these situations, formulation as an aqueous suspension (or flowable) rather than an E.C. may be the best choice.

Table II. FIFRA Hazard Classification Comparisons of Various Fungicide Formulations

Formulation Type	FIFRA Classification				
	Oral	Dermal		Ocular	Inhalation
		Irritation	Tox.		
E.C. (1 lb/gal)	III	II	III	II	III
E.C. (1 lb/gal) With Adjuvant	III	II	III	I	III
A.S. (1 lb/gal)	III	IV	III	III	III
WP (12 percent)	III	IV	III	III	III

When formulating aqueous suspensions, however, similar "surprises" can occur. Several years ago we developed a "standard" flowable base for preparing small quantities of new actives to be evaluated by the plant scientists. The formula contained typical lignin suspending agents, thickeners, an antifoam agent, and a wetting agent (either an alkylphenol ethoxylate or alkylether ethoxylate). A higher than normal level (10 percent) of the wetting agent was used to insure good wetting with possibly difficult actives, as well as to give the optimum spreading properties when the product was sprayed onto foliage. This water-based blank was tested for eye irritation and resulted in a FIFRA I rating. When the formula was revised to contain 5 percent surfactant, the rating dropped to FIFRA Category III. These, as well as many other surfactants, are known to have irritating properties in their concentrated state, but the degree of eye irritation on dilution to 10 percent was a surprise. Situations like this demonstrate the need to select surfactants with low irritation properties. Most surfactant manufacturers publish the acute toxicological properties of their products, and these can be of value in surfactant selection.

Increased Safety of Liquid Formulations

There are other possible ways to increase the safety of liquid formulations.

Increasing the Concentration of Active Ingredient in an E.C. If the solubility properties of the solvent system will allow, a higher concentration of active may result in lower irritation properties. This would indicate greater irritancy of the emulsifier/solvent system than of the active ingredient.

Microencapsulation of the Active. There are products on the market in which the microencapsulated formulation is less hazardous than the conventional formulation. This is particularly true if the active itself has high inherent toxicity. The encapsulation of methyl parathion in PENNCAP-M is an example of the successful use of this process.

Concentrated Emulsions (CE). These are pre-emulsified concentrates where part of the solvent is replaced with water. Our experience with a herbicide CE formulation has demonstrated reduced eye irritation when compared to a conventional E.C. of the same concentration, (FIFRA III versus FIFRA II).

Of course, it may also be appropriate to consider replacing the liquid formula with a dry form that can be applied through spray equipment. Sprayable solid formulations generally include wettable powders (WP) and water dispersible granules or dry flowables (WDG or DF). During the past few years we have seen the development of a variety of WDG's, in some cases supplementing or replacing a WP of the same active. Wettable powders are dusty when handled and may present a concern to the mixer-loader. However, unless the active itself has inherent toxic

properties, the WP may demonstrate safe levels of inhalation toxicity. We have also seen the replacement of WP products with aqueous suspensions. This has been achieved in cases where the active has low solubility in water and is chemically stable in a water-based vehicle.

A dry flowable formulation should be as hard and attrition-free as possible to reduce the formation of dust during shipping and handling. The hardness or durability properties must be balanced against the need for good dispersion properties in water. Packaging of dry flowables is usually important and should consist of fairly rigid containers with the package as full as possible to reduce attrition of the product.

Nonsprayable formulations such as granules, pellets, and briquettes should be as dust-free and resistant to attrition as possible. In the development of a granular product, the use of a harder LVM clay rather than the softer RVM clay carrier may be of value. The use of high-boiling liquids such as mineral oil to bind the dust may be helpful.

Dust may also be minimized in a granular product by selecting the correct particle-size range where fines are eliminated by screening. This can usually be accomplished by selecting specifications with the supplier. As with dry flowables, attention to correct packaging will minimize product attrition and dust formation.

Other forms of granular carriers are certainly possible. Clay carriers are most frequently used because of their low cost, but other carrier materials can be developed to provide variations in release of the active, particularly if a conventional clay granule demonstrates excessive human, avian, or even phytotoxicity. Granule carriers such as the starch matrix developed by the USDA, ARS in Peoria, may find applications to improve the safety of granular products.

Elanco Products has developed a series of different types of formulations for the same active ingredient. In Table III the respective FIFRA categories for the E.C., the powder concentrate, the DF, and the granule are presented. It is obvious from this example that the ocular irritation can be very different for different formulations of the same active ingredient, and that changes in the other toxicity categories may also occur.

Table III. Comparison of Different Formulation Types for the Same Active Ingredient

Formulation Type	FIFRA Categories				
	Oral	Dermal		Ocular	Inhalation
		Irritation	Tox.		
E.C. No. 1 (1.5 lb/gal)	III	III	IV	I	III
E.C. No. 2 (1.5 lb/gal)	III	III	IV	II	III
DF (60 percent)	III	III	IV	III	III
2.5 G (30/60 mesh)	IV	IV	IV	III	IV
Powder Concentrate (50 percent)	IV	IV	IV	III	IV

Packaging

Packaging concepts also offer some useful opportunities with wettable powders. These products can be packaged in water-soluble film packets which may be directly added to the spray tank, thereby avoiding exposure to the operators. The user exposure data presented in Table IV demonstrate the difference in contact to the mixer-loader and the applicator when using a conventional 50 WP and one in a water-soluble packet.

Table IV. Mixer/Loader/Applicator Exposure Data for an Experimental 50W - Plant Growth Regulator

Route of Exposure	Package Type	
	Conventional Bag	Water Soluble Packet
Inhalation, $\mu\text{g}/\text{lb}$ a.i.	3.8	0.47
Dermal, mg/lb a.i.	2.4	0.041

Water-soluble packets may also have utility in reducing exposure to products formulated as E.C.'s. A few years ago we investigated the compatibility of an E.C. formulation with conventional polyvinyl alcohol films. The product showed good compatibility with the film and could be filled in pouches of up to at least eight ounces. The only problem was the ability to completely avoid leakage, the liquids being more successful than a powder in finding an imperfect seal. The results were encouraging, however, and I believe the concept could be developed for an E.C. that may have irritating properties.

Acute Hazard of Granules to Wildlife

Avian toxicity from granules may be minimized by selecting the correct particle-size range and using a low concentration of active ingredient. Studies have indicated that particles below 30-mesh are infrequently selected by birds. If the active ingredient concentration is low, the bird may be repelled by the particle rather than developing a toxic response. Highly colored granules should also be avoided. In general, the safety of a granule will be increased if the granule blends in with the soil.

The suggestions presented here for improvements in product safety will not present solutions to all of our situations. At the same time I hope that some of the ideas will be helpful in our formulation efforts, and that less hazardous product formulations can be produced.

RECEIVED December 28, 1987

Chapter 12

Use of Selected Surfactants To Reduce Dermal Toxicity of Insecticides

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Microencapsulation has proven to be a useful technique to reduce the dermal toxicity of insecticides. However, often in order to reduce dermal toxicity to the extent desired, the rate of release from the microcapsules needs to be reduced to the point where insecticidal activity falls below an acceptable value. A class of surfactants has been discovered which when solubilized in the aqueous phase of an insecticide microcapsule dispersion can form a second barrier in addition to the microcapsule wall. It is speculated that this second barrier forms at the skin-water interface. By the addition of the surfactant the desired dermal toxicity reduction can then be achieved without lowering the release rate from the microcapsules to the extent where insecticidal activity falls below an acceptable value. An example will be shown where this dermal toxicity reduction technique is applied to a Dyfonate microcapsule dispersion.

Percutaneous absorption represents an important route of exposure for agricultural and household pesticides. It has been shown that deposition on skin is 20-1700 times the amount that may be inhaled (1). Chemicals exposed to the skin may absorb from 0.2% to greater than 50% of the applied dose into systemic circulation. For example, three common insecticides, Malathion, Parathion, and Carbaryl, are absorbed at 8.2%, 9.7%, and 73.9% of the total applied topical dose (1). Washing of the skin cannot reliably prevent the dermal absorption of insecticides or other materials. For example, a solution of polychlorinated biphenyls was applied to guinea pig skin and immediately washed with water and acetone. After this procedure, only 59% of the applied dose was actually removed from the skin (2). With these results and the fact that the skin is the most important route of exposure to most pesticides, protection of the skin from exposure is vitally important.

0097-6156/88/0371-0131\$06.00/0

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The skin is the largest organ in the human body and accounts for approximately 10% of the total body weight (3). This organ consists of two fundamental layers, the epidermis and dermis (Figure 1). The thinner portion, the epidermis, accounts for the major portion of biochemical transformations that occur in the skin; however, it constitutes approximately 5 to 10 percent of the total mass of human skin. The epidermis and dermis are approximately 0.1 millimeter and 2 to 4 millimeters thick, respectively. The outermost layer of the epidermis is the stratum corneum. This layer consists primarily of dead, keratinized epithelial cells. These form horny scales that are constantly worn away and replaced by the living cells underneath. This layer forms the primary protection against foreign materials from penetrating into the systemic circulation. The living cell layer below the stratum corneum is avascular and serves as a secondary level of defense. Absorption into the systemic circulation occurs in the dermis, which is highly vascular.

One method used to reduce dermal toxicity of insecticides is microencapsulation. With this technique, the rate of release from the microcapsules can be controlled to the extent that dermal toxicity can be reduced considerably. However, in order to produce this type of toxicity reduction, the rate of release may need to be reduced to the point where insecticidal activity falls below an efficacious value. A class of surfactants has been found which further reduces acute dermal toxicity when used in conjunction with insecticide microcapsules. It is speculated that this class of surfactants forms a barrier at the skin surface to protect against absorption of lipophilic insecticides. The formulation technique in this paper consists of combining a hydrophilic surfactant with microencapsulated Dyfonate (a registered trademark of ICI Americas Inc.) to further reduce its dermal toxicity without changing the release rate from the microcapsules so that insecticidal activity does not fall below an acceptable level.

Materials and Methods

Microencapsulation. A Dyfonate microcapsule suspension was prepared using Stauffer Chemical Company interfacial polymerization technology. Electron micrographs of the microcapsules are shown in Figures 2 and 3. The Stauffer microencapsulation process is based on *in situ* interfacial condensation polymerization of polyisocyanate monomers (4). This process is unique because the monomers reside only in one phase (organic dispersed phase). This process has been used to produce pesticide microcapsule formulations containing 4-5 lbs of active ingredient per gallon.

The first step of the Stauffer microencapsulation process consists of dispersing an organic pesticide phase (containing isocyanate monomers) into an aqueous phase containing an emulsifier and a protective colloid. The isocyanate monomers used in the process are polymethylene polyphenylisocyanate (PAPI) and toluenediisocyanate (TDI) (Figure 4). The wall-forming reaction is initiated by heating the batch to an elevated temperature at which point the isocyanate monomers are hydrolyzed at the interface to form amines which, in turn, react with unhydrolyzed isocyanate monomers to form the polyurea microcapsule wall (Figure 5).

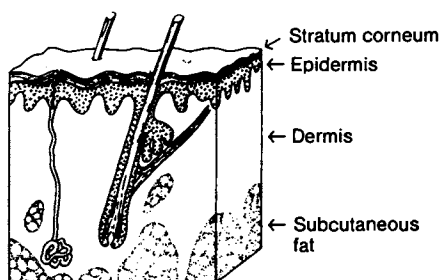


Figure 1: Structure of skin.

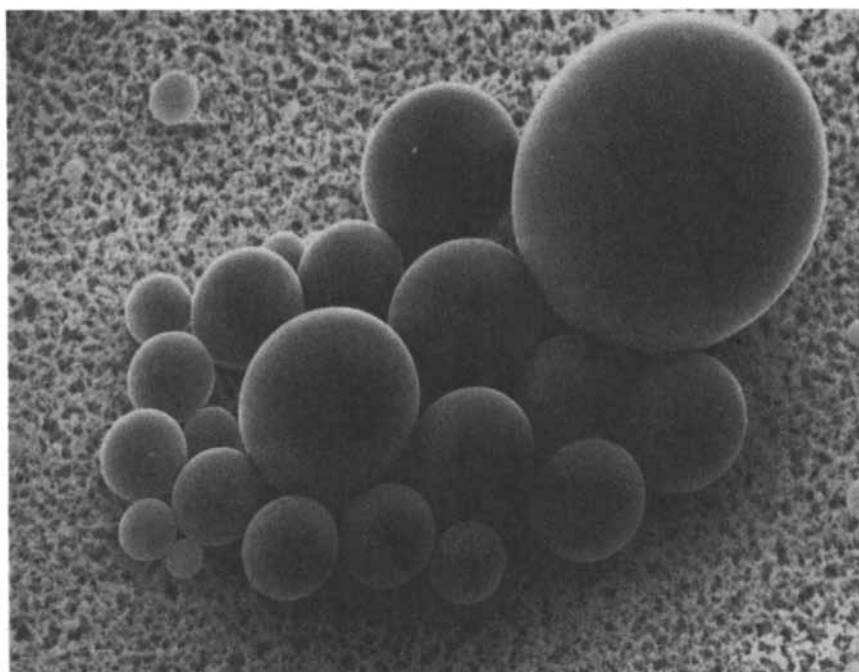


Figure 2: Electron micrograph of a microcapsule on filter paper (1000x).

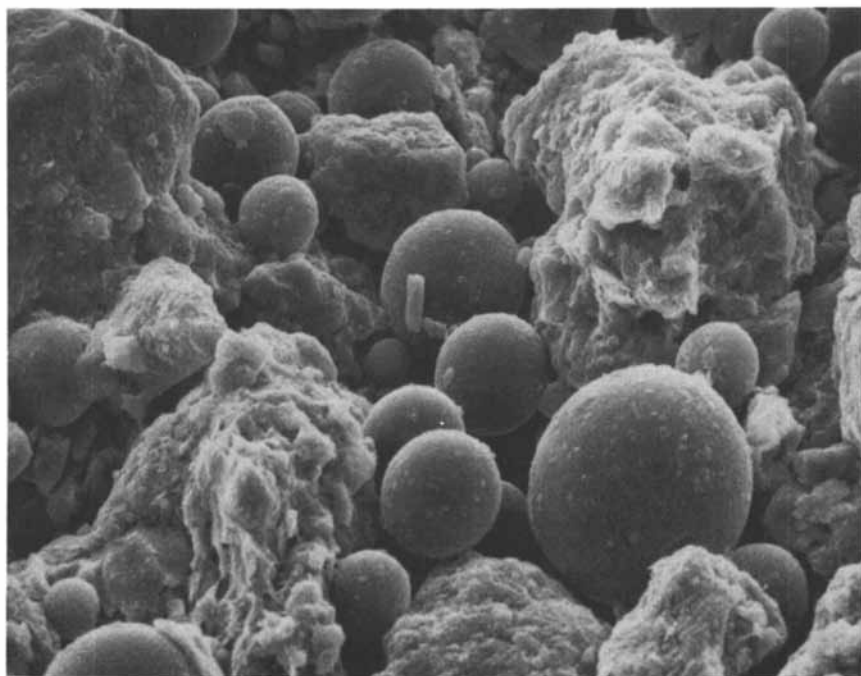
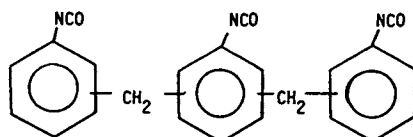
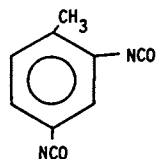


Figure 3: Electron micrograph of microcapsules on soil (1000x).



PAPI



TDI

Figure 4: Structures of the isocyanate monomers, PAPI and TDI that are used in wall formation.

The release rate of this microcapsule system can be varied by varying microcapsule particle size (i.e. total surface area per pound of pesticide), wall thickness (weight percent isocyanate monomers in organic phase) and wall permeability. The wall permeability can be varied by varying the crosslink density of the polyurea (ratio of PAPI to TDI), by varying the wall microporosity (solvent effect), by limiting crosslinking (ammonia addition) and by varying the isocyanate monomer chemical composition. In addition, mixtures of microcapsules with different wall thickness and wall permeability can be produced by this process by sequential dispersion of different organic phases into the same aqueous phase (5).

Surfactants. Igepal DM-970 and Igepal CO-990 were obtained from General Aniline and Film Corp. The structures are shown in Figure 6. (Igepal is a registered trademark of GAF Corp.)

Animal Test Method. Acute dermal toxicity testing was performed according to the OECD guidelines (6). The test animal used was Stauffland albino rabbits, 5 of each sex per dose, (a cross between New Zealand and Florida white strains, Phillips Rabbitry, Soquel, California). The abdominal areas of the rabbits to be dosed were shaved 24 hours prior to treatment. A dosage of test material was pipetted onto a piece of rubber damming, and the area of the rubber damming containing the test material was placed directly on the shaved area of the rabbit. This rubber damming was then secured to the rabbit with surgical tape and covered with gauze. The gauze and the damming were removed 24 hours after the test material application. The dose site was wiped with gauze and rinsed with distilled water to remove the remaining test material. The abdomen of the rabbit was then rewrapped with clean gauze to prevent the rabbit from grooming the dose site and ingesting any residual material. A group of four rabbits were sham-treated and served as controls for each dose level. All test animals were observed for up to 14 days and mortalities were recorded. The median lethal dose (LD50) values for each test material were calculated using the method of Litchfield and Wilcoxon (7).

Results and Discussion

Dose-mortality plots for the acute dermal toxicities of Dyfonate microcapsule dispersions are shown in Figure 7. From these plots the LD50 value for each formulation was determined and listed in Table I. A concentration of 3% Igepal CO-990 or DM-970 in the dispersion approximately doubled the LD50 value. Potency ratios (i.e. LD50 value for the microcapsule dispersion with Igepal divided by the LD50 value for the dispersion without Igepal) were calculated for each microcapsule dispersion and shown in figure 8. No significant protective effect of Igepal CO-990 was observed at a 2% concentration, however, a 3% concentration of either Igepal CO-990 or Igepal DM-970 produce a significant decrease on acute dermal toxicity (i.e. an increase in potency ratio).

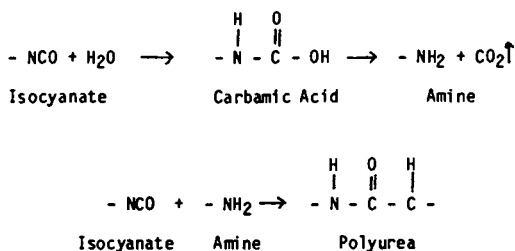


Figure 5: Microcapsule wall forming reaction.

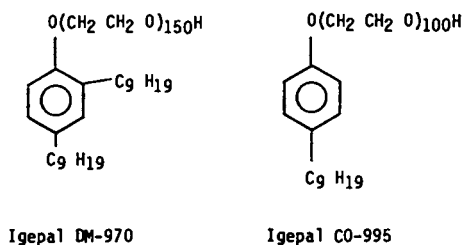


Figure 6: Structures of Igepal CO-990 and Igepal DM-970. (Igepal is a registered trademark of GAF Corp.)

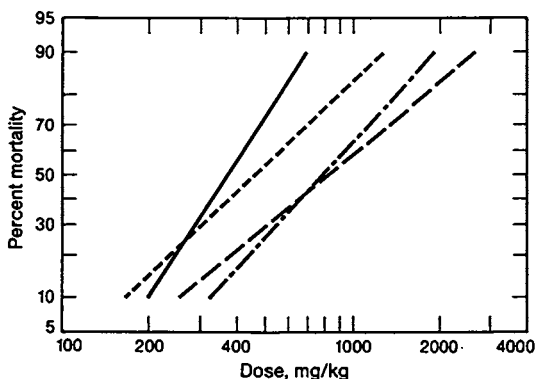


Figure 7: Log-Probit plots of acute dermal toxicity dose-mortality curves for Dyfonate microcapsule dispersions without Igepal (-), with 2% Igepal CO-990 (--), with 3% Igepal CO-990 (-.-) and with 3% Igepal DM-970 (— —). (Dyfonate is a registered trademark of ICI Americas Inc.)

TABLE I: Acute Dermal LD50 Values for Dyfonate Microcapsule Dispersions with and without Igepal

Igepal Surfactant (a)	Acute Dermal LD50 (mg/kg)
None	370 (285-480) (b)
2% CO-990	457 (350-596)
3% CO-990	794 (585-1078)
3% DM-970	809 (564-1160)

(a) The microcapsule portion was identical in each formulation.

(b) Values in parenthesis are 95% confidence limits.

Mammalian skin is highly lipophilic (3), and this property represents an important barrier function of the stratum corneum. Lipophilic substances like Dyfonate can easily be absorbed by the stratum corneum and transferred into systemic circulation. In an effort to reduce this absorption, the material can be microencapsulated, thus reducing the availability at the skin surface.

Acute dermal toxicity of the microencapsulated material could be decreased further by increasing the thickness and/or the cross-link density of the capsule wall. In the case of the Dyfonate microcapsule dispersion, this approach caused the insecticidal efficacy to fall below an acceptable value. However, addition of Igepal to the microcapsule dispersion did further reduce the dermal toxicity without effecting the insecticidal efficacy. It is speculated that Igepal formed a secondary barrier at the skin surface. This is schematically shown in Figure 9. The lipophilic end of the Igepal molecule is adsorbed on the skin surface. Since Dyfonate is highly lipophilic, it is speculated that the secondary barrier's protection resides in the hydrophilic layer associated with the long hydrophilic chains of the surfactant. This barrier further reduces the amount of Dyfonate available at the skin's surface for absorption, thus reducing toxicity.

Addition of either Igepal DM-970 and Igepal CO-990 to a Dyfonate microcapsule formulation has been shown to decrease the dermal toxicity and increase safety of the concentrated formulation. The presence of Igepal in this type of formulation provides a decrease in dermal toxicity of the concentrated formulation without altering the insecticidal efficacy of the diluted dispersion on soil.

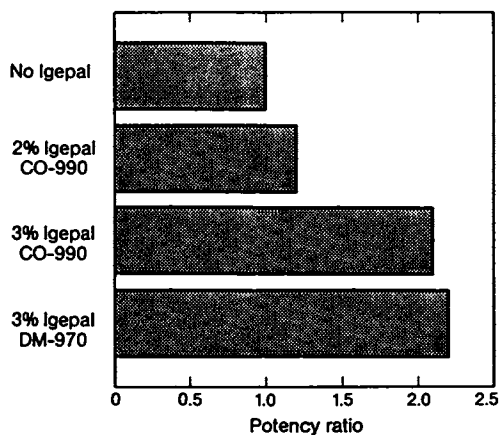


Figure 8: Potency Ratios for the microcapsule dispersions with and without Igepal.

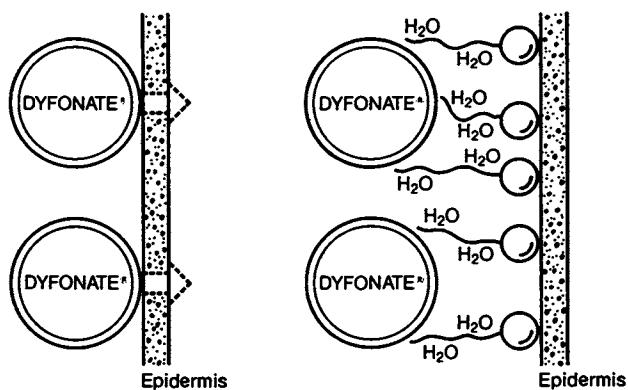


Figure 9: Schematic representation of the Dyfonate microcapsule dispersion with and without addition of Igepal.

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RECEIVED December 28, 1987

Chapter 13

Dynamic Surface Tensions of Spray Tank Adjuvants

New Concepts and Techniques in Surfactants

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The Dynamic Surface Tensions of several spray tank adjuvants were measured using the maximum bubble pressure method (MBP). The effect of concentration and water hardness on the dynamic surface tension was studied. The correlation between dynamic surface tension and wetting and soil penetration was determined. A good correlation was found for both. No differences in dynamic surface tension was found due to changes in hardness although this may be due to the nature of the surfactants selected which were designed to be insensitive to changes in water hardness. Using the MBP technique, the dynamic surface tension was found to be concentration dependent and increases in the rate of surface tension lowering were measured well above the CMC. Based on the experimental results, the MBP technique was judged to be a rapid, simple, sensitive, and accurate procedure for determining the dynamic surface tension of agricultural spray tank adjuvants.

This study is part of a series which involves the application of new or improved laboratory techniques to study the surface and interfacial properties of surfactants employed in the agricultural industry. In this particular exercise, the dynamic surface tensions of several spray tank adjuvants are determined by the maximum bubble pressure technique using laboratory equipment designed and built at the Department of Chemical Engineering of Illinois Institute of Technology.

Several different types of adjuvants have been studied as shown in Table I. In this first study, no attempt was made to study variations in each particular adjuvant formulation, however, this is the intent of future work. Kao (1) has determined the dynamic surface tensions for research and industrial grade sodium dodecylsulfate and found considerable differences between the two. In this work, we

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have worked with industrial grade surfactants and have made no attempt to further purify them. The effect of selective absorption due to mixtures present in industrial grade surfactants has not been considered. It is hoped that this work will help the formulator design the most effective products for field application. We intend to demonstrate that dynamic surface tensions can be obtained easily with the maximum bubble pressure technique and that the values obtained are significant in determining the speed and effectiveness of surfactant blends used as wetting agents.

Table I. Adjuvants Used in Investigation

Product	Application	Active Ingredient
Adsee 775	Sticker	Copolymer
Adsee 799	Soil Cond	Fatty Acid Ester
Adsee 801	Wetting	Alcohol Ether
Adsee AK31-64	Foaming	Sulfate/Sulfonate
Adsee AK31-69	Spray Oil Emul	Nonionic Blend
Sponto 168D	Compatibility	Phosphate Ester
Emcol H-3AM	Activator	Sulfosuccinate

THEORY

The technique of measurement of dynamic surface tension has recently been reviewed by Mysels (2) and has been used by various investigators in the past (1,3,4,5). The maximum bubble pressure method depends on the fact that if a small bubble of a gas (e.g. air) is blown at the tip of a capillary immersed in a liquid, the pressure in the bubble increases initially, while the bubble grows and its radius of curvature decreases. If the bubble is small enough to be considered as spherical, the maximum pressure occurs when it becomes a hemisphere, and at this point, the radius of curvature is at its minimum value. Growth beyond this point results in a drop in pressure, liquid rushes in, and the bubble is blown from the tip of the capillary. A theoretical treatment and justification of the technique is described by Joos and Rillaerts (6).

In practice, the pressure increases within the capillary at a constant gas flow rate until the bubble appears at the tip of the capillary orifice. The orifice has been immersed in the liquid to a known depth (h). The pressure difference between the inside and the outside of the bubble is related by the Laplace equation:

$$p - p' = 2\gamma/r + dgh$$

where γ is the surface tension, d is the density of the liquid, p' is the atmospheric pressure, p is the pressure within the bubble, g is the gravitational acceleration and r is the radius of the capillary.

APPARATUS

The maximum bubble pressure apparatus used for measuring the dynamic surface tension is illustrated in Figure 1.

The T shaped capillary tube (A) with a radius of 67 microns, was fused into the tensiometer container (TC) built by Reliance Glass Works, Bensenville, IL. Initially, air is blown into the tensiometer container to keep the tip of the capillary dry. The sample solution is then introduced into the tensiometer container to a predetermined depth. The air flow rate is adjusted with a Cole Parmer Masterflex speed controller (PC) and any irregular bubbling at the tip of the capillary is eliminated using a Swagelock fine metering valve (MV).

The time effect on the surface tension of a freshly formed bubble is studied by generating bubbles from the tip of the capillary tube. The frequency of bubble formation is measured using an optical technique. A pair of co-linear glass rods direct a light beam across the capillary tip. A light diode (L) is attached to one of the glass rods for transmitting light and a photodiode detector (PD) located on the other glass rod is attached to a frequency counter (FC) available from J. Flude Mfg., Model 1953A, to monitor the bubble generating frequency within the accuracy of ± 0.005 Hz. The pressure within the bubble is measured with a digital manometer (M) available from Meriam Instruments, Model LP-200I, and is monitored with an oscilloscope (OS) from Leader Instruments, Model LBO-5825.

The accuracy of the maximum bubble pressure method was checked by determining the surface tension between deionized water and air, known in the literature to be 72.3 dyne/cm at 25°C. Separately, the capillary was calibrated by measuring the orifice using a differential interference microscope. Comparison of both measurements gave a 0.6 micron difference which corresponds to a 0.1 dyne/cm error. The sensitivity of the method was found to be ± 0.02 dyne/cm with a total uncertainty of ± 0.30 dyne/cm.

DISCUSSION

The results of measuring dynamic surface tensions at various bubble generating rates for the various adjuvant solutions at 0.1% weight percent in 342 ppm water is shown in Figure 2. These results show that several of the samples show significant surface tension reduction even after 40 milliseconds while others show hardly any change over the entire time frame. Of those that show significant rapid surface tension reduction, ADSEE 801, is the most pronounced, followed by SPONTO 168D and ADSEE AK31-64. Table II shows the differences in surface tensions after 30 and 180 milliseconds as well as the static surface tensions obtained with a Du Nouy ring (7) at 25°C. Although the static surface tensions of all the spray tank adjuvants are similar at 0.1%, their surface tensions after small time increments differ considerably from each other. Because of the pronounced effect with ADSEE 801, it was chosen for further study to determine the effect on dynamic surface tension of changes in concentration and water hardness.

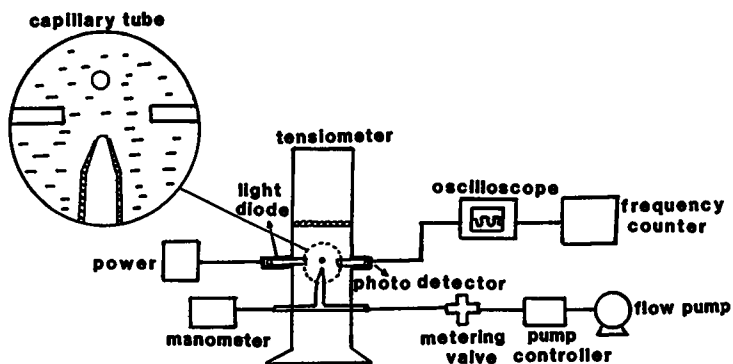


Figure 1. Schematic Diagram of the maximum bubble pressure apparatus.

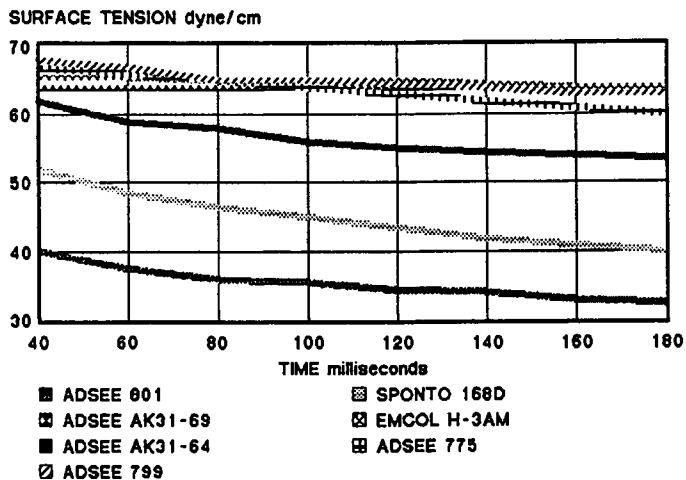


Figure 2. Dynamic Surface Tensions at 25°C, 342 ppm, 0.1% for various spray tank adjuvants.

Table II. Surface Tensions for Various Adjuvants
0.1%, 342 ppm H₂O, 25°C

Product	30 MSEC	180 MSEC	Static
Sponto 168D	51	40	32
Emcol H-3AM	66	64	28
Adsee 775	67	67	31
Adsee 799	66	66	31
Adsee 801	44	32	29
Adsee AK31-64	63	54	28
Adsee AK31-69	64	64	31

Concentration studies (Figure 3) show a drastic change in dynamic surface tension values upon reducing the concentration of ADSEE 801 from 1.0% to 0.001%. The CMC of this product and several of the others is shown in Figure 4. From the values, it can be readily concluded that the concentrations used in our studies are at or above the CMC. Table III shows the values at 30 and 180 milliseconds and static surface tensions at 0.01%. The values show no significant dynamic effect at the lower concentration, although it is above the CMC for all products.

Table III. Surface Tensions for Various Adjuvants
0.01%, 342 ppm H₂O, 25°C

Product	30 MSEC	180 MSEC	Static
Sponto 168D	66	65	33
Emcol H-3AM	67	66	28
Adsee 775	69	69	32
Adsee 799	69	69	38
Adsee 801	68	64	49
Adsee AK31-64	69	67	53
Adsee AK31-69	66	66	32

The results obtained for variations in water hardness, while keeping the concentration constant at 0.1%, are shown in Figure 5. No significant changes in surface tension values can be seen for ADSEE 801 in the three different waters. Groves, Banzon, and Woofrey (7) recently measured the effect of salt concentration and bubble generation rate on the dynamic surface tension of solutions of sodium dodecylsulfate and found changes in salt concentration have a pronounced effect on this surfactant.

Table IV compares the Draves (9,10) wetting times with 30 millisecond and static surface tensions for the various adjuvants. It is apparent that conclusions about wetting times cannot be drawn from the static surface tension values. The 30 millisecond values, however, do show that a low dynamic surface tension gives rapid wetting times. ADSEE 801, which is by far the fastest at lowering surface tension, is also the fastest wetter. This seems logical since wetting is a function of surface tension and contact angle all related by Young's equation.

$$W = \gamma (1 + \cos \theta)$$

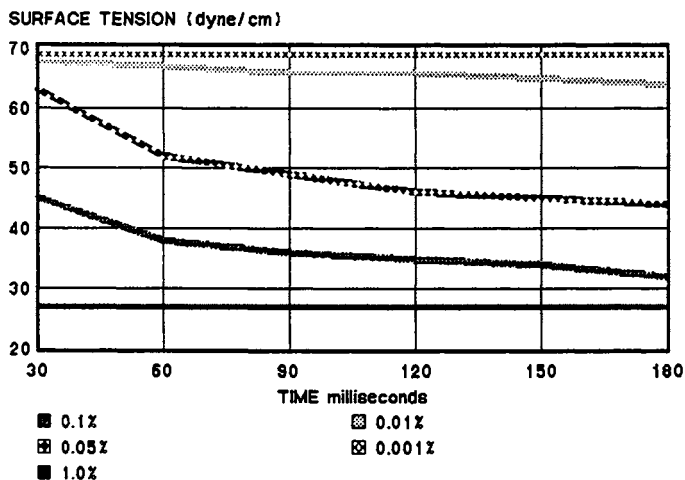


Figure 3. Adsee 801 - Effect of concentration on Dynamic Surface Tension, 25°C, 342 ppm.

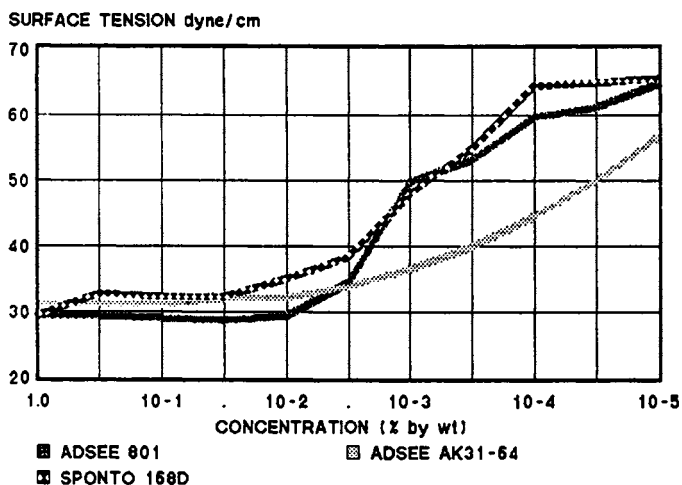


Figure 4. CMC values at 25°C, 342 ppm.

