Physical and

Chemical Properties

Of Organic

Pesticides

As Related to

LLOYD L. ISENHOUR and GEORGE L. BROWN
Rohm & Haas Co., Philadelphia, Pa.

FORMULATION AN

Proper formulation can make the difference between poor and effective pesticide action ... The right formulation depends on the properties of the pesticide

THE ULTIMATE ACTIVITY of a pesticide depends primarily upon its chemical constitution and its capability of entering into a suitable biological reaction. Realization of this ultimate capability depends upon proper formulation and application, which primarily answer the problem of handling the toxicant so that it can be distributed adequately to reach a specific pest in a specific area. We must economically answer that problem without chemically or physically destroying, reducing, or masking the attributes which makes a chemical compound the good toxicant which we are trying to formulate and apply.

For the purpose of this discussion we must assume that the toxicant has been evaluated as to its basic activity. It will be classified as an insecticide, miticide, fungicide, bactericide, and/or herbicide. I hope that in the not too distant future we will be able to include "virusides" in discussions such as this. Within one or more of these categories the pesticide will be used as a contact or residual poison. The residual effect may result from surface deposits or from absorption into plant tissues.

Distribution Requirements

It is obvious from even a casual glance at the mathematics involved that the particle size of pesticides must be quite small in order to be dispersed adequately. On an acre of cropland we can estimate that the exposed foliage surface area may be four to five times the soil surface area. In certain orchard crops it may be more. In round figures this may mean a minimum of 200 million square centimeters of foliage surface to be covered. With concentrate spraying at 10 gallons per acre and all droplets 50 microns in diameter, we approximate 300 drops per square centimeter. Figure 1 shows that the surface is not completely covered, however, even when we assume perfect distribution and no loss from drift. It has been shown (*16*) that water drop-

lets containing a wetting agent will spread to approximately three times their original diameter. This would make the droplet almost cover the area apportioned to it. Oil droplets may spread over fifteen times their original diameter and thus compensate for incomplete coverage. In the case of the same number of dry particles, there is a disconcerting portion of uncovered surface even under these assumed perfect conditions. This must be taken into consideration when deciding how to formulate a material that acts only as a contact insecticide or miticide. Distribution of 10 micron particles would increase the number 125 times and theoretically would solve the coverage problem. It has been shown (*16*), however, that particle sizes in excess of 30 microns are needed for good deposit and adherence.

All efforts in this mechanical operation of application must be a compromise. The ultimate in distribution is the formation of molecular vapors. In an

some problem when it is desired to use them in dry carriers as wettable powders or dusts. Unless the dry carrier is relatively absorbent the powder becomes wet and sticky with only a small percentage of added toxicant. This interferes mechanically with the dispersion of the individual particles. A carrier which will absorb 25% or more of nonvolatile liquid, and hold it as a dry base, may fail to release it adequately under many use conditions. We have seen several demonstrations of this situation with formulations of 2-chloroethyl 2-(*p-tert*-butylphenoxy) isopropyl sulfite. A 25% wettable power has shown adequate toxicity to mites when used in water spray dispersions. In the presence of water and wetting agent combination the toxicant is released from the absorbent powder in lethal amounts. When this same 25% dry concentrate is further diluted with nonabsorbent dust carriers such as pyrophyllite, talc, or silica, the resulting 5% dust is relatively ineffective. A separate preparation of 5% liquid toxicant onto the same dust diluent, but avoiding the more absorbent carrier needed for the concentrate, gives an effective miticide dust. These observations were made on commercial field applications and detailed comparative figures cannot be quoted. This problem does not appear with compounds such as the organic phosphates which exhibit enough volatility to escape from absorbent carriers.

Even when used as a spray dispersion, the wettable powder containing the 2-chloroethyl 2 - (*p - tert* - butylphenoxy) isopropyl sulfite only slowly releases its toxicant. Ebeling and Pence (6) have compared the 25% wettable powder formulation with a 25% emulsifiable concentrate under closely controlled conditions. Their figures show the emulsion formulation to be toxic at a significantly lower concentration than the suspension of wettable powder against 2-spotted mite when counts are made 48 hours after application. Residual activity is retained over a longer period of time by the reservoir system supplied by the wettable powder. In contrast, O,O-diethyl O-*p*-nitrophenylthiophosphate was more toxic during the first 48 hours when used as a wettable powder, and the powder also maintained a longer residual action. This result with the parathion will be referred to in more detail during the discussion on emulsions.

