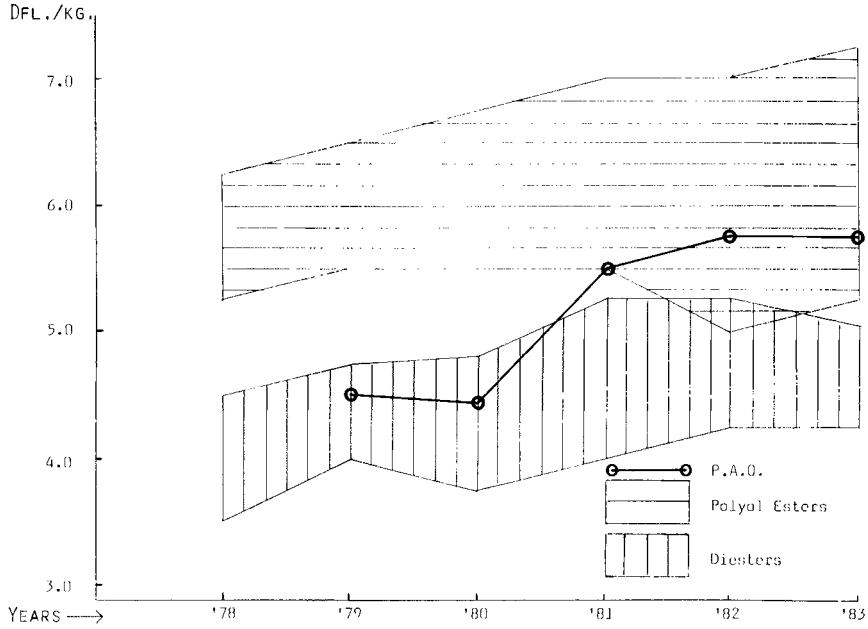

FIG. 1. Price development of esters and poly-alpha olefins for synthetic automotive lubricants (Western Europe).

scenarios of these two base fluids.

Although the change in relative costing seemed to improve prospects for oleochemical-based fluids, the future of di- and polyolesters in each of the many segments of the synthetic lubricant business largely remains crystal ball watching. Close contacts, alertness, flexibility and adequate responses to changes will continue to dictate the chance of success in this industry.

Important aspects to consider for present development programs are:

—the relative price developments in 1984/1985,
—the security of supply,
—the captive status of oil companies,
—advances in additive technology,
—engine builder trends,
—developments in cost of crude oil and fuels,
—consumer spending power,
—legislation and importance of energy conservation,
—cost of developments in relation to the future commercial benefit (product registration).

Antimicrobial Agents Derived from Fatty Acids

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ABSTRACT

The author reviews his research, since 1966, for the ideal germicide. The relationship between structure of fatty acids, their corresponding esters, and antimicrobial activity is presented. Saturated fatty acids have their highest activity when the chain length is twelve carbons (C_{12}) long; monounsaturated fatty acids reach their peak with palmitoleic acid ($C_{16:1}$); the most active polyunsaturated fatty acid is linoleic. *Trans* isomers are not active against microorganisms. The esterification of fatty acids to monohydric alcohols leads to inactive derivatives, whereas esterification to polyhydric alcohols increases biological activity. Examples of glycerol and sucrose esters are reviewed. In general, the lauroyl derivatives are the most active. A few examples of esters as active pharmacological agents against organisms causing bovine mastitis are presented as well as the use of monolaurin (Lauricidin®) as cosmetic and food preservatives. The safety and efficacy of fatty acid esters as potential germicides offer new and expanded roles for oleochemicals.

INTRODUCTION

"If all the drugs in the pharmacopoeia save three were dumped into the ocean, it would be so much better for the patient and so much worse for the fish." — Wendell Homes

These words by an American physician are prophetic and "foresaw" the problems of today's environmental contamination. The chemical industry has helped create a veritable arsenal of weapons against microorganisms and insects. In our narcissism with this extraordinary technology developed since the early part of the 1900s, the specter of danger to ourselves and the environs was overlooked. It is only in the past few years that *Silent Springs* (1) and other similar publications started to warn us of our folly.