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In Pesticide Formulations; Cross, F. et al.;

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Table IV. Effect of Surface Tensions on Wetting
at 25°C, 342 ppm H₂O, 0.1%

Product	Static dyne/cm	30 MSEC dyne/cm	Wet sec
Adsee 801	29	44	8
Emcol H-3AM	28	66	50
Adsee 775	31	66	50
Sponto 168D	32	51*	70
Adsee 799	29	66	73
Adsee AK31-64	28	63	90
Adsee AK31-69	31	64	300

*50 MSEC

Here W is the work of adhesion - i.e., the work required to separate the liquid from the solid, γ is the liquid surface tension and θ is the contact angle measured in the liquid. Both the surface tension and the contact angle vary with time and therefore, the work of adhesion must also vary with time. The lower the surface tension and the smaller the contact angle, the lower is the work required to spread the liquid.

Table V also shows the Draves wetting values for various concentrations of ADSEE 801, the spray tank adjuvant formulated as a wetting agent. The static surface tension values show that all concentrations are at or above the CMC for this formulation. The wetting power of the product at the various concentrations cannot be predicted by the static surface tension values. The surface tension values after 30 millisecond, however, do enable one to distinguish between the fast wetting concentrations and the very slow wetting concentrations.

Table V. Effect of Conc on Wetting
ADSEE 801 - 342 ppm H₂O, 25°C

Conc % By Wt.	Static (dyne/cm)	30 MSEC (dyne/cm)	Wetting (seconds)
1.0	29.6	27.4	0
0.1	29.0	44.0	8
0.01	29.4	66.3	267

Table VI compares the penetration rates for 1.0% solutions of several adjuvants with their static surface tensions and the surface tensions measured after 30 milliseconds. The penetration rates were measured at 25°C using 75 ml of surfactant solution and 100 ml of soil in glass cylinders. The cylinders were carefully packed to give the same height of top soil and the time required for the surfactant solution to penetrate the entire column of soil was determined for each of the four adjuvants. As in the wetting experiments, it can be shown that the penetration rate is very dependent on the dynamic surface tension properties of the surfactant and not related to the static surface tensions. Products lowering surface tension rapidly give faster penetration than those which are slower, although the final surface tensions may be very similar. Penetration studies at 0.1% did not show any difference between the products.

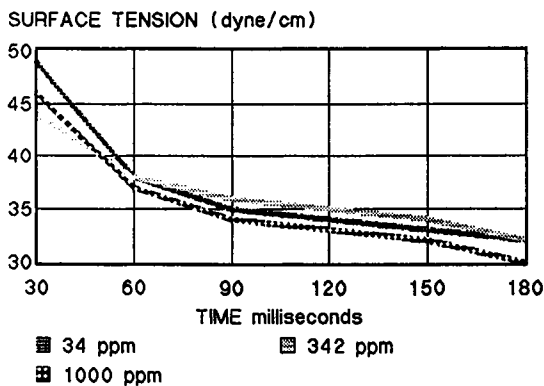


Figure 5. Adsee 801 - Effect of water hardness at 25°C, 0.1% on Dynamic Surface Tension.

Table VI. Soil Penetration Tests
75 ml Adjuvant at 1.0% in 100 ml Soil

Adjuvant	Static (dyne/cm)	30 MSEC (dyne/cm)	Penetrate (sec)
Adsee 801	29.6	27.4	115
Sponto 168D	29.6	35.3	190
Emcol H-3AM	27.5	59.3	230

Both these experiments show that the performance of surfactants is very much related to the dynamic surface properties and that performance may continue to improve well above the CMC where time is a factor in overall effectiveness. The maximum bubble pressure technique gives a means of measuring dynamic surface tensions at and above the CMC and of predicting the time related performance characteristics of surfactant solutions.

CONCLUSIONS

The maximum bubble pressure technique is an accurate and rapid method for the determination of dynamic surface tensions for times of 30 milliseconds and above. For the series of nonionic and anionic spray tank adjuvants investigated, the effect of water hardness is minimal on the surface tension values at various times. The effect of concentration is quite pronounced and there is a good correlation between rapid surface tension lowering and rapid wetting using the Draves wetting test. Dynamic surface tension values can be obtained at concentrations at or above the CMC. The values obtained at these concentrations indicate that time related surface phenomena such as wetting rates are not maximum at the CMC but may continue to increase above the CMC and are related to the rate at which low surface tensions are achieved.

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RECEIVED February 4, 1988

Chapter 14

Determination of Cohesive Energy Density Parameters for Developing Pesticide Formulations

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The art of developing agricultural pesticide formulations requires an understanding of the interactions of solute and solvents, of colloidal particles and surface active agents, and of liquids and emulsifiers. The applications of the concepts of Cohesive Energy Density is of value in increasing one's understanding of these phenomena. Detailed explanations of the Cohesive Energy Density principles and concepts are presented in current literature. When applying these concepts the practitioner will on occasion encounter organic compounds or aqueous solutions for which he will not find accurate CED values. This paper will demonstrate methods which can be used in determining these parameters and data points. The first section includes unpublished data calculated by the late Dr. Allen Beerbower, as well as by this author. The second section deals with a method for the determination of the Cohesive Energy Density values of inorganic aqueous solutions.

The pioneer researchers in the field of "Cohesive Energy Density" (C.E.D.) have been few. In 1986 we lost a dedicated and brilliant worker in C.E.D. research, Dr. Allen A. Beerbower. At his wish this unpublished work concerning the molecular group contributions is presented, to give those pursuing C.E.D. research access to his expanded data base.

This paper is dedicated to Dr. Allen Beerbower and is a result of personal communiques from him. He spent many of his post-retirement years developing the data in Table I.

The principles of C.E.D. were first propounded by Hildebrand (1) during his research into the principles governing solubility. He found that dividing the heat of vaporization by the molar volume of a solvent yielded a meaningful parameter for comparative purposes. If the parameters of two liquids are within + 2 Hildebrands the solvents are miscible. Hansen (2) found that solids could be included and accuracy increased by expanding the bulk parameter from

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a single to a three-parameter system. Again, if the set of three parameters for two substances are close, the materials will dissolve in each other. Beerbower improved the qualitative nature of these parameters. The results were more quantitative than suspected, allowing him to define, numerically, the nature of emulsions and surfactants. Extending Beerbower's method (3) gives a descriptive surfactant selection procedure. The technique was further refined into a surfactant "near neighborhood" optimization procedure as described in "Computer Optimization of Emulsifiers for Pesticide Emulsifiable Concentrates". (4)

Intuition is the strong right arm of the experienced, but fails the novice and those who search for the principles which govern the art of formulation. Those who use C.E.D. as an engineering approximation for chemical formulations are seeking a rational starting point. One of the main difficulties in using this procedure is determining C.E.D. parameters. This paper presents one approach to alleviating some of that difficulty if chemical structures are known.

Determination of C.E.D. Parameters from Chemical Structures

With Table I of molecular/chemical group values, the researcher is able to use a chemical structure to develop a functional set of C.E.D. parameters. The practitioner can then determine approximate values for the heat of vaporization, boiling point, specific gravity, solvency/solubility, emulsifiability, etc.

A problem encountered in developing Table I concerned the evolution of the C.E.D. parameters. The three base variable C.E.D. system was published originally by Hansen (2) and presented a set of parameters for various materials. Hansen's approach was based on the heat of vaporization, solubility of solvents with selected polymers, and physical properties. A second complete set of parameters for a wide variety of solvents was later co-authored by Hansen and Beerbower, published in the "Encyclopedia of Chemical Technology" (9) in 1971. The Hansen and Beerbower method of developing C.E.D. parameters involved a physical-chemical basis and statistically combining the data with expected heats of vaporization. Their 1971 article (as noted in a personal communiqué from Charles Hansen) was a compromise of these two methods. Later, Hoy published a third set of values. All three sets of C.E.D. parameters are included in Allan F.M. Barton's publication. (5) It is this author's experience that these sets of values are accurate enough for most emulsion and emulsifier selection work. Table I was based on all three data sets and yields results on that compromise basis. (Refer to Table I, and accompanying Figures.)

C.E.D. Parameters for Strong Electrolyte Solutions

The second part of this paper develops a mathematical basis for the determination of C.E.D. parameters for aqueous solutions of multivalent, strong electrolytes; and demonstrates the accuracy of the proposed method by evaluating surface tension data for a series of dissimilar ionic specie solutions.

The first step in determining the C.E.D. for strong electrolyte solutions is to determine an average or apparent molar volume. This is approximated using the following procedure:

Assume the hydrated ions are spherical and determine their volume fraction. This is done using the Einstein equation based on viscosity of an electrolyte solution. His equation is expressed as:

$$\phi = (\nu/\nu_0 - 1.0)/2.5 \quad (1)$$

where ϕ is the volume fraction of the hydrated ions in the water solution, ν equals the solution viscosity and ν_0 equals viscosity of water at 20° Centigrade.

If we consider the volume of 1000.0 grams of solution ($1000.0/d_T$) multiplied by the volume fraction of the hydrated ions (ϕ), we obtain the volume occupied by the hydrated ions. Thus the expression is formed:

$$V_I = M_N \times V_{MSW} = (1000.0/d_T) \times \phi \quad (2)$$

where d_T = density at 20/4

V_{MSW} is the average molar volume. The number of moles of the ion species (M_N) is determined directly by a calculation based on the freeze point depression. The usual arrangement of terms is as follows:

$$F_D = K_F \times (1000) \times (G_2/G_1) \times (M_2) \quad (3)$$

where F_D equals the freeze point depression and K_F is a factor, usually 1.86, G_2 equals the weight of solute, G_1 equals the weight of solvent, and M_2 equals molecular weight of material in question.

By a rearrangement of terms and only slight modification of salt addition, we obtain the following expression:

$$G_2/M_2 = M_N = F_D \times G_1 / (K_F \times (1000.0)) = \quad (4)$$

$$(F_D) \times (1000.0 - 10.0 \times P_S) / (K_F) \times 1000.0$$

where P_S is the percent salt in the solution.

Now combine equations 1 and 4 to determine the average molar volume of the hydrated ions:

$$V_{MSW} = (1.0/M_N) \times (M_N) \times (V_{MSW}) \quad (5)$$

The moles of water (N_W) not bound by hydration is calculated directly by this expression:

$$N_W = (1000.0/d_T - M_N \times V_{MSW}) / 18.018 \quad (6)$$

Table I. Molecular Group Contributions for Molecular Volume and Cohesive Energy Parameters

Group	Group Name or Chemical Composition
M_W	Molecular Weight
V	Apparant Molar Volume
VxD	Molar Volume multiplied by C.E.D. Dispersion Parameter
VxP	Molar Volume multiplied by C.E.D. Polarity Parameter
Vx(H ²)	Molar Volume multiplied by C.E.D. Hydrogen Bonding Parameter Squared

(Temperatures assumed to be 25 Degrees Centigrade but not specified)

GROUP	M_W	V	VxD	VxP	Vx(H ²)
-CH ₃	15.038	31.737	205	0	0
-CH ₂ -	14.027	16.572	132	0	0
>CH-	13.019	-1.000	39	0	0
>C<	12.011	-19.200	-34	0	0
=CH ₂	14.027	32.100	197	46	70
=CH-	13.019	12.400	109	34	70
=C<	12.011	-5.700	22	34	70
5/6 Ring	0.000	13.500	93	0	0
Conj - Chain	0.000	-1.700	0	0	275
Cis - Configuration	0.000	0.000	-200	0	0
Conj - Ring	0.000	0.800	21	0	-111
-O-	15.999	3.800	49	196	717
>C=O	28.011	10.545	142	376	478
-OCO-	44.011	18.959	191	239	1672
>PO ₄ -	95.974	28.000	362	489	3106
-CN	26.011	22.400	210	538	597
-NO ₂	45.998	24.000	244	523	358
-NH ₂	16.016	17.930	181	205	1574
-NH-	15.008	4.500	78	103	741
>N-	14.000	-9.000	15	73	179
-N=	14.000	4.000	80	647	860
-CONH-	43.018	16.800	252	621	2926
-CON<	42.010	13.200	147	601	2333
-OH	17.008	10.465	103	244	4778
-COOH	45.018	27.834	259	205	2389
>SiO<	44.085	3.800	130	150	450
-CL	35.453	25.300	205	300	100
-CL Aromatic	35.453	24.000	161	269	38
(-CL) ₂ Adjacent	70.906	51.200	440	538	430
>C=O	28.011	10.000	142	376	478
-F	18.998	18.000	108	265	0
-BR	79.904	29.000	258	300	500
-BR Aromatic	79.904	30.000	269	196	215
(-BR) ₂ Adjacent	159.808	54.000	538	454	1576
-I	126.904	32.200	320	325	1000
-COO- Ester	44.009	8.200	326	250	1250
-COO- Ester Aromatic	44.009	8.200	326	250	800
-O-	15.999	3.600	115	200	1150
-O- Aromatic	15.999	3.800	49	196	717

Table I. Continued

	M_W	V	VxD	VxP	Vx(H ²)
-NH ₂ Amide	15.018	25.100	327	500	2700
-S-	32.064	8.000	222	177	108
Phenyl-	77.107	75.400	733	59	100
Phenyl<	76.099	60.400	645	65	100
-NO ₂ Aromatic	45.998	24.000	244	523	358
-NH- Aromatic	15.008	4.500	78	103	741
>N- Aromatic	14.000	-9.000	15	73	179
>CO ₃	60.008	22.000	313	108	1098
>CO ₃ Ring	60.008	22.000	372	747	462
HCOO- Formate	44.009	32.500	265	121	1577
-CO-O-CO- Anhydride	72.019	30.000	330	538	2365

See Figure 1, which demonstrates the use of Table I and illustrates the accuracies that can be expected.

NO. x Group	M_W	V	VxD	VxP	$Vx(H^2)$
2x(-CH ₃)	2x(15.038)	31.737	205	0	0
6x(-CH ₂ -)	+6x(14.027)	16.572	132	0	0
	<u>114.238</u>	<u>162.906</u>	<u>1202</u>	<u>0</u>	<u>0</u>

For N-Octane Density= M_W/V_W at 20/4, $D=VxD/V_W$, $P=VxP/V_W$, $H=\sqrt{Vx(H^2)}/V_W$

N-Octane	Density	D	P	H
Calculated	.701	7.38	0	0
Reported By:				
(1.) Density as found in "Handbook of Chemistry and Physics 53 Edition" (7)	.703*	---	---	---
(2.) "CRC Handbook of Solubility Parameters and other cohesion parameters" @ 25°C. Hoy (5)	.698	7.5	0	0
(3.) "Encyclopedia of Chemical Technology" @ 25°C. Hansen-Beerbower (9)	.699	7.6	0	0
N-Butane CH ₃ (CH ₂) ₂ CH ₃	.601	6.98	0	0
(1.) Density	.601	---	---	---
(2.) Hoy	.572	6.6	0	0
(3.) Hansen-Beerbower	.573	6.9	0	0
Decane CH ₃ (CH ₂) ₈ CH ₃	.726	7.48	0	0
(1.) Density	.730	---	---	---
(2.) Hoy	.725	7.72	0	0
(3.) Hansen-Beerbower	.726	7.7	0	0
Monochlorobenzene	1.118	8.47	2.9	1.1
(1.) Density	1.106	---	---	---
(2.) Hoy	1.098	8.50	4.5	0.0
(3.) Hansen-Beerbower	1.102	9.3	2.1	1.0
Chloroform	1.342	5.16	6.4	3.5
(1.) Density	1.446	---	---	---
(2.) Hoy	1.477	5.38	6.7	3.1
(3.) Hansen-Beerbower	1.479	8.7	1.5	2.8
1,4 Dioxane	1.192	8.47	5.3	4.4
(1.) Density	1.034	---	---	---
(2.) Hoy	1.028	8.0	4.9	3.4
(3.) Hansen-Beerbower	1.028	9.3	.9	3.6

*Densities standardized at 20/4 degrees Centigrade except N-Butane where the density is standardized at 0/4

As demonstrated, the Beerbower table is a compromise between the earlier Hansen & Beerbower data set and the later Hoy parameters as reported by Barton.

Figure 1. Calculated Molecular Volume and CED Parameters Using Table I and Comparisons with Reported Values.

We are now able to calculate the mole fractions (X_S) of the hydrated salt ions and the remaining water (X_W) in the solution as:

$$X_S = (M_F)/(N_W + M_N); X_W = (N_W)/(N_W + M_N) \quad (7)$$

$$\text{where: } X_S + X_W = 1.0 \quad (8)$$

With these values we can determine an average molar volume for the aqueous salt solution by the expression:

$$V_S = (X_S) \times (V_{MSW}) + (X_W) \times (18.018) \quad (9)$$

where 18.018 is the molar volume of water.

The second step in determining the C.E.D. parameters is to calculate the heat of vaporization for an aqueous system. Since salt in solution normally changes the vapor pressure of the water, this is used as the key to determining a heat of vaporization of the aqueous system. Torquato and Stell's (6) derivation serves as a beginning model for a mixture of benzene and carbazole. This author proposes modifying their equation, to develop the expression:

$$D_H = (V_S/V_W) \times D_{HW} - (K) \times ((V_S/V_W) \times (D_{HW} - (V_S) \times (D_{HS}))) \quad (10)$$

where:

D_H = heat of vaporization of the salt solution (ΔH_V)

V_S = the molar volume of the salt solution

V_W = the molar volume of water

D_{HW} = the heat of vaporization of water (as back calculated from Beerbower's C.E.D. parameters)

K = a calculated equilibrium constant

D_{HS} = a modified Clausius - Clapeyron heat of vaporization value for the salt solution.

D_{HS} is determined using the vapor pressure, at a salt solution temperature equal to or less than boiling, designated as P_1 . Use the steam tables (7) to determine the temperature of water corresponding to pressure P_1 , and label that temperature as T_1 . Next locate the point in the steam table which is next to P_1 , T_1 and use that point as P_2 , T_2 . Then insert these data points directly into the Clausius - Clapeyron equation to give a modified heat of vaporization for salt water.

$$\ln\left(\frac{P_2}{P_1}\right) = \frac{\Delta H_V}{R} \left(\frac{1}{T_1} - \frac{1}{T_2}\right) \quad (11)$$

To change the modified heat of vaporization to the normal value, a constant was introduced to yield $(K \times \Delta H_V) = D_{HS}$.

The equilibrium constant (K) is related to the pressure, temperature, solubility, and ionization of the salt in solution, and can be expressed as:

$$\begin{aligned} \ln(K) = A_0 - A_1/(R) \times (T) + (A_2) \times (\ln(T/R)) + \\ (A_3) \times (T/R) + (A_4)/(2) \times (R) \times (T^2) \end{aligned} \quad (12)$$

Equation 12 was derived by Adamson (8) and can be simplified as:

$$\begin{aligned} K = \text{EXP} (A_0 - A_1/T + (A_2) \times (\ln(T)) + (A_3) \times (T) + \\ (A_4)/(T^2)) \end{aligned} \quad (13)$$

Using Adamson's expression, the heat of vaporization for salt water is:

$$D_H = K \times (D_{HW} - D_{HS}) \quad (14)$$

where D_{HW} is the heat of vaporization of water near the temperature in consideration.

Now that the parameters have been set for the equilibrium constant, we are ready to calculate a set of C.E.D. parameters for the electrolyte solutions.

It was found from the salt data that:

$$K = ((T - T_0)/T)^2 \times 18.018 \times (\text{EXP}(-4.0 \times M)) \quad (15)$$

Equation 15 has only one constant, $T_0 = 273.15$, with T being the average temperature in degrees Kelvin and M equaling the molar concentration.

Equation 14 was combined to form a modified heat of vaporization.

The heat of vaporization value is used to calculate a C.E.D. value for salt water using Beerbower's expression:

$$\delta^2 = (D_H - R \times T)/V_M \quad (16)$$

Adjustment of the heat of vaporization for water is needed so that a ratio of volume to volume basis is maintained. This is accomplished by multiplying the calculated heat of vaporization for water by the ratio of the calculated molar volume of the salt solution, then dividing by the molar volume of water. Thus the value for the heat of vaporization is expressed as:

$$D_X = (D_{HW} - D_{HS}) \times (V_S) \times K \times (V_S/V_W) \quad (17)$$

$$D_H = (D_{HW}) \times (V_S/V_W) - D_X \quad (18)$$

We can now calculate the total solubility parameter value for the salt solution by the expression:

$$\delta^2 = ((D_H) - (R) \times (T))/V_S \quad (19)$$

The Hansen dispersion parameter (δ_D) is calculated with the expression derived by Beerbower using the refractive index value. The published expression is:

$$\delta_D = 4.22 \times (\eta_D^2 - 1.0) + 3.746 \pm .5 \quad (20)$$

(4.32 was used for the solution calculations)

where η_D equals the refractive index at 20°Centigrade.

The calculations give a reasonable data fit when using a slightly modified surface tension expression also derived by Beerbower. (9) (See equation 21)

To determine the polarity (δ_P) and hydrogen bonding value (δ_H), Hansen's equation can be used:

$$\delta_P^2 + \delta_H^2 = \delta^2 - \delta_D^2 \quad (21)$$

The original surface tension equation was:

$$\gamma = (.0715) \times (V_S^{1/3}) \times (\delta_D^2 + .632 \times (\delta_P^2 + \delta_H^2)) \quad (22)$$

and was used successfully for melted metals and fused salts. The modified expression used for salt water solutions is:

$$\gamma = (.0715) \times (V_S^{1/3}) \times (\delta_D^2 + .678 \times (\delta_P^2 + \delta_H^2)) \quad (23)$$

An example of the calculations using the expressions above is seen in Figure 2.

A set of surface tensions has been correlated and an accompanying set of C.E.D. parameters for KOH, KCl, LiCl, NaCl, NaBr, and NaNO₃ were evaluated in 20 different concentrations with an overall error of less than 3.0%. The error was the same using divalent salts such as BaCl₂, H₂SO₄, MgSO₄ and Na₂CO₃.

See Table II for results of surface tension calculations versus reported results.

Conclusion

Application of these additional calculation methods, to determine C.E.D. parameters and data points, allows the formulation chemist to consider the interaction of emulsions, dispersions, solutions and colloids as a more unified system. These C.E.D. parameters have been successfully used in surfactant selections and solubility evaluations to predict interactions and solubility. The D_x factor was found to be minimal in its contribution and can be dropped without a loss in accuracy. That leaves the equation dimensionally correct as well as accurate.

$$\text{KOH } .5\text{M}, 2.75\% \text{ AI}, 1.022 \text{ Sp.Gr.}, \eta_D = 1.3384, \Delta T_F = 1.724$$

$$\eta/\eta_0 = 1.051, \Delta P = 15.0, \gamma @ 2.73\% = 73.95$$

$$P = 760 - 15 = 745.0 \text{ from steam tables @ } P = (743.85, 749.2);$$

$$\Delta H = \frac{.014232806}{.000020201} = 704.5410$$

$$T = (99.4, 99.6)$$

$$\phi = (1.051 - 1.00)/2.5 = .0204$$

$$M = (1.724) \times (1000 - 27.5)/(1.86) \times (1000) = .90139$$

$$MV_S = (1000/1.002) \times (.0204) = 19.96086$$

$$V_S = (1/.90139) \times (19.96086) = 20.3593$$

$$N = (1000/1.022 - 19.96086)/18.02 = 54.2834$$

$$X_{\text{M}} = .90139/(54.2834 + .90139) = .01633$$

$$X_{\text{N}} = 54.2834/(54.2834 + .9039) = .9837$$

$$V_{\text{SS}} = 17.7257 + .3325 = 18.0582$$

$$\Delta H_S = 709.2816 - 704.5410 = 4.7406$$

$$\Delta H_W = (7.6^2 + 7.8^2 + 20.7^2) \times 18.018 + 1.986 \times (298.15) = \\ (547.09) \times (18.018) + 592.1259 = 9857.46762 + 592.1259 = 10449.59352$$

$$\Delta H_{\text{SS}} = 10449.59352 - (4.7406) \times (18.07) = 10449.59352 - 85.74181 \\ = 10363.85171$$

$$\Delta H_{\text{SS}}^1 = 10363.85171 - 592.1259 = 9771.72581$$

$$\delta^2 = 9771.72581/18.018 = 542.3313$$

$$\delta_D = 4.22 (\eta_D^2 - 1) + 4.32 = 4.22 \times (1.3384^2 - 1) + 4.32 = \\ 4.22 (.7913) + 4.32 = 7.6593$$

$$\delta_P^2 + \delta_H^2 = 542.3313 - 58.6656 = 483.6657$$

$$\gamma = (.0715) \times (15.0867)^{1/3} \times (58.6656 + .678 \times (483.6657)) = \\ .0715 \times (2.6236) \times (386.59096) = 72.52$$

$$\% \text{ Error} = 100 - (100) \times (72.52)/73.95 = 1.94\%$$

Figure 2. Calculation of Surface Tensions.

Table II. Comparison of Calculated and Observed Surface Tensions

Salt	Molar	Calculated Surface Tension	Observed Surface Tension
H ₂ SO ₄	0.50	73.7	72.3
	1.00	74.4	72.6
	2.00	75.5	73.4
HClO ₄	0.61	72.8	70.3
	1.01	72.4	70.3
	3.15	70.1	68.7
	7.87	79.1	69.2
KOH	0.50	73.1	74.0
	1.00	73.3	74.9
KCl	0.50	72.5	73.5
	1.00	72.1	74.2
	2.00	71.5	75.6
LiCl	0.50	73.4	72.9
	1.00	73.8	73.6
	2.00	74.3	75.4
	3.00	74.9	77.2
NaCl	0.50	73.1	73.8
	1.00	73.3	74.4
	2.00	73.7	76.1
	3.00	74.5	77.7
	4.00	75.5	80.0
BaCl ₂	0.50	73.7	73.5
MgCl ₂	0.50	74.6	74.0
NaBr	0.50	72.8	73.5
	1.00	73.3	74.1
MgSO ₄	0.50	77.2	73.8
	1.00	85.1	76.8
Na ₂ CO ₃	0.50	75.6	74.1
NaNO ₃	0.50	72.8	73.8
	1.00	72.9	74.0
	2.00	73.5	75.3
	3.00	74.7	76.7

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RECEIVED March 18, 1988

Chapter 15

Effects of Solvent on Microemulsion Phase Behavior

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The formulation of pesticides in the form of emulsifiable concentrates requires selection of a suitable solvent and surfactant package. Thermodynamically stable microemulsions provide an alternative approach to conventional kinetically stable, coarse emulsions. A knowledge of the interactions between surfactant, water and solvent is needed to provide the formulation design basis. We have studied these interactions by measuring phase behavior for several surfactant systems in a large number of model and commercially available solvents. These studies have demonstrated the importance of oil molar volume, aromaticity, chain linearity and the presence of polar groups on the solvent. The hydrophilic/lipophilic (H/L) properties of the surfactant are then adjusted to compensate for variation in solvent properties. Surfactant H/L properties can also be modified to accommodate variations in pesticide molecular structure.

Solvents are used in pesticide formulations to dissolve and deliver the active ingredients to the desired target. The solvents include aromatics (e.g., Aromatic 100), aliphatics (e.g., Isopar L), as well as oxygenates such as MIBK, isophorone, and Exxate 600. The criteria for solvent selection include solvency for the active ingredient, volatility, toxicity including phytotoxicity, cost, and the effect of the solvent upon emulsion stability. Emulsion stability and the ease of dilution are particularly important for delivering active ingredients in the form of emulsifiable

0097-6156/88/0371-0163\$07.75/0

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concentrates. These consist of emulsifiers and active ingredients dissolved in a suitable solvent and are readily dispersed in water forming stable emulsions for ease of delivery to plant surfaces. The solvent, surfactant, and active ingredient all contribute to emulsion stability and concentrate dilutability. Typically, a conventional emulsion system is formulated by using blends of surfactants to adjust hydrophile/lipophile (H/L) characteristics, while holding all other formulation parameters constant. However, other parameters such as solvent type and water hardness or aqueous phase salinity also need to be considered since they affect emulsion stability and concentrate dilutability.

Microemulsification can provide an improved approach to the formulation of active ingredient delivery fluids. The blend of surfactants can be chosen to provide a concentrate which will disperse with minimum energy upon dilution with water to form a thermodynamically stable fluid called a microemulsion. A critical parameter in the selection of the surfactant is its ability to absorb or solubilize water and/or oil. This characteristic can be quantified through phase behavior measurements which define the relative and absolute amount of water and oil held by a surfactant mixture as a homogeneous phase. Many microemulsion phase behavior studies directed at chemically enhanced oil recovery (CEOR) have been described (1-5). Parameters, such as surfactant H/L properties, solvent type and aqueous phase salinity, which affect emulsion stability and concentrate dilutability, also control microemulsion phase behavior. Thus microemulsion phase behavior can be used to provide basic information on the compositional and thermodynamic variables which control emulsion stability and concentrate dilutability.

This report will describe microemulsion phase behavior studies with particular emphasis on the effects of solvent type and surfactant H/L properties. We have found that polar solvents require more hydrophilic surfactants (i.e., higher H/L) than nonpolar solvents. Our data is also consistent with the trend that the higher boiling solvents within a homologous series require more lipophilic surfactants (i.e., lower H/L) (4). The effect of solvent structure on microemulsion phase behavior and surfactant performance, has been studied in terms of solvent molar volume, aromaticity, alkyl chain branching, alkyl chain cyclization, and the type and location of polar functional groups. Using a nonionic/anionic surfactant couple, solvent/water microemulsions for 35 different solvents including paraffins, cycloparaffins, aromatics, esters and ketones were prepared. This phase behavior data should provide a useful tool when formulating new emulsifiable concentrates or reformulating existing concentrates with new solvents.

Microemulsion Fundamentals

Before delineating the results of our studies, the properties of microemulsions and microemulsion phase behavior will be described briefly. Microemulsions are thermodynamically stable, transparent or translucent mixtures of oil, water (which may contain salts), and one or more surfactants or cosurfactants (6). Throughout this paper, oil and solvent will be used interchangeably since most of

the solvents discussed have very limited solubility in water. The clarity of microemulsions results from the very small droplet sizes of the dispersed phase, sizes ranging from 50-1400Å in diameter. Macroemulsions are opaque and have limited stability due to the large droplet sizes of the dispersed phase. Microemulsions form spontaneously with simple mixing as opposed to the high shear required for macroemulsions. They may be water- or oil-continuous and under certain conditions may be bi-continuous. It is generally true that the physical properties of an emulsion, micro or macro, are similar to those of the emulsion component which is the continuous phase. Table I compares the properties of microemulsions to those of macroemulsions.

Microemulsions can exist as a single phase fluid or in equilibrium with excess oil, excess water, both excess oil and water, or in some cases other microemulsion phases. Microemulsion phase behavior and the parameters that influence it have been studied by many laboratories including Exxon's (3,4,7). Microemulsion phase behavior, as referred in this paper, is determined by equilibrating mixtures of surfactants with equal volumes of solvent and aqueous solutions followed by measuring the volumes of microemulsion and excess solvent and/or aqueous phase (1). Measurements are taken as a function of surfactant H/L ratio, temperature, or aqueous and solvent phase compositional parameters. Surfactant H/L ratio as used in this paper refers to the weight ratio of two surfactants, one of which is primarily hydrophilic and the other is lipophilic. Hydrophilic surfactants in this context, partition into water while lipophilic surfactants partition into oil. Relative H/L character of the surfactant mixture is adjusted by changing the weight ratio of the two surfactants.

The equilibrated systems consisting of solvent, water, and surfactants, as first described by Winsor (8), exist as one of four types:

Two phases with the lower microemulsion phase in equilibrium with excess solvent (Winsor Type I).

Two phases with the upper microemulsion phase in equilibrium with excess water (Winsor Type II).

Three phases with the middle microemulsion phase in equilibrium with both excess solvent and water (Winsor Type III).

Single phase when the surfactant concentration is sufficiently high (Winsor Type IV).

Upper (u), middle (m), and lower (l) phase microemulsions exist at relatively low surfactant concentrations and are described in Figure 1. The dashed lines represent the shift in the microemulsion phase boundaries with varying H/L ratio, temperature, or composition. The transition from upper to middle to lower phase microemulsion is called a hydrophilic shift, since it progressively involves the absorption of water and the rejection of solvent. Lower phase microemulsions provide a water like environment. A hydrophilic shift is obtained by increasing the H/L ratio of the emulsifier, increasing the temperature (for sulfonate surfactants), or increasing the alkane number or molar volume of the oil or

TABLE I**Macroemulsions vs. Microemulsions**

<u>Macroemulsions</u>	<u>Microemulsions</u>
Large droplet size	Small droplet size (<1400Å)
Milky white	Translucent or transparent
Kinetically stable	Thermodynamically stable
Low interfacial surface area	High interfacial surface area
High interfacial tension	Low interfacial tension
High mixing energy	Form spontaneously

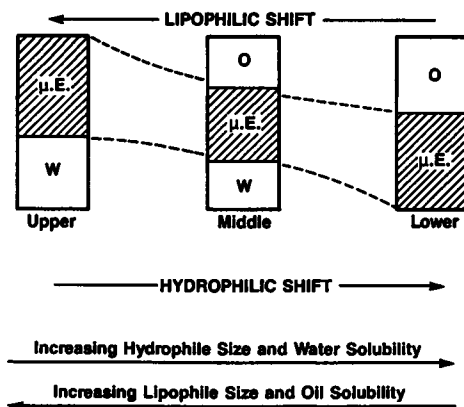


Figure 1. Microemulsion phase behavior scans.

solvent. If one decreases the salinity of the aqueous phase, the surfactant becomes more water soluble which results in a hydrophilic shift. The reverse transition, lower to middle to upper phase microemulsion is called a lipophilic shift and involves the absorption of solvent and the rejection of water. Upper phase microemulsions provide a solvent like environment. A lipophilic shift can be obtained by decreasing the H/L ratio of the surfactants, increasing the salinity of the water, increasing the oil aromaticity, and increasing the temperature (for ethoxylated surfactants). Increasing the salinity of the aqueous phase causes the surfactant to be salted out of the aqueous phase into the organic phase. This translates into a lipophilic shift. Parameters which can cause a hydrophilic shift can be offset by those causing a lipophilic shift. For example, the effects of increasing temperature (ethoxylated surfactants), salinity of the aqueous phase, or oil aromaticity can be offset by increasing the H/L ratio of the surfactant. Also, the effects of increasing oil alkane carbon number or molar volume, and temperature (sulfonated surfactants) can be compensated for by decreasing the H/L ratio of the surfactant. Thus, surfactant composition can be adjusted to account for changes in conditions and oil or solvent composition (2).