APPLICATION

enclosed space these give true fumigation and perfect coverage, but only a tiny fraction of our agricultural operations can be carried out in a fumigation tent or a greenhouse. If we expose to the air individual particles which are too small we have excessive evaporation and drift. The toxicant simply disappears into the atmosphere. For application we obtain one or two microns, or even fractional micron dispersions of a toxicant, however, by incasing it in water dispersions or emulsions, in solvent solutions, or by attaching it to larger particles of a dust carrier.

Volatile Toxicants

Vapor formation makes possible the smallest particle sizes and best distribution but these vapors must be adequately confined or maintained. Obviously highly volatile substances are limited to contact applications for immediate toxicity. Toxicants in this category are the easiest to formulate and apply. For straight fumigation effects the undiluted toxicants can be mechanically dispersed. Highly potent ingredients may need to be diluted into solutions or emulsions in order to bring the dosage within the capacity of available mechanical equipment. Volatile toxicants may be impregnated on absorptive powders for use either in dust or spray dispersions. The powder deposits may serve as a reservoir to maintain a suitable vapor concentration over a period of time in unconfined space. This is a familiar technique with tetraethyl pyrophosphate.

Liquid Toxicants

Toxicants which are liquid below temperatures of 30° to 40° C. may present

Solid Toxicants

Toxicants melting above 50° C. can be distributed in dry nonabsorptive-type carriers in order to formulate them into a state of adequate subdivision. Mathematical calculation and field experience .have established that the old inorganic toxicants such as calcium ar-

New types of sprayers as well as dusters are increasing capacity as well as efficacy. The right type of formulation is important in getting best results
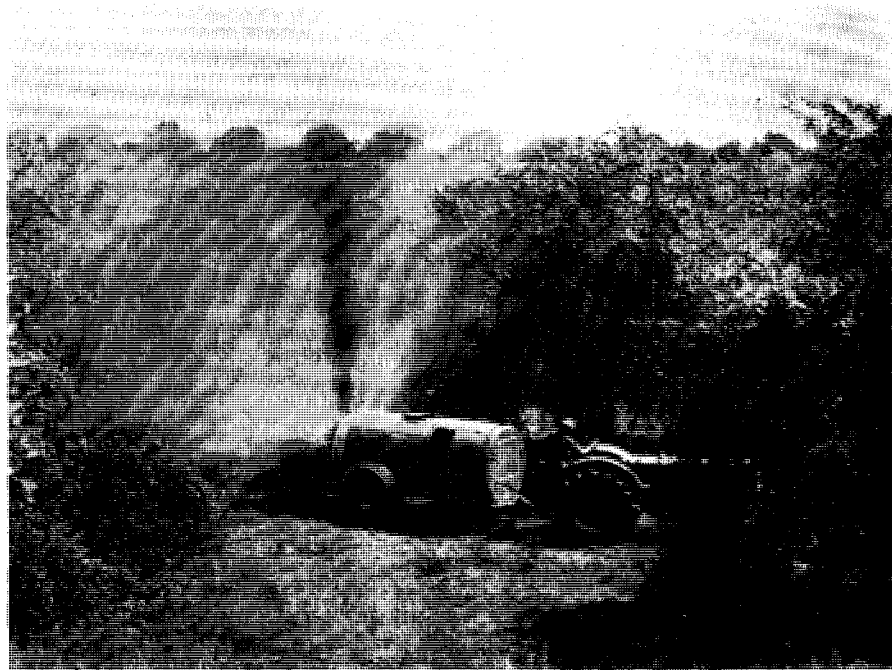
senate or cryolite require an average particle diameter of 40 to 50 microns maximum in order to obtain effective distribution and deposition (16, 21) at dosages of 20 to 30 pounds per acre in full foliage. Studies have also shown this to be an optimum average particle size for carriers. When we use a more potent organic insecticide such as dichlorodiphenyltrichloroethane at a dosage of only 1 or 2 pounds per acre it is axiomatic that we must produce at least this same number of particles from the smaller quantity. Theoretically, where experience has shown a 40 micron particle diameter is optimum for a toxicant used at 30 pounds per acre, a 1 pound dosage would require a particle diameter of approximately 13 microns. Experimental evidence has been reported (2, 9, 12, 20, 22) to show that insecticidal potency increases with decrease in particle size. This factor is due to both better distribution and better availability. Many times there is a temptation to compromise on the specification for particle size in order to reduce the difficulty and cost of preparing the formulation. This is a too common practice on toxicants which have a melting point sufficiently high to permit grinding. If 1 pound of active toxicant is mixed with 19 pounds of diluent of the same density and both with an average particle diameter of 40 microns, the number of toxicant particles per particle of diluent is shown on the left side of Figure 2. There would be one particle of toxicant surrounded by 19 particles of diluent. The chart does not show every particle because in an aggregate not all of them would be visible in one plane. At 20 microns for the toxicant we would have eight active particles still surrounded by 19 particles of diluent. At 10 microns the toxicant outnumbers the diluent particles over three to one but the figure shows clearly that the carrier still tends to mask the availability of toxicant. At 4 microns, as shown on the right, adequate distribution is readily apparent. It is equally obvious that too small a particle size on the carrier would mask the toxicant still more. This problem is well recognized as evidenced by the effort and thought that has been expended (4, 10, 11, 14) in an effort to improve the ease of grinding of DDT. In actual commercial formulating practice it is too frequently ignored.