Today, questions about our chemical world are being raised by government, industry and consumers. How can we continue to battle the microorganisms which damage crops, are responsible for so many diseases, and in general cause much mischief to man, and not add to the problem? Sulfa drugs and antibiotics certainly have been useful — but at a price. The administration of these powerful agents has created side effects which have become more a part of the problem than the solution. The growing resistance of microorganisms to germicides is but one example.

The solution to this ever-growing problem of using chemicals to eradicate disease and pestilence is to "return to nature": to find natural (nontoxic) agents which will kill bacteria, fungi, etc., but will do little or no harm to

Man or animal. In our case, this has resulted in a quest since 1966 to find the ideal germicide which could act on select cells and not have random effect on all cells. It was with this in mind that our attention was directed to the effect of fatty acids on microorganisms.

Soaps (saponified fatty acids) have been used by man since antiquity as a means for cleaning and disinfecting. The first recorded mention of "soap" was made on a 4,000-year-old clay tablet uncovered at Tello, Mesopotamia. In ancient times, soap was manufactured in the home from animal fat and wood ashes or lye. It was only in the 8th century A.D. that the making of soap became an industry in Italy and Spain (2).

Besides their general cleaning characteristics, soaps have been shown to be a useful antiseptic agent. Much of the early literature on the subject can be found in reviews by Bayliss (3), Kodicek (4) and Nieman (5). In subsequent years, the antifungal and bactericidal properties of fatty acids have been extensively investigated (6-8). Other reports point to the inactivation of viruses by various soaps (9-12).

Since 1966, our laboratory has been studying structure-function relationships to enable us to understand better the mechanisms of action of fatty acids and fatty acid derivatives. Since then, over 500 lipophilic compounds have been screened. Only a small portion of the data has been reported because of the proprietory nature of some of the findings. Much of our published work can be found in a number of recent reviews (13-16). This paper reviews only briefly the highlights of past research (Table I) and focuses more closely on the present and potential use of nontoxic germicidal agents originated from fatty acid derivatives.

MATERIAL AND METHODS

Because of the broad scope of this conference, it would be less than fair to present complete details of our screening methods. It is sufficient to say that both natural and synthetic lipids were tested in a liquid broth. Lipids were obtained from usual industrial sources and/or were kindly provided by numerous colleagues. Their cooperation played a vital part in our research effort, particularly since funds for this type of research were scarce. Many of the details used in our screen can be found in several earlier papers by our group (17, 18).

Basically, the information obtained was based on effects noted after placing the compound to be evaluated in direct contact with a spectrum of different microorganisms. The minimal inhibitory concentration (MIC) at 37 C could thus be determined. It is important to point out that the usual disc method used for water-soluble antibiotics gives false information for lipophilic compounds, since the amount of inhibitory activity (zone of inhibition) is limited more by a compound's failure to move off the disc (insolubility) than by its lack of biological activity per se. The disc method is never justified in screening for activity of lipophilic agents.

TABLE I

Antimicrobial History of Fatty Acids (FA) and Their Esters

Clark, J.R.	Effect of soaps on fungi	1899
Reichenbach, H.	Effects of FA on *E. coli*	1908
Kiesel, A.	Antimycotic action of FA	1919
Eggerth, A.H.	Alpha-Bromo FA	1926
Bayliss, M.	Structure-function relationship	1936
Stock, C.C, and T. Francis	Effects on viruses	1943
Rothman, S., et al.	Undecylenic acid	1946
Kodicek, E.	Unsaturated FA	1949
Franke, W.	Activity of *cis*-form	1949
Nieman, C.	Comprehensive review	1954
Gershon, H., and R. Parmegiani	Fluoro-fatty acids	1967
Kabara, J.J., et al.	Nonionic fatty acid derivatives	1972
Kabara, J.J., et al.	Isomeric unsaturated FA	1973
Kabara, J.J., et al.	Monolaurin (Lauricidin)	1977

Lipids as Antimicrobial Agents

Table II represents a good summary of our experiences in testing fatty acids, both saturated and unsaturated. Several generalities can be noted. First, saturated fatty acids exhibit their highest activity with a chain length of C_{12} (lauric acid). Second, the introduction of a *cis* double bond increases the antimicrobial activity of the fatty acid. Maximum effect was dependent, however, on chain length. In the case of monounsaturated fatty acid, maximum antimicrobial effects were found for the $C_{16:1}$ derivatives (palmitoleic acid). Third, only the *cis* isomer was active. *Trans* fatty acids have been shown to be inactive. Fourth, whereas the addition of a second double bond (linoleic acid) increased activity, a third double bond (linolenic acid) lowered activity.