Two important concepts have been used to describe the influence of composition and thermodynamic variables on the phase behavior of microemulsions; namely, the idea of balance related to so-called optimal parameters and the measure of surfactant efficiency related to solubilization at balance. Balanced microemulsions occur when water and solvent uptakes by a surfactant are equal as shown in the middle of Figure 1, where the microemulsion is in equilibrium with equal volumes of solvent and aqueous phase. The balanced condition is often called the optimal value of the specific variable, e.g. 'optimal salinity' when salinity is the variable. Optimal salinity can be used to describe the effect of a change in oil composition on the H/L properties of the surfactant. For example, if the optimal salinity for oil A is greater than that of oil B, *ceteris parabis*, then the surfactants are said to behave more hydrophilic (i.e. exhibit a hydrophilic shift) in oil A relative to oil B. Recall that a hydrophilic shift required an increase in salinity to restore balance. While optimal salinity can be used to characterize the relative H/L properties of the surfactant for a given water and solvent, it does not address the issue of surfactant efficiency. The volume of the microemulsion phase at balance relative to the excess solvent and aqueous phase volumes depends upon surfactant concentration and efficiency. The larger the middle phase volume at balance for a given concentration of surfactant, the greater the solvent and water uptake by the surfactant. Thus high oil and water uptakes, defined as the volume of solvent and water held in the microemulsion phase by a given volume of surfactant, signify high surfactant efficiency. Shinoda and Friberg (9) have shown that increasing the hydrophile and lipophile groups on nonionic surfactants while keeping the phase inversion temperature, PIT, the same results in an increase in solubilizing power. The PIT for nonionic surfactants (ethoxylates) is the balance condition when temperature is the variable. Solvent and water uptake at balance

also depend upon surfactant type as well as surfactant H/L ratio, salinity, alkane carbon number, oil aromaticity, and temperature (4).

In the previous phase behavior discussion, the effect of oil or solvent on the microemulsion phase behavior was described by two parameters, alkane carbon number (10) or oil molar volume (4) and oil aromaticity (2). These parameters have been widely used in many phase behavior studies, particularly those relating to enhanced oil recovery. However, these parameters may not account for all the changes in solvent or oil structure that may influence microemulsion phase behavior. These structural changes include alkyl chain branching, alkyl chain cyclization, and the presence and position of various hydrophilic functional groups in the solvent. For example, as will be described later, n-heptane and 2,3-dimethylpentane are both paraffinic and have similar molar volumes, but the alkyl chain branching of the latter imparts more lipophilic character to the anionic/nonionic surfactant blend used to prepare the microemulsion. What follows is a description of the results of our phase behavior studies in which we systematically examined the effect of solvent structure and composition on microemulsion phase behavior.

EXPERIMENTAL

Surfactant systems. The nonionic/anionic surfactant couple used in these studies consisted of an equal weight mixture of dinonylphenol ethoxylate and the monoethanolamine salt of a branched C₁₂- α -xylyl sulfonic acid (C₁₂*XS-MEA). These surfactants are shown in Figure 2. Three different dinonylphenol ethoxylates, having different degrees of ethoxylation, were used depending upon the particular solvent studied. These were Igepal DM-530 containing 9 EO groups, Igepal DM-710 containing 14-15 EO groups, and Igepal DM-730 containing 24 EO groups. The H/L properties of the surfactant blend could be varied in a controlled manner by either changing the degree of ethoxylation on the nonionic component or by changing the weight ratio of the nonionic to anionic components. In this study we have arbitrarily fixed the weight ratio of the two surfactants and varied the degree of ethoxylation in order to explore the effects of H/L on microemulsion phase behavior.

Solvents. The solvents studied are commercially available solvents and pure model compounds. As shown in table II, the solvents cover a broad range of molar volumes, degree of branching, alkyl chain cyclization, aromaticity, as well as types and positions of functional groups. Norpar, Isopar, Exxol, Aromatic and Exxate describe normal paraffins, branched paraffins, alkyl cycloparaffins, alkyl aromatics, and alkyl esters respectively. The former are tradenames of solvents supplied by Exxon Chemical. In addition several pure hydrocarbons were included. Each group of solvents consists of an homologous series with increasing hydrocarbon molecular weight from top to bottom. The solvents embrace the major structural parameters that we wish to understand in terms of microemulsion phase behavior which is controlled by

TABLE II
Solvents Evaluated in Microemulsion Phase Behavior Studies

	<u>Compound</u>	<u>Molar Volume</u>
<u>n-Paraffins</u>	n-heptane	146
	Norpar 10	190
	Norpar 12	217
	Norpar 13	245
	Norpar 15	280
<u>Branched Paraffins</u>	2,3-Dimethylpentane	144
	Isopar C	162
	Isopar E	171
	Isopar G	200
	Isopar H	211
	Isopar K	216
	Isopar L	223
	Isopar M	244
	Isopar V	273
<u>Alkyl Cycloparaffins</u>	Exxol D40	183
	Exxol D60	205
	Exxol D80	224
	Exxol D100	240
<u>Alkyl Aromatics</u>	Toluene	108
	Ethylbenzene	123
	n-Butylbenzene	156
	Aromatic 100	139
	Aromatic 150	151
	Aromatic 200	174
<u>Esters</u>	Exxate® 600	165
	Exxate® 700	181
	Exxate® 800	197
	Exxate® 900	213
	Exxate® 1000	229
	Exxate® 1300	277
<u>Ketones</u>	Methyl Isobutyl Ketone	125
	2-Heptanone	141
	4-Heptanone	140
	Diisopropyl Ketone	141
	Diisobutyl Ketone	168

varying the H/L properties of the surfactants, salinity of the aqueous phase, and solvent composition.

Phase behavior. Phase volumes were measured on mixtures containing 2 g/dl of the surfactant couple in 1/1 (v/v) solvent/aqueous phase. The phase volumes were determined as a function of aqueous phase salinity on phase equilibrated mixtures at 24°C. Water and oil uptakes (solubilizations) were calculated from phase volumes assuming all the surfactant resides in the microemulsion phase (1). Water (V_w/V_s) and oil (V_o/V_s) uptakes are defined as the volume of water or oil held in the microemulsion per unit volume of surfactant. Optimal salinity is determined as the salinity at which water and oil uptakes are equal (1). Optimal salinity depends on the H/L properties of the surfactant as well as solvent structure. For a fixed solvent, optimal salinity provides a measure of the H/L properties of the surfactant at balance while the uptakes at balance provide a measure of the efficiency of the surfactant. In this paper we will first describe the effects of solvent structure on optimal salinity and uptake at optimal salinity. We will then relate optimal salinity to the more familiar HLB scale (13,15).

RESULTS AND DISCUSSION

Previous phase behavior studies have been done with paraffinic and isoparaffinic solvents in microemulsions prepared with nonionic/anionic surfactant couples (11). A similar approach using a nonionic/anionic surfactant couple has been followed here for a number of paraffinic, cycloparaffinic, aromatic, ester, and ketone solvents. The phase behavior of the surfactant systems was studied as a function of solvent structure and oil molar volume (OMV). Following the presentation of this phase behavior data in terms of an optimal salinity scale and uptake at optimal salinity, we will provide an approach for correlating this data with the conventional HLB scale.

To evaluate optimal salinity and uptake, we measured equilibrated phase volumes as a function of salinity. Figure 3 gives a typical result with Exxate 700 as the solvent phase and 1/1 C₁₂* XS-MEA/Igepal DM-710 as the surfactant. Optimal salinity occurred at 1.38 wt % NaCl with an upper phase boundary (UPB) at 2.0 wt % NaCl and a lower phase boundary (LPB) at 0.85 wt % NaCl. An uptake at optimal salinity of 5.4 was observed. Similar phase plots were derived for the other solvents studied. The data is summarized in Tables IIIA and IIIB and Figure 4.

General trends with oil structure

A number of points can be made from the data in Tables IIIA and IIIB and Figure 4. Microemulsion phase behavior depends upon solvent structural parameters such as oil molar volume (OMV) and oil aromaticity. Other parameters such as alkyl chain branching, alkyl chain cyclization, and the presence and position of functional groups also influence phase behavior. Figure 4 shows that the optimal salinity increases with increasing OMV within a homologous series of solvents, e.g., Isopar solvents, Exxsol D solvents, Exxate solvents, and alkylbenzenes. The alkylbenzenes,

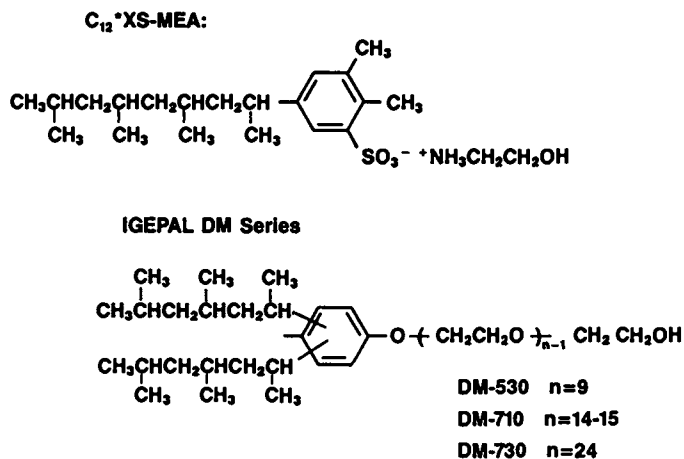


Figure 2. Surfactant systems and structures.

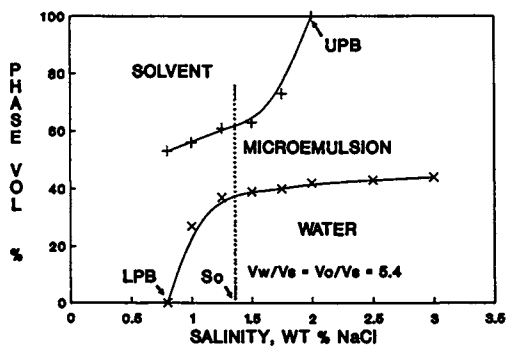
Figure 3. Microemulsion phase volumes as a function of salinity for DM 710/C₁₂Xs-MEA:1/1; Exxate 700/water:1/1; Cs=2 g/dl; T = 24 C.

TABLE III^A Microemulsion Phase Behavior Data
for C₁₂*XS-MEA Igepal DM-530

<u>Solvent</u>	<u>Solvent Class</u>	<u>Molar Volume</u>	<u>LPB¹</u>	<u>Opt. Sal</u>	<u>UPB²</u>	<u>Uptake at Opt. Sal.</u>
Isopar E	Paraffinic	171	1.77	2.09	2.70	9.6
Isopar C	Paraffinic	162	1.98	2.35	3.24	8.8
Isopar G	Paraffinic	200	2.53	3.12	4.02	6.4
Isopar H	Paraffinic	211	2.53	3.14	4.23	5.5
Isopar K	Paraffinic	216	2.81	3.32	4.40	5.4
Isopar L	Paraffinic	223	2.97	3.52	4.39	5.2
Isopar M	Paraffinic	244	3.04	3.73	4.90	4.1
Isopar V	Paraffinic	273	3.30	4.47	5.81	3.5
Norpar 10	Paraffinic	190	2.52	3.02	3.65	5.9
Norpar 12	Paraffinic	217	3.24	4.05	5.32	5.0
Norpar 13	Paraffinic	245	3.72	4.65	6.99	4.0
Norpar 15	Paraffinic	280	4.0	6.9	9.06	2.1
Exxsol D40	Naphthenic	183	2.07	2.61	3.49	8.2
Exxsol D60	Naphthenic	205	2.68	3.10	4.10	7.0
Exxsol D80	Naphthenic	224	2.57	3.33	5.28	6.5
Exxsol D100	Naphthenic	240	2.98	4.05	5.5	5.8
Aromatic 100	Aromatic	139	0.50	0.57	0.63	11.5
Aromatic 150	Aromatic	151	0.60	0.67	0.76	11.8
Aromatic 200	Aromatic	174	0.61	0.68	0.78	9.0
Exxate 600	Ester	165	0.47	0.56	0.67	7.3
Diisobutyl Ketone	Ketone	168	0.93	1.14	1.47	5.9

¹ LPB - Lower Phase Transition

² UPB - Upper Phase Transition

TABLE IIIB Microemulsion Phase Behavior Data
for C₁₂*XS-MEA Igepal DM-730

<u>Solvent</u>	<u>Solvent Class</u>	<u>Molar Volume</u>	<u>LPB</u>	<u>Opt. Sal.</u>	<u>UPB</u>	<u>Uptake at Opt. Sal.</u>
Isopar C	Paraffinic	162	9.1	13.6	20.5	2.75
Heptane	Paraffinic	146.5		14.2		9.07
Decane	Paraffinic	194.9		17.7		4.94
Exxsol D40	Naphthenic	183	10.7	16.0	20.0	3.0
Aromatic 100	Aromatic	339	3.49	4.32	5.35	8.6
Toluene	Aromatic	106		1.60		12.72
n-Butyl Benzene	Aromatic	156		3.5		11.4
Exxate 600	Ester	165	2.67	3.85	5.20	6.2
Exxate 1300	Ester	277	4.22	8.4	12.6	5.6

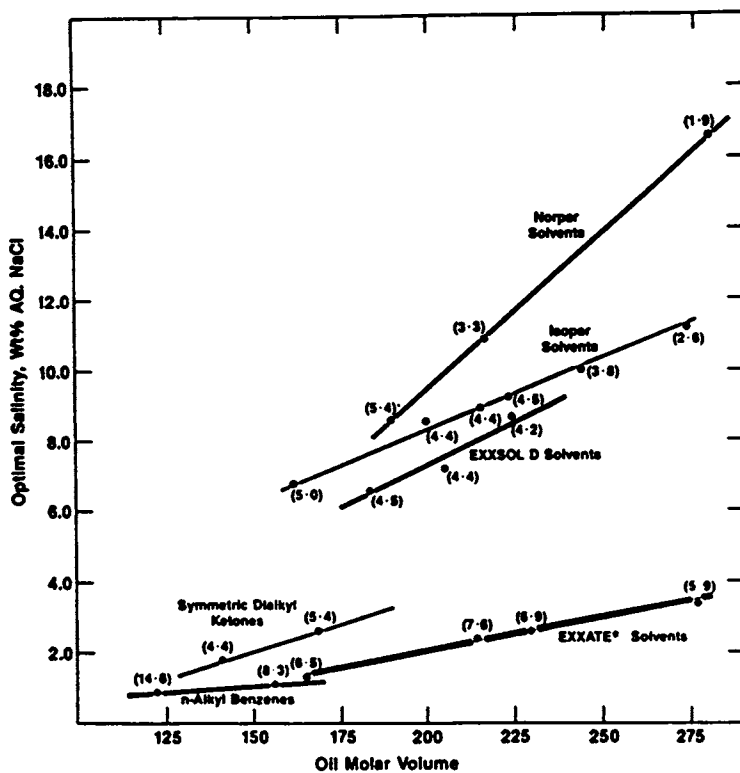


Figure 4. Effect of solvent structure on microemulsion phase behavior for Igepal DM 710/C₁₂XS-MEA:1/1; solvent/water:1/1; Cs=2 g/dl; T = 24 C.

acetates and ketones show a similar optimal salinity dependence on OMV and optimal salinities which are significantly lower than those of normal paraffins of comparable OMV. Thus, the surfactants are more lipophilic in these solvents than in alkanes of a similar OMV. At a constant OMV, optimal salinity decreases (or surfactants become increasingly more lipophilic) in the following order: n-paraffins (Norpar solvents) < branched paraffins (Isopar[®] solvents) < cyclic paraffins, alkylcycloparaffins (Exxsol solvents) < ketones \leq esters (Exxate solvents \approx alkylbenzenes (Aromatic solvents)). Figure 4 also gives uptake at optimal salinity (numbers in parentheses) as a function of OMV. In general, uptake decreases with increasing OMV within an homologous series. Those solvents imparting lower optimal salinity to the surfactant, e.g. Exxates and n-alkylbenzenes, also tend to increase surfactant efficiency (higher uptakes).

Chain branching. At a constant OMV, a surfactant behaves more lipophilic in a branched paraffin than in a n-paraffin. This is shown by comparison of the branched Isopar[®] solvents with the linear Norpar solvents in Figure 4. Increased surfactant lipophilicity with branching in the oil is demonstrated more clearly with the model compounds heptane and 2,3-dimethylpentane which have similar OMV, but optimal salinities of 6.0% NaCl and 4.5% NaCl respectively (Table IV). One way to view this result is in terms of the solubility of the surfactant in the oil. The solubility of this surfactant is greater in a branched hydrocarbon than in a linear hydrocarbon and hence less salt is required to obtain comparable water-oil partitioning.

Cyclic groups. At constant OMV the presence of a cyclic group in a paraffin also results in the surfactant behaving more lipophilic. This can be shown by comparing Exxsol D solvents (ca. 50% cyclic paraffins and 50% acyclic paraffins) to Norpar solvents or Isopar solvents. Again the effect is even more evident with the model compounds, e.g., hexane vs. methyl cyclohexane, which have optimal salinities of 4.7% NaCl and 2.7% NaCl, respectively (see Table V). Recall that a reduction in optimal salinity compensates for a lipophilic shift in surfactant phase behavior.

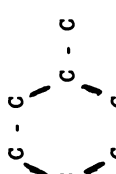
Polar Groups. A lipophilic shift in the surfactant can be obtained when a hydrophilic functional group such as a carbonyl (ketone) or carboxyl (ester) group is introduced into a paraffinic solvent at a constant OMV. Compare the data for Exxate 900 and Isopar K which have similar OMV (see Table VI). The large shift in optimal salinity, 8.9 to 2.4 on going from Isopar K to Exxate 900 indicates that the surfactant behaves more lipophilic in the Exxate 900 than Isopar K. In addition, the increased uptake of Exxate 900 indicates that it interacts more strongly with the surfactant than does Isopar K. Unlike paraffins, alkyl chain branching in esters and ketones has little or no effect on the observed optimal salinity. However, moving the functional group of the ketone or ester from the end to the middle of the molecule at constant OMV increases the optimal salinity, thus imparting less lipophilicity to the surfactant. See the data in Table VII for comparison.

TABLE IV
 Branching of Alkyl Groups Causes
 Lipophilic Shift in Paraffin/Water Microemulsions

<u>Solvent</u>	<u>Structure</u>	<u>Molar Volume</u>	<u>Opt. Salinity</u>	<u>Uptake @ Opt. Salinity</u>
n-Heptane	C-C-C-C-C-C	146	6.0	6.0
2,3-Dimethyl Pentane	C C C-C-C-C-C	144	4.5	7.2

1/1 C₁₂* XS-MEA/Igepal DM-710; 1/1 Paraffin/H₂O; C_S = 2 g/dl; T = 22°C

TABLE V
 Cyclization of Alkyl Group Causes
 Lipophilic Shift in Paraffin/Water Microemulsions

<u>Solvent</u>	<u>Structure</u>	<u>Molar Volume</u>	<u>Opt. Salinity</u>	<u>Uptake @ Opt. Salinity</u>
Hexane	C-C-C-C-C-C	130	4.7	6.1
Methyl Cyclohexane		127.5	2.67	10.0

1/1 Solvent/H₂O; 1/1 C₁₂* XS-MEA/Igepal DM-710; C_S = 2 g/dl; T = 22°C

TABLE VI

Microemulsion Phase Behavior Affected by Presence
of Hydrophilic Functional Group in Solvent(1)

Solvent	Functional Group	Molar Volume	Opt. Salinity	Uptake @ Opt. Salinity
Isopar K	--	216	8.9	4.4
Exxate® 900	$\begin{array}{c} \text{O} \\ \\ \text{- C - O -} \end{array}$	213	2.4	7.6

(1) 1/1 Solvent/H₂O; 1/1 C₁₂* XS-MEA/Igepal DM-710; C_S = 2 g/dl; T = 22°C

TABLE VII
Phase Behavior Depends On Location of
Functional Group and Branching of Alkyl Groups

Solvent	Structure	Mogas Volume	Opt. Salinity	Uptake @ Opt. Salinity
2-Heptanone	$\begin{array}{c} \text{O} \\ \\ \text{C-C-C-C-C-C-C} \end{array}$	141	0.88	5.2
4-Heptanone	$\begin{array}{c} \text{O} \\ \\ \text{C-C-C-C-C-C-C} \end{array}$	140	1.73	4.5
2,4-Dimethyl-3-Pentanone	$\begin{array}{c} \text{O} \\ \\ \text{C-C-C-C-C} \\ \quad \\ \text{C} \quad \text{C} \end{array}$	141	1.78	4.4

1/1 Solvent/H₂O; 1/1 C₁₂* XS-MEA/Igepal DM-710; C_S = 2 g/dl; T = 22°C

The data in Table III and Figure 4 show that uptakes at balance generally decrease with increasing OMV within a homologous series of solvents. This is particularly true with the homologous series of paraffins and alkylbenzenes. However, within the homologous series of esters and ketones, there appears some anomalous behavior with solvents having lower OMV, such as diisopropylketone and Exxate 600. These anomalies will be addressed shortly. In general, alkylbenzenes, cyclic paraffins, alkyl cycloparaffins, and esters exhibit higher uptakes than the acyclic paraffins, indicating that they interact more strongly than the acyclic paraffins with the surfactants studied. At a constant OMV alkyl chain branching has little effect on the uptake at balance as does the position of the functional groups in the esters and ketones.

As mentioned above, the lower esters and ketones appear to exhibit anomalous behavior with respect to the trends in uptakes with respect to OMV displayed by the paraffins and alkylbenzenes reported both herein and by other laboratories (4). One plausible explanation for the observed anomalies could be due to the presence of the hydrophilic functional groups in these solvents. These functional groups can allow the solvent to interact not only with the lipophilic portion of the surfactant but also the hydrophilic portion of the surfactant and the aqueous phase as well. Alkanes and alkylbenzenes, having no hydrophilic functionality, can be assumed to have little or no interaction with the hydrophilic portion of the surfactant or the aqueous phase.

Microemulsion phase behavior studies have been done with paraffins and alkylbenzenes in which a small amount of a polar solvent, typically alcohols, have been added to the oil/water/surfactant system(1,4,7,12). The alcohols used in these studies, such as various butanols and pentanols, are primarily oil-soluble and thus partition into the solvent phase. Thus adding an alcohol is qualitatively like adding a polar group to the solvent. The only difference is that with the paraffin/alcohol system the added polar group is on a separate molecular species while with the esters or ketones it is present in the same molecule. The alcohol generally decreases the uptakes at balance for the given hydrocarbon; with the effect being more pronounced with increased alcohol concentration. By analogy we expect a similar decrease in uptake as the polarity of the solvent is increased. As the molecular weight of ester or ketone decreases, the weight fraction of the polar group increases. In view of the observation that the uptakes decrease as the fraction of alcohol increases, we expect and observe that the uptakes decrease as the ester or ketone molecular weight (or OMV) decreases. This is true at least for low OMV esters and ketones. For the higher OMV esters and ketones the effect of the large hydrocarbon moiety dominates the effect of the hydrophilic functional group and the normal trend of increasing uptakes with decreasing OMV is observed.

One last item worth noting is that for the compounds studied, decreasing the H/L of the surfactant blend by going from Igepal® DM-730 to Igepal DM-710 to Igepal DM-530 decreases the optimal salinity and increases the uptakes at balance. This is illustrated in Table VIII.

TABLE VIII

Lipophilic Shift in Surfactant Blend
Increases Uptakes at Optimal Salinity

Solvent	Structure	Opt. Salinity	Uptake @ Opt. Salinity
Isopar C	1/1 C12 * XS-MEA/Igepal DM-530	2.35	8.8
	1/1 C12 * XS-MEA/Igepal DM-710	6.8	5.0
	1/1 C12 * XS-MEA/Igepal DM-730	13.6	2.8
Exxsol D40	1/1 C12 * XS-MEA/Igepal DM-530	2.61	8.2
	1/1 C12 * XS-MEA/Igepal DM-710	6.6	4.5
	1/1 C12 * XS-MEA/Igepal DM-730	16.0	3.0
Exxate® 600	1/1 C12 * XS-MEA/Igepal DM-530	0.56	7.3
	1/1 C12 * XS-MEA/Igepal DM-710	1.35	6.5
	1/1 C12 * XS-MEA/Igepal DM-730	3.85	6.2

In summary, the results obtained with the anionic/nonionic surfactant blend are consistent with data developed previously for n-alkanes and alkylbenzenes and with data reported in the literature(4). However, we have demonstrated that microemulsion phase behavior depends on a number of structural parameters in addition to the alkane carbon number of OMV and oil aromaticity previously used to describe the effect of oils on phase behavior. We have shown that alkyl chain branching, alkyl chain cyclization, and the presence and position of hydrophilic functional groups in the solvents profoundly influence the observed phase behavior.

Surfactant HLB

Up to now, the effect of solvent structure on microemulsion phase behavior has been expressed in terms of aqueous phase salinity, i.e., wt % aq. NaCl. The aqueous phase salinity is used to adjust the hydrophile/lipophile character of the surfactant couple with an increase in salinity resulting in a decrease in the H/L character of the surfactant. The phase behavior data in Table III and Figure 4 expressed in terms of aqueous phase salinity can be translated from a salinity scale to the more familiar HLB scale (13,15). HLB's are generally calculated using a weight average blending rule for surfactant mixtures (13). The HLB values for the Igepal DM series of surfactants are proportional to the weight fraction of ethylene oxide (EO) in the surfactant molecule and listed in McCutcheon's (14). Using a weight average blending rule for surfactant mixtures, HLB values for the various surfactant blends studied were calculated by assuming various HLB values for the monoethanolamine salt of dodecylxylene sulfonic acid. A linear relationship was found between these HLB values and the measured optimal salinity when the assumed HLB for the anionic surfactant was $9.7 \pm .2$. Based on an HLB of 11.7 for salts of dodecylbenzene sulfonic acid (14), this value seems reasonable since replacement of the benzene group with xylene should make the surfactant more lipophilic resulting in a lower HLB. In addition it should be realized that HLB's are normally evaluated in mineral oil (e.g. Nujol which is a paraffinic white oil) (13). We used optimal salinity data generated in decane and its equivalent commercial solvent, Norpar 10 as a white oil analog with a somewhat lower OMV. These differences would also result in slightly higher values for the HLB. The HLB values used in all subsequent calculations and correlations are listed in the following table.

The HLB's for the surfactant couples listed were then plotted against the optimal salinity for a given solvent. Examples of such plots are given in Figure 5. Note that each solvent has its own HLB vs. optimal salinity plot. For a given solvent homologous series, plots for the higher molar volume members lie below the plots for the lower molar volume homologs e.g. the HLB required for Norpar 15 is less than that for Norpar 12 at the same salinity. This is consistent with the previously mentioned fact that an increase in oil molar volume results in a hydrophilic shift which must be compensated for by a decrease in HLB to restore balance. This is also consistent with the concept of HLB requirement of the oil which is a basic part of the HLB system (15).

HLB's¹ for C₁₂*XS-MEA/Igepal DM Blends

<u>Surfactant(s)</u>	<u>HLB</u>
C ₁₂ *XS-MEA	9.7
Igepal DM 530	10.6
Igepal DM 710	13.0
Igepal DM 730	15.1
C ₁₂ *XS-MEA/DM530 = 1/1	10.15
C ₁₂ *XS-MEA/DM710 = 1/1	11.35
C ₁₂ *XS-MEA/DM730 = 1/1	12.40

¹ HLB of Blend = \sum wt. fract. x HLB of individual surfactants

For a given solvent homologous series at fixed optimal salinity, HLB vs. molar volume can be determined from the correlations given in Figure 5. Strictly speaking, the HLB scale is defined only at zero salinity. Since the plots of Figure 5 exhibit too much curvature at low salinity making extrapolation to zero salinity inaccurate, we decided to compare HLB's vs. solvent molar volume at higher salinity, for example 2% NaCl. At an optimal salinity of 2% NaCl, HLB values for the various oils of known molar volume can be obtained from the correlations given in Figure 5. The HLB's at this chosen optimal salinity can then be correlated with the molar volumes of the various oils as shown in Figure 6. From this figure and the molar volumes of the various oils given in Table II, we can read the HLB required for a given oil. Table IX gives the oil molar volume and surfactant HLB required to form a balanced microemulsion at an optimal salinity of 2% NaCl. Becher (15) discussed the HLB requirement of the oil. The values cited for aromatic and paraffinic mineral oils (p. 249) are similar to those found for the Aromatics and Isopars listed in Table IX. By using these correlations between optimal salinity, oil molar volume, and surfactant HLB, one can describe the effects of oil composition and structure on microemulsion phase behavior in terms of HLB rather than optimal salinity. The identical conclusions

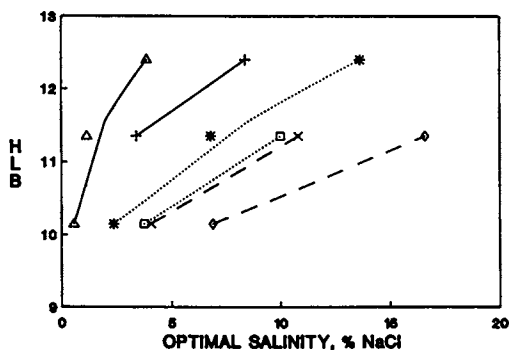


Figure 5. HLB: Optimal salinity correlation for Igepal DM/C₁₂XS-MEA blends; Cs = 2 g/dL; T = 24 °C; Δ, Exxate 600; +, Exxate 1300; *, Isopar C; □, Isopar M; ×, Norpar 12; and ◇, Norpar 15.

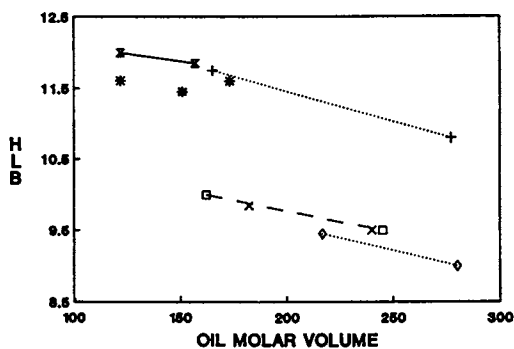


Figure 6. HLB: Oil molar volume correlation. X, alkyl benzenes; +, Exxates; *, aromatic series; □, Isopars; ×, Exxol D series; and ◇, Norpars.

TABLE IX

Microemulsion Data for Selected Solvents

<u>Class</u>	<u>Molar Vol.</u>	<u>Required HLB</u>
Toluene	106	12.15
Aromatic 150	151	11.45
Isopar C	162	10.0
Isopar K	216	9.70
Isopar L	223	9.65
Isopar M	244	9.50
Isopar V	273	9.35
Exxate 600	165	11.75
Exxate 900	213	11.35

1/1 Igepal DM Series/C₁₂XS-MEA; 2 g/dl

Solvent/Water = 1/1; T = 22 C, 2% NaCl

regarding the effects of solvent structure on the HLB requirements for a balanced microemulsion are obtained from this data and from the data expressed in terms of aqueous phase salinity.

Emulsion Stability and Concentrate Dilutability

The parameters that control microemulsion phase behavior also influence emulsion stability and concentrate dilutability. In general, conditions leading to higher uptakes at balance also result in more stable emulsions and more readily dilutable concentrates. Graciaa et al (7) report that in emulsion systems containing no alcohol or salt "the absolute stability is considerably enhanced over systems containing alcohol and salt." We have already pointed out that salt and alcohol lead to lower uptakes. Therefore, in view of Graciaa et al(7), lower uptakes correlate with reduced stability. Likewise adjusting H/L ratio to the lower phase region near balance leads to more stable O/W emulsions requiring very little mixing energy (7). With regard to concentrate dilutability, it is well known (1,10) that higher uptakes at balance lead to reduced ultralow interfacial tension (IFT) between oil and water. This lower IFT should result in easier mixing of solvent and aqueous phase and, hence, improved dilutability. Thus, solvent structure which affects surfactant H/L ratio will also affect emulsion stability and concentrate dilutability in the same manner as microemulsion phase behavior described above.

Now that we understand the effects of solvent structure on microemulsion phase behavior, and therefore emulsion stability and concentrate dilutability, how can the formulator use the data developed herein? We feel the data is particularly useful when one is reformulating from one solvent to another. By referring to the data in Tables III and IX and Figures 4 and 6, one will know qualitatively and semi-quantitatively how to change the surfactant HLB to maintain emulsion stability and concentrate dilutability. This data should save considerable time when reformulating. If one wishes to formulate an emulsion using a solvent not specifically listed in the data, one can approximate the relative surfactant HLB required for the solvent from the data as long as one knows its structure and molar volume. Perhaps the use of the phase behavior data developed herein is best illustrated by a few examples. Suppose one is using the C₁₂* XS-MEA/Igepal DM710 surfactant couple to microemulsify an active ingredient dissolved in toluene into water. If one desires to simply replace the toluene with Aromatic 150, then what changes have to be made in surfactant HLB? Here we have increased the molar volume of an aromatic solvent as well as changed the homologous series and according to the data in Table IX and Figure 6, a slight decrease in surfactant HLB may be required to maintain emulsion stability and concentrate dilutability. Recall that these properties are linked to microemulsion phase behavior (7). This can be achieved by either increasing the salinity of the aqueous phase or by decreasing the HLB of the surfactant couple, in this case by replacing some of the Igepal DM 710 with DM 530.

As another example, one wants to replace the Isopar V currently used as a carrier solvent in a pesticide emulsifiable

concentrate with the more volatile Isopar L. This involves only a decrease in molar volume within a homologous series of solvents. The decrease in molar volume upon going from Isopar V to Isopar L will require an increased surfactant HLB, as shown in Table IX and Figures 4 and 6. This can be achieved either by decreasing the aqueous phase salinity or by replacing some of the Igepal DM 710 in the C₁₂*XS-MEA/Igepal DM 710 surfactant blend with the more hydrophilic Igepal[®] DM 730. Note that the influence of molar volume on the surfactant HLB required to emulsify solvents is much more predominant with paraffinic and cycloparaffinic solvents than with aromatics, esters, and ketones.

The last example of using the microemulsion phase behavior to reformulate an emulsion upon changing the solvent involves a change in molar volume and solvent structure. The isoparaffinic Isopar M (MV = 244) is replaced with the Exxate 600 (MV = 165). The decrease in molar volume will require a more hydrophilic surfactant. Also, the change in structure upon going from branched paraffin to an ester will require an additional increase in HLB of the surfactant couple. This can be obtained as described above with the Isopar solvents.

In all the above cases, no specific numbers were put upon the magnitude of the change in HLB required as one changed solvents in a microemulsion or macroemulsion. This is because the exact value will depend upon a number of formulation parameters including the amount of solvent, the amount of water, the amount and type of surfactant, and the amount and type of active ingredient. Recall that data presented herein are based upon formulations with the following parameters: 1/1 (v/v) mixtures of solvent/water emulsified with 2 vol % of 1/1 C₁₂*XS-MEA/Igepal DM surfactants. No active ingredient is present. However, in spite of this limitation, the data relating solvent structure to microemulsion phase behavior will be qualitatively and semi-quantitatively correct regardless of the specifics of the formulation. For solvents of equivalent molar volume, the HLB of the surfactants required to emulsify the solvents in water will increase in the following order: n-paraffins (Norpar) < branched paraffins (Isopar[®]) < cyclic paraffins (Exxsol) < esters (Exxate) ≈ ketones ≤ aromatics (Aromatics). Also within a homologous series of solvents, those with a greater molar volume, will require a more lipophilic surfactant. This trend is more pronounced with paraffinic solvents than with aromatics, esters, or ketones.