Emulsion Formulations

Many factors involved in the economical choice of solvents and emulsifiers have been recently summarized by Selz (17), and these comments need not be repeated. As previously indicated, formulation has as a primary purpose the development of a mechanism of adequate dispersement of the pesticide. Many
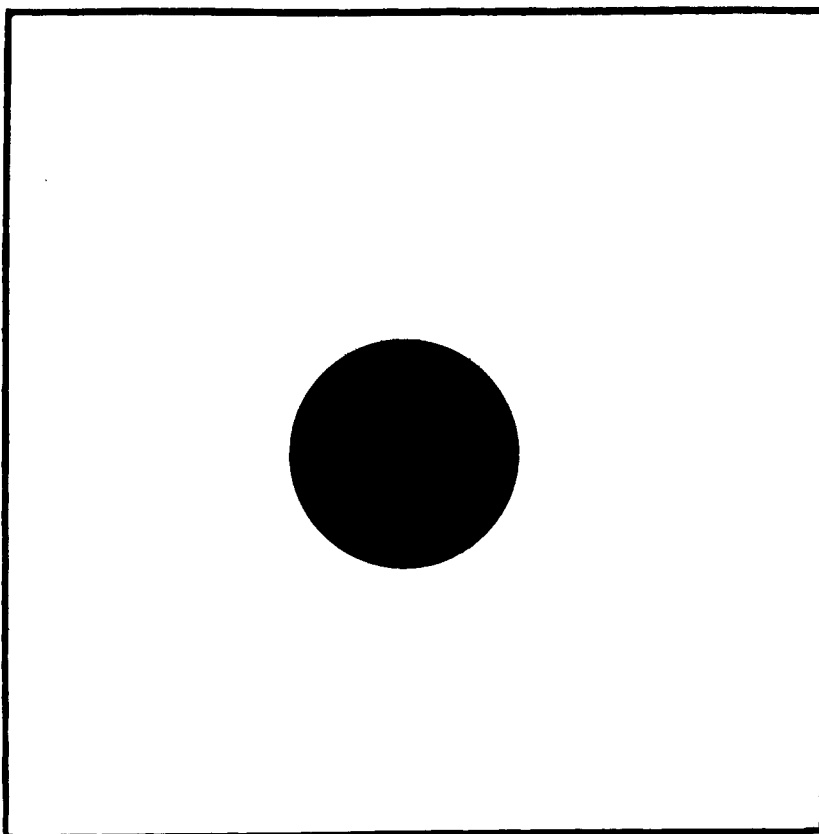