Unsaturated fatty acids represented by acetylenic linkages tend to be less active against some types of bacteria then ethylenic unsaturation (3). In a comparative study in our laboratory, we found the acetylenic derivatives to be

TABLE II

Minimal Inhibitory Concentration (mM) of Saturated and Unsaturated Fatty Acids

Fatty acid	Organism			
	Pseudomonas aeruginosa	*Streptococcus* Group A	*Staphylococcus aureus*	*Candida albicans*
Caproic	NI	NI	NI	NI
Caprylic	NI	NI	NI	NI
Capric	NI	1.45	2.9	2.9
Lauric	NI	0.12	2.5	2.5
Myristic	NI	0.55	4.4	4.4
Myristoleic	NI	0.11	0.44	0.55
Palmitic	NI	3.9	NI	NI
Palmitoleic	NI	0.1	1.0	0.5
Stearic	NI	NI	NI	NI
Oleic	NI	1.77	NI	NI
Elaidic	NI	NI	NI	NI
Linoleic	NI	0.09	NI	0.46
Linolenic	NI	0.35	1.79	NI
Linoelaidic	NI	NI	NI	NI
Arachidonic	NI	NI	NI	NI

slightly more active (17).

The reader is urged to study the monograph "The Pharmacological Effect of Lipids" for greater details relating fatty acid structure to biological activity (19).

Having surmised which effects chain length and unsaturation had in relation to antimicrobial activity, it was of interest to compare the effect of changing the carboxyl group by reduction to either an aldehyde or alcohol group (Table III). Under these conditions the C_{12} acid, alcohol and aldehyde had approximately the same activity: a slight edge in biological activity going to the alcohol as compared to the acid (20). However, an interesting feature was that, when lauric acid was esterified to a monohydric alcohol, that antimicrobial activity was completely lost. This was true whether the alcohol was as simple as methanol or complex, as in the case of the cholesteryl laurate; both of these compounds were inactive. Also, when the terminal end of lauric acid was oxidized so that a dodecanedioic acid was formed, the dicarboxylic acid was also completely inactive. Included in this series, for reasons that were not completely clear, we also tested hydroxy lauric acid. Our results showed that this derivative was also active but not as active as lauric acid. However, in this case, esterification of the hydroxy lauric acid yielded an ester which did not lose activity as in the case of methyl laurate. This made us think that the hydroxyl group was important to the biological activity.

Because of this observation we decided to study the effects of esterification with polyhydric alcohols (21). Some of the more readily available derivatives were those of glycerol ester. A complete series of glycerol monoesters were studied, ranging from glycerol acetate all the way up to glycerol linoleate (Table IV). The glycerol-1-laurate was the most active derivative found in our screen. Interestingly, the unsaturated fatty acids, when esterified to glycerol, became less active than their corresponding fatty acid. In the case of the straight-chain fatty acid, lauric acid, the ester was more active. All the monoglycerides were esterified in the alpha position. When we compared the glycerol-2-laurate, or beta position, with glycerol laurate in the alpha position, we found for all practical purposes that the monoesters were identical in biological activity.

To confirm further the effect of esterification with glycerol, we studied a whole series of mono-, di- and triglycerides (20). For ease of presentation, only esters containing C_{10} or C_{12} fatty acids are listed (Table V). One can see from the table that the monoester was much more active than the C_{10} (capric acid) derivative. The 1, 3,-dicaprin has no activity. In the case of lauric acid, esterification to glycerine to form a monoester makes the derivative more active. Again the 1- and 2-monolaurin had identical activities, whereas the diesters (whether the 1,2- or the 1,3-dilaurin) had no activity. The trilaurin was totally inactive. These data suggested that it was only the monoester which had biological activity and this point continues to be emphasized in our subsequent work.