Note that we have not addressed the role that the active ingredient plays in the phase behavior of a pesticide formulation. The principle reason for this is that we are not a pesticide manufacturer and do not have the laboratories equipped to handle most actives safely. Certainly, the active will contribute to the microemulsion phase behavior but to what degree will depend upon the concentration and structure of the particular active. Most actives, such as triazines and phenolics, have considerable polar character and should interact with the aqueous phase and the polar portion of the surfactant molecule. This should lead to phase behavior similar to that noted for systems with added alcohols and the polar aromatic and ester solvents. Thus, an increase in surfactant HLB would be required to form a stable emulsion when actives are present. The magnitude of this shift is dependent upon

the active, its concentration, and the other formulation variables including the solvent and water composition.

The microemulsion phase behavior data that we have presented with solvent/water microemulsions prepared with the C₁₂*XS-MEA/Igepal DM surfactant couple, shows the effect of solvent structure on phase behavior to be more complicated than previously thought. Prior to this work most descriptions depended upon two solvent parameters, alkane carbon number or molar volume, and the aromaticity. We have demonstrated that alkyl chain branching, allyl chain cyclization, and the presence and position of hydrophilic functional groups in the solvents profoundly influence the observed phase behavior. The observed trends are that, within a homologous series of solvents, when oil molar volume increases, either the salinity of the aqueous phase must increase or the HLB of the surfactant must decrease to maintain the condition of balance. At constant solvent molar volume, the surfactant HLB must increase to maintain balance when the solvent structure changes as follows: n-paraffin < branched paraffin < cyclic paraffin < ester ≤ aromatic. We believe these trends are general enough to be translated to other microemulsion formulations, regardless of the surfactants and other additives within the formulations. This should even hold true for macroemulsions since microemulsion phase behavior, emulsion stability and concentrate dilutability are controlled by the same formulation parameters. We feel that the phase behavior data described herein will provide a valuable framework with which the formulator can efficiently reformulate existing products with new solvents as well as prepare new formulations.

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RECEIVED March 16, 1988

Chapter 16

Mechanism of Action of Hydroxyethylcellulose as a Structure Agent for Suspension Concentrate Formulations

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The suspension concentrate (SC) formulation for pesticidal active ingredients is conventionally prepared by a milling or comminution process using a wetting agent and/or dispersant to effect production of a colloidally stable suspension of an active ingredient in an aqueous continuous phase. This suspension is a thermodynamically unstable system, and will undergo spontaneous sedimentation of the dispersed phase. The sediment formed is generally dilatant in rheological terms and thus will not readily redisperse to give a homogeneous suspension. Structure agents, usually water soluble polymers, are added to such suspensions, in order to inhibit or slow down the sedimentation rate. The mechanism by which these structure agents function is often poorly understood and thus we have set out to determine the mechanism of action of one specific structuring agent, hydroxyethyl-cellulose (HEC), as part of a wider programme of suspension characterisation.

The formulation of plant protection agents in the form of suspensions has many advantages, not least the fact that one can avoid the use of organic solvents in the formulation. Often biological activity can be maintained at levels comparable with emulsifiable systems with the judicious use of formulation oils and adjuvants.

The main problems associated with suspensions is that while they are relatively easy to produce as colloidally stable systems, they have an inherent tendency to become heterogeneous on storage, with the active ingredient sedimenting under the influence of gravity to yield what are referred to as dilatant clay sediments.⁽¹⁾ The rheological properties of these "clays" means that they are not readily redispersed by inversions since they tend to thicken, or the viscosity increases with increasing shear rate. The sediment may pack to the close packed limit if sedimentation is uncontrolled.

0097-6156/88/0371-0190\$06.00/0

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It is common practice to add what are usually referred to as structure agents to the formulation in order to retard the sedimentation rate. These are either water soluble polymers or flocculated clays such as bentonite.(2) The water soluble polymers usually function by inducing a controlled level of flocculation between the suspended particles of the system. The suspended particles would be regarded as residing in a minimum of the particle pair interaction potential curve.(3) There are at least two principal mechanisms proposed by which a water soluble polymer may induce flocculation of suspended particles, and hence retard sedimentation and reduce the tendency to formation of dilatant clays. One is the bridging mechanism by which an adsorbing polymer may simultaneously adsorb to more than one particle,(3) leading to a network-like formation in the suspension. This mechanism by implication requires that the polymer being used adsorbs strongly.(3) It is usually found that in such systems the optimum conditions for bridging flocculation are when the polymer is adsorbed to less than complete surface coverage of the particle by the polymer. Complete surface coverage is usually ascertained by examination of the adsorption isotherm, where the level of polymer addition required to reach the plateau in the adsorption isotherm often corresponds to complete surface coverage. Lesser additions of polymer may result in bridging and observable flocculation of particles, although not invariably. The alternative mechanism of flocculation is by the depletion mechanism, where a non-adsorbing polymer produces a depletion layer (4) or region of negative adsorption around the particle, which may be shown to lead to attractive interactions between particles, resulting from attractive osmotic forces due to excluded polymer.

The flocculation of the particles may be monitored by a number of techniques, such as sediment volume measurements,(3) turbidity fluctuation,(5) or indicated by dispersed phase volume fraction measurements. The latter technique is a new experimental technique involving ultrasound velocity measurements carried out in a vertical scanning manner,(6) further developed in these laboratories for applications with optically opaque concentrated suspensions. Our initial findings show that the technique can be used to quantify the state of flocculation of suspended particles in terms of a volume bulk modulus using the measured volume fraction at various vertical positions in a suspension.(7) The prime advantage is that the development of the structure can be observed because the non-intrusive nature of the technique allows repeated scans of a given suspension, over a period of days, weeks or even months.

Details of the adsorbed state of the structure agent, hydroxyethylcellulose (HEC), has been discerned using an EPR technique, where a spin labelled derivative of the polymer was produced using a covalently attached nitroxyl spin label (to a very low degree of labelling).(8) The rotational correlation time of the spin label is highly environment dependent, and thus to a first approximation we can determine whether the label and hence the polymer segment associated with it is in a loop or tail configuration (mobile) or in a train-like or flat configuration (immobile).(9) This information correlates with the adsorption

isotherms and may indicate the state of flocculation of the suspension.

Materials

Suspension Preparation. The suspensions used were produced from technical 2-[[4-chloro-6-(ethylamino)-1,3,5-triazin-2-yl]amino]-2-methylpropanenitrile, (cyanazine), using a proprietary polycarboxylate/polyisobutylene block copolymer as dispersant. The dispersions were 46% v/v when milled in a Mini 250 Motor mill (Eiger Engineering Ltd, Warrington) with 2 mm glass media and a dispersant level of 17 g/kg was used. Product was milled to a particle sizes of 1.2 to 2.1 μm VMD (volume mean diameter), determined by Coulter counter (model TA 2), using cyanazine saturated electrolyte. Suspensions were diluted with distilled water.

Natrosol JXR 250 (Hercules Ltd), an HEC of degree of substitution, 2.5 hydroxyethyl groups per glucose residue and $M_w = 1.0 \times 10^7$ was used to structure suspensions at the indicated levels and added to the suspensions post-milling, in the form of a pre-dissolved concentrate.

Preparation of Spin Labelled Polymer. Preparation of the spin labelled HEC was performed using a variation of the technique of Cafe *et al.*, (8,9) originally developed for labelling of Na-carboxymethylcellulose. The spin label used was 2,2,6,6 tetramethyl-piperidino-oxyl (TEMPO). Cyanogen bromide was used to activate the HEC, but the activation reaction was carried out for only 1 hour, compared to the 4 hours recommended for Na-CMC, and the pH of the reaction medium was maintained at a constant value of 10, for both the activation stage and the linking stage. The higher values recommended for the reaction with Na-CMC led to unacceptably low values for the degree of labelling. Care was taken to ensure that the HEC did not cross-link during the activation stage by not exceeding 5g/l concentration of the HEC in the reaction medium, and this was further checked by measuring the intrinsic viscosity of the HEC in water, both before and after the labelling process, where it was established that the increase in intrinsic viscosity was negligible and within the experimental error of the technique. The samples of spin labelled polymer were freed of excess non-covalently linked spin label by exhaustive dialysis of the samples against distilled water and checking the dialysate for the presence of an EPR signal. EPR spectra were recorded on a Bruker ER 200 spectrometer.

Methods

Adsorption Isotherms. Suspensions of colloiddally stable unstructured cyanazine particles were prepared at the stated volume fractions, using a concentrated (46% v/v) stock suspension. Appropriate amounts of stock aqueous solutions of Natrosol JXR 250 were added to the concentrated suspensions with water. Samples were equilibrated by tumbling overnight, followed by centrifuging at 12000 rpm. Supernatants were assayed for their hydroxyethyl-cellulose content using the phenol-sulphuric acid reaction. (10)

Flocculation Monitoring

Sediment Volume Determination. These were performed on 7% v/v cyanazine suspensions contained in conical based measuring cylinders, with various doses of HEC added. The samples reached a reasonable degree of consolidation within two weeks, after which the sediment volume was read.

Turbidity Fluctuation. The turbidity fluctuation technique has been described in detail by other workers.(5) It was successfully applied here to the same 7% v/v suspensions used in the sedimentation volume measurements, after gentle inversions of the suspensions. The equipment used was a PDA 2000 photometric dispersion analyser (Rank Bros, Bottisham, Cambs, U.K.), and the output was monitored via the ratio channel.

EPR Studies of Adsorbed Polymer. Samples for adsorbed polymer configuration studies were prepared by addition of appropriate amounts of spin labelled Natrosol JXR 250 in a pre-dissolved state, to colloidal stable suspensions of cyanazine, diluted to the appropriate volume fraction from a concentrated stock suspension. The suspensions were allowed to equilibrate with tumbling for 18 hours, which preliminary experiments had shown was sufficient time to reach an equilibrium distribution of polymer. Suspensions were then centrifuged at 12000 rpm, and the supernatant removed, followed by redispersal in cyanazine saturated water. This procedure was repeated approximately 5 times or until no detectable spin labelled polymer was found in the supernatant. The polymer coated cyanazine particles were then redispersed in the minimum amount of water and the EPR spectrum taken, using an aqueous solution type EPR cell to minimise dielectric losses.

Ultrasound Velocity Studies of Suspensions. The technique has been described in some detail previously, in its application for studying creaming phenomena in emulsion formulations.(6) It has been further developed in these laboratories and applied to the study of sedimentation in suspensions. In essence we measure the time of flight of an individual, short duration (single cycle of RF) ultrasound pulse of 6 M Hz frequency, through a cell of 32 mm internal path length. The internal path length of the cell is measured at 1 mm vertical intervals, using two calibration liquids of known ultrasound velocity, water and n-heptane at 20°C. All measurements were carried out at 20°C, in a waterbath controlled to $\pm 0.01^\circ\text{C}$. A schematic diagram of the essential electronic components is shown in reference 6. In addition to this there is a microcomputer controlled chassis holding the transducers which is capable of logging the transducer height and time of flight of the ultrasonic pulses, from which the velocity (and hence volume fraction) is calculable. A parabolic relationship between ultrasound velocity through the suspension and dispersed phase volume fraction was shown to hold over a volume fraction range of at least 0 to 0.4, the so-called Urlick relationship,(11) and it was considered reasonable to apply the relationship to volume fractions up to the close-packed limit. Volume fraction/height

profiles were obtained, with a precision of 1 mm of vertical displacement. This is obtained using 10 mm diameter immersible transducers, since in the far field the ultrasound intensity is concentrated within a cylindrical element approximately 1 mm from the axis of the cylindrical transducer. Outside of this element the ultrasound intensity drops by about -20 dB. (12)

Results and Discussion

The preparation of the spin labelled HEC derivative was determined to have labelled the polymer to less than one sugar residue in approximately 40, and thus it was concluded that the spin labelled derivative had similar physico-chemical properties to the unlabelled analogue. The intrinsic viscosity value of the derivative similarly indicated that there was no significant cross-linking in the activation process, see Table I.

Table I. Intrinsic Viscosity and Molecular Weight Data for Natrosols

Type	Intrinsic Viscosity (ml/g)	Molecular Weight*
JXR	216	1.01×10^5
JXR (labelled)	226	1.07×10^5

$$* [\eta] = 9.5 \times 10^{-5} M^{0.85}$$

Fig 1 shows the adsorption isotherms for the unlabelled polymer adsorbing onto colloiddally stable cyanazine particles of 1.2 um volume mean diameter, where the adsorption experiments were performed on suspensions of 0.07 and 0.40 dispersed phase volume fraction suspensions of cyanazine respectively. It may be seen that when the adsorption experiment is carried out at the lower volume fraction, $\phi=0.07$, the isotherm is apparently much more like the classic high affinity type of isotherm, where the change over from the high affinity region to the plateau level of polymer adsorption is over a much more critical concentration range. For the adsorption experiment carried out at the higher volume fraction of particles, the isotherm is observed to curve gently away from the high affinity region, and in the concentration range of HEC investigated, not to reach the plateau level of polymer adsorption reached for the low volume fraction experiment. This is due to polydispersity of the adsorbing HEC influencing the adsorption isotherm. (13,14) This effect has been noted by previous workers, and a definitive theoretical treatment has been given in which it has been shown that for a given particle surface area to volume of continuous phase ratio, i.e. a "concentration" of surface, there will be only one molecular weight of polymer in the continuous molecular weight distribution which is simultaneously adsorbed on the particle and free in the continuous phase. Thus the polymer

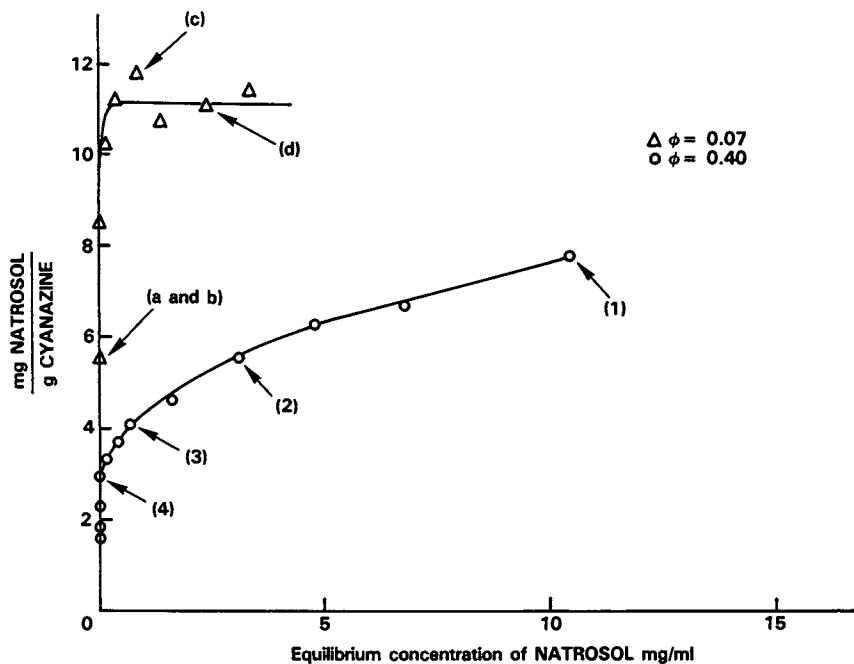


Fig 1. Natrosol JXR 250/cyanazine adsorption isotherms at volume fractions of cyanazine 0.07 and 0.4.

effectively is fractionated, the higher molecular weight fractions being adsorbed on to the particle and the lower molecular weight fractions remaining soluble in the continuous phase. The effect of this on the adsorption isotherms as a function of volume fraction is that at the higher volume fractions of particles, a much larger dose of HEC is required to achieve the same degree of surface coverage of the particles by the HEC as is obtained with the lower volume fraction suspensions.

This is complemented by the observations of the adsorbed polymer configuration. It may be seen in Fig 2, where the EPR spectra of the surface adsorbed labelled HEC for suspensions made at the lower particle volume fraction of 0.07 are shown for different points on the adsorption isotherm. The EPR spectra for the points in the high affinity region, i.e. areas of low surface coverage, show the broad structureless features to be expected of a fairly immobile spin probe adsorbed with polymer residues lying in trains on the particle surface, see Fig 3. It is worth comparing these spectra with the spectrum of the completely free polymer in aqueous solution, see Fig 4. As the degree of surface coverage of the cyanazine particle by HEC is increased, at higher polymer doses, the spectra of the surface adsorbed HEC takes on a much more mobile character, and this can be rationalised as the polymer having to take on a much more loopy configuration with a high proportion of the residues in the form of loops and dangling tails as the available surface for adsorption becomes much more restricted, see Fig 3. The spectra in Fig 2 were all obtained from 0.07 volume fraction suspensions. In Fig 5, the spectra for different HEC doses equilibrated with 0.40 volume fraction suspensions are shown. Even at the highest polymer dose the spectra have the characteristics of an immobile spectrum. At no polymer dose was a mobile spectrum obtained for surface adsorbed HEC in the 0.4 volume fraction suspensions. This is consistent with the adsorption isotherms, where at the comparable levels of surface coverage in the low volume fraction suspensions, only immobile behaviour was observed.

In Fig 6, it may be seen that the effect of addition of higher levels of the dispersant, with the spin labelled HEC, does not appear to inhibit adsorption of the HEC, although it does influence the adsorbed HEC configuration. As the level of dispersant is increased, the adsorbed HEC takes on a more mobile conformation, presumably because it competes for the available space, forcing the HEC to loop more into the continuous phase. At the highest level of addition of dispersant, the adsorbed HEC is remarkably mobile, having an EPR spectrum with almost the same line width characteristics as the free polymer. The observation of surface adsorbed spin labelled HEC that cannot be removed by washing unequivocally shows that the HEC does not flocculate the suspension by a depletion mechanism.

Flocculation Studies. In Fig 7, the results of the sediment volume and turbidity fluctuation studies are presented. The studies are restricted to the 0.07 volume fraction suspensions for practical reasons. They show that the colloidal stability of the cyanazine particles are sensitive to the concentration of added HEC. There

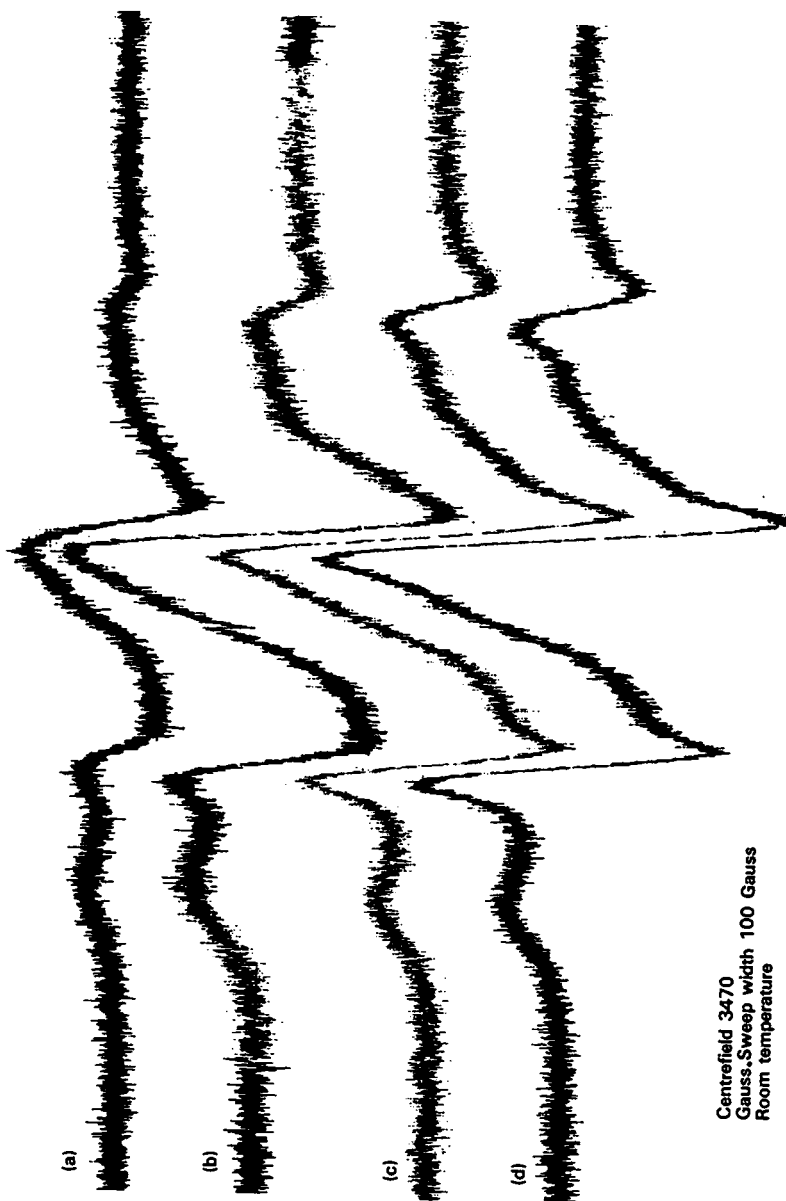


Fig 2. Electron spin resonance spectra of surface adsorbed spin labelled Natrosol JXR 250 as a function of initial polymer dose. Volume fraction of cyanazine = 0.07.

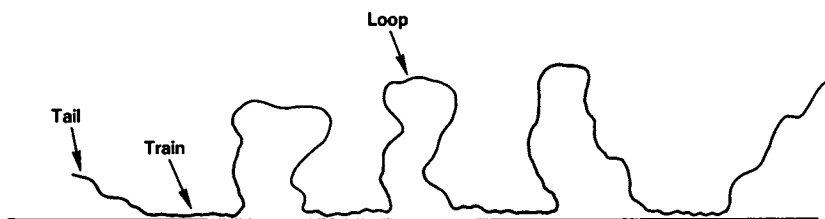


Fig 3. Figure of a polymer adsorbed in loops and tails.

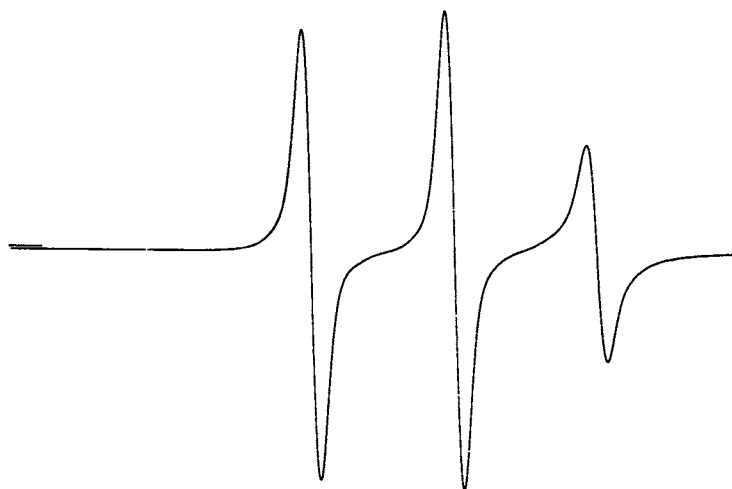


Fig 4. Electron spin resonance spectrum of free spin labelled Natrosol JXR 250 in water.

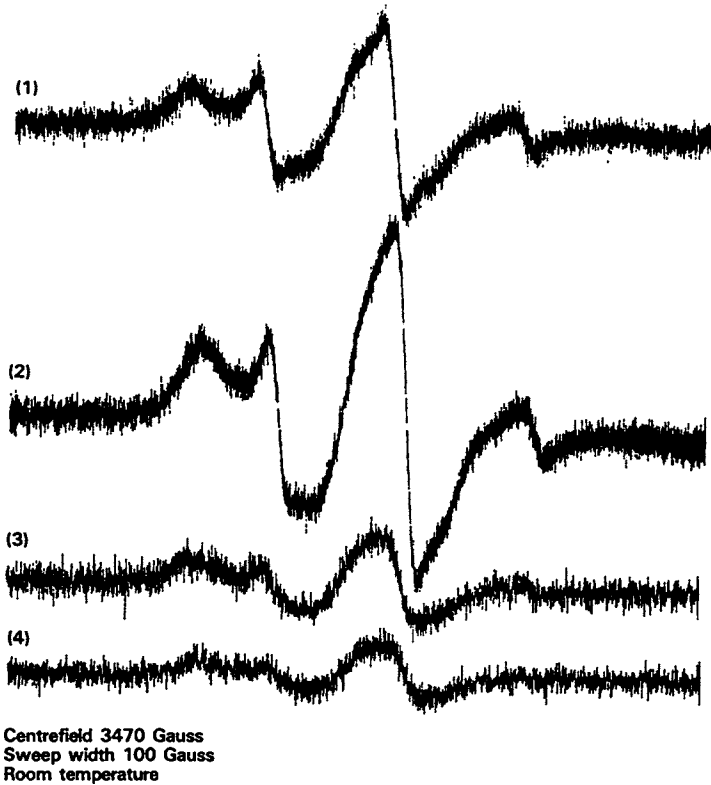


Fig 5. Electron spin resonance spectra of surface adsorbed polymer as a function of polymer dose, volume fraction of cyanazine = 0.4.

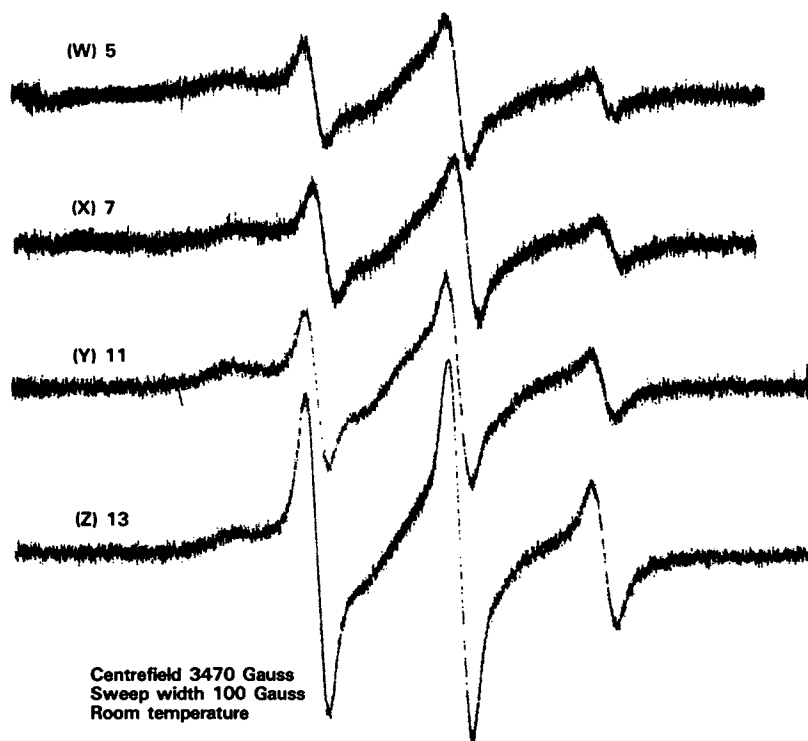


Fig 6. Electron spin resonance spectrum of Natrosol JXR 250, as a function of dispersant dose.

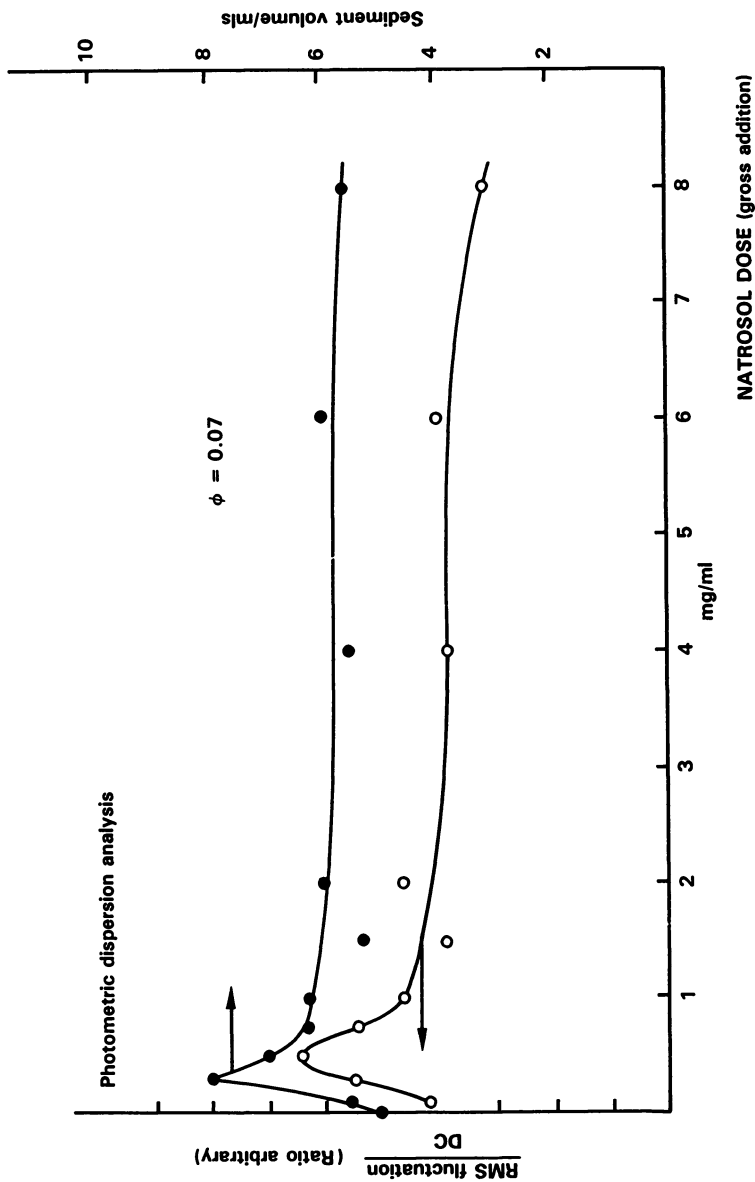


Fig 7. Flocculation monitoring of low volume fraction cyanazine suspensions, using photometric dispersion analysis.

is a polymer dose corresponding to less than complete surface coverage at which the cyanazine particles flocculate. This is quite clearly seen by both flocculation monitoring techniques. The sediment volume measurements show that at less than surface coverage a low density sediment is formed, consistent with flocculation and the turbidity fluctuation technique complements this by indicating a larger average particle size for the same polymer dose.

Thus at less than complete coverage the HEC may flocculate the cyanazine particles by a bridging mechanism, whereby a network is formed by an HEC molecule, simultaneously adsorbing to more than one particle. Colloidal stability is re-achieved at higher polymer doses, as might be expected since at these higher coverages, when the polymer is loopy, as shown by the EPR studies, some additional steric stabilising capacity may be derived from the HEC.

For the higher volume fraction suspensions, however, in the range of HEC doses investigated, complete surface coverage is never achieved, and thus the suspension is always in a state of weak flocculation as a result of the presence of the HEC.

Ultrasonic Velocity Studies. Since there are no techniques presently available for monitoring flocculation in concentrated suspensions, we have developed a technique using ultrasound velocity scanning in sedimenting systems which may be applied to flocculation monitoring and also following such processes as dilatant clay formation in suspension concentrates.

In Fig 8 we show the results obtained for sedimentation studies on a concentrated (40% volume fraction) suspension of unstructured colloidally stable cyanazine particles, where the sample was repeatedly scanned over a period of 105 days. The build up of dilatant clay at the cell base can quite clearly be seen, where the particles pack to the random close packed limit ($\phi=0.65$), although this value may be influenced by the polydispersity of the particles.

In Fig 9 we show a similar scan over a comparable time period, but it may be seen that, at the base of the cell, the limiting volume fraction in the cyanazine enriched layers is approximately 0.48. If the HEC were serving to structure the system simply by the influence it would have on the viscosity of the continuous phase, then we could expect to find a limiting volume fraction in the layers at the base of the cell largely the same as that found in the unstructured system. Thus the findings for the HEC structured systems indicate that the system must be weakly flocculated, and we propose that the flocculation is by a similar bridging mechanism to that observed in the low volume fraction suspensions, since the EPR data indicate that the configuration and extent of surface coverage by the adsorbed HEC polymer in the concentrated suspensions ($\phi=0.4$) is similar.

Conclusions

This study demonstrates quite clearly that the mode of action of the structure agent HEC in the system under investigation is that it induces controlled flocculation by a bridging mechanism. The

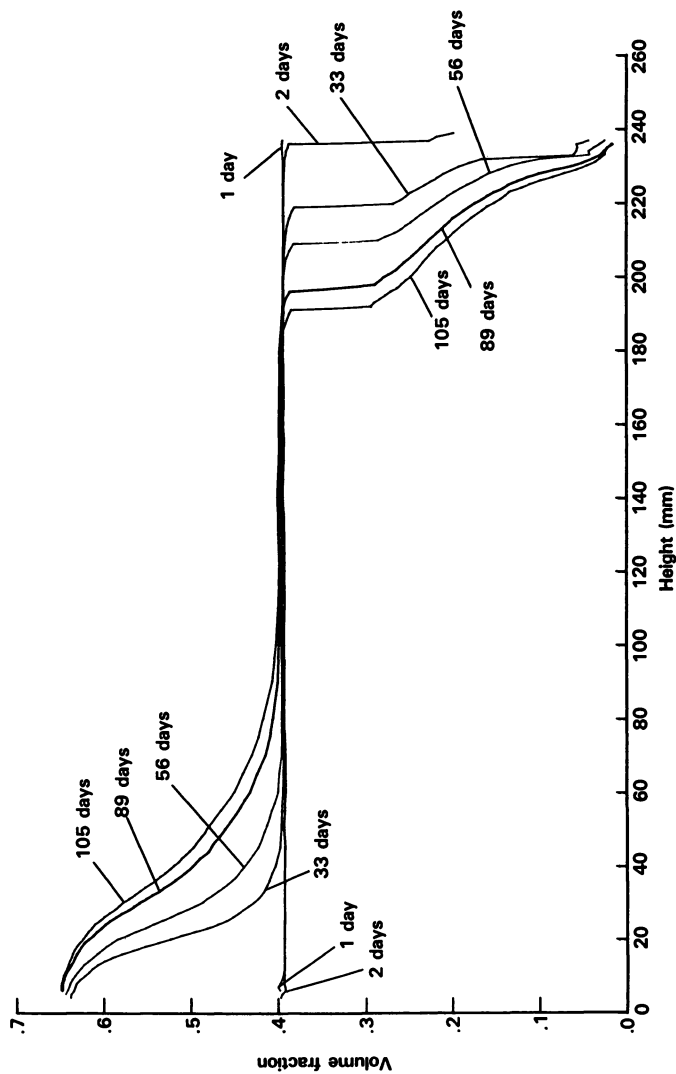


Fig 8. Ultrasonic velocity sedimentation scans as a function of time for 40% v/v cyanazine suspensions without a structure agent.