Figure 1. Comparative area. 10 gallons in 50 micron drops on 5 acres foliage surface

commercial formulators, however, place false emphasis on ease and economy at the possible expense of adversely affecting the potency of the toxicant. It is not enough simply to observe spontaneous dispersibility and emulsion stability in a graduated cylinder. We have seen how inadequate grinding or highly absorbent carriers can mask the effectiveness of toxicants dispersed in dry carriers. We need further keep in mind that every toxicant displays certain effectiveness correlated with its ability to penetrate a biological system (5). Theoretically an excellent solvent or wetting agent could improve that penetration. Such benefits from wetting agents have been reported in the case of herbicides (7, 8, 13, 18). I believe that most such benefits are due more to better adherence and distribution rather than to any effect on the penetration or the biological reaction of the toxicant. Some herbicides are selective, for example, because the formulation does not wet and adhere to certain types of foliage where the toxicant would be phytocidal if actually deposited on the foliage surface. A good toxicant is good partially because it has in itself the hydrophile-lipophile balance required for penetration to the site of the desired biochemical reaction. We should avoid solvents and emulsifiers which may physically reduce the pene-

trating ability of the toxicant. We believe that this may be a factor in the work reported by Ebeling and Pence (6). The parathion showed more potency in impregnated wettable powder than in emulsions. They do not report the solvent used but it perhaps stayed with the parathion and interfered with its absorption but did not reduce volatility and loss into the atmosphere. On the other hand-the volatility and inherent solvent power of the straight toxicant enabled it to free itself from the absorbent dry carrier and penetrate to sites where it could exert its biological activity.

From the viewpoint of safety and convenience in handling we desire to use solvents with low volatility. This must be balanced against the advantage of having the solvent evaporate rapidly so that it does not inhibit the fundamental biological activity of the toxicant. In the case of a pesticide such as DDT, where we need small well distributed crystals for maximum surface residual effect, the crystal size and general insecticidal effectiveness will be inversely proportional to the volatility of the solvent (2, 3, 20).

Water Solubility

To this point our consideration of the solubility of pesticides has been directed

toward the solvents used for liquid formulations. Many obvious and well recognized points are being ignored or barely mentioned in order to stay within the time limit. We have indirectly referred to the solubility of the toxicant in the biological system to which it is to be applied. This point relates primarily to *basic* toxicity. We must formulate in a manner to take advantage of, and particularly not to interfere with those intrinsic properties. During formulation and storage, and during and after application, we always have water with us. Water constitutes a major percentage of any biological system. The degree of water solubility of the toxicant will have a primary effect on the way it can be used.

High water solubility, on any biologically active material, dictates that the compound may be phytocidal to an objectionable degree. As an example, disodium ethylene bisdithiocarbamate is sold as a fungicide in a water concentrate solution. It has little practical value, however, until it has been insolubilized and made safer by reaction with a heavy cation such as zinc or iron. Tetraethylpyrophosphate is insecticidal within concentrations safe to plants but its water solubility contributes to phytotoxic properties which make it hazardous to apply in concentrate solutions.

Water solubility in the range of a hundred parts per million or more will prevent the use of a toxicant as a surface residual insecticide, miticide, or fungicide. Moisture precipitation will quickly remove such residues. Such solubility may, however, contribute greatly to the successful application of the pesticide as a systemic poison. Water solubility facilitates translocation within a plant. Octamethyl pyrophosphoramide and O-[2(ethylmercapto)-ethyl] O,O-diethylthiophosphate are two well-known examples of this in the insecticide field. Otherwise, such water soluble compounds are limited to use as contact insecticides or herbicides, or as eradicant fungicides and bactericides. No known method of formulation will change their classification.