A rather complete comparison of the antifungal and antibacterial activity of glycerol and sucrose esters was made by Shibasaki et al (22). Glycerol esters and sucrose esters esterified with either C_8, C_{10} or C_{12} fatty acids were screened for activity. Two methods were used to measure activity: an agar dilution method and a broth dilution method. Using either method, C_{12} glycerol ester was the most important derivative in terms of antifungal activity (Table VI). Both the sucrose mono- and diesters show little activity compared to the glycerol esters.

In Table VII, the same derivatives were compared for their antibacterial activity. All three monoesters of lauric acid were active. Although the diesters of sucrose, particularly the C_8 and C_{12} derivatives, were active, they were not as active as the lauroyl derivative. The lauroyl derivative was about 10 times as active as either the C_8 or C_{10} derivatives and the ester was about 10 times as active as lauric acid itself.

Indication of how biological activity was influenced by pH is shown in Table VIII. Here, lauric acid, monoglyceryl monolaurate and its sucrose monoester were compared at various pH. In all cases, the biological activity of the esters do not change in the same degree as one would expect for the fatty acid. Being nonionic, the monoesters are not influenced by pH, although the activity is slightly higher at the lower pH. This represents an effect of pH on the growth of the organism rather than the effect of pH on the

TABLE III

Minimal Inhibitory Concentrations

Dodecyl derivative	Microorganism (gram-positive) *Pneumococci* (mM)	Group A *Streptococcus* (mM)
Lauric acid	0.06	0.12
Lauryl alcohol	0.07	0.07
Lauryl aldehyde	0.14	0.14
Methyl laurate	>4.6	>4.6
Cholesteryl laurate	NI	NI
Dodecanedioic acid	NI	NI
α-OH lauric acid	–	0.23
Methyl, α-OH laurate	–	0.54

TABLE IV

MIC for α-Monoglycerol Esters (mM) (21)

	Streptococcus Group A	*Staphylococcus aureus*
Glycerol acetate	>7.46[a]	>7.46[a]
Glycerol butyrate	>6.17[a]	>6.17[a]
Glycerol caproate	2.63	>5.26[a]
Glycerol caprylate	2.29	>4.59[a]
Glycerol pelargonate	2.16	>4.13[a]
Glycerol caprate	0.20	1.00
Glycerol laurate	0.05	0.09
Glycerol myristate	0.17	>3.31[a]
Glycerol stearate	>2.79[a]	>2.79[a]
Glycerol oleate	>2.81[a]	2.81[a]
Glycerol linoleate	1.41	>2.82[a]
Glycerol-2-laurate	0.09	0.19

[a]No inhibition, maximum concentration tested listed.

TABLE V

MIC Comparison (mM): Free Acid Form vs Glyceride Form (21)

Compound	Organism *Pneumococci* (mM)	Group A *Streptococcus* (mM)
Capric acid	1.45	1.45
1-Monocaprin	0.10	0.20
1, 3-Dicaprin	a	a
Lauric acid	0.06	0.12
1-Monolaurin	0.09	0.05
2-Monolaurin	b	0.09
1, 2-Dilaurin	a	a
1, 3-Dilaurin	a	a
Trilaurin	a	a

[a]No inhibition at concentrations tested.

[b]Test not performed.

TABLE VI

Comparison of Antifungal Activities of Fatty Acids and Their Esters (22).

Drug	MIC (mM) By agar dilution method[a]				By broth dilution method[b]
	A. niger	*P. citrimum*	*C. utilis*	*S. cerevisiae*	*C. utilis*
C_8	4	2	2	1	2
MC_8	4	2	4	4	>2
SMC_8	>4	>4	>4	>4	>2
SDC_8	>4	2	>4	4	>2
C_{10}	1	1	1	0.5	1
MC_{10}	0.5	0.5	0.5	0.5	0.5
SMC_{10}	>4	>4	>4	>4	>2
SDC_{10}	>4	>4	>4	>4	>2
C_{12}	>4	4	4	>4	1
MC_{12}	0.5	0.5	0.5	0.5	0.063
SMC_{12}	>4	>4	>4	>4	>2
SDC_{12}	>2	>2	>2	>2	>2

MIC: Minimum inhibitory concentration.