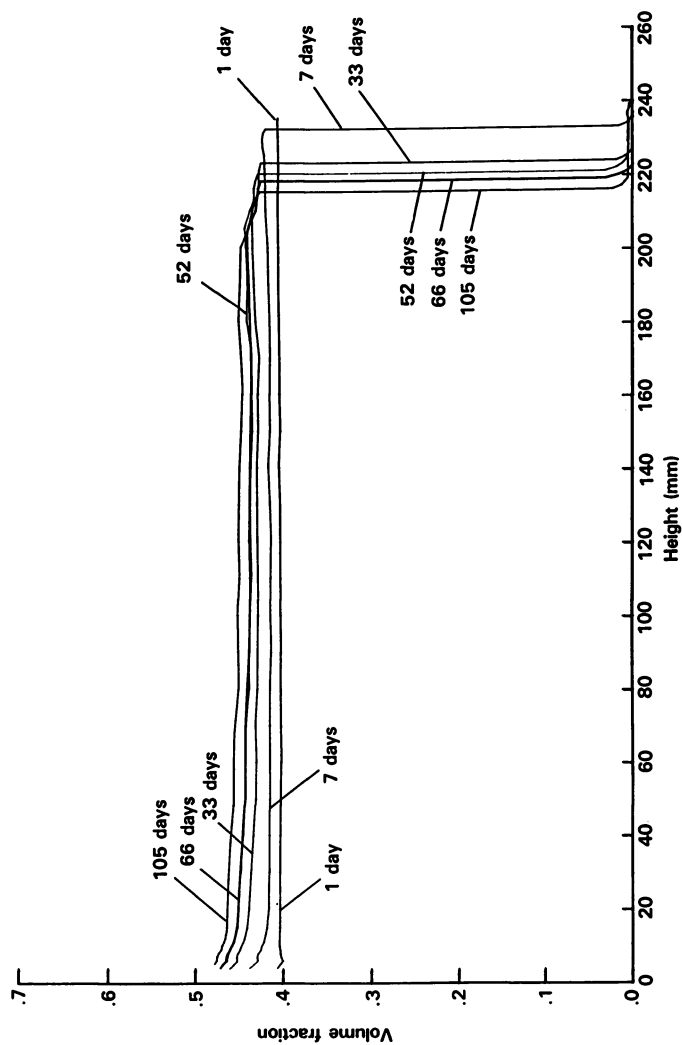


Fig 9. Ultrasonic velocity sedimentation scans for 40% v/v cyanazine suspensions flocculated with Natrosol JXR 250, as a function of time.

polymer has an inherently high affinity for the colloiddally stable cyanazine particle, since it is never completely displaced by a competing block co-polymer dispersant, but maintains its adsorbed state and takes on an adsorbed configuration that has a high proportion of loops and tails when in competition with the block co-polymer. This is quite surprising since it would not be expected that a homopolymer would adsorb so strongly. It may be a consequence of some residual hydrophobic character in unsubstituted regions of the cellulose chain. It is recognised for example that the water insolubility but swellability of cellulose is a consequence of configuration of the glucose sub-units in cellulose⁽¹⁵⁾ where the axial hydrogen atoms above and below the glucose ring are hydrophobic in nature, and the equatorial hydroxyl groups are hydrophilic. This is why the cellulose molecule can crystallise in layers by hydrophobic interactions, and yet maintain a high affinity for water. The foregoing argument is consistent with a bridging mechanism for the controlled flocculation but not with a depletion mechanism.

Acknowledgments

The technical assistance of T Reid, A Lidstone and I Fabris is gratefully acknowledged.

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RECEIVED January 11, 1988

Chapter 17

Advanced Polymeric Systems for Site-Specific Release Control of Insecticides in Foliar Applications

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Chlordimeform (CDF), an insecticide/acaricide commonly used for foliar applications in cotton, as well as its desmethyl analogue (CMF) have been converted into polymeric controlled release systems with tailored site-specific release characteristics. Based on the microenvironmental conditions prevailing on cotton leaves, as the site of the insects action and of the pesticides' application, alkali-catalyzed hydrolysis, photolysis and cation exchange were employed to trigger the release by cleavage of susceptible chemical bonds connecting the active agents with a macromolecular carrier. Corresponding polymers comprise ethyleneglycol carbamate and benzoin carbamate either as hydrolyzable or light-sensitive spacer groups, or they contain CDF bound as a salt to sulfonic acid groups in the resin. In vitro and in vivo investigations provide evidence for the benefits of the site-specific release principle with respect to improved efficiency and safety of pesticides in practical use.

In conventional applications of pesticides certain inherent loss factors can often result in a partially useless waste of the chemicals and in their undesired distribution to the environment and to non-target animals. In recent years controlled release systems based on the use of polymers have shown a considerable potential to overcome those disadvantages and risks (1-17). With respect to agrochemicals the current controlled release technology covers mainly three different approaches how to govern the active agents' bioavailability in crop protection.

The pesticide can be physically dissolved, adsorbed or dispersed in a polymer matrix, in order to control its release by diffusion or by matrix erosion.

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0097-6156/88/0371-0208\$06.00/0
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- The pesticide can be physically entrapped in polymeric reservoir systems, such as microcapsules hollow fibers etc., its release is regulated by permeation, osmosis or evaporation.
- The pesticide can be chemically bound to macromolecular carriers, either as part of the polymer backbone or as a pendent moiety, and its release is governed by the cleavage of susceptible chemical bonds.

A large variety of different polymers and copolymers has been used in numerous devices of various forms and dimensions. The main goal in the development of all those controlled release pesticide systems has so far been the reliable control of the active ingredient's release rate, in order to keep its temporal bioavailability at a constant optimum level. The localized release control by targeting the pesticide's delivery specifically to the particular pest or crop has hardly been drawn any attention to, although targeting of drugs is an established and intensively studied subject in the pharmaceutical field (18). Our own research in this field has been focussed on the achievement of additional site-specificity in the release control of insecticides. It is the aim of this paper to shortly review some of the work accomplished or presently in progress within our laboratory.

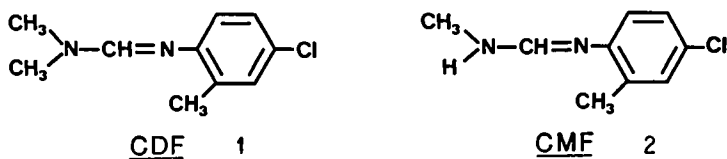
Concepts and Objectives for Site-specific Release Control in Cotton

The most distinguished characteristic of site-specific release control is the fact that the release of a bioactive material is in particular triggered and governed by a specific phenomenon occurring in the target biosystem. Regarding the three fundamental approaches to release control by polymers we came to the conclusion that a chemically bound system only implies a dimension of activation energy, which meets the requirements for the high selectivity in the pesticide release aimed at. Accordingly the general model of a polymeric site-specific pesticide release system is thought to be composed of a polymeric backbone containing comonomers and/or crosslinking agents besides a monomer connected with the pendent pesticide molecule (Figure 1). Whereas the components of the polymer chain should enable a certain fine-tuning of the release characteristics, the key position in the system is held by a tailored spacer group and a susceptible bond linking the pesticide to the polymeric carrier. Both these elements finally determine mechanism, rate and selectivity of the release process.

N²-(4-chloro-o-tolyl)-N¹ N¹ dimethyl-formamidine 1, (Chlor-dimeform, CDF), has been selected as a model pesticide for feasibility studies on the site-specific release concept. CDF is an insecticide/acaricide commonly used in foliar applications to fight pests in cotton e.g. *spodoptera littoralis*, *heliethis* and others (19).

Unfortunately Chlordimeform lacks a suitable functional group which could be utilized for the chemical binding to a polymeric carrier. The corresponding monomethyl compound, N²-(4-chloro-o-tolyl)-N¹ methylformamidine 2 (CMF), usually referred to as N-Desmethyl-chlordimeform, shows an identical spectrum of biological

activity and is in fact the active form of 1 generated in vivo by demethylation (20, 21).



Due to the reactive secondary amino group CMF 2 was used in this study for the synthesis of those systems which imply the covalent binding to a macromolecule. CDF 1 was used for systems based on heteropolar linkages to polymers, and in bioassaying experiments it was employed as a standard for comparison.

With respect to site-specificity in the release a detailed knowledge of the biosystem one is going to deal with, is by all means an inevitable requirement for the realization of the targeting principle. With CDF 1 and CMF 2 the actual target is of course the insect which destroys leaves and seed capsules of the cotton plant. Since these insecticides are active against quite a variety of insect pests in cotton, a general alignment of the release trigger with the metabolism of all these insect species was regarded as not feasible. Therefore we have directed our search for possible triggering effects to the cotton leaf as the site where the insects' eggs, larvae and adults appear. Consequently a specific property in the cotton leaf's microenvironment was to be utilized as a specific release trigger. However, checking the microenvironmental conditions prevailing on cotton leaves resulted in three different phenomena (Figure 2) probably employable for release triggering by cleavage of chemical bonds according to the basic idea:

- pH values in the range of 8-10 existent on the leaf surfaces caused by alkaline excretions (22)
- the optimum orientation of the leaves to sunlight with it's photochemical potency
- cation concentrations of 18-20 m moles/ltr. found in cotton leaf dew (23).

As a consequence alkali-catalyzed hydrolysis, photolysis and cation exchange have been identified as the most promising target-specific triggers to be utilized in the new site-specific release systems.

Synthesis of Polymer-Bound Insecticides

The first approach based on hydrolysis as a release mechanism required as a weak link between the polymer backbone and the pendent insecticide moiety a labile bond to be hydrolyzed in a desired way under the cotton leaves alkaline conditions. Previous investigations (24) with model compounds containing CMF 2 linked with aliphatic moieties via urea-, amide-, ester-, carbamate- and phosphonitrilic amide bonds, had conclusively proven only the carbamate linkage to be

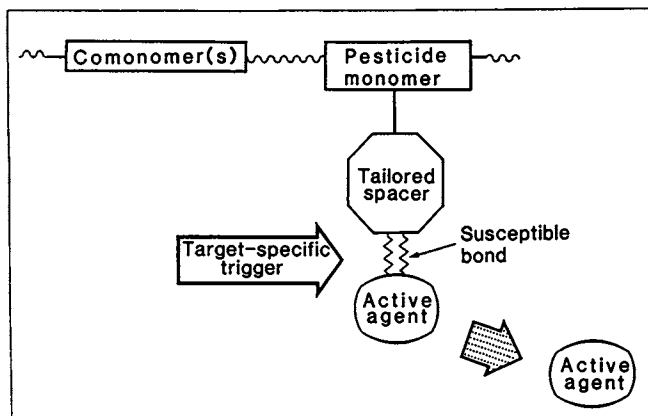


Figure 1. General model for site-specific controlled release pesticides

Atmosphere

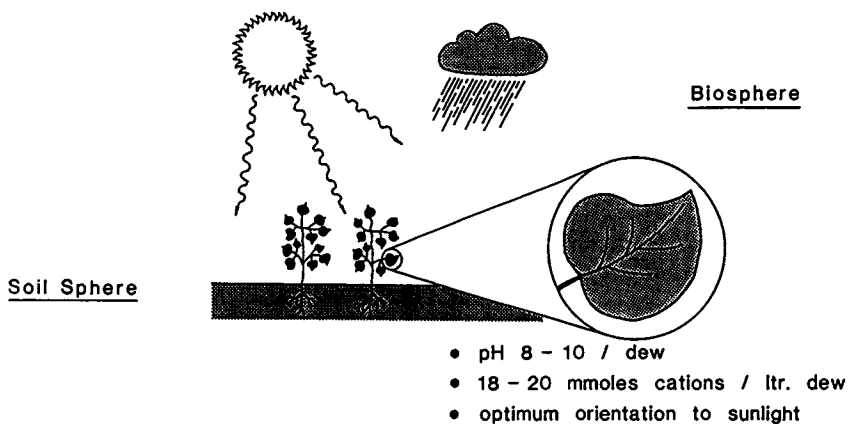


Figure 2. Microenvironmental conditions prevailing on cotton leaves

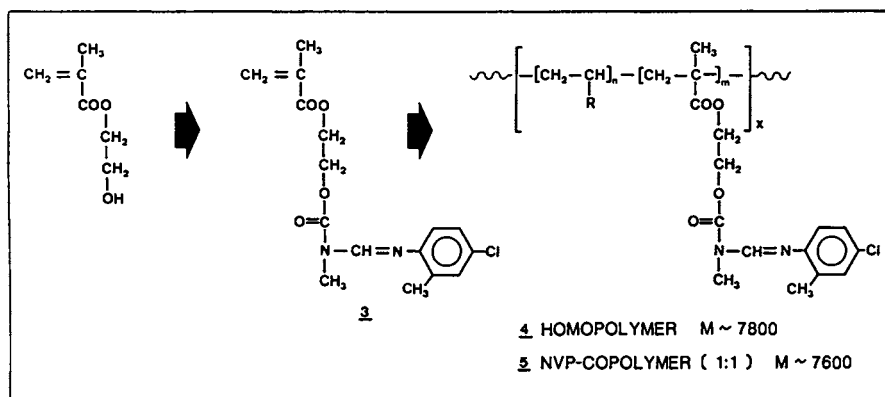
suitably hydrolyzed at the pH value concerned. By reaction of 2-hydroxyethyl-methacrylate, phosgen and CMF 2 the CMF derivative 3 is obtained which can subsequently be polymerized by radical techniques to form homo- or copolymers (Scheme 1). The polymers thus obtained containing the ethyleneglycol ester unit as a spacer group and the carbamate moiety as a susceptible bond are in perfect accordance with the model lead structure (Figure 1). The homopolymer 4 and the more hydrophilic 1:1 copolymer with N-vinylpyrrolidone (NVP) 5 were set to modest molecular weights favouring conventional foliar application by spraying.

The second concept based on the idea of a photolytic cleavage of the susceptible bond as a release trigger required a suitable photoresponsive spacer group. Among various model compounds including a number of photoremovable protecting groups (25-27) connected with CMF 2 by carbamate linkages, finally the benzoin-carbamate of CMF 2 was found to undergo the desired photofragmentation under formation of CMF (28). A corresponding polymeric system can be synthesized from 4-methacrylamido-benzoin 6 by reaction with the carbamoylchloride of CMF (24) and by radical polymerization of the monomer 7 thus obtained (Scheme 2). The 1:1 methyl-methacrylate copolymer 8 and the corresponding N-vinyl-pyrrolidone copolymer 9 were adapted in the molecular weights to the hydrolytic systems 4 and 5. A detailed investigation of the photochemistry of the monomeric and polymeric CMF-benzoin-carbamates using CIDNP-NMR techniques (29, 30) confirmed the cleavage of the benzoin moiety as an absolutely predominant process resulting in the formation of CMF, CO₂ and 2-phenyl-benzofuran moieties (Scheme 3).

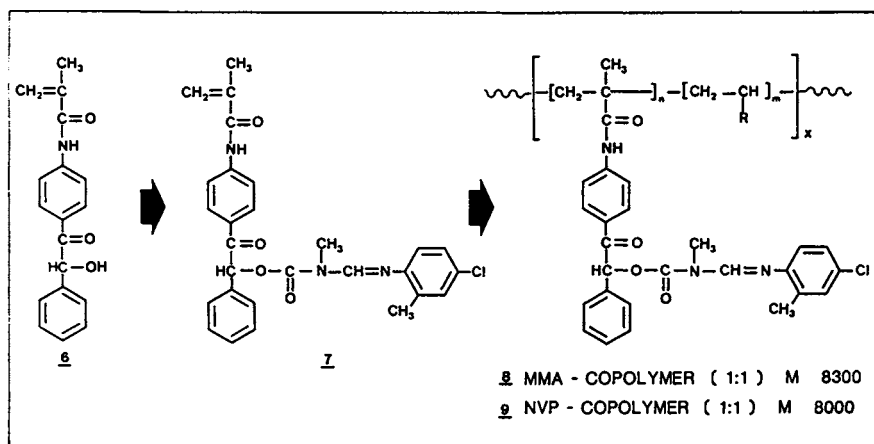
The third approach we were thinking of is based on the utilization of the relatively large cation concentration prevailing on cotton leaf surfaces as a release trigger. Since Chlordimeform 1 is a weak base it is capable of forming stable salts with strongly acidic polymeric sulfonic acids. Among various linear and crosslinked aliphatic and aromatic polymeric sulfonic acids those CDF-resinates formed with sulfonated highly porous styrene/divinyl benzene copolymers showed by far the most superior stability and release capacity (Scheme 4). The release process of CDF could be simulated in vitro with spray deposits on filter paper obtained from aqueous formulations of the products. Whereas a deposit obtained from conventional CDF emulsion concentrate (EC) is completely depleted after 5 days due to CDF-evaporation, deposits obtained from the CDF resinate 10 do not lose any active agent for weeks. Subsequent spraying with distilled water has no influence. Only when increasing amounts of sodium bicarbonate are sprayed onto the CDF-resinate deposits there are gradually well-defined portions of CDF released and exposed to regular evaporation. The complete release of CDF from the resinate requires under these conditions almost 4 equivalents of cations (Figure 3).

Physicochemical and Biological Properties of the Site-Specific Controlled Release Systems

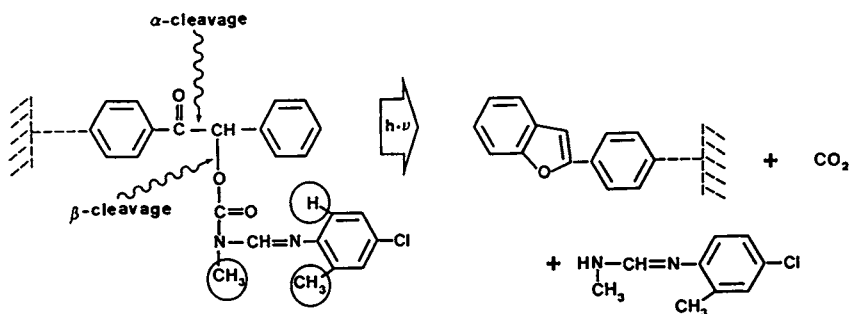
Evaporation, wash off by rain, leaching and chemical degradation are among the most important loss factors which often decimate a pesticide's bioavailability in open field applications within a short



Scheme 1. Hydrolytic systems: monomer synthesis and polymerization (NVP=N-vinyl-2-pyrrolidone)

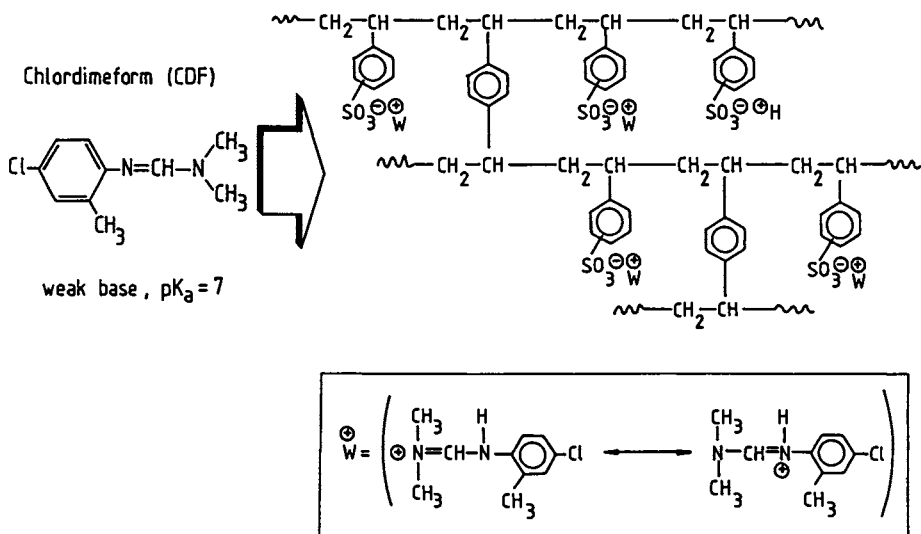


Scheme 2. Photolytic systems: monomer synthesis and polymerization (MMA=methyl-methacrylate; NVP=N-vinyl-2-pyrrolidone)



Scheme 3. Photocleavage of benzoin-CMF-carbamates

CHLORDIMEFORM - ION EXCHANGER SALT



Scheme 4. Preparation of CDF-resinates

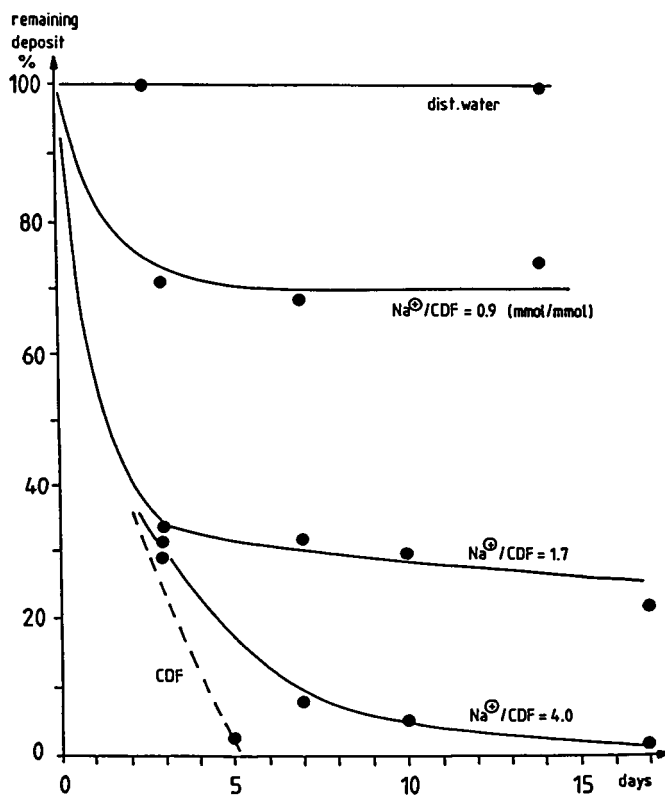


Figure 3. CDF evaporation from CDF resin spray deposits (CDF, dotted line: deposits from conventional CDF emulsion concentrate). (Reproduced with permission from ref. 31. Copyright 1987 Controlled Release Society.)

period of time. Table I summarizes some physicochemical properties of the three different types of new controlled release systems. In comparison to CDF 1 and CMF 2 the polymers 4, 5, 8, 9 and 10 show a decrease in vapour pressure and water solubility by several orders of magnitude. In the absence of those triggering influences which the respective design of the system is based on aqueous formulations of the polymers exhibit highly improved stabilities and do not contain detectable amounts of free CDF. Two days after aerial applications in cotton plantations, CDF recoveries on the crop were determined to be 40-60 % increased when the new polymers were used compared to the conventional CDF emulsion concentrate. This result exemplifies clearly the substantially reduced environmental losses obtained with the new site-specific release systems - a factor of considerable importance with regard to economical and ecological aspects.

After the feasibility of the three different site-specific release mechanism had been verified by simulating *in vitro* experiments, the new systems were to be tested on the real biological target under practical conditions. In greenhouse experiments laboratory-reared *spodoptera littoralis* larvae of the first instar on young cotton plants (30 cm) were used for the bioassaying experiments. Larval mortalities were assessed 4 and 8 days after treatment of the plants with wettable powder (WP)-, emulsion concentrate (EC)- or flowable (FO)-formulations of the new polymers 4, 5, 8, 9, 10. Some of the polymers were also tested in field experiments and naturally occurring eggs and larvae were used for assessing the activities. The results (Table II) give evidence of the two photolytic systems (8, 9) as well as the CDF-resinate (10) being at least equal in their insecticidal potency to the standard CDF. EC- and FO-formulations are always more efficient than the corresponding WP-formulations, presumably due to their favourable film-forming properties. The bioactivity of the hydrolytic systems 4 and 5 is found to be not completely satisfactory. The lack of dew in greenhouse experiments - occurring every night in the field - might result in an insufficient level of hydrolysis-triggered CMF-release. Further investigations require a careful simulation of dew formation in greenhouse experiments and additional field trials under practical conditions to give evidence of the actual efficiency of the hydrolytic systems under practical conditions.

Since the aqueous formulations of the new polymeric release systems do not contain distinct amounts of free CMF or CDF, the results from the bioassaying experiments provide clear proof of the site-specific release mechanisms conceived being effective in the target biosystem. On the other hand due to the absence of free insecticides the practical formulations showed no toxic effects during oral and dermal studies on rats. Thus site-specificity of the release mechanism can contribute in a substantial way to handling safety and environmental clearance of pesticides.

The forementioned environmental losses in conventional applications of pesticides lead to insufficient duration of the pesticidal activity. Therefore prolonged duration of activity is another main goal advanced controlled release systems aim at. A longterm activity test with the polymers 5, 9 and 10 has been performed in such a way that cotton plants in a greenhouse after the treatment with aqueous formulations of the polymers were stored for

Table I. Physicochemical Properties of Site-Specific Release Systems

Controlled Release Polymer	\bar{M}_n	CDF (CMF) Content % weight	Water Solubility 20°C ppm	Vapour Pressure 20°C mm Hg	Stability
Hydrolyt. Systems	Homopolymer <u>4</u>	53	$\ll 0,5$	$\ll 10^{-7}$	hydrolytically stable at pH 5 - 7,5
	NVP-Copolymer (1:1) <u>5</u>	40	$\ll 0,5$	$\ll 10^{-7}$	
Photolyt. Systems	MMA-Copolymer (1:1) <u>8</u>	30	$\ll 0,5$	$\ll 10^{-7}$	stable in lighttight containers
	NVP-Copolymer (1:1) <u>9</u>	24	$\ll 0,5$	$\ll 10^{-7}$	
Ion Exchange	CDF-Resinate 10 <u>cross-linked</u>	30	$\ll 0,5$	$\ll 10^{-7}$	stable in absence of cations
Standards	CMF <u>2</u>	100	350	$7,2 \cdot 10^{-5}$	sensitive to
	CDF <u>1</u>	100	250	$3,6 \cdot 10^{-4}$	H ₂ O, O ₂ , light

Table II. Bioactivities of Site-Specific Release Systems
(greenhouse experiments: *Spodoptera littoralis* larvae L1 on cotton plants; field experiments: naturally occurring eggs and larvae of *Spodoptera littoralis*; WP=wettable powder, ED=emulsion concentrate, FO=flowable)

Controlled Release Polymers	GREENHOUSE EXPERIMENTS			FIELD EXPERIMENTS	
	WP-25 (4)	EC-50 (4)	EC-50 (8)	eggs	larvae
Hydrolyt. Systems	Homopolymer 4	80	64	43 (WP)	-
	NVP-Copolymer (1:1) 5	90	82	74 (WP)	-
Photolyt. Systems	MMA-Copolymer (1:1) 8	98	90	-	88 (EC)
	NVP-Copolymer (1:1) 9	-	97	-	-
Ion Exchange CDF-Resinate 10	92	98 (FO)	92 (FO)	76 (FO)	96 (FO)
Standards	CMF 2	94	98	78	-
	CDF 1	100	96	90	72 (EC) 90 (EC)

increasing periods of time before infestation with *spodoptera littoralis* larvae and assessment of the larval mortality. The results thus obtained from greenhouse experiments are shown in Figure 4. The photolytic NVP-copolymer 9 exhibits by far the highest duration of activity in comparison to the hydrolytic NVP-copolymer 5, the CDF-resinate 10 and the CDF standard. Under these conditions this particular polymer keeps the insecticidal potency on a high level of 80-100 % for a period of four weeks compared to 10 days only found for the CDF standard. We assume that the minor efficiency of the polymer 5 and the CDF-resinate 10 observed in the longterm studies are again due to the fact that there is water involved in the release processes concerned, hydrolysis and cation exchange. Under the influence of dew in open fields the longterm activity of the latter systems might turn out more positively than the behaviour in the greenhouse.

Finally it was to be proved that the photolytic systems, also containing carbamate linkages, not only *in vitro* (s. Scheme 3) but also *in vivo* are subject to the particular photoreaction under release of CMF. For this purpose a number of cotton plants was treated with aqueous formulations of the polymer 8. When the plants were stored under reduced light intensity in the shade the larval mortalities found on those plants dropped to 15 % only within 10 days, compared to 98 % larval mortality after 10 days obtained with plants stored under full daylight. With CDF used as a standard the larval mortalities undergoe in both cases only the regular longterm decrease to 76 % within 10 days. Based on these results, light is considered to be the actual release trigger in the polymer 8 thus confirming the feasibility of the original concept.

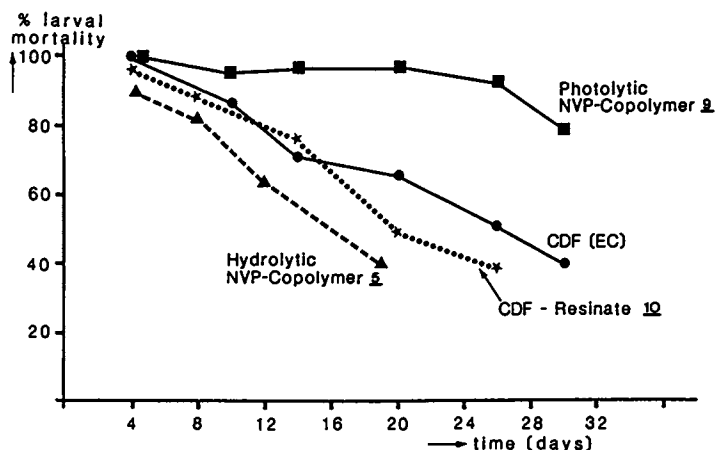


Figure 4. Longterm bioactivity of site-specific release systems (*spodoptera littoralis* larvae L1, greenhouse, cotton plants 30 cm high)

Conclusions

The new polymerbound controlled release systems exhibit site-specific release characteristics, which are specifically directed to cotton leaves as a target biosystem. Hydrolysis, photolysis and cation exchange as release mechanisms can selectively be triggered under the biosystem's conditions. Reduced environmental losses and a general detoxification is found as a benefit in all the three systems. The preparation of the new polymers includes relatively simple and unexpensive processes, with the CDF resinate being at the head. Conventional formulation and spraying techniques can be used for the practical application. Preliminary greenhouse and field experiments have given evidence of the advantages of site-specific release systems. Especially light-triggered release as a concept showed most promising results with respect to a remarkably prolonged duration of activity. Further investigations will be directed to the transfer of the new concepts to various types of bioactive materials.

Acknowledgments

The authors are grateful to Dr. G. Rist for the NMR-spectroscopic investigation of the photorelease mechanism and to Dr. F. Bourgeois, F. Buholzer, Dr. V. Flück, Dr. E. Neuenschwander and Dr. H. Schwitulla for the extensive biological testing.

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RECEIVED January 11, 1988

Chapter 18

Long-Term Controlled Release of Herbicides

Root Growth Inhibition

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Research on controlled-release of pesticides has resulted in products designed to extend bioactivity for periods of several days, months, or at most, several years. However, recent research directed toward solving problems associated with plant-root penetration through caps and liners that are designed to minimize leaching or movement of buried nuclear and chemical wastes has resulted in development of a long-term controlled-release herbicide delivery system designed to stop root growth for periods of up to 100 years. Through the unique combination of polymers with a herbicidally active dinitroaniline, a cylindrical pellet (9 mm long and 9 mm in diameter) was developed that continuously releases a herbicide for a period of up to 100 years. Equilibrium concentration of the herbicide in soil adjacent to the pellet and the bioactive lifetime of the device can be adjusted by changing the size of the pellet; the type of polymer; the type, quality, and quantity of carrier; and/or the concentration and type of dinitroaniline used. Commercial products that have been developed under a Federal Technology Transfer Program that utilize this technology include: 1) **ROOT-SHIELD**, a root repelling sewer gasket for concrete, clay, and PVC sewer lines, 2) **BIOBARRIER**, a spun-bonded polypropylene geotextile fabric developed to prevent root growth from invading septic tanks; penetrating under roadways, and along the edge of sidewalks, airport runways, and tennis courts, and for landscaped areas; and 3) **ROOT-GUARD**, a plastic drip irrigation emitter designed to protect buried drip irrigation systems from being plugged by roots.

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The problem of retaining nuclear and chemical wastes within burial sites has been the subject of research for well over two decades. For example, there are more than 90 million metric tons of uranium mill tailings which release radioactive radon gas (^{222}Rn) at ~25 inactive sites throughout the United States. The Uranium Mill Tailings Control Act of 1978 (Public Law 95-604) directed the U.S. Department of Energy (DOE) to take steps to provide for "the stabilization, disposal, and control in a safe and environmentally sound manner of such tailings in order to prevent or minimize radon diffusion into the environment and to prevent or minimize other environmental hazards from such tailings." Initial research efforts developed physical sealing techniques or "Barriers" for tailings to trap the radon gas. Physical barriers consisted of multilayer clay/aggregate material (1), asphalt emulsions, (2) and, more recently, thick polymeric covers (e.g., ~10 mil-thick black polyethylene). In all cases the barriers are covered with compacted soil and planted with a grass or a native plant species. The compacted soil minimizes water infiltration into the waste and protects the barrier from degradation by oxidation and ultraviolet radiation. The plants serve as hydrologic pumps, reducing water infiltration, and stabilizing the soil from wind-induced erosion. However, many of these physical barriers were breached by the roots of the plants growing in the soil cover, creating a route for release of the ^{222}Rn and for water infiltration and subsequent mobilization of the waste. Similar problems exist at low-level radioactive waste burial sites, with translocation of radioactivity by deep-rooted plants. Breaching of these physical barriers illustrated the need to develop an alternate method of controlling root growth over periods of 100 to 300 years.

Plant roots also penetrate sewer lines and septic drainfields and damage sidewalks, streets, tennis courts, etc. In 1984 the city of Charlotte, NC, which maintains over 1,800 miles of sewer lines, spent in excess of \$500,000 for root control and system repairs caused by root invasion (3). In 1986 the city of Sunnyvale, CA, spent over \$1,000,000 to repair damage to streets and sidewalks caused by tree roots (4). These problems are not isolated to city-owned sewers and streets; home owners also experience intrusion of roots into sewer lines or under driveways and sidewalks. Even with the recent development of extremely tight-fitting gasketed PVC pipe the only truly effective solution for sewer lines that have been penetrated by roots is to physically remove them. However, physical root-removal is only a temporary solution. With PVC sewer pipe, repeated root removal will eventually damage the pipe, making major repairs necessary. Existing methods for stopping or controlling plant roots from cracking, pushing up or damaging sidewalks, streets, driveways, and airport runways are limited. After the damage has begun there are only two solutions available: physically removing the tree or plant, or trenching along the edge of the invaded area to cut the roots. The latter option typically induces additional lateral root growth, thus exacerbating the problem. When planting new trees one can use physical shields, to attempt to force the roots to grow down.

The concept of using herbicides to rid sewer systems of invading roots is not new. Phytotoxic chemicals, such as copper sulphate, have been flushed through the sewer system or forced under pressure (U.S. patent 2,976,191) through the sewer pipe joint into the soil to kill roots. The soil around the gaskets or the gasket itself has been treated with herbicides like 2,4-D to stop the penetration of roots (U.S. patent 3,231,398). Neither approach has proven to be very effective as evidenced by current lack of commercial use. Also, flushing chemicals through the system does not eliminate the physical mass of the roots that block the line. Furthermore, chemicals can damage the aboveground vegetation as well as the sewage-digesting microorganisms. The second solution, namely the use of herbicides, while correct in concept, has been a problem in the past since the herbicides that have been selected significantly damage or kill the vegetation growing above the treated sewer line while not remaining active for very long periods of time. At best, all these methods to this age-old problem have been temporary, requiring repeated treatments rather than providing a long-term solution.

Methods for controlling plant root intrusion into waste burial sites, sewer lines, and under sidewalks, streets and similar areas have been the subject of research at Battelle's Pacific Northwest Laboratories since 1978. Original efforts for the U. S. Department of Energy (DOE) were directed toward developing plant "Biobarriers" that would prevent roots from penetrating waste repositories (5-8) without killing the aboveground plant. Two basic requirements were imposed on development of the biobarrier system. First, the chemical root-growth inhibitor (in this case, trifluralin) had to be environmentally safe and acceptable. Thus, it had to have a reasonably short environmental half-life, exhibit little soil mobility (which would prevent any contamination of surface and/or groundwaters), and limit plant root growth without adversely affecting the growth of aboveground biomass. Inherent in these criteria was the requirement for a method that would allow for long-term controlled delivery of a herbicide from a reservoir that would provide for inhibiting root growth. Second, because a buried system was required (e.g., 1 or more feet below the surface), the cost of placement dictated that the root-growth-inhibiting herbicide remain bioactive within the reservoir for an extended period of time (up to 100 years). Since completing the research for the DOE, attention has been focused on transferring this technology to industry and developing commercial products (9-14).