Water solubility to the extent of 2 to 10 p.p.m. is permissible for pesticides which exhibit surface residual effects. Protective fungicides require such solubility because otherwise they are not available to poison the water in which the spores germinate. Such water solubility explains how imperfect coverage of fungicide particles, as shown in Figure 1, is extended to cover the remaining surface where disease spores are germinating in the film of moisture. Such fungicides must be effective at these low concentrations in water. At higher degrees of solubility it would be impossible to main-

tain residual deposits which serve as reservoirs for active fungicide under conditions of moisture formation. It has been postulated that exudates of the plant or fungus may dissolve and activate a fungicide. This can be a factor but it does not eliminate the need for slight water solubility. Zinc ethylene bisdithiocarbamate is an excellent fungicide. The iron salt is effective. One might expect the cupric salt to be doubly effective because of the added value of the copper. Actually this copper salt is so insoluble that it is of little value. It is imperative to recognize that where water solubility is necessary in the biological reaction we must not formulate in a manner to inhibit completely that solubility. To a limited extent we might advantageously reduce the rate of water solubility and thus increase the length of the residual surface activity. One mechanism for this would be to solubilize the toxicant in, or coat it with, a hydrophobic but slowly volatile material. This is a poor substitute, however, for having a toxicant with the needed solubility factors, and then formulating so as to not mask those properties.

Solubility in Biological Systems

Ebeling and Pence (6) have done a commendable piece of work in demonstrating the multiple benefits of toxicants that have relatively lower water solubili-

Figure 2

TOXICANT DISTRIBUTION in 5% Dust

TOXICANT   DILUENT

370 MESH   20 MICRONS   10 MICRONS   4 MICRONS
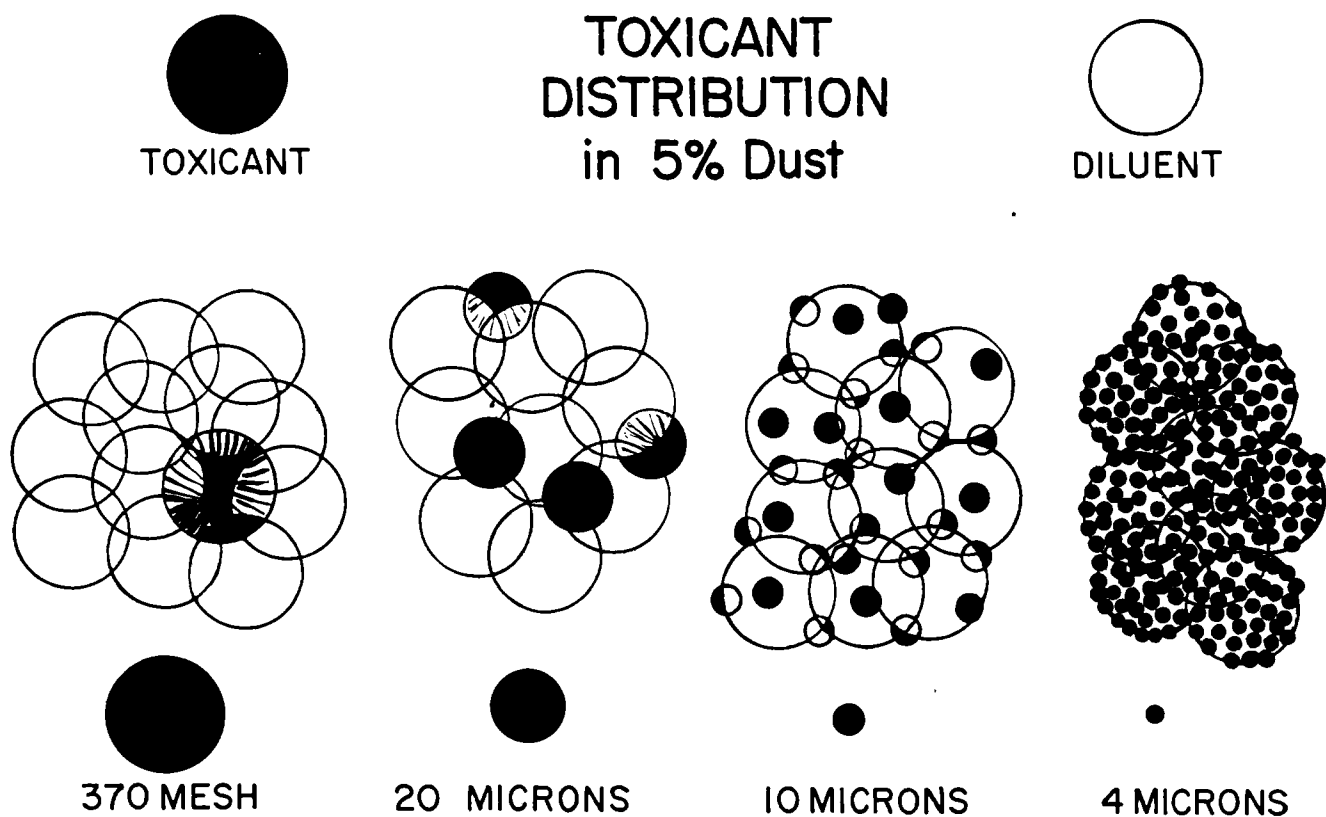
ties along with enough lipid solubility to permit penetration of foliage cuticle and cell tissue. Miticides such as 2-chloroethyl 2-(p-tert-butylphenoxy) isopropylsulfite, 4,4'-dichlorobenzilic acid ethylester, and O,O-diethyl O-p-nitrophenylthiophosphate give in the field results which exceed any normal expectation based on average surface coverage. They show that these results are due as much to a unique combination of solubilities as to high biological potency against mites. These and other compounds are able to penetrate foliage but do not have enough water solubility to be readily translocated as true systemics following foliage application. This creates a localized subcuticular toxic reservoir within the sprayed foliage and serves as a stomach poison to mites which feed thereon. With this mechanism miticides applied to one side of a leaf will kill mites feeding from the other side. This permits effective pest control in spite of marginal application techniques.