[a]On Czapek Dox's agar medium (supplemented with 0.25% yeast ext. and peptone, pH 5.6), after 30 C, 48 hr incubation.

[b]In Czapek Dox's medium (supplemented with 0.25% yeast ext. and peptone, pH 5.6), after 30 C, 24 hr. incubation.

TABLE VII

Comparison of Antibacterial Activities of Fatty Acids and Their Esters (22).

Drug	MIC (mM) By agar dilution method[a]				By broth dilution method[b]
	B. subtilis	*B. cereus*	*M. lysodeikticus*	*Staph. aureus*	*B. subtilis*
C_8	>2	>2	>2	>2	>2
MC_8	2	2	1	2	2
SMC_8	>2	>2	>2	>2	>2
SDC_8	0.125	0.125	0.125	0.125	0.5
C_{10}	2	1	2	>2	>2
MC_{10}	0.5	0.5	0.5	0.5	0.5
SMC_{10}	>2	>2	1	>2	>2
SDC_{10}	>2	0.5	0.125	>2	>2
C_{12}	>2	>2	>2	>2	0.5
MC_{12}	0.063	0.063	0.063	0.063	0.063
SMC_{12}	2	2	0.5	>2	>2
SDC_{12}	>2	>2	>2	>2	>2

[a]On nutrient agar medium (pH 7.0), after 37 C, 24 hr incubation.

[b]In nutrient broth medium (pH 7.0), after 37 C, 24 hr incubation.

TABLE VIII

Effect of pH on Antibacterial Activities of C_{12} Compounds Towards *B. subtilis* (22)

pH	MIC (mM)[a]		
	C_{12}	MC_{12}	SMC_{12}
5	0.016	0.032	0.25
6	0.125	0.063	>2
7	0.5	0.063	>2
8	>1.0	0.063	>2

[a]By broth dilution method.

antimicrobial agent.

In Tables IX and X, the antifungal activities of monocaprin and monolaurin were compared with some commonly used preservatives that are most popular either in the cosmetic industry or the food industry. These include the parabens, lauryl sulfate, sorbic acid and dehydroacetic acid. Both the C_{10} and the C_{12} derivatives have about the same activity against these fungi. However, when the monolaurin is compared with some of the other preservatives, the activity of the monoester is as high or higher than most of the presently used preservatives. This is particularly true when compared with sorbic acid. Monolaurin is about 10 or more times as active as sorbic acid itself.

Recent papers by Beuchat (23) and Shibasaki (24) have supported the findings that the lauric acid monoglyceride is very active. Beuchat showed that monolaurin had a low MIC against *Vibrio parahoemulyticus*. Monlaurin (at 5.0 μg/mL or less) was more effective than sodium benzoate (300 μg/mL) or sorbic acid (70 μg/mL).

These same ester preservatives were compared for their antibacterial activity (Table X). Again, it can be seen that the C_{12} derivative of glycerol was the most active ester. In this example, we screened the sucrose diester of C_8 fatty acid. This diester was active under these conditions but was not as active as the monoester of glycerine. Butyl parabens, which is one of the more active parabens used in the cosmetic industry, and sorbic acid, a common food preservative, show only low activity under the testing conditons.

Further comparisons were made with monolaurin vs sorbic acid, phenol, methyl- and propylparabens. Table XI shows the very high activity of the monoester for gram-positive organisms, much more effective than sorbic acid. The limitation of the activity of these lipid antimicrobial

TABLE IX

Comparison of Antifungal Activities of Fatty Acid Esters with Some Commonly Used Preservatives (22)

Drug	MIC (μg/mL)[a]		
	A niger	*C. utilis*	*S. cerevisiae*
MC_{10}	123	123	123
MC_{12}	137	69	137
BpHB	200	200	200
SLS	100	400	100
SA	1,000	1,000	1,000
DHA	100	200	200

BpHB: butyl *p*-hydroxybenzoate; SLS: sodium lauryl sulfate; SA: sorbic acid; DHA: dehydroacetic acid.

[a]By agar dilution method.