Biobarrier technology based products that have been laboratory and field tested include a root repelling sewer gasket (ROOT-SHIELD) for concrete, clay, and PVC sewer lines, a spun-bonded polypropylene geotextile fabric (BIOBARRIER) with nodules or pellets equally spaced over the geotextile developed to prevent root growth from invading septic tanks; and for penetrating under roadways, and along the edge of sidewalks, airport runways, and tennis courts; and into landscaped areas; and an impregnated plastic drip irrigation emitter (ROOT-GUARD) designed to protect buried drip irrigation systems from being plugged by roots. The lack of environmental concerns related to these applications has led to the rapid approval of an extended-use label for technical-grade trifluralin by the U.S. Environmental Protection Agency.

The Biobarrier Technology is based on the principle of long-term controlled-release by means of a polymeric delivery system. The system acts as a reservoir for the herbicide, protecting it from photochemical, chemical, and biological degradation, while providing a method for controlled release. Thus the bioactive chemical is released slowly, in a controlled manner, to the soil adjacent to the device. This polymeric delivery system maintains an effective dose for a substantial length of time, in contrast to single application methods, which result in higher than necessary concentrations immediately after treatment followed by rapid degradation to a level below the minimum effective dose required for control (Figure 1). This figure represents a theoretical model of 0-order controlled-release from a polymeric reservoir for which there is 6 years of field test data for validation purposes.

MATERIALS AND METHODS

Trifluralin

Pure trifluralin, which is produced as a 95% technical-grade compound, is a yellow-orange crystal that melts at 49°-50°C and thermally decomposes at 275°C. It is readily soluble in organic solvents, has low solubility (0.3 ppm) in water, and photodegrades rapidly if exposed to ultraviolet light (photochemical half-life is approximately 2 hours) (15).

The family of chemicals known as dinitroanilines, of which trifluralin (trade name, TREFLAN) is the most widely used, inhibits the division of cells by inhibiting spindle formation at the end of the root tip in such a way that the root is unable to grow. It is effective, through direct contact and in vapor phase within soils, on the roots of both grasses and broadleaf plants. It is not known to bioaccumulate in plants (i.e., it is not systemic); thus it will not be transported through the food chain to wildlife, domestic animals, or humans. In the application of trifluralin for biobarrier-based products, the growth of the aboveground portion of trees, shrubs, or grasses will not be adversely affected except through the limiting root mass.

All dinitroanilines affect root growth in a similar fashion, some more or less than others. However, the herbicidal activity, physical and chemical properties, and environmental characteristics make trifluralin ideal for incorporation into polymers for controlled-release as a biobarrier. In Table 1 the physical properties of several dinitroaniline-type compounds marketed as preemergence herbicides are compared.

Biobarrier Device Preparation

Special preblends were prepared (5-6) by the following technique: polyethylene powder (35 to 50 mesh) was mixed thoroughly with carbon black (18%) and the mixture warmed in an oven to 60-70°C. Trifluralin was melted in a beaker and heat, under agitation to 100-110°C. This molten trifluralin was the slowly blended into the warm polyethylene-carbon black mixture with constant mixing until cooled, producing a friable black powder for use in injection molding.

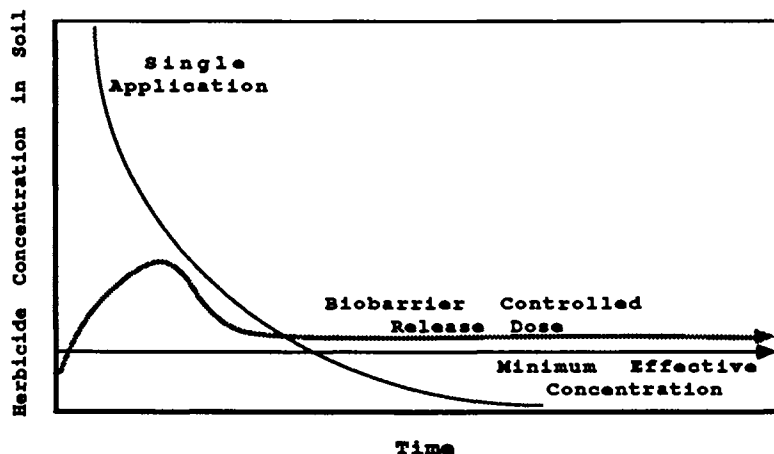


Figure 1. Comparison of Single Application and Controlled-Release Method.

Table 1. Physical Properties of Dinitroaniline Herbicides

Common Name	Trade Name	Melting Point (°C)	Vapor Pressure (mm Hg)	H ₂ O Solubility (ppm)
Trifluralin	Treflan(a)	49-50	1.1×10^{-4}	0.3
Benefin	Balan(a)	67-68	2.8×10^{-5}	0.1
Isopropalin	Paarlan(a)	-	2.7×10^{-5}	0.08
Oryzalin	Surflan(a)	140-142	1.0×10^{-7}	2.5
Ethalfuralin	Sonalan(a)	57-59	8.2×10^{-5}	0.3
Pendimethalin	Prowl(b)	56-57	4.0×10^{-5}	0.3
Profluralin	Tolban(c)	65-66	3.0×10^{-5}	<0.5

(a) Trade Names for Elanco Products Company, Division of Eli Lilly and Co., Indianapolis, Indiana

(b) Trade Name for American Cyanamid Co., Wayne, New Jersey

(c) Trade Name for CIBA-Geigy Corp., Hawthorne, New York

Evaluation of Release Rate from Biobarrier Devices

The experimental system was designed to optimize and control temperature and flow rate conditions that influence release rates and that are governed by trifluralin solution concentration, vapor pressure, and diffusion. The experimental systems consisted of a series of continuous flow-through test cells, maintained at selected temperatures by temperature controlled jackets (Figure 2). *In vitro* test cells were used to provide data to estimate minimum effective lifetime for various trifluralin-polymer devices. Three primary temperatures, $12 \pm 1^\circ\text{C}$, $25 \pm 1^\circ\text{C}$, and $39 \pm 1^\circ\text{C}$, were chosen to simulate a range of average soil temperatures with depth or location of usage. The resulting data can be extrapolated to other temperatures and use conditions by plotting release rate versus $1/T$, with T in degrees Kelvin ($^\circ\text{K}$) (5). This test system, utilizing temperature control, provides a means of **accelerated aging** of the biobarrier devices to determine the useful bioactive life of the devices (which must range up to 100 or more years) in a period of only four to six months.

The extracting eluent (water containing 10% methanol and 0.1% Tween 40 to enhance the solubility of the trifluralin) was pumped through the test cell (Figure 2) at a rate of 50 to 200 ml per day ("sink" conditions) depending on concentration and temperature. The eluent was collected in darkened glass containers.

The volumes perfused over the devices are dependent on loading levels in the device and on release rates; the goal is to flow sufficient eluent by the device to enable detection and quantitation of trifluralin, yet not approach 10% of the trifluralin solubility in the eluent. All lines leading into and leaving the flow cell were stainless steel to prevent the absorptive loss of trifluralin that occurs with plastic lines. Trifluralin was directly analyzed in the flow cell effluent at 3- to 5-day intervals. The daily release rate was calculated from the concentration of trifluralin in the sample aliquot, the length of time over which the sample was collected, and the volume of the sample collected in that time period. Because "sink" conditions were maintained within each flow cell, eluent flow rate only affected sample volume and was not used directly in calculating the *in vitro* daily release rates.

Chemical Analysis of Trifluralin

Aliquots (50-200 μl) of device extracts or test cell eluents were analyzed by high-pressure liquid chromatography (HPLC) using a C-18 μ -Bondapak column and 80% methanol mobile phase; detection and quantitation of trifluralin was performed using its ultraviolet (uv) absorbance peak at 273 nm. This method permitted separation of interfering constituents from trifluralin and its degradation products.

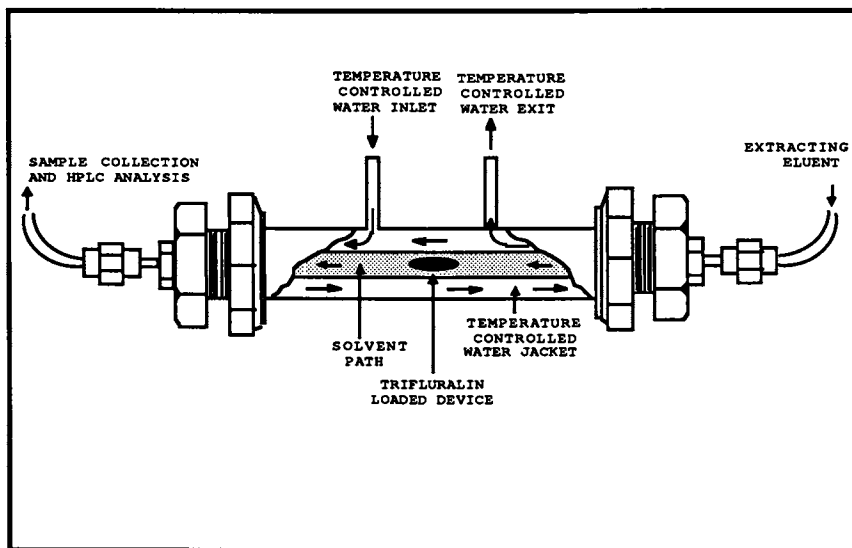


Figure 2. Details of Continuous-Flow Diffusion Cell.

Calculation of Useful Life Expectancy of Devices

In Vitro Effective Life (IVEL)

Laboratory measurements of release rates, based on temperature responses obtained from the *in vitro* test cell, can be used to calculate an absolute worst-case condition with respect to bioactive longevity of the biobarrier device. This calculation is based on a very conservative assumption that the concentration of trifluralin at the soil/device interface, as mimicked in the flow through diffusion cells, would be nearly zero. However, since in fact a significant concentration of the herbicide exists on the surface of the device as well as in the soil surrounding the device, the release rate for a pellet in the soil will be less than the calculated rate for the same device in the *in vitro* system. Based on 1) the estimated daily release rates from the devices *in vitro*, and 2) the total trifluralin content, the *in vitro* effective life of the device can be calculated. This assumes that there is not chemical degradation of the trifluralin, for which there is supporting data, and that there is no physical deterioration or erosion of the polymeric device.

Soil Effective Life (SEL)

In practice, the *in vitro* effective life of the biobarrier device is extended by 1) the presence of trifluralin on the surface of the device, 2) the soil trifluralin concentrations

that slow the rates of diffusion from the devices, and 3) the seasonal depressions in soil temperature that occur in many areas. The fluctuating temperatures in the soil also slow diffusion and increases the useful life of the device. Given these considerations, soil effective life of the biobarrier device can be calculated from the following formula:

$$\text{SEL in years} = \frac{2.4 \times \text{trifluralin content of device in } \mu\text{g}}{\text{in vitro release rate in } \mu\text{g/day} \times 365 \text{ days/yea.}}$$

The constant of 2.4 shown in the formula was empirically derived from laboratory *in vitro* and soil studies using a range of polyethylene devices sizes (5) and validated based on six years of field test data (8 and 11). The constant compensate for the diffusion gradients established at the interface between device and soil, thus permitting *in vitro* data to be used when extrapolating to field behavior. The temperature-dependence relationship, which is crucial to device performance and longevity, must be specified for a particular device. The temperature affects the daily release rate used in the equation; the rate at any temperature is determined from the temperature versus release rate plots.

Laboratory and Field Efficacy Experiments

Greenhouse Microcosms

Several replicated experiments were conducted in the greenhouse to evaluate the performance of various biobarrier devices. The microcosms that were constructed in 1984 and as shown in Figure 3. These microcosm were designed to simulate a typical leaking sewer gasket. The microcosm was designed for multiple years evaluation of the 1) actual release rates of trifluralin at greenhouse temperatures compared to *in vitro* flow-cell rates, 2) soil accumulation profiles, and 3) effectiveness of various concentrations of trifluralin-impregnated gaskets (9-10) in preventing root intrusion into the leaking pipe. The microcosm itself represents a modification of previously used designs (16). The microcosm was contained in a rectangular wooden box, constructed of marine plywood, 60 cm wide, 60 cm deep, and 90 cm (36 in.) high. The front panel was fabricated of a sheet of polycarbonate, 1.9 cm thick. A hinged plywood door, prevent the entry of light, allowed periodic soil sampling, and permitted visual observation of root growth.

Within the microcosm test system a 20-cm PVC elbow, fitted with either a control or one of three different trifluralin-treated 1.6-cm-diameter gaskets, was attached with clear silicone adhesive to the clear front panel (Figure 3). The gasket was perforated at three locations (both sides and top) to permit aqueous nutrient solution contained within the pipe to enter the otherwise dry soil. The holes in the gasket were 0.63-cm in diameter to optimize the potential for penetration of roots through the gasket into the PVC pipe. A series of soil-sampling ports were placed in the clear front panel, radiating outward from the soil/gasket interface.

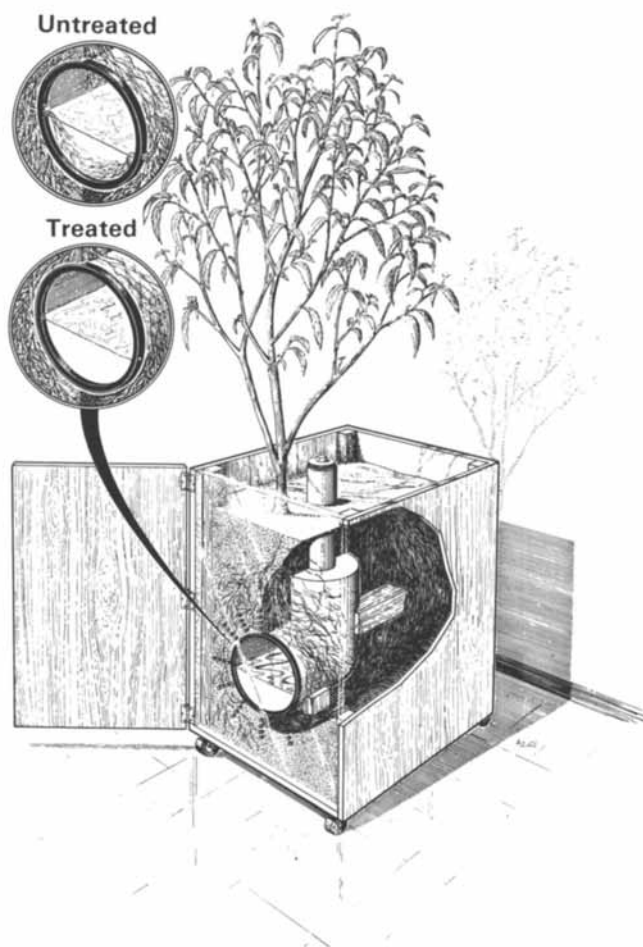


Figure 3. Microcosms Used to Evaluate Performance of Trifluralin-Containing Sewer Gaskets.

Once trees were established, the only moisture provided was either via purposeful overflow of the aerated solutions through the two side holes within the pipe or via water-saturated air contacting the soil when the water level was below the holes. All microcosms were planted with Yellow Willow (*Salix alba*, variety Vitellina), an aggressively rooting variety of willow. A total of twelve microcosms were fabricated; allowing for three replicates each of three different trifluralin-containing gaskets and three controls. Microcosms were completed and functional in December 1984. In the middle and at the end of each growing season soils were sampled for trifluralin content and those gaskets that were breached by roots were removed and extracted for remaining trifluralin. These test systems were held for 4 growing seasons and to assure that gasket performance is indeed adequate to inhibit root invasion into the sewer pipe, and to quantify soil trifluralin concentration profiles at various distances from the gasket over extended periods of time.

Field Validation Experiments

After several years of testing biobarrier devices in both the greenhouse and laboratory, two DOE nuclear waste disposal field sites, Grand Junction, CO, and Maxey Flats, KY, were identified for a multi-year test of the biobarrier technology. Laboratory studies indicated that 9 mm x 9 mm biobarrier devices placed on 5.0-cm centers should yield a sufficient concentration of trifluralin in the soil to prevent root elongation through the barrier zone. Based on these data two densities of pellets were used in field tests: 1,600 pellets per square meter (2.5-cm centers) and 400 per square meter (5.0-cm centers). Different protective seals (i.e., compacted clay, and asphalt) were selected and biobarrier pellets were placed over them. To ensure precision of placement of the pellets, two templates were constructed with 1.6-cm holes on 2.5- and 5.0-cm centers. In late August 1981, the following steps were completed at the Grand Junction site: 1) 5-cm of top soil was placed over the physical barrier, 2) the biobarrier pellets placed on the proper centers using the appropriate templates, 3) an additional 25- to 60-cm of top soil spread on top of the biobarriers by heavy earth-moving equipment, 4) the site seeded with a native grass, and 5) the locations of each plot recorded. At the Maxey Flats study site a series of in situ field lysimeters were established for evaluating the performance of the biobarriers(8).

Since initiating these studies, several trips have been made to each site to evaluate biobarrier performance. During these trips an inspection trench is dug over each type of barrier and 1) replicate samples of the vertical soil profile are taken for trifluralin analysis, 2) rooting depth is measured at both treatment and control sites, and 3) biobarrier pellets are removed to determine remaining trifluralin content. Three different concentrations of trifluralin in polyethylene. Figure 4 represents a plot of data for the high concentration devices tabulated in Table 3. The response of release rate to temperature is marked; rates vary by a factor of ~100 over a 25°C change in temperature. At the lower temperature, release rates were measured at 0.5- to 0.7- μg trifluralin/day, sufficient to develop and maintain a root-growth-inhibiting zone in the soil approximately 3 cm in diameter.

RESULTS AND DISCUSSION

Compatibility and Release Rates from Polymers

The original biobarrier studies, conducted for DOE (5-8), evaluated several polymers that could be used to provide controlled release of trifluralin to soil. Those polymers included polyethylene, polypropylene, polyvinyl acetate, polyurethane, polyvinyl chloride, ethylene propylene rubber, polyester, thermoplastic elastomer, and silicone rubber. A formulation consisting of ~60% powdered polyethylene, ~18% carbon black, and ~22% trifluralin was used for field studies at both Grand Junction, and Maxey Flats and has proven to be an effective system for root-growth control (see Materials and Methods for description of method of preparation of biobarrier devices. The material was injection-molded into individual cylindrical pellets of two sizes (7-mm diameter by 7-mm high and 9-mm diameter by 9-mm high). The pellets were incorporated into soil on a horizontal plane on both a 2.5- and 5.0-cm spacing.

Over the last several years various polymers have been evaluated for compatibility and for steady-state release rates of trifluralin. This study permitted an evaluation of polymers suitable for use in the biobarrier products. Some of the polymers tested and their release rates are shown in Table 2. In each case the polymer was loaded with approximately 10% technical-grade trifluralin in a homogeneous mixture and a sheet formed. The sheet was placed in the continuous flow *in vitro* system until release rate had reached quasi-steady state. Depending on the polymer used, release rates varied over a 60-fold range, indicating the range in rates that may be attained for this herbicide from a relatively small number of potential polymers.

Temperature-Dependent Release Rate

Temperature-dependent release rates have been measured in flow cells for all commercial products developed from the biobarrier technology. Table 3 shows the results obtained for

Table 2. Release Rates of Trifluralin from Different Polymers

Polymer Type	Release Rate ($\mu\text{g}/\text{day}/\text{cm}^2 \pm \text{SD}$)
Poly(ethylene-vinylacetate)A	9.3 \pm 3.3
Poly(ethylene-vinylacetate)B	13.3 \pm 0.6
Polyester	7.3 \pm 1.7
Poly(ether urethane)	3.4 \pm 1.0
Polyethylene (A)	1.5 \pm 0.2
Polypropylene (A)	4.2 \pm 0.4
Polypropylene (B)	3.9 \pm 0.4
Silicone rubber (B)	91.7 \pm 16.8

SOURCE: Data from ref. 5.

Table 3. Temperature-Dependent Release Rates and Equilibration Time for Polyethylene Biobarrier Devices Containing Low (3-5%), Medium (7-10%), and High (15-20%) Concentrations of Technical-Grade Trifluralin (Avg \pm SD, n=3)

Trifluralin Concentration	Temperature (°C)	Equilibration Time (days)	Rate of Trifluralin Release ($\mu\text{g/day/device} \pm \text{SD}$)
Low	38.9	30	11.4 \pm 9.2
	26.0	12	4.8 \pm 0.5
	12.5	-	not detected
Medium	37.3	18	49.8 \pm 25.4
	25.2	12	7.4 \pm 0.9
	12.0	12	≤ 0.7
High	37.7	18	110.1 \pm 41.0
	24.5	14	9.6 \pm 3.1
	12.6	20	1.3 \pm 0.4

Useful Life Expectancy

Estimated values of the soil effective lifetime (SEL) of the 7- and 9-mm devices developed for DOE are provided in Figure 5. The functional life of the 9-mm device based on ~22% trifluralin concentration would be approximately 60% longer *in vitro* life than that of the 7-mm device containing ~19% trifluralin. This significant increase in device longevity results from the change in ratio of volume to surface area with each incremental change in diameter. Thus, as the diameter of the pellet increased from 7-mm to 9-mm the surface area increased by ~19%, and the volume by ~31%. Actual measurements of trifluralin loading in the two different sized devices showed an increase in content from 40- to 65-mg trifluralin. Thus, the increased device size provides improved confidence with respect to establishing an effective root-growth-inhibiting zone for an extended period of time. The 9-mm device is expected to provide a slight increase in release rate per device, decreasing the lag-time for an effective root-growth inhibiting trifluralin concentration (~2 ppm to 10 ppm) to be built up around the device. The Soil Effective Life (SEL) of the 7-mm device ranges from 1.7 years at ~38°C to 68 years at ~12°C. The MEL for the 9-mm device ranges from 2.5 years at ~38°C to 104 years at ~12°C.

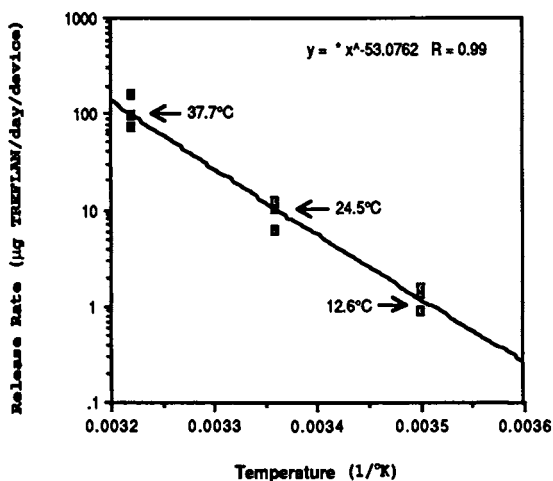


Figure 4. Relationship Between Release Rate and Temperature (1/T, where T=°K) for High Concentration Polyethylene Device.

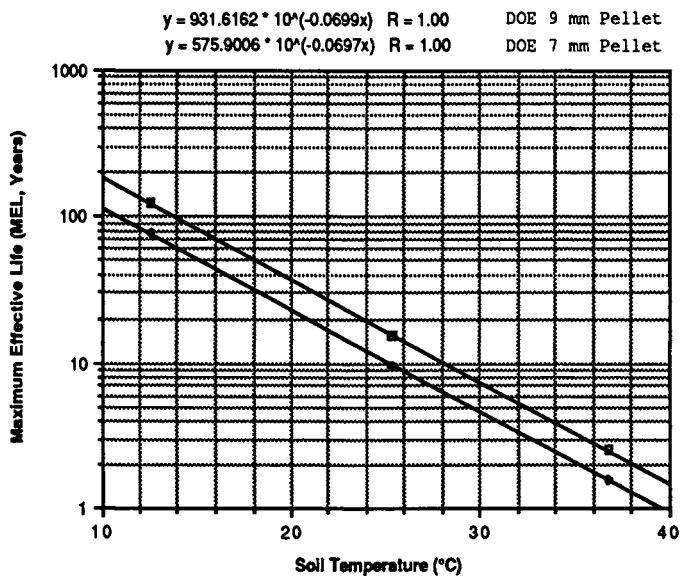


Figure 5. Soil Effective Life (SEL) for 7- and 9-mm Polyethylene-based Biobarrier Devices.

Greenhouse Microcosm Experiments

The results presented in Table 4 show soil concentrations of trifluralin at 2- to 5-cm from the gasket/soil (Burbank-loam) interface over the 2 years of testing. As noted earlier, the trifluralin concentrations in soil increase with gasket concentration, and equilibrium appears to have been reached after six months for the 1 and 5 % gaskets. Two of the three gasket concentrations, appear to release sufficient trifluralin to inhibit root elongation effectively; however, it takes approximately 6 months for the concentration to reach the necessary levels in the adjacent soils. Although this effective zone is some 2-5 cm away from the gasket, a ROOT-SHIELD gasket containing medium and high concentrations of trifluralin has a sufficient surface concentration of the herbicide to effectively protect the sewer line from root penetration while the concentration is building up in the adjacent soil.

Within several months of establishing the microcosms in the greenhouse, control gaskets were penetrated by roots. The first low treatment level gaskets containing between 0.5% trifluralin was breached in eight months, while medium (1% trifluralin) and high (5% trifluralin) treatment levels developed root barrier zones ranging from 2.5- to 5.0-cm into the soil. This is illustrated in Figure 6, which shows a split-image of a treated and a control (with root penetration) gasket. Gaskets containing lower percentage concentrations of trifluralin were found to be ineffective and were determined to have too short a SEL. However, the higher gasket loadings allowed for rapid development of a root exclusion zone, and had a sufficient concentration of trifluralin on the surface of the gasket to inhibit root penetration immediately after installation. Additionally, as determined by the accelerated aging tests, the reservoir of herbicide is sufficient to provide bioactive lifetimes of between 25 and 50 years for the size gasket typically used for municipal sewer lines.

Table 4. Influence of Equilibration Time on Trifluralin Concentrations (ppm \pm SD) in Soil Adjacent to Trifluralin-Impregnated Sewer Gaskets

Equilibration Time (days)	Concentration of Trifluralin in Gasket		
	0.5%	1.0%	5.0%
50	0.76	5.0	14.5
112	7.0	10.1	29.5 \pm 15.3
142	12.2 \pm 1.2	14.5 \pm 8.9	45.7 \pm 26.9
175	8.4 \pm 1.2	15.7 \pm 3.9	63.3 \pm 7.1
234	3.7	11.2	14.2
733	2.0 \pm 1.4	4.2 \pm 1.5	14.2 \pm 1.6

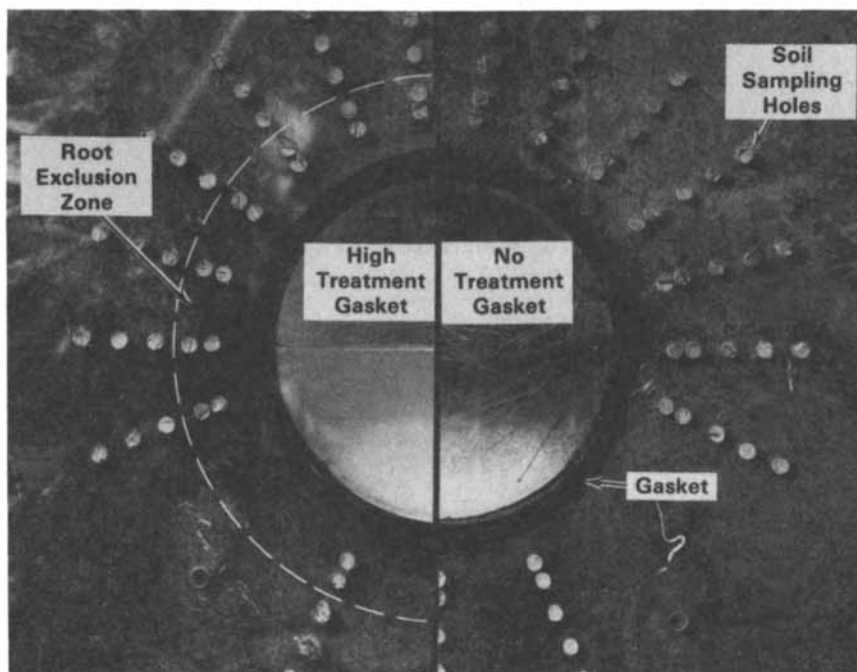


Figure 6. Split Image of Efficacy of High Concentration ROOT-SHIELD Gasket Compared to Control Gasket.

One final parameter that must be addressed is the ability of plant roots to be physically pushed through narrow zones of trifluralin concentrations. This phenomenon is frequently observed in small lysimeters, where narrow zones of normally inhibitory trifluralin concentrations are present and stop root elongation, but then roots are forced through the narrow inhibitory zone by secondary root expansion. Therefore, the depth or width of the inhibitory zone around the gasket becomes important in addition to the absolute soil concentration. The data shown in Table 5 address this aspect of the problem. If, on the basis of the plant root growth inhibition studies, we assume that a level between 5 and 10 ppm is adequate to inhibit root growth and if a level between 10 and 15 ppm is preferred, then we can estimate the width of the effective soil zone. Based on the results shown in Table 5, gaskets containing low (0.5-1.0%) and medium (2.0-3.0%) concentrations of trifluralin have an effective root-growth-inhibiting zone at 142 days of at most 3 cm from the gasket, while the high concentration gaskets (5.0-6.0%) have an effective zone as much as 5 cm from the gasket. Again, it should be stressed that these systems may not yet be at equilibrium, although we would assume that as equilibrium is attained, the effective zone will be increased.

Table 5. Soil Trifluralin Concentration (ppm \pm SD) Profiles Resulting from Three 1.25-cm diameter Gaskets Impregnated with Different Concentrations of Trifluralin

Distance from Gasket (cm)	Concentration of Trifluralin in Gasket		
	0.5-1.0%	2.0-3.0%	5.0-6.0%
2	12.2 \pm 1.2	14.5 \pm 8.9	45.7 \pm 26.9
3	8.7 \pm 2.3	10.4 \pm 7.1	30.9 \pm 16.6
5	5.9 \pm 3.3	2.2 \pm 2.1	8.5 \pm 4.7
7	3.6 \pm 4.4	0.3 \pm 0.5	2.2 \pm 2.1
9	0	0	0

Similarly, we would expect that the maximum soil concentration at each radial increment will increase to some slightly higher value. Because trifluralin was not detectable at distances of ≥ 10 cm from the device, which is supported by research performed by scientists at EPA Corvallis (17), therefore no groundwater contamination problem is foreseen.

Field Validation Studies

Results from the Grand Junction field site are shown in Table 6. The concentration of trifluralin in the soil near the devices, after five years in the field, exceeded the concentration (5 to 10 ppm) necessary to stop root elongation at the barrier zone. Roots of grasses that were planted and those native species that invaded the sites were observed to terminate in swollen tips approximately 7- to 9-cm above the biobarrier devices. Soil concentration for pellets placed on 2.5-cm centers indicate that the devices are placed closer together than necessary for root control. When devices are placed on 5.0-cm centers, the soil concentrations after five years meet or exceed the concentration necessary to inhibit root penetration. Results from Maxey Flats field tests also show concentrations of trifluralin in soil profiles sufficient to stop root growth (8).

Biobarrier pellets retrieved from Grand Junction were extracted for trifluralin content to determine the percent reduction in herbicide content compared to control pellets that had been maintained in sealed storage in the laboratory. Results are shown in Table 7. The control pellets contained an average of 188 mg of trifluralin or a 28% loading level. At manufacture, a concentration of 24% was estimated based on the theoretical losses caused by volatilization during fabrication. In comparison, the pellets recovered from Grand Junction had an average loading of 177 mg of trifluralin, representing a 5% loss over the control pellets or a 2% loss over the original estimate of 24%. Simple linear extrapolation assuming a 0-order release rate, which we do not expect to hold after $\sim 2/3$ of the herbicide has been depleted, would suggest that these devices will continue to release trifluralin for approximately 80 more years. This estimate compares favorably with the *in vitro* based effective lifetime for the 9-mm pellets of 104 years.

Table 6. Soil Trifluralin Concentration Profiles after 5 Years for Three Different Pellet Placement Configurations at Grand Junction, Colorado

Distance Above or Below Biobarrier (cm)	Trifluralin Concentrations (ppm)		
	Device Centers <u>Above Clay Barrier</u>		Device Centers <u>Above Asphalt Barrier</u>
	2.5-cm	5.0-cm	2.5-cm
+13 - 15	0	0	0
+10 - 13	0	0	0
+7 - 10	1.1	4.1	1.8
+5 - 7	4.2	10.1	4.1
+2.5- 5	10.2	22.1	9.4
0 - 2.5	16.7	45.7	14.2
0	-	-	-
-2.5- 0	23.8	50.7	27.7

Table 7. Trifluralin Content of Grand Junction and Laboratory-stored Control Pellets after 5 Years (a)

Device	Device Weight (mg)	Trifluralin Content (mg)
Control	674 ± 16	188 ± 8
Grand Junction	696 ± 18	177 ± 5

(a) Mean and standard deviations for 3 replicates containing 3 pellets each.

CONCLUSIONS

This report describes research performed on several biobarrier-based commercial products and provides data and support information which indicate that a maximum effective bioactive lifetime on the order of 100 years can be achieved. When placed in a layer of soil, the biobarrier system will prevent roots and shoots from penetrating through that layer without harming the overlying vegetation. Equilibrium concentrations in soil can be adjusted by varying the type of

dinitroaniline, the type and crystallinity of the polymer, the size and percentage trifluralin of the device (i.e., wall thickness for Fickian diffusion), the type and quantity of the carrier used with the trifluralin, and the geometric pattern or spacing on which the biobarrier devices are placed.

Commercial products designed, fully tested, and ready to enter the market place include: 1) ROOT-SHIELD, a root-repelling sewer gasket for concrete, clay, and PVC sewer lines, 2) BIOBARRIER, a spun-bonded polypropylene geotextile fabric with biobarrier nodules evenly spaced on the geotextile developed to prevent root growth from invading septic tanks; penetrating under roadways, and along the edge of sidewalks, airport runways, and tennis courts; and for landscaping; and 3) ROOT-GUARD, an impregnated plastic drip irrigation emitter designed to protect buried drip irrigation systems from being plugged by roots.

Acknowledgment

Research supported by the following: U.S. Department of Energy, Contract DE-AC06-76RLO-1830, Mantaline Corporation, Mantua, Ohio, Reemay, Incorporated, Kennett Square, Pennsylvania, and AGRIFIM Irrigation International, Inc. San Francisco, California.

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RECEIVED February 4, 1988

Chapter 19

Formulation of Living Biological Control Agents with Alginate

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Alginate is a water-soluble polysaccharide gum that has excellent gel-forming properties. Living organisms that are capable of biologically controlling a variety of agricultural pests can easily be entrapped in a calcium alginate matrix by a fast, gentle, aqueous, room temperature process. The gel beads, granules, or seed coatings that are produced by the process are biodegradable in the environment. Weed-killing fungi (Alternaria, Fusarium, and Phyllosticta spp.), antagonistic fungi (Trichoderma, Glilotadium, Talaromyces, and Penicillium spp.) and bacteria (Pseudomonas and Bacillus spp.) which can control soilborne plant disease pathogens, and insect-killing nematodes (Steinernema and Heterorhabditis spp.) have all been formulated successfully using alginate. This relatively new use of alginate properties to formulate biocontrol agents is a versatile and promising development in agricultural research which is reviewed in this paper.