Solubility in water is an important factor affecting the suitability for use and the efficiency of any toxicant in a pesticide category. The solubility potential in water should be determined as a part of the evaluation of any toxicant. Changes in the molecule to modify water solubility could be a significant factor toward improving the performance of a compound.

When formulating an emulsion concentrate it is important to find solvents which have little or no solubility in water. Otherwise, during emulsification, there will be a partitioning effect in the water. If the toxicant has been employed close to the saturation point in the organic solvent it will be precipitated out of solution. This factor has been well impressed upon those formulators who have attempted to find suitable solvents for making emulsion concentrates of isopropyl N-phenylcarbamate.

Chemical Stability

The major chemical reactions concerning us in the formulation and application of pesticides are those which affect decomposition. In any formulation it is obviously necessary to avoid the use of any carrier, solvent, or emulsifier which could react with the toxicant. Constant attention should be paid to possible hydrolysis by water, either alone or in the presence of alkalis, acids, or natural enzymes. It is possible, even though not always economical, to avoid harmful amounts of acid or alkali in formulation and storage. The highly chlorinated organics, for example, may release free chlorine which forms hydrochloric acid in the presence of water. This catalyzes further decomposition in addition to corroding the container. A basic solution to this problem is to have the formulation free of water contamination

and to incorporate inhibitors. It is seldom practical to formulate in order to buffer against the low or high pH conditions which may be encountered during and after application. We simply must choose toxicants and emulsifiers which are sufficiently stable under the use conditions. We must make this same type of selection in order to avoid objectionable inactivation under enzymatic influence, and recognize that the enzyme source may be in the plant, the pest, or incidental microbial flora (1, 19).

As indicated above, water is always with us in pesticide applications. Wherever we make spray mixtures we must also remember the effect of those heavy metal salts which cause what we call water hardness. Such ions as calcium, iron, and magnesium may react directly to insolubilize and inactivate such toxicants as amine or sodium salts of 2,4-dichlorophenoxyacetic acid. They also interfere with the activity of many emulsifiers and spreaders (17).