TABLE X

Comparison of Antibacterial Activities of Fatty Acid Esters with Some Commonly Used Preservatives (22)

Drug	MIC (μg/mL)[a]		
	B. subtilis	*B. cereus*	*Staph. aureus*
SDC_8	74	74	149
MC_{10}	123	123	123
MC_{12}	17	17	17
MpHB	400	200	200
SLS	100	100	50
SA	4,000	4,000	4,000

[a]By agar dilution method.

agents was seen in the fact that they have little or no activity against gram-negative organisms.

This lack of activity against gram-negative organism was a matter of concern. The reason for this resistance can be seen in Figure 1. The bacterial envelope of the gram-positive and gram-negative organisms are completely different. With the gram-negative organism, there is a membranous wall composed primarily of lipopolysaccharide layers which inhibit the insertion of the antimicrobial lipid into the membrane. Both the gram-negative envelope and the gram-positive envelope have a peptidoglycan membrane. However, in the case of the gram-negative envelope, the outer membane has an additional lipopolysaccharide barrier. There are techniques for the removal of this barrier. The most effective method is to add a chelating agent. A chelating agent (lactic acid/ethylenediaminetetraacetic acid, EDTA) will combine with the cation bridge(s) that hold the lipopolysaccharide layer to the peptidoglycan envelope. When the metal bridge is removed, the lipopolysaccharide layer is stripped off. Under these conditions, gram-negative and gram-positive organisms react similarly to the monoglyceride. In this manner, use of a chelating agent overcomes the limitation of the fatty acid esters to gram-negative organisms.

Figure 2 shows the complex membrane of a yeast (25). In this case, the outer membrane is composed of mannan which apparently does not strongly influence the ability of the ester to insert itself into the membrane. Thus yeast, molds and fungi are susceptible to monolaurin.

An electron micrograph of an envelope virus shows that the outer coating of the virus is very similar to gram-positive organisms and consequently these types of viruses are easily penetrated by lipid agents. In in vitro tests by Sands (12) and Hierholzer and Kabara (26), it was found that monoglycerides can affect susceptible viruses like Herpes I and II. Indeed, all lipid-coated viruses of this nature are susceptible to the effect of the monoglyceride. In some in vivo work currently being done in a number of laboratories, early indication reveals that indeed we may have a very effective antiherpes agent. This lead is currently being followed and we do have some anecdotal information from a double-blind clinical experiment showing that a cream composed of monolaurin was effective against *Herpes labialis.*

PRACTICAL APPLICATIONS OF LIPID ANTIMICROBIAL AGENTS

Bovine Mastitis Teat-Dip

It was of interest to seek out a number of clinical problems which we felt were amenable to solutions by the findings just presented. One of the problems identified was bovine mastitis. Because the organisms involved in mastitis were those most affected by monolaurin (Lauricidin®), we felt that this animal problem would represent a good clinical model. Lauricidin, the commercial form of monolaurin, was incorporated into a formula which had a very fast kill on *Staphylococcus aureus.* In our first series of studies, we compared our formulae with teat-dip products that are or were on the market. When our early formula of Lauricidin teat-dip was compared with products from four other sources, it was obvious, except for a dip which contained Chlorhexadine, that all the other teat dips were relatively inactive (Table XII). The three germicides that were used in that teat dip formulae were an iodophor, 8-hydroxyquinoline derivative, or a Bronpol derivative. It is interesting to note that all of these germicides are very active when tested by themselves but, when formulated into the teat dips, particularly in the presence of glycerol, they lost their activity and consequently were totally ineffective.

Preservation of Cosmetics

The real test of a germicide is its use in a complex system. Cosmetic emulsions represent a whole spectrum of such systems. In data presented to the cosmetic industry (27, 28), monolaurin was shown to be a very effective and safe preservative. One example from these studies is the results obtained on preserving a protein-containing emulsion (Table XIII). In these initial experiments, high levels of

TABLE XI

MIC (μg/mL) of the Test Materials

Compounds – organisms	Glycerin-1-monolaurin	Sorbic acid	Phenol	Methyl paraben	Propyl paraben
Staphylococcus aureus	39	1,000	1,250	5,000	2,500
Bacillus subtilis	39	1,000	1,250	5,000	2,500
Escherichia coli	>2,500	1,000	2,500	2,500	5,000
Pseudomonas aeruginosa	>2,500	2,000	1,250	5,000	>10,000
Aspergillus niger	>2,500	1,000	1,250	2,500	2,500
Candida albicans	>2,500	1,000	1,250	2,500	2,500