Alginate is a linear, (1-4)-linked copolymer of α -L-guluronate and β -D-mannuronate that is a unique, water-soluble polysaccharide gum (1). Most of the alginate of commerce is extracted from Macrocystis pyrifera, a giant kelp, but it is an important structural component of all Phaeophyceae, the brown seaweeds.

Gel-forming, thickening, suspending, film-forming, and stabilizing properties make alginate solutions ideal for many food, pharmaceutical, cosmetic, agricultural, and industrial applications. As an adjuvant for pesticide spray formulations, alginate acts as a suspending and filming agent (1). Viscous solutions of sodium alginate containing the herbicide diquat dibromide have been extruded into water to control submerged aquatic weeds (2-4).

Sodium alginate solutions can easily be gelled by reaction with certain metal cations such as calcium by a mechanism that is known as ionotropic gelation. Alginate gels have been widely used for many years in food products (1). More recently, they have been used to immobilize microbial cells and enzymes for use in flow-through

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biochemical reactors (5-7) to produce useful chemical compounds such as ethanol, and to immobilize a fungus which decolorizes kraft mill effluent (8). In agriculture, the gelling property of alginate has been utilized in recent years for the preparation of controlled-release formulations of chemical pesticides (9-17).

Living organisms such as fungi, bacteria, and nematodes can be readily entrapped in a non-toxic calcium alginate matrix by a gentle, room temperature, aqueous-based process in which the organism is added to a sodium alginate (1-2% by wt.) solution and the resulting mixture is then added dropwise to a calcium chloride (3% by wt.) solution. Each droplet is gelled at the surface almost immediately upon immersion in the calcium chloride (gellant) solution to form a spherical gel bead. A residence time of 1-20 minutes in the calcium solution allows gelation to proceed from the bead surface toward the center as the Ca^{+2} ions diffuse inward and react with the carboxylate groups of the alginate. Gel beads containing the organism may be harvested and used in their "hydrated" state, or dried to form small pellets or granules. Organic or inorganic fillers, nutrients, or other adjuvants are normally added to the alginate/organism mixture before gelation in order to improve the final product.

Biodegradable, non-polluting alginate gel beads containing beneficial rhizosphere bacterial inoculants (18, 19) have been described. The alginate technique is also useful for the preparation and storage of large quantities of inoculum for field evaluation of disease resistance and fungicide evaluation as was done by Boyette and Walker (20) with the soybean-destructive fungus Cercospora kikuchii.

Biological control strategies are vitally important in today's agriculture because of the increased number of pests that are resistant to chemical pesticides and because of contamination of surface and ground water supplies by chemical pesticides. This paper reviews the use of alginate gel technology to prepare formulations containing living biological control agents such as fungi, bacteria, and nematodes for the control of agricultural pests such as weeds, soilborne plant pathogens, and insects.

Weed Control Applications

Granular formulations of fungal plant pathogens (mycoherbicides) can be applied preemergence to attack weed seedlings as they emerge from the soil when they are the most vulnerable to infection. Alginate granules containing indigenous weed-killing fungi (Table 1) were first prepared by Walker and Connick (21). Phyllosticta sorghicola, isolated from johnsongrass [Sorghum halepense (L.) Pers.], was included as a representative pycnidium-forming fungus. Each fungus was cultured and formulated separately. The fungi were grown in a commercial fermentor, the mycelium and growth medium were homogenized, and sodium alginate, water, and kaolin filler were added. Granules that contained the mycelium dispersed throughout were prepared by dropwise addition of the alginate mixture to a calcium chloride solution, and then air-drying the resulting gel beads.

To determine the number of conidia (spores) produced per gram of formulation when sporulation was induced after 10 weeks storage, granules were placed on moist filter paper in petri dishes and were periodically exposed to light from sunlamps. At designated intervals, the conidia were washed from the granules using a dilute surfactant solution and counted under magnification.

The total number of conidia per gram of sample harvested 2, 5, 7, and 9 days after rewetting was compared to the number of conidia from a single harvest at 9 days (Table I).

Table I. Conidia obtained in single and multiple harvests from alginate granules

Fungus	Conidia (no. x 10 ⁶ /g Formulation)	
	Multiple Harvest ^a	Single Harvest ^b
<u>Alternaria cassiae</u>	1.5	0.64
<u>Alternaria macrospora</u>	2.4	1.40
<u>Fusarium lateritium</u>	9.6	13.0
<u>Colletotrichum malvarum</u>	11.3	28.0
<u>Phyllosticta sorghicola</u>	520	580

^a The same samples of the granules were rewetted and induced to sporulate after harvest at 2, 5, 7, and 9 days. No conidia were present initially.

^b A single harvest of conidia was made 9 days after rewetting the granules.

SOURCE: Data from ref. 21.

All of the fungi that were tested produced new conidia after each harvest during the washing and rewetting cycles to give a beneficial sustained-release effect. Multiple harvests gave higher conidia production for the two Alternaria species than did the single harvest at 9 days. Field observations have confirmed that the pathogens used in this study, when formulated and packaged as dried granules without conidia, sporulated readily under field conditions provided that adequate moisture was present. The ability of A. cassiae to infect and kill sicklepod (Cassia obtusifolia L.) seedlings has been demonstrated in field plots where the granules were applied preemergence (22).

Pycnidium-forming fungi are difficult to produce by conventional techniques, and only a few species have been studied as potential mycoherbicides. In the Walker and Connick (21) study, the Phyllosticta species produced numerous pycnidia on the granules. It appears that this method of alginate formulation may be ideal for pycnidium-forming fungi because the conidia need not be removed from the pycnidia for field application, thus offering better protection for the fungus against adverse environmental conditions.

The application of these alginate/fungus granules to soil is their most direct use. However, the granules can also be used as a matrices from which spores can be grown and harvested for other uses such as the formulation of foliar sprays.

Boyette and Walker (23) studied the weed control efficacy of the biocontrol fungus Fusarium lateritium Nees ex Fr. formulated as a conidial spray or incorporated in alginate granules. The formulations were applied in the greenhouse to corn, cotton, and soybeans that were infested with velvetleaf (Abutilon theophrasti Medic.) and prickly sida (Sida spinosa L.), and applied in the field to soybeans infested with these same weeds. In the greenhouse, both weeds were effectively and equally controlled with the postemergence conidial spray or the preemergence alginate/F. lateritium granules (Table II). The field test data in Table II also show that the spray and granule applications gave about the same weed control, which was low because of drought conditions that year.

Table II. Biological control of velvetleaf and prickly sida in soybeans with Fusarium lateritium in greenhouse and field tests

Treatment	Weed Control (%) ^a			
	Greenhouse ^b		Field ^c	
	Velvetleaf	Prickly sida	Velvetleaf	Prickly sida
Conidial spray	91	94	30	36
Alginate/ <u>F. lateritium</u> granules	89	92	35	38

^a Controls consisting of surfactant-only spray and granules without fungus gave 0-9% weed control. Weed control was determined by percent stand reduction after 4 weeks.

^b Spray: postemergence, sprayed to runoff, 1.5×10^6 conidia/ml; granules: preemergence, 1120 kg/ha rate.

^c Spray: postemergence, applications 1-week apart, 1.5×10^6 conidia/ml; granules: preemergence, 1120 kg/ha rate.

SOURCE: Data from ref. 23.

The alginate/*F. lateritium* granules served a dual purpose: (a) they were applied directly to test plots in a conventional manner; and (b) they were used to grow conidia for the spray formulations. In the latter case, fungus-infested granules were placed in trays and hydrated with distilled water. The trays were covered with plastic film and the granules were incubated and exposed periodically to ultraviolet light from sunlamps. The fungus sporulated profusely on the granules and the macroconidia were rinsed from the granules with water.

Lindow conducted a field experiment in which a conidial suspension of an *Alternaria* species that is a specific biocontrol agent for Italian thistle (*Carduus pycnocephalus* L.) was compared with an alginate granule preparation containing the fungus plus soy flour and cornmeal (50/50) as nutrients and fillers (Lindow, S., University of California, Berkeley, personal communication, 1987). The results (Table III) show that the granules, when used with Italian thistle seedlings (2-4 cm high) in the presence of rain splash, were effective in delivering viable, infectious propagules to the thistles. The infection obtained (judged after 3 weeks) with the granules was better than with the conidial spray formulation. However, in other trials where hard rain was not encountered or where the thistle plants were taller, infection was not as severe. This seems to be due to a lack of sufficient dispersal of spores to the target plant from granules that rest on the soil surface. Even though the granules are thickly covered with *Alternaria* spores, there is usually not much air movement at ground level to effectively disperse the spores. This is a limitation inherent in any granular formulation of a fungus like *Alternaria* that produces spores which attack the aerial portions of a weed.

Table III. Severity of foliar necrosis incited by *Alternaria* sp. on Italian thistle (*Carduus pycnocephalus*). (Lindow, S., personal communication, 1987).^a

Treatment	Infection (Percent of leaf) ^b
Control	0.02
Conidial suspension ^c	41.0
Alginate/ <i>Alternaria</i> granules	50.5

^a The fungus was applied to 2-4 cm tall plants in a field plot. At least one rain shower occurred during the 3-week duration of the test.

^b Three weeks after treatment.

^c About 10^5 conidia/ml.

Granules are, however, an almost ideal vehicle for applying soilborne fungal weed pathogens. Weidemann (24, 25) used the alginate gel technique to formulate the endemic, soilborne fungus Fusarium solani f. sp. cucurbitae for the control of Texas gourd (Cucurbita texana) in Arkansas soybean fields. This fungus causes a collar rot and root rot which leads to a rapid wilt and collapse of the weed. Alginate granules that were amended with the nutritional adjuvant soyflour (2% w/v) and applied at a rate of 112 kg/ha and 224 kg/ha, and granules amended with ground oatmeal (2% w/v) and applied at 224 kg/ha gave >80% weed control within 6 weeks. Spores washed off the granules into the soil after rainfall, thereby contacting the target weed at the soil level and below to cause infection. The number of fungal spores produced is greatly increased in the soil when a nutritional component is incorporated in the formulation. Both pre- and postemergence (seedling stage) applications of the alginate granules were effective.

Soilborne Plant Disease Control

Alginate granule formulations containing antagonist microorganisms have been an innovative and promising approach for the control of soilborne plant pathogenic fungi. The spherical, biodegradable granules can be applied to soil using conventional agricultural equipment.

Fravel, et al. (26) incorporated conidia and/or ascospores of isolates of Talaromyces flavus, Gliocladium virens, Penicillium oxalicum, or Trichoderma viride, or cells of the bacteria Pseudomonas cepacia in alginate granules with a pyrophyllite filler. The soilborne plant disease targets of these and similar biocontrol organisms are shown in Table IV. Many crops worldwide are severely impacted by disease-causing microorganisms. Rhizoctonia solani, for example, is a fungal pathogen of about 200 economically important crops.

Viability of the biocontrol agents in formulations gelled with calcium chloride and calcium gluconate were compared after 12 weeks and it was found that calcium gluconate enhanced the survival of encapsulated bacteria and fungi better than the chloride. Bashan (19), however, found that calcium chloride was a satisfactory gellant for use with bacteria when a secondary multiplication of the bacteria was induced by incubation of the gel beads in fresh nutrient broth medium.

Fravel, et al. (27) have subsequently shown that an alginate/pyrophyllite/T. flavus formulation suppressed Verticillium wilt incidence in potatoes under actual production conditions. A significant amount of protection carried over to the following year without further treatment (28). Papavizas, et al. (29) thoroughly studied alginate granule formulations of T. flavus, particularly the survival and multiplication of the fungus in soil and survival of propagules during storage. Conidia in alginate-bran granules gave the highest population density in soil, but ascospores survived best in storage (5-25°C).

Table IV. Biological control agents incorporated in alginate granules to combat soilborne plant pathogens

Biocontrol Agent	Plant Disease Target	Disease Pathogen	Bioassay Crop
<u>Talaromyces flavus</u>	Verticillium wilt	<u>Verticillium dahliae</u>	potato, eggplant
<u>Trichoderma hamatum</u>	Rhizoctonia damping-off	<u>Rhizoctonia solani</u>	cotton, sugar beet
<u>Trichoderma harzianum</u>	"	"	"
<u>Trichoderma viride</u>	"	"	"
<u>Gliocladium virens</u>	"	"	"
<u>Pseudomonas cepacia</u>	Phythium damping-off	<u>Phythium ultimum</u>	soybean

Lewis and Papavizas (30) and Lewis, et al. (31) first demonstrated that when an organic nutritive filler, wheat bran, is incorporated in alginate granules with Trichoderma or Gliocladium instead of an inert clay, proliferation of the biocontrol fungus in soil is significantly increased. These alginate granules containing a food base were capable of reducing the inoculum density of the pathogen Rhizoctonia solani and preventing damping-off disease of cotton and sugar beet seedlings in different soil types. Shelf life of the formulations was good.

The Lewis process allows the use of wet fungal biomass of Trichoderma or Gliocladium directly from fermentation vessels. Interestingly, relatively low amounts of wet biomass were as effective as high rates when they were incorporated in alginate granules (32). Fungal biomass is an ideal inoculum for granules because it can easily be prepared in large quantities and because it contains abundant chlamyospores, the hardy, resistant, and effective propagule of these biocontrol fungi.

The considerable body of encouraging results obtained with alginate granules containing biocontrol fungi applied to soil for the control of soilborne plant disease indicates a good commercial potential for these formulations in selected applications. However, more research is needed to further improve effectiveness and shelf life.

Alginate Seed Treatments for Disease Control

Placing a biological control agent directly on a crop seed insures its presence where the protection is needed. Fravel, et al. (28) incorporated two beneficial bacteria together in an alginate-pyrophyllite seed coating for soybean. Pseudomonas cepacia

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suppressed postemergence damping-off disease and Rhizobium japonicum effectively nodulated the soybean roots for nitrogen fixation. A multi-purpose formulation such as this involving compatible microorganisms has obvious advantages, and is worthy of additional research.

Garber, et al. (33) coated cotton seed with T. viride, G. virens, or Bacillus subtilis incorporated together with oat bran in a hard, strong, adherent matrix of alginate-pyrophyllite. Positive seedling disease control was obtained. The biocontrol fungi were easily isolated from seedlings taken from plots where they were applied as seed coatings. Results obtained the following year (34) when the oat bran was sterilized before use were not as good. It was postulated that a high, natural population of Bacillus spp. present in the unsterilized bran had provided an additional protection against Pythium spp. or R. solani. Particularly good results were obtained when fungicides were applied in combination with the biocontrol seed treatments.

Encapsulation of Nematodes

Kaya and Nelsen (35) recently opened a new area of research in insect control with the encapsulation of biocontrol nematodes in alginate gel beads. In order to perform their function as biocontrol agents, the nematodes must somehow escape or be liberated from encapsulation to seek out hosts. Infective stages of the nematodes Steinernema feltiae or Heterorhabditis heliothidis were encapsulated at a concentration of about 300 nematodes per gel bead (capsule) and fed to larvae of beet armyworm (Spodoptera exigua). The nematodes were released when the insect larvae bit into the gel beads. The kill rate was excellent as long as adequate moisture was present to prevent desiccation of the nematodes (Table V). The S. feltiae formulation maintained its population and infectivity when stored for 8 months in closed containers at 4°C.

Table V. Control of beet armyworm (S. exigua) larvae exposed to nematodes encapsulated in alginate gel beads ^a

Nematode Genus	Number of Larvae	
	Alive	Dead
<u>Heterorhabditis</u>	2	35
<u>Steinernema</u>	0	38
Control ^b	36	0

^a Larvae and gel beads were placed on moist filter paper.

^b Gel beads without nematodes.

SOURCE: Data from ref. 35.

Infective stages of *S. feltiae* (= *Neoalectana carpocapsae*) and *H. heliothidis* were also encapsulated in alginate capsules by Poinar, et al. (36). The *S. feltiae* capsules were placed in several habitats and, with adequate moisture, most of the nematodes were able to migrate out of the capsules by one week. When bacteria were abundant in the surrounding environment, they decomposed the capsule matrix and accelerated release of the nematodes.

Kaya, et al. (37) recently devised a technique to place a quantity of *S. feltiae* nematodes and a tomato seed into each alginate gel bead. Nematodes are released from the beads when the seeds germinate and are therefore already in position to protect the seedlings from insect attack. Successful bioassays with these gel bead formulations were conducted in sterilized and nonsterilized soil against larvae of the greater waxmoth (*Galleria mellonella*). Insect larvae were killed even without seed present in the soil-applied capsules which indicates that some nematodes managed to escape from the capsules through their own ability.

Calcium is removed from complexation with alginate by the action of phosphate (19, 26) or citrate (37) buffer solutions which preferentially bind the calcium and solubilize the alginate matrix. In this way, calcium alginate gel beads or granules can be dissolved so that entrapped organisms can be counted easily. It should be noted that phosphate fertilizer would also act to weaken or degrade the structure of calcium alginate formulations in soil and accelerate the release of active ingredients.

Conclusions

Alginate technology has proven to be useful for the formulation of a variety of biological control agents. Dried or hydrated calcium alginate matrices can protect living organisms in storage and in the environment, yet permit the escape of entrapped agents to attack the target pests. Combinations of biocontrol agents or combinations of chemical and biological pesticides in a single alginate formulation show great potential. With such combinations, a broader spectrum of pest control could be achieved from a single application. It is now time to study in detail the economics of alginate formulations. Cost-effective formulations of biocontrol agents are of paramount importance for the success of biocontrol technology, and research in this area needs to be increased.

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RECEIVED January 11, 1988

Chapter 20

Development of Solid Pesticide Formulations by Fluidized-Bed Technology

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The fluidized bed granulator is versatile. Its application to pesticide formulation includes granulation, drying, coating and mixing products. In a fluidized bed granulation process, the granulation and drying are concurrent process in the same unit. It offers several advantages over the most common process, pan granulation method, in making water dispersible granules. The fluidized bed granulation can also be used to convert a liquid formulation containing a surfactant into a solid product. Some water soluble pesticides are the examples of this application.

Fluidized bed technology has been known and used for many years. Its drying, mixing, granulating and coating efficiency has been applied to a wide variety of material in the food, chemical, pharmaceutical, mineral and ceramic industries (1). In recent years, the interest of this technology has been increasing in pesticide formulation development.

The object of this study is to demonstrate the application of Fluid Bed Granulation for the development and manufacturing of new and improved agricultural formulations.

The mechanism involved during granulation are layering and coalescing (agglomerating) (2,3). Layered granules come from particles enlarged by consecutive layering of material on nuclei; these granules usually have a smooth spherical shape and their cross sections look like that of onions (Fig. 1). Conversely, coalesced granules are formed when fine particles are incorporated rapidly into granule clusters (raspberry-like) which tend to have irregular shapes and rough surfaces (Fig. 2). Both mechanisms will occur simultaneously during granulation but one of them will predominate.

By adjusting the operating parameters of the system and by carefully selecting the physical properties of the formulation ingredients, the growth mechanism can be controlled. Since the growth mechanism

0097-6156/88/0371-0251\$06.00/0

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will ultimately determine the physical properties of the final granular products, i.e., shape, particle size distribution, and flowability, its importance cannot be overstated.

A fluid bed granulator transforms pumpable and atomizable granulating liquids, such as solutions, melts, slurries, or pastes, into granules by making feed particles grow. Such growth is achieved by spraying, mixing, granulating, and drying in one enclosed vessel.

The formation of a fluidized bed happens when air is passed upward through a bed of solid particles resting on a retention screen. In lab models, air-flow necessary for fluidization is generated by a fan but on large production units it is generated by suction-fans that create negative pressure. A useful feature is the ability to heat the air being used which is used to dry the product while it is being made. The material to be processed can be placed into the product container or it can be part of the granulating liquid. The perforated plate at the bottom of the container has a fine mesh screen to prevent the solid particles from falling into the machine. On top it has exhaust filters that allow air to escape while retaining small particles and dust. A diagram of a typical fluidized bed granulator is shown on Fig. 3.

Two types of solid pesticide formulations that have gained interest are the Water Dispersible Granule (WDG) and Water Soluble Granule (WSG). The WDG offers many advantages over Wettable Powders (WP) and Liquid Flowables (F) because it reduces hazardous dusting, hard packing, and settling problems. At the same time, it is easy to measure and can be concentrated with active ingredients. Moreover, it is easy to handle, package, ship and warehouse. From a cleaning standpoint, spills of WDG's and WSG's are much easier to clean than WP's and F's.

Just as interesting as the WDG is the conversion of water soluble pesticides into granular forms. The WSG offers the same advantages of the WDG and then goes one step further by being soluble in water.

Most of the granulation processes produce a hard pack granule that do not meet the performance requirements of a WDG so only a few methods are applied to formulate it; extrusion, for example, makes a granule by compaction but it is not suitable to formulate WDG. Compaction, however, is not a problem for WSG's since the granules are soluble.

At present, one popular method is Pan or Disc Granulation. It is a simple operation. Details on WDG formulation by pan granulation are available in the literature (4-6). Despite its popularity, pan granulation has some shortcomings that can be pointed out when it is compared to fluidized bed granulation. For comparison purposes, it will serve well to see how both systems are used to formulate a WDG.

Experimental

Water Dispersible Granule (WDG). A 1 kg laboratory fluidized bed granulator (Aeromatic size 1, Aeromatic Inc., NJ) and a 16" pan granulator (Ferro-Tech, Wyandotte, MI) were used to formulate a WDG whose composition is given in Table 1. Captan technical was used as the active ingredient.

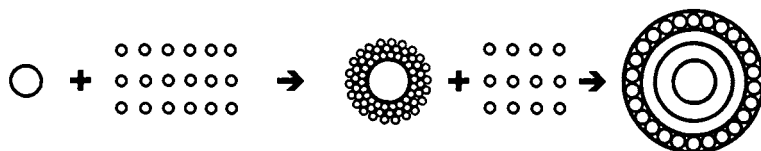


Figure 1. Particle Size Enlargement by Layer Mechanism.

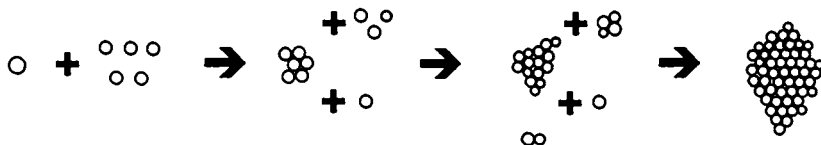


Figure 2. Particle Size Enlargement by Coalescence Mechanism.

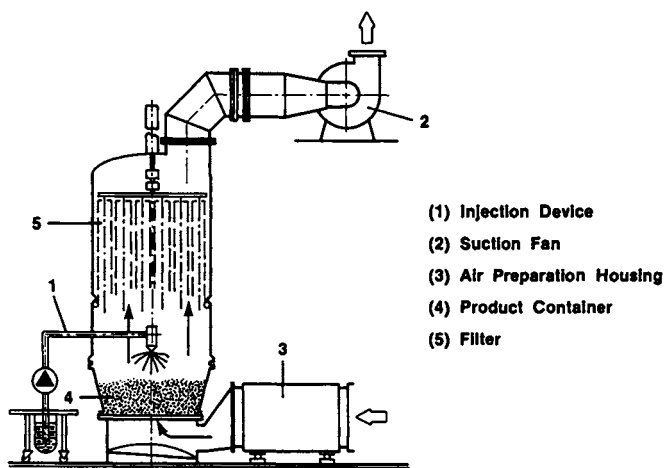


Figure 3. Fluid-Bed Spray Granulator.

Table 1. Composition of WDG

<u>Ingredients</u>	<u>Wt %</u>
Active Ingredient	40-90
Wetting Agent	1-4
Dispersant	1-12
Diluent	0-45
Binder	0-2

In fluidized bed granulation, all ingredients are first blended and micronized to a desired particle size then loaded into the granulating container. The granulating liquid can be water or a binder solution which is sprayed onto the fluidized particles. The process of inter particle collision in the presence of spray liquid causes the particles to agglomerate and layer; consequently, the particles are enlarged. The product is dry since the fluidized bed granulator is using heated or room temperature air but if it still needs drying, it can continue to dry without spraying. Finally, the finished dry granules can be easily sieved to the required size.

Another way to make a WDG using the fluid bed granulator is to spray a slurry of ingredients onto a small amount of powdery seed material. In this case, the slurry can be wet-milled to the desired size keeping in mind that the slurry must consist of WDG ingredients mixed with enough water to make it pumpable and sprayable. Water will again be removed by the heated air and sieving will follow.

Pan granulation like fluidized bed granulation uses blended dry ingredients that have been micronized. After spraying and granulating, however, the granules are wet and need post-drying before they can be sieved. In lab operations, the wet granules are dried in ovens or in hoods but in scale-up operations a moving fluidized bed set at elevated temperatures is usually used for further drying; sometimes the excessive heat will harden the granules so much that they will not disperse readily.

Water Soluble Granule (WSG). The same machines were used for this experiment. The materials that were used were soluble pesticides like 2,4-D (2,4-Dichlorophenoxyacetic acid) and Round-Up™ (41.09% Isopropylamine salt of Glyphosate). A common composition for WSG is shown on Table 2.

Table 2. Common Composition for WDG

<u>Ingredients</u>	<u>Wt %</u>
Active Ingredient	30-60
Soluble Carriers	40-70

The fluidized bed granulation is conducted just like that of a WDG but the critical part in making a WSG is finding soluble carriers which can function as granulation nuclei. The carriers, in general, consists of water soluble materials. The commercially formulated pesticidal products are used as granulation liquids and sprayed onto the carriers.

Results and Discussion

In fluidized bed granulation, several factors i.e., nozzle air flow, height of spray nozzle, spray angle, formulation composition and inlet air temperature etc., can influence the physical properties of granules. By adjusting the process parameters, a Captan WDG produced by a fluidized bed granulator tends to be agglomerated by coalesced mechanism and forms predominately a cluster type particle (Figure 4). While a WDG made by a pan granulation usually is enlarged by layering mechanism and forms a rather smooth spherical shape particle (Figure 5). The raspberry cluster type granules have large surface area which disperse better than the smooth shape ones. Again, in the fluidized bed granulation, the granulation and drying are simultaneous; while pan granulation needs an additional drying step. Since the fluidized bed granulator has a very efficient drying capability, the products can be dried with either ambient or elevated temperature depending on the formulation compositions. On the other hand, drying in pan granulation requires, most of the time, much higher temperatures which sometimes causes poor dispersibility. Both micronized wettable powders and wet-milled slurries can be used as feed stocks in a fluidized bed granulation but not in pan granulation. Therefore, a low melting technical can be wet-milled and granulated in a fluidized bed granulator. With the proper adjusted conditions, the finished WDG from fluidized bed granulation has a narrow mesh size distribution (Figure 6). A typical experimental run generates a very small amount of oversize granules. The fines usually can be recycled in the subsequent batch. Unfortunately, the oversize materials in a pan granulation process is higher. To recycle the oversize WDG, materials have to be crushed, blended and milled again and this high recycling rate increases the overall cost of production.

A fluidized bed granulator operates with an explosion proof container and processes under negative pressure. It is an enclosed system that can substitute inert gases for fluidized air or it can be equipped with a solvent recovery system for a non-aqueous liquid operation. Therefore, a hazardous technical can be safely processed in a fluidized bed unit to minimize the risks of operational exposures. In contrast, a pan granulator is usually run in the open environment. Sometimes it causes hazardous dustiness. Table 3 summarizes the major differences between these two granulation methods.

A fluidized bed granulator is a versatile equipment. Its powerful drying and granulating capability can be utilized to convert an aqueous pesticide formulation into a solid soluble granule. Water soluble pesticides are usually formulated as aqueous concentrates. However, sometimes it is desirable to have a solid formulation for the ease of handling and spill cleaning as well as reducing the costs of transportation, and warehousing, etc. By properly selecting the carriers for granulation nuclei, a water soluble granule can be successfully produced by spray-granulating an aqueous pesticide concentrate. A 2,4-D granule is shown in Figure 7.

Optionally, dyes or polymeric materials can also be incorporated in the unit to coat granules. By this means, some controlled release products can be formulated.

Table 3. Major Differences Between Fluidized Bed Granulation and Pan Granulation

	<u>Fluidized Bed Granulation</u>	<u>Pan Granulation</u>
o Process Steps	Two Steps	Three Steps
o Feed Stocks	Air-mill Powder or Wet Mill Flowable	Air-Mill Powder
o Drying Equipment	Same Unit	Separate Unit
o Drying Temperature	Elevated or Ambient	Elevated
o Operational Exposure	Enclosed	Open
o Initial Capital Investment	High	Low

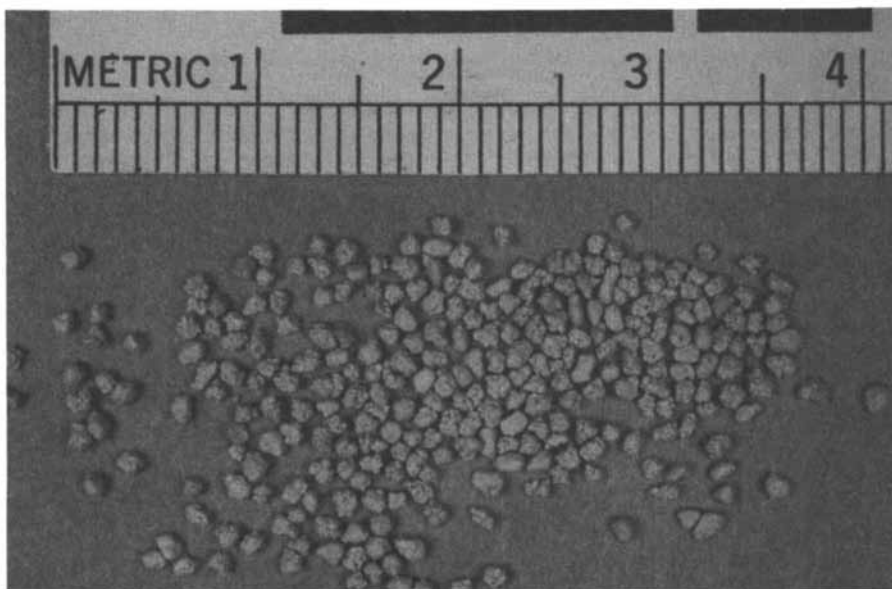


Figure 4. Captan WDG by Fluidized Bed Granulation.

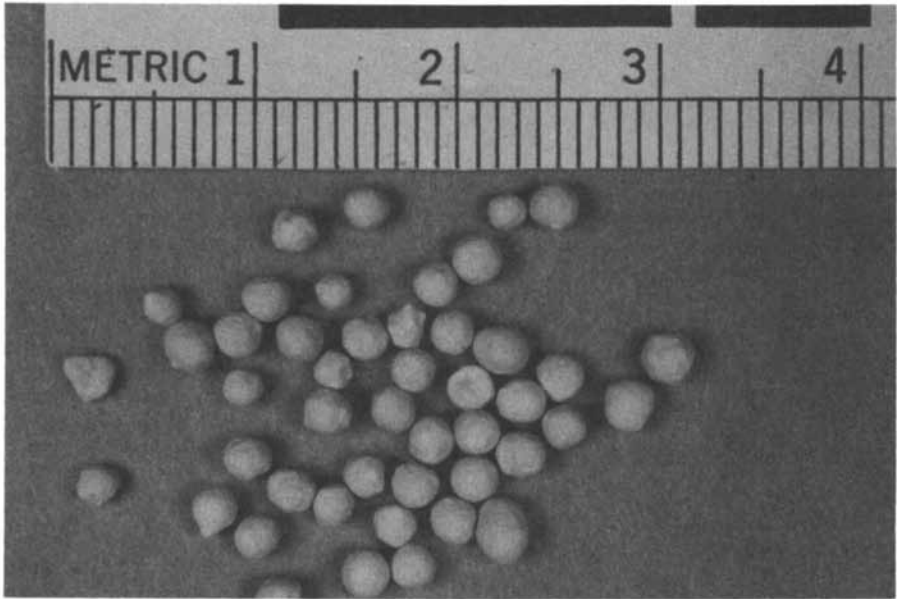


Figure 5. Captan WDG by Pan Granulation.

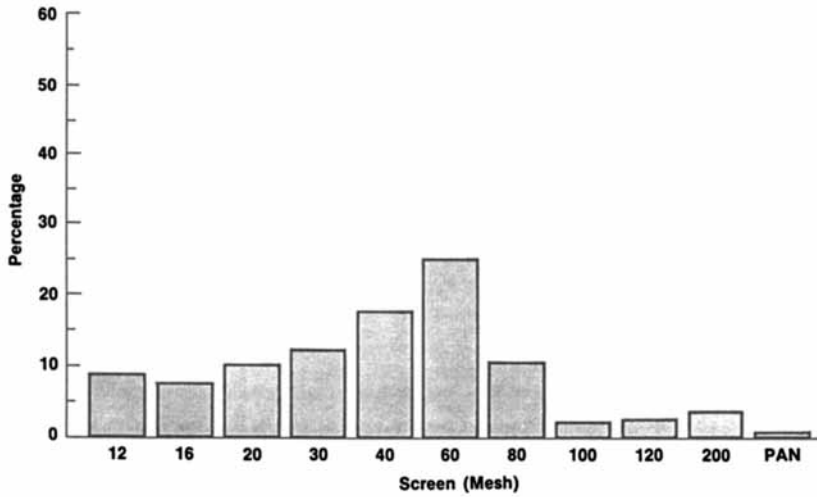


Figure 6. Sieve Analysis Profile.

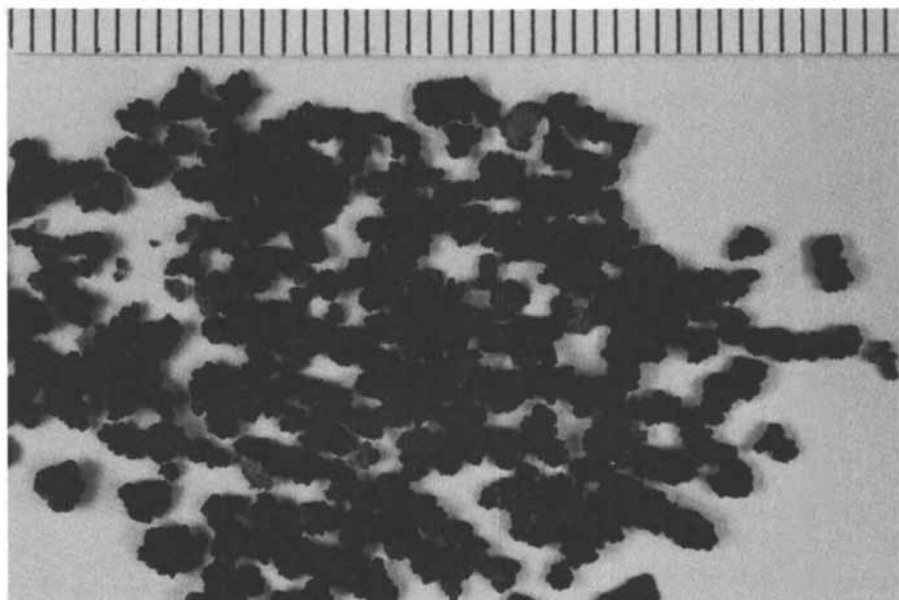


Figure 7. 2,4-D WSG by Fluidized Bed Granulation.