Oxygen is another substance in nature which we have always with us, and it is very potent. If a toxicant has reducing properties, and it is exposed to oxygen during storage, it will lose potency. Disodium ethylene bisdithiocarbamate is stable almost indefinitely in water solution in full containers. If the consumer holds a partially full container, and agitates it occasionally, the compound will slowly react with the available oxygen, and lose potency. After application this same compound, in a thin spray deposit intimately exposed to the air, is fungicidal only a few hours. The slightly soluble zinc and iron salts are not so reactive. They maintain available potency over several days. Similar effect from oxygen, in varying degrees, can be anticipated with almost all organic pesticides.

We know that photoradiations can have a catalytic effect on organic pesticide decomposition. There have been few specific reports identifying the interrelationship of the various causative factors of chemical decomposition. Typical reports (15) simply attribute loss of activity to the combined effects of sunlight, heat, wind, and rain.

Enzymatic decomposition of DDT in resistant flies (19) has been reported, as has the decomposition of 2,4-dichlorophenoxyacetic acid in soil. We cannot formulate or apply pesticides in a manner to avoid such enzymatic effects. We must avoid them by our selection of toxicants or combination of toxicants.

These decomposition factors may actually be a blessing in disguise. It would be most embarrassing in this world if nothing decomposed. We would have serious difficulty in producing uncontaminated and safe food if insecticide residues remained in their full potency over an indefinite period.

One other point should be considered

by every worker who designs, uses, or advises on the use of application equipment. Insecticides and miticides which give surface, systemic, or subcuticular residues and the hormone-type herbicides are effective even with relatively incomplete coverage of foliage surfaces. This has encouraged habits of careless application and the use of low capacity equipment. Available fungicides have not yet reached this approach to perfection. Thorough coverage is essential on all foliage surfaces where plant diseases present a threat of epidemic loss. We might even find ourselves returning to the use of less spectacular contact toxicants if insects and mites continue to adapt themselves to the remarkable nerve poisons now in use. Good equipment and carefully used equipment are necessary if we are to realize the full benefits of even the best pesticide formulation.

Literature Cited

(1) Aldrich, R. J., J. AGR. FOOD CHEM., 1, 257–60 (1953).
(2) Barlow, F., and Hadaway, A. B., Bull. Entomol. Research, 42, 769–77 (1952).
(3) Barnes, S., Ibid., 36, 373–82 (1945).
(4) Bruce, E., U. S. Patent 2,453,076 (Nov. 2, 1948).
(5) Crafts, A. S., Proc. Fifth Ann. Calif. Weed Conf., pp. 73–6 (1953).
(6) Ebeling, Walter, and Pence, Roy J., J. AGR. FOOD CHEM., 1, 386–97 (1953).
(7) Engel, R. E., and Wolf, D. E., Agron. J., 42, 360–1 (1950).
(8) Gertsch, M. E., Weeds, II, p. 33 (1953).
(9) Hadaway, A. B., and Barlow, F., Bull. Entomol. Research, 43, 281–311 (1952).
(10) Hayward, C., U. S. Patent 2,656,396 (Oct. 20, 1953).
(11) Kallok, J., U. S. Patent 2,590,544 (March 25, 1952).
(12) Keiser, I., and Henderson, C. F., J. Econ. Entomol., 44, 646–52 (1951).
(13) Laning, E. R., and Aldrich, R. J., Proc. Northeast States Weed Control Conf., pp. 7–12 (1951).
(14) Little, K., U. S. Patent 2,453,076, (Nov. 2, 1948).
(15) Mistric, W. J., Jr., and Gaines, J. C., J. Econ. Entomol., 46, 341–9 (1953).
(16) Potts, S. F., J. Econ. Entomol., 39, 716–20 (1946).
(17) Selz, Edgar, J. AGR. FOOD CHEM., 1, 381–6 (1953).
(18) Staniforth, D. W., and Loomis, W. E., Science, 109, 628–9 (1949).
(19) Sternberg, J., Vinson, E. B., and Kearns, C. W., J. Econ. Entomol., 46, 513–5 (1953).
(20) van Tiel, N., Bull. Entomol. Research, 43, 413–19 (1952).
(21) Wilson, H. F., and Jackson, M. L., J. Econ. Entomol., 39, 290–5 (1946).
(22) Woodruff, N., and Turner, N., J. Econ. Entomol., 40, 206–11 (1947).