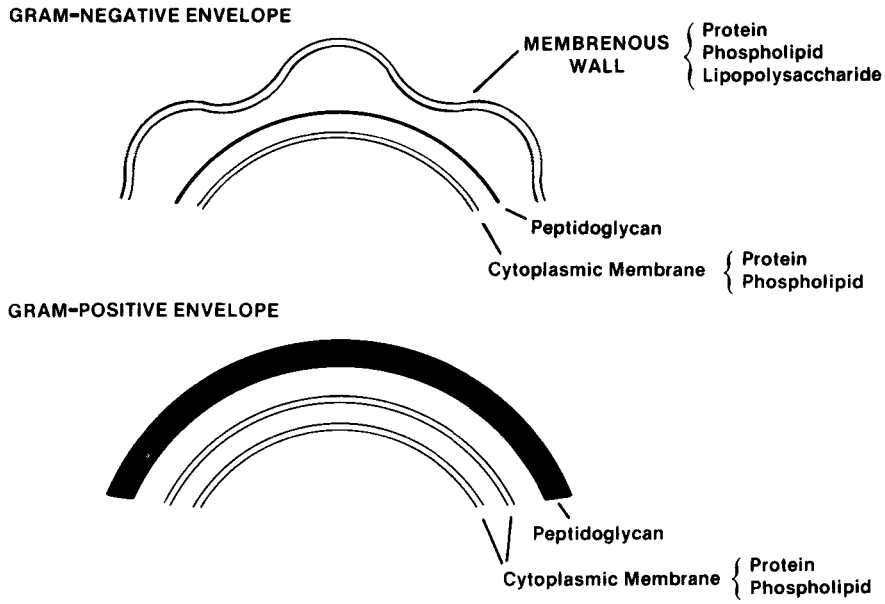

FIG. 1. Structure of the cell envelope of gram-negative and gram-positive bacteria.

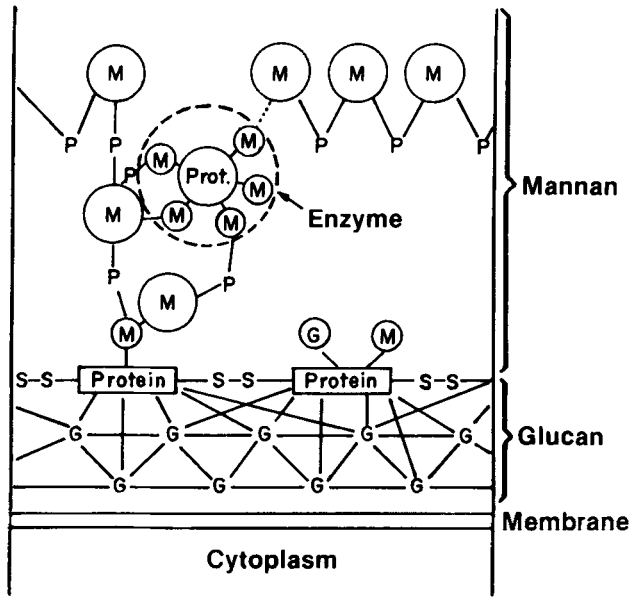

FIG. 2. Schematic structure of the yeast cell wall (25). M indicates mannan; G, glucan; P, phosphates; S, sulfur.

TABLE XII

Comparison of Commercial Teat-Dip Preparations

Formula tested	*Staph. aureus* vs time 5 min	15 min	30 min	60 min
H_2O only	6.9×10^5	8.5×10^5	8.6×10^5	8.6×10^5
Lauricidin-TD	5.9×10^3	<100	<100	<100
Company A	9.1×10^5	5.1×10^5	3.9×10^5	3.5×10^5
B	3.8×10^5	2.2×10^5	1.9×10^5	1.3×10^5
C	9.7×10^5	1.1×10^6	1.1×10^6	7.8×10^5
D	<100	<100	<1000	<100
H_2O only	1.1×10^6	–	1.1×10^6	1.1×10^6

TABLE XIII

Protein Hair Treatment Formula

Deionized water
Hydrolyzed animal protein
Cetyl alcohol
Glyceryl stearate and PEG – 100 stearate
Quaternium – 31
Hydrolyzed milk protein
Oat flour
Cherry kernel oil
Sunflower oil
Quaternium – 41
PEG – 5 soya sterol
Glycerin
Guar hydroxypropyl trimonium chloride
Titanium dioxide
Wheat germ glycerides
Fragrance
Autolyzed yeast
PEG – 75 lanolin
Panthenol

preservative were used (formula A). In a second series, the usual glyceryl stearate in the formula was substituted by monolaurin (27). Regardless of the challenge organisms, both cosmetic formulae were shown to resist large challenges of organisms (3.0×10^5 to $2.0 \times 10_6$ CFU/mL, Table XIV). These initial results were followed by studies in which optimal ratios of monoglycerides, parabens and chelator were determined (28). In these experiments of the preservative system ratio (1:1:1) was shown to be effective even at low levels (<0.3%). This was true whether O/W or W/O emulsions were used as model systems.

Preservation of Food

An unusual accumulation of reports on the use of monolaurin in food products can be found in two issues of the *Journal of Food Safety* (Vol. 3, No. 2, 1981; Vol. 4, No. 1, 1982). Both issues are devoted exclusively to papers on the subject. It behooves the reader who is seriously following the progress of food preservation to review these two volumes. Space and time does not allow more specific information on all these findings except to point out that Lauricidin was generally found to be more active at high rather than low temperatures. This means that, for many products, long shelf-life can be accomplished at room temperature after three days, has had its shelf life extended

TABLE XIV

Microbial Challenge

Interval		Initial	48 hr	96 hr	7 days	4 days
Pseudomonas aeruginosa	A	3.0×10^5	100	–	–	–
	B	3.0×10^5	5.0×10^4	5.0×10^4	–	–
Staphylococcus aureus	A	3.0×10^5	–	–	–	–
	B	3.0×10^5	–	–	–	–
Candida albicans	A	2.0×10^6	1.1×10^3	–	–	–
	B	2.0×10^6	5.5×10^3	1.5×10^3	400	–

A: Lauricidin (0.3%), methyl paraben (0.3%), propyl paraben (0.1%) and EDTA (0.2%).
B: Lauricidin (4.8%) and EDTA (0.3%).

to over four months using a monolaurin and lactic acid combination (Lauri-Lac).

FUTURE POSSIBILITIES

There is a wealth of accumulated information in a decade and a half of work on this subject. Although it was impossible to summarize all the data on fatty acids and their esters, I hope that these few examples will create interest and show the industry that fatty acid esters of polyhydric alcohols offer new and expanded roles for oleochemicals. Those who would like more information on this subject should obtain a copy of "The Pharmacological Effect of Lipids," printed by the American Oil Chemists' Society in 1978. This volume offers a good background on antimicrobial lipids. It is being updated by the publication of a second volume representing a symposium on the subject held in Chicago in May, 1983. Both books will give even the casual reader a firm foothold into the literature on the subject.

I believe our work has opened a number of interesting possibilities for the oleochemical industry. The examples that I gave were but a few. Monolaurin is probably the most important of the lipids found after screening over 500 derivatives. Applications for this material in the food, cosmetic and pharmaceutical fields are rapidly expanding. Not only can products be chemically preserved but also a chemical can be added which gives protection without toxicity. Monolaurin (Lauricidin®) is accepted by all governments as being completely nontoxic and therefore can be used in products as a substitute for more toxic germicides. The replacement of mercury, formaldehyde and other toxic preservatives, in the cosmetic, food and pharmaceutical areas, represents a tremendous opportunity for formulators to produce not only microbiologically safe products but also products that when applied to the skin are compatible with those lipids already present on the surface.

REFERENCES

1. Larson, R., Silent Springs, Houghton Mifflin, Boston, MA, (1962).
2. Adams, R.M., in *Occupational Skin Disease*, Grune and Stratton, New York, 1983, chap. 12, pp. 192