Conclusion

Various granulation techniques can be used for producing uniform, free-flowing, dustless granules. Unfortunately, most processes cannot produce a WDG that disperses readily in water to form a uniform and stable suspension much less a WSG.

Nevertheless, a fluidized bed granulator is versatile enough to work with inert gases since it operates in an enclosure. It eliminates operator exposure which is a problem anytime one deals with powders. It provides dust explosion protection with its explosion proof design. With modification, it can recover solvents that are used during granulation and has the capability to coat granules for controlled-release formulations. In addition, the process is environmentally safe.

It is unfortunately that the high initial capital investment needed for a fluid bed granulator and the limited availability of scale-up facilities are still obstacles that prevent people from looking into its capabilities. Yet, the overall quality of solid pesticide formulations resulting from this agglomeration technology should make a fluid bed granulator a useful tool in agricultural formulations.

Acknowledgments

I am grateful to the Agricultural Chemicals Division of Chevron Chemical Company for supporting this work. I also thank Mr. A. Karczewski, Mr. B. Hance and Mr. J. Smith for their assistance.

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RECEIVED February 4, 1988

Chapter 21

Pesticide Formulations and Other Parameters Affecting Dose Transfer

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The biological effect of a pesticide, properly timed, depends upon the toxicological properties of the AI, its formulation, the concentration and pattern of the dose at the point of action. Monosize droplet atomization techniques allow a precise examination of droplet/plant/pest relationships. The effects of droplet size, pattern, and formulation changes on the dose transfer process in various insects and mites involve delivery, impingement, retention, toxicity, behavioral and resistance phenomena. Separation of drop size, concentration, and formulation effects can be useful in understanding toxin activity and developing accurate parameters for specific targets and crop protection agents. High speed cinematography, computer image analysis, and fluorescence photography were used to study atomization, droplet formation and transport, deposition and deposit formation phenomena with various pesticide/additive combinations. Predictive responses in spatial disruption and age structure of specific pests are essential to the design of useful formulation/application protocols of each AI.

Pesticides provide innumerable benefits for the control of various pests which destroy almost 33% of all food crops. However, the use of such agents has also resulted in significant costs to public health and the environment (1). In general, the amount of agrichemicals released into the environment has risen 1900% in the 50 year period between 1930 and 1980 (2). Although the improved efficacy of the more recent pesticides has allowed a reduction in use rates as low as a few grams per hectare, the capability to effectively deliver these smaller amounts of agrichemicals to specific targets has become increasingly difficult to achieve (3).

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Spray application is a complex and dynamic process involving many interdependent components. As summarized by Young (4), the factors of atomization, transport to target, impaction, deposition formation, movement in/on plant, and biological effect are influenced by each other, the external factors of environment and operating conditions, target properties, as well as the formulation, and the active ingredient (AI). Improvements in pesticide use efficiency will require a more intensive study of the physical and physiochemical parameters controlling droplet dynamics, deposition on defined targets and biological response (Figure 1). The biological effect, properly timed, depends upon the toxicological properties of the AI, its formulation, the concentration and pattern of the dose at the point of action. Droplet deposition and biological response of pests and diseases have complex relationships, sometimes not well correlated and Hislop (5), Graham-Bryce (6) and Ford and Salt (7) suggest that there is a lack of basic understanding of the dose transfer processes.

Graham-Bryce (6) discussed the increasing efficacy of modern chemicals and suggested that further improvements in efficacy may not be as rewarding to agriculturists as unlocking such secrets as biological availability and developing bio-targeting via improved delivery methodology. Geissbuhler et al. (8) predicts that future activities for research in agrichemicals will be governed by such things as 1) advances in the knowledge of crop biochemistry and pest biology, 2) decreased successes in conventional approaches, 3) increased use of electronic information and data development and transfer, and 4) increased economic and ecological pressures leading to a modified crop technology and regulatory environment. As a consequence of this environment we will see 1) biotechnology becoming an increasing component of research, 2) more "biorational" designs, 3) more sophisticated evaluations, and 4) development of targeted oriented delivery systems.

Restructuring the placement of a pesticide (i.e., as close to the target as possible) is clearly fundamental to good pest management. As Courshee (9) concluded, the actual target needs to be defined in terms in both space and time. The proportion of pesticide which finally reaches the target and the form available to the pest must be enhanced if we are to increase the efficiency of pesticides. With respect to insects, increased knowledge of the biology should reveal the stage of greatest vulnerability and a greater understanding of insect movement and probability of impingement or encounter (with a residue) within a crop structure (i.e., canopy). This understanding will dramatically increase our ability to select or design more accurate schemes, improve timing or develop resistance management, some of which could only be implemented if improved application technology existed. Under current conditions, savings in pesticide inputs are not being fully realized.

While pathogens and weeds (i.e., *Phytophthora*; *Amaranthus* spp., respectively) also elicit a number of difficulties in targeting, one of the major problems resides in identifying the specific target site and subsequent protocols. Matthews (10) has

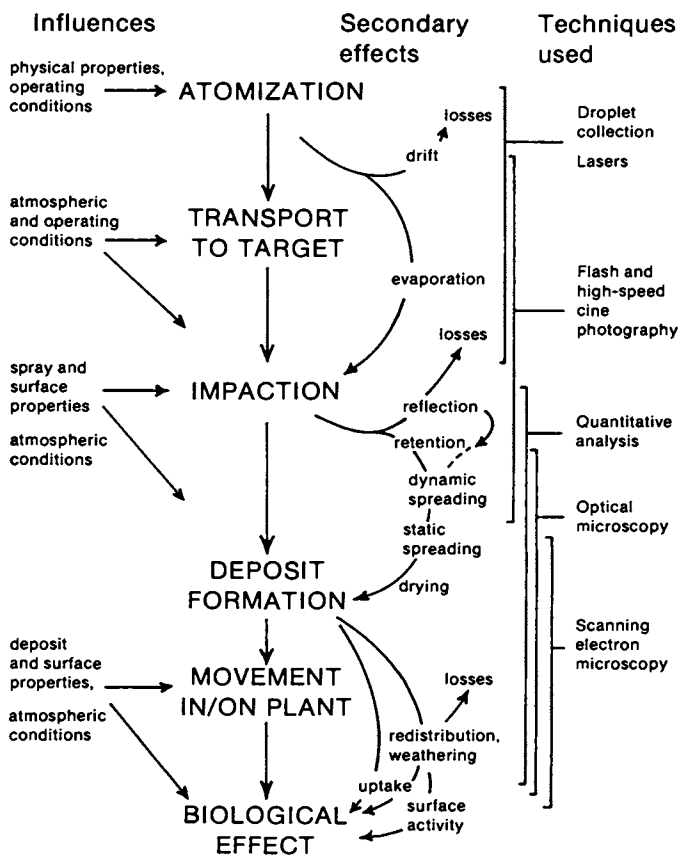


Figure 1. The many interactions of foliar atomization (modified after 4 with permission).

summarized our problems with regard to insects, pathogens and weeds and the parameters of equipment selection, modifications, spray volumes, and drop sizes. It is apparent that much has been accomplished in defining these principles. However, there remains many opportunities for improvement in the selective placement of toxicants within the crop environment. Graham-Bryce (6) succinctly identified one of our major problems of placement efficiency when comparing lab and field toxicities of DDT and deltamethrin (Table I). While obviously gaining an enormous increase in chemical efficacy, deltamethrin loses a significant amount of this efficacy advantage (vs. DDT) when placed in a field situation. Additionally, while we know in general terms, an optimum range of droplet sizes for selective targets (Table II), we lack in many instances the ability to deliver that pesticide to that target (10). Additionally, we also have a great deal yet to learn about the optimum placement strategies and criteria for our major pests (5). Additional guidance for nozzle selection has been obtained with the issuance of more practical recommendations for various crop applications (Southcombe, personal communication). The BCPC Nozzle Selection Handbook is an attempt to better educate the user about preferred spray qualities for specific targets. Foliar target areas may be much greater than land areas in terms of surface area, although pesticide recommendations are still generally expressed in terms of 1/ha. Some researchers have attempted to relate dosages per plant surface area while others have selected spray volumes based upon orchard tree row volumes (10-12). With the increasing pressures from ecologists, economists, and environmentalists (i.e., groundwater contamination), it is now clearly up to the crop protection specialists to delineate these parameters which would allow more precise delivery and usage of agrichemicals. Clearly, availability to the target, physicochemical properties, and a fundamental understanding of the biological characteristics of a population (tolerance) and some explanation of substrate specificity of the target process and resistance mechanisms will be fruitful areas for needed research.

Atomization of a pesticide and its subsequent fate in the environment will depend in part upon the properties of solubility, volatility, partition characteristics and stability. Considerations of these properties are reviewed and discussed by Hartley and Graham-Bryce (13) and more recently by McCann and Whitehouse (14). Past studies of pesticide formulations have tended to focus on reliability, ease of handling, and safety. Clearly these are important, but Graham-Bryce (6) succinctly illustrates that enhancement of biological activity via formulation and application research deserves more attention than it has thus far received. While applications made at different dosages may give similar areas of deposit, the rates of volatilization in a given environment may be the same. However, the loss represents a greater proportion of the toxicant applied at the lower dose. Therefore, losses may become more serious for more active compounds applied at lower rates (14). In order to pursue a fundamental understanding for optimizing formulation/

Table I. Comparison of intrinsic activities and application rates for representative insecticides (after Graham-Bryce, 1983)

Insecticide	Typical application rate, g/ha	Relative application rate	Relative lethal dosage ^a
DDT	1000	50	1600
Dimethoate	500	25	1039
Deltamethrin	20	1	1

^a Mean value calculated from data for four species; *Phaedon cochleariae*, *Anopheles stephensi*, *Choristoneura occidentalis*, and *Musca domestica*.

Table II. Optimum droplet size ranges for selected targets (after Matthews, 1979)

Target	Droplet sizes (um)
Flying insects	10-50
Insects on foliage	30-50
Foliage	40-100
Soil (and avoidance of drift)	250-500

application effects on dose transfer, there first must be a definition of the droplet pattern in space and time required for an optimum biological effect. Thereafter, application and formulation methodology designed for a specific distribution and release rate can be devised. Heretofore, the comprehension of volume, droplet size, and formulation interactions on biological effects have been partly hidden because of the wide range of droplet sizes produced from most conventional nozzles. The development of controlled droplet application (CDA) nozzles has lessened the range of droplet sizes and some success has been obtained with the use of laboratory monosized droplet devices. It is these devices which offer the unique opportunity to study the effects of formulation on the biological effect as it is influenced by droplet size, pattern of distribution, and concentration (15).

Examination of Dose Transfer

Examination of the biological effect may also be divided into more or less immediate and well defined direct effects (mortality) and those which are classified as sublethal effects. With the development of the synthetic pyrethroids and other new chemistry, the behavioral changes which occur and contribute to significant population effects, especially under low volume (small droplet)

conditions, must be studied if we are to develop a better understanding of the dose transfer process.

The study of pest behavior and how insects or mites move about their environment, find food, avoid being eaten, etc., is both challenging and important. The adaptations, requirements and mechanisms of gaining experience for various insect and mite pests all show a wide diversity of behavior. Understanding the mechanisms underlying behavior requires first understanding the behavior itself. The observations can be assembled into a series of quantitative parameters including latency - time to onset; frequency - number of occurrences; duration - length of time of pattern; and intensity - number of acts/unit time. We need to know how sublethal levels of toxicants can affect pest behavior and whether such changes are a meaningful contribution to overall crop protection. Consequently, as we attempt to use more potent toxicants and target them specifically, the measurement of how a pest acts and reacts to a toxin becomes more important.

In an attempt to better understand the interaction of drop size, distribution, and dosage on the efficiency of the dose transfer process, systems for generating uniform drops and providing various patterns of distribution have been developed and utilized in these studies (Figure 2) (16,17). Coupling video technology to the systems enhances our ability to better understand pest behavior in response to droplet encounters, i.e., tobacco budworm, *Heliothis virescens* F, cabbage looper, *Trichoplusia ni* (Hubner), and twospotted spider mite, *Tetranychus urticae* Koch (16). Video techniques, documented over time, allow a further elucidation of the behavioral responses of pests to a toxin. For example, video recordings can document the detection process by a pest, and when this feature is diminished by formulation, droplet drying (oil vs. water), or residue decline (time or rainfall).

Droplet sizes and oviposition of *T. urticae* (Figures 3 & 4) appear to be related in that decreasing sizes of droplets increase the effect with decreasing amounts of bifenthrin (18). In recent tests with fenpropathrin (19), placement of toxicant was accomplished with an automated microsyringe, calibrated to deliver 1-5 μ l droplet, 5-1 μ l droplets, and 10-1/2 μ l droplets per 1.3 cm diam discs. Five adult *T. urticae* females were placed on each disc (8 replicates) after droplets had dried and feeding, aversion, and oviposition responses were observed after 48 hr. One other observation clearly denoted in Table III, particularly with feeding responses, is that as the same amount of toxicant is delivered in an increasing number of smaller droplets, the response is generally greater than with fewer but larger droplets/disc. The normal random search behavior of mites thus appears to allow more frequent encounters with the toxicant and hence a more effective transfer. Initial interest in dispersal responses of mites was intensified after studies by Iftner and Hall (20) showed that *T. urticae* adults could not only detect, but also respond to deposits of pyrethroids (Table IV). It is not yet known whether this displacement, in response to residues of pyrethroids, is a result of (1) mere increased movement

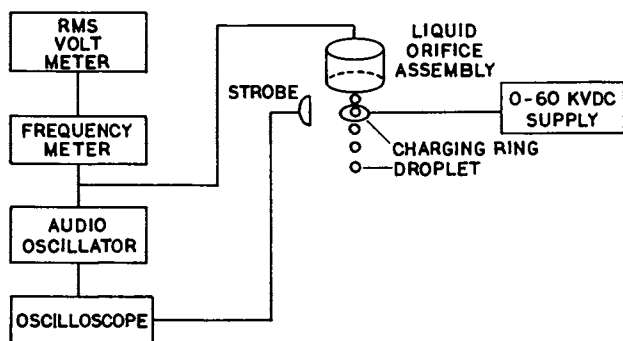


Figure 2. Schematics of components used to produce and charge uniform size drops.

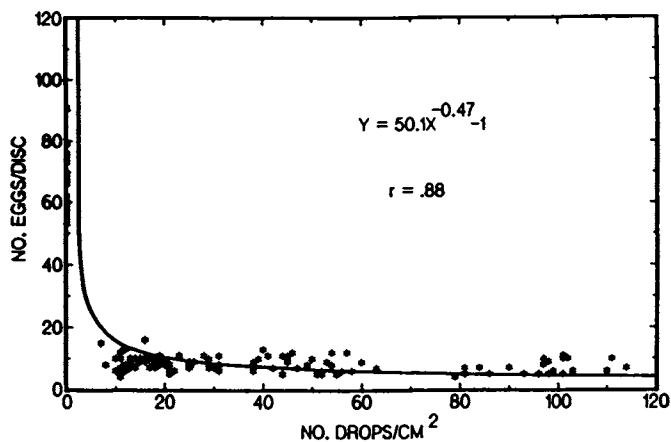


Figure 3. Effect of number of 200 μ drops/cm² of bifenthrin on *T. urticae* egg production at 48 hr.

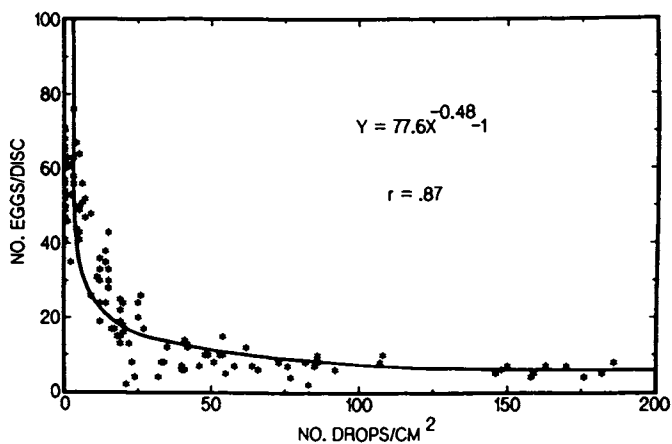


Figure 4. Effect of number of 120μ drops/cm² of bifenthrin on *T. urticae* egg production at 48 hr.

Table III. Fenpropathrin and *T. urticae* behavior - 48 hr^a

Treatment & Number of droplets	Avg % in water	Avg number eggs/disc	Avg number feeding scars/disc
2.4 EC^b			
1 - 5 ul	0.5 ab	27.88 b	136.88 b
5 - 1 ul	2.5 c	5.88 a	18.13 a
10 - 1/2 ul	2.75c	4.38 a	9.38 a
Check	0.00 a	45.88 c	282.50 c

^a Means in each column followed by same letter are not significantly different using DNMRT ($P < 0.05$).

^b Fenpropathrin used at 0.090 gm AI/l.

(hyperactivity) and hence a "random chance" location of untreated areas or (2) an active search for untreated areas which do not yield some perceived excitatory nerve response. These data do suggest that coverage (number droplets/cm² and patterns of placement) could have a significant effect upon dose transfer and hence ultimate biological effects in field situations.

Formulation Induced Pest Responses

In studies involving observations of mite feeding behavior (21), changes in formulation resulted in a change in perception and, hence, resulting behavior of females (Tables V & VI). Permethrin droplets deposited by the Electrodyn (ED) caused a reversal in proportion of time in a feeding state in comparison to that recorded for the standard EC formulation of permethrin. Cypermethrin in the ED (waterless) formulation caused dramatic changes in mite feeding behavior in response to the density of Electrodyn generated drops/disc. The data shows that as few as one droplet/disc has enough toxicant to disrupt normal behavioral functions (a 50% reduction in feeding scars). Thus, the reduction in feeding activity is achieved at doses that are not in themselves lethal. Increased density of drops elicited an increasingly disruptive reaction. Feeding impairment, or excitatory behavior may contribute to depletion of pest resources and population potentials may be limited.

In a series of more sophisticated studies of toxicity and behavioral responses of mites to various formulation, it was found that, in comparison to the standard cyhexatin (Plictran) 50% WP formulation, other formulations may have distinct advantages in terms of biological response (Table VII). In these tests, lima bean discs (1.3 cm diam) were dipped into agitated solutions of cyhexatin formulations and allowed to dry. Adult females (*Tetranychus urticae* Koch) were placed on the discs and observed over 48 hours under laboratory conditions after the techniques of Hall (15, 16). With 8 replications and 5 mites per disc, the results differentiated the formulations in mortality, oviposition and aversion to feeding. The formulations of cyhexatin had minor changes in particle size and the increase in % with less than 12 microns (211-C) was thought to be useful in eliciting a greater overall biological response. In a subsequent series of tests with 211-C included for additional evaluation, it was observed that the 30 EC formulation was far superior to other formulations in short term evaluations of dose transfer (Table VIII). Although mortality was not high, there was a significant decrease in both oviposition and feeding. A significant change in the energy budget of a mite population could lead to an overall reduction in population potentials (in the absence of other modifying parameters).

In further tests, lima bean plants (2 cotyledon leaves) were sprayed in a chamber at 3.2 km/h at 275 kPa (Spraying System 8001E nozzle) ca. 50 cm above the targets and allowed to dry. *T. urticae* females were placed on 1.3 cm diam. discs for observation over 48 hr. With 8 replications and 5 mites per disc, the results

Table IV. Location of mites 24 h after spray application

Material ^b	Total no. of mites by location ^a					
	UL*	LL*	UR	LR		
Fenvalerate	0	0	0	56(4)		
Permethrin	0	1	0	59		
Phosmet	0	0	0	60		
Water (check)	0	0	0	60		
	χ^2 Value = 15.18					
	UL'	LL'	UL*	LL*	UR*	LR
Fenvalerate	7	24	1	3	2	4(19)
Permethrin	1	30	0	3	1	4(21)
Phosmet	0	1	0	4	0	55
Water (check)	0	0	0	1	0	59
	χ^2 Value = 173.83					

^a Values in parentheses represent mites lost to walkoff, spindown, or vaseline. *Treated surface. ' = untreated outer half of left dicotyledon leaf.

^b Fenvalerate 2.4 EC and permethrin 2.0 EC and at 60 gm AI/100 l, and phosmet 50 WP used at 60 gm AI/100 l.

Table V. Examination of droplet density and formulation on behavioral responses of *T. urticae*^a

Treatment	1 Droplet/Disc		4 Droplets/Disc	
	Walk	Feed	Walk	Feed
Ambush 3 ED ^b	45.7	254.3	251.8	48.1
Ambush 2 EC ^c	--	--	63.8	236.2
Water	--	--	59.9	240.1

^a Data in seconds.

^b ED = Electro-dyn generated permethrin at 0.1 ml/s flow rate.

^c EC used at concentration of 0.06 g AI/l.

Table VI. Response of *T. urticae* to Electro-dyn droplets of cypermethrin^a

Drops per Disc	Water Check	Avg No. of Feeding Scars/Disc	
		Tracer alone	Cypermethrin + tracer
1	--	134.2	84.2
2	--	165.0	48.3
3	--	215.0	21.6
4	--	150.1	31.2
5	192.5	149.1	25.0

^a Electro-dyn* with cypermethrin 3 ED at 0.1 ml/s flow rate.

Table VII. Effects of cyhexatin formulations on *T. urticae* at 48 hr^{ab}

Formulation	Avg % Dead	Avg No. Eggs/Disc	Avg No. Feeding Scars/Disc
114-1 50 WP	32.5 bc	18.1 bc	41.9 a
114-2A 50 WP	25.0 b	13.4 ab	41.9 a
114-2B 50 WP	40.0 bc	16.0 ab	36.2 a
211-C 50 WP	52.5 c	14.6 ab	25.0 a
Plictran Std. 50 WP	77.5 d	9.38 a	22.5 a
Check	0.0 a	24.3 c	123.1 b

^a Means in each column followed by same letter are not significantly significant ($p = 0.05$; DNMRT).

^b Cyhexatin used at 0.148 gm AI/l.

Table VIII. Effects of cyhexatin formulations on *T. urticae* at 48 hr^{ab}

Formulation	Avg % Dead	Avg Eggs/Disc	Avg Feeding Scars/Disc
Plictran 200 EC	15.0 abc	22.1 b	74.4 b
Plictran 30 EC	35.0 c	3.9 a	6.9 a
Plictran Std. 50 WP	7.5 ab	36.4 c	203.1 c
211-C 50 WP	30.0 bc	19.8 b	71.3 ab
Check	0.0 a	53.4 d	236.9 d

^a Means in each column followed by same letter are not significantly different ($p = 0.05$; DNMRT).

^b Cyhexatin used at 0.148 gm AI/l.

clearly differentiated the formulations in dispersal into water (repellency), fecundity and aversion to feeding (Table IX). Further tests at 1/2 and 1/3 the rate of cyhexatin followed this same trend in formulation differences, i.e., cyhexatin 80 WDG had the least influence followed by the standard 50 WP formulation while the EC was the most effective treatment for decreasing both oviposition and production of feeding scars. Thus, sublethal behavioral responses (how or if a toxin is encountered or perceived by a mobile pest) may be evoked by (individually or interacting) formulation, droplet density, concentration of AI or total dose/unit area.

Controlled release formulations, combining a biologically active agent and a polymer for example, control the release rate of a pesticide and may allow the product to be biologically available for a longer period of time (Figure 5) (22). Encapsulation has been reported to change pest responses to a toxicant (19). A series of encapsulated formulations of fenpropathrin, supplied by Sumitomo Chemical Co., had a significant range in cell wall thickness. Leaf dip tests were conducted with fenpropathrin using the complete array of encapsulated formulations (Table X). This test showed that the thicker cell wall formulations (R712 and R713) provided "protection" from detection of the irritant, a response that was prevalent in the thin walled microcapsule (R705) and the standard EC formulation. There is yet no evidence of the identity of the sensing organs nor have we elucidated the meaning of this short term response on long term growth potential in a field population of mites. The site-specific controlled release formulation of chlorodimeform (CDF) in a targeted use on cotton is an excellent example of a designed formulation modification (23). CDF is bound (heteropolar) to insoluble polymeric sulfonic acids of the cation exchange type and offers added bioactivity in the field. Beyond utilizing plant cations to trigger the release of AI, this new CDF-resinate implies greater safety and reduced environmental losses during application. To date, however, utilization of controlled release formulations on plant protection has not yet been fully exploited. It may be that we should be looking for a more enhanced and efficient "short term" release process rather than the traditional "extended residual," i.e., over two weeks. Seasonal growth patterns (new unprotected foliage) may preclude extended strategies unless increases in handling safety are the predominant factors.

Discussion

The concept of dose transfer involves the delivery of a toxicant (atomization to deposit) to a point where there is sufficient contact with an organism to result in a measurable, predictable biological response. It is clear that this is a complex, dynamic process which can be very inefficient, depending on the pest, its location and delivery (deposition uniformity). With the arrival of CDA, an ultra-low volume (ULV) pesticide application system,

Table IX. Response of *T. urticae* to various formulations of cyhexatin (0.148 gm AI/l) at 48 hr after treatment ^a

Formulation	Avg % in Water	Avg No. Eggs/Disc.	Avg No. Feeding Scars/Disc.
Cyhexatin 50 WP	55.0 c	18.9 b	61.3 b
Cyhexatin 30 EC	17.5 b	3.3 a	6.3 a
Cyhexatin 5F	45.0 c	5.8 a	10.6 a
Cyhexatin 6F + 1% silicone	50.0 c	4.3 a	8.7 a
Cyhexatin 80 WDG	17.5 b	44.4 c	186.3 c
Water Check	0.0 a	61.4 d	321.3 d

^a Means in each column followed by same letter are not significantly different ($p = 0.05$; DNMRT).

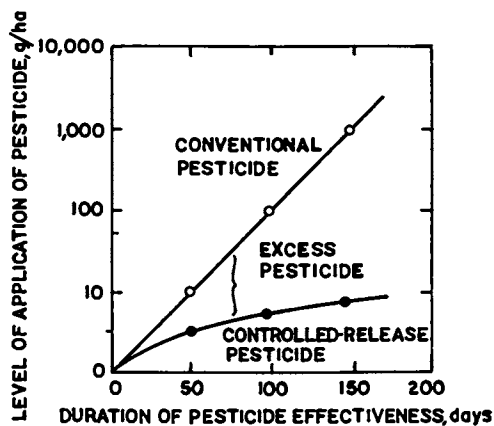


Figure 5. Relationship between level of application and duration of action for controlled release and conventional formulations (modified from [22] with permission).

changes may also occur in wash-off, volatility, and drift potentials, as well as redistribution phenomena.

Pest responses to distribution of discrete droplet patterns are a unique feature of the pest control function. The question thus remains, what does a behavioral response to a toxicant mean in short-term vs long-term population responses? Will sublethal levels of toxicants disrupt stable age distributions (SAD) and result in unintended surges in pest populations (24)? Can an aversion response evoke an increased probability of encounter? Will disruptions in energy budgets, oviposition, movement, or communication be meaningful in crop protection? The measurement of behavioral changes is frequently imprecise and can be strain and compound dependent (25). In addition, such observations are frequently dependent upon environmental conditions (26). However, the inclusion of quantitative measures of behavioral responses to toxicants may enhance our understanding and hence predictability (via modeling efforts) of optimum conditions of the dose transfer process (7).

It has often been noted that there is frequently a poor correlation of spray volume and the biological effect (5,27). Monosize droplet generators and image analysis represent added versatile tools with which to address this issue. The meaning of this capability (especially interfaced with more refined formulations) is that biologists now are faced with the task of indicating optimum conditions of toxicant placement for maximum biological effect. In other words, what is the impact of changing drop size, crop architecture, or spray volume? Dial-A-Drop capability is getting closer to reality in field delivery systems (28,29) and we'll have a better understanding of what placement requirements are needed for optimizing biological effects (with minimal environmental hazards).

Crop architecture under field spraying conditions often masks the effects of leaf surface properties, drop concentration, and formulation and may not reflect results of many detailed leaf studies on these factors. Secondary air entrainment (shrouding acting as scoops) may capture more small droplets and aid deposition to selected sites within crop canopies (Reichard, personal comm.) as well as reducing off-target placement. The impingement efficiency of droplets in entrained air may also be aided by specific formulation adjuvants. Such improvements in deposition may not be seen at higher air velocities or with larger drops, when evaporation (surface area/mass) is sufficiently high to allow increased evaporative losses.

In laboratory studies, droplet bounce (impingement) phenomena as dynamically captured on film by Reichard and co-workers (30) currently lack sufficient correlations between static surface tension values, and bounce values. This illustrates the need for more detailed research utilizing dynamic surface tension measurements as a more accurate indicator of rebound potentials. Anderson et al. (31) recently suggested that retention as determined by dynamic surface tension and droplet spreading (determined by equilibrium values) could be modified independently of each other to optimize the transfer process.

Actual hits (of arthropod pests on a leaf surface) have been frequently observed as being <10% in our laboratory studies, irrespective of "good" coverage. Consequently, the retention, diffusion, and redistribution characteristics of a toxicant at the biological interface (leaf surface) may be more important in our attempts to correlate lab/field data (32). For example, how long does a deposit remain in an effective transfer state whereby contact by walking insects will allow sufficient transfer to the pest cuticle? If retention or tie-up in wax layers is such that the forces of pick-up are greater than physiodynamics retaining the toxicant to the leaf surface, than an effective transfer can occur (33). It is at this interface (not masked by initial changes in toxicity) that observations on sublethal and subtle behavioral effects of a pesticide (i.e., the encounter process) may indeed provide greater insight into dose transfer phenomena. Crease and Ford (33) recently demonstrated that large increases in transfer efficiency (shown in laboratory studies) as a result of rather simple changes in formulation could be documented in field trials.

New innovative pesticide molecules continue to be developed offering more elaborate and yet specific methods of species disruption. The question of how to best utilize these more active compounds can only be answered by more detailed evaluation studies of the biological interface, i.e., plant surface, AI, the encounter process, and the factors governing mobility in the environment (6,8). Research aimed at understanding the deposition/formulation influences on the biological effect will be aided by dial-a-drop systems (16,17). This must occur if we are to take advantage of the increasing efficacy of the new chemistry or to fully utilize the biorational approaches of disrupting pest development i.e., membrane integrity, hormonal interference, etc. (6).

The process of crop protection is an imprecise process in that farmers frequently operate under uncertainty with a number of unidentified parameters, such as pest numbers or unidentified pests in the crop area. In addition, we also frequently assume that all crop production functions are accomplished in a precise (optimum) manner which frequently is not the case. Clearly, if we are to continue to provide agricultural chemical tools, then a more adequately identified pesticide benefits assessment has to be presented to the user (8). Geissbuhler (8) predicted that, given the current state of uncertainty in agriculture, industry will have to demonstrate to the user, sound economic benefits (as well as technical aspects) of proposed chemical solutions for pest problems. In addition, such solutions must take into account the political and socio-economic conditions. Users lacking a high level of farm efficiency will not be able to take full advantage of fine-tuning techniques such as IPM, biological control, formulation and innovative delivery techniques or strategies. Methodologies that stimulate such advancements encompassing decision support via computers in educational and analytical criteria (34) as well as other decision aids (Figure 6), should prove useful for the advancement of more precise strategies and

Table X. Fenpropathrin formulations and *T. urticae* responses after 48 hr^a

Formulation	Estimated Cell Wall Thickness	Avg Eggs/Disc	Avg Feeding Scars/Disc
R705 10 MC	.01	0.5 a	0.0 a
R711 10 MC	.02	14.6 b	58.1 b
R712 10 MC	.04	32.0 d	171.3 c
R713 10 MC	.08	24.6 c	141.3 c
2.4 EC	--	0.0 a	0.0 a
Check	--	34.0 d	220.6 d

^a Means in each column followed by same letter are not significantly different ($p = 0.05$; DNMR).

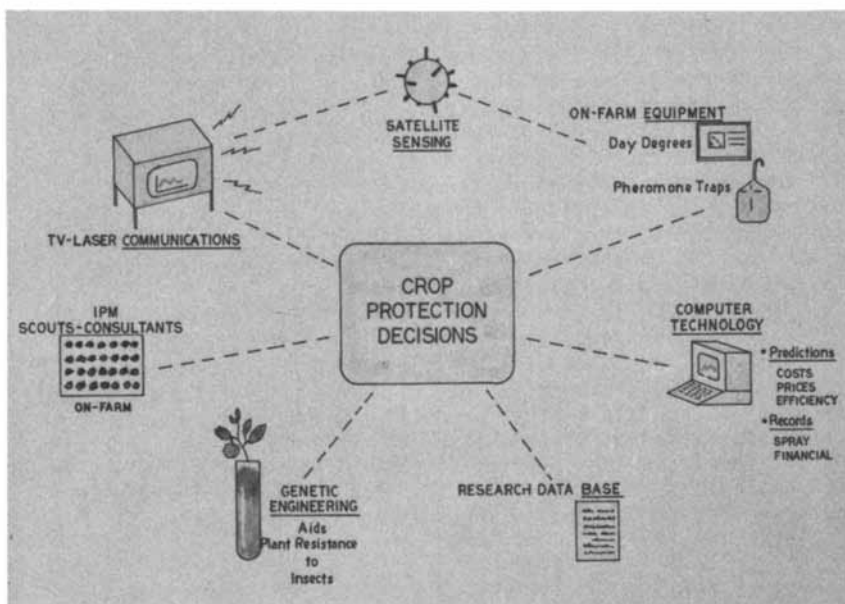


Figure 6. High technology implementation aids grower decisions for optimizing plant protection programs.

techniques in crop protection. With increasing regulations and environmental pressures on the pesticide industry (and the users of pesticides), any technique that increases the perception and development of more prescriptive methods/techniques will allow agricultural chemicals to be fully utilized into the year 2000.

Conclusions

Pest behavior can be significantly modified by changes in both formulation, the quality of the distribution, as well as AI (sublethal responses). As summarized by Lockwood (25), behavioral resistance can be characterized as pest actions in response to selective pressure by a toxicant which enhances the ability of a population to avoid lethal responses to the toxicant. Dispersal, hyperactivity and other reactions to particular distributions of new classes of pesticides are beginning to be commonplace (35). Georghiou, in his review of pesticide resistance management (36) concludes that both formulation and application technology have to be integrated into future resistance management strategies.

Can we actually develop a definitive statement of concentration patterns in space and time for specific AI/pest combinations for an optimum effect? This effectiveness should perhaps be based, not on pest control, but rather on the protection of the crop (yield and quality). Defining the requirements will remain a major obstacle for improvements in dose transfer efficiency. Hislop (5) concludes that striving for "the optimum droplet size," for example, may be counter productive, for indeed there will be many diverse situations for maximizing a biological effect. However, studies which examine and separate the myriad of relationships between toxicant, quality of placement, and the biological effect as modified by formulation will prove useful as the new, more efficacious agents are developed. The incentives for improvement of the dose transfer process in agriculture are being modified by costs/benefit issues, as well as the increasing pressures of socio-economics, and environmental and legislative activists.

Improvements in dose transfer will require active multidisciplinary teams and cooperative industry/academia programs. The delivery of a practical, optimal dose transfer system still lacks expertise on decision rules, on-farm records management, accurate weather predictions, and most importantly, basic information on placement rules. Formulation and pesticide application technology specialists have to be more closely aligned with biologists, if significant advances in delivery efficiency and dose transfer are to be attained as part of a rational pesticide strategy.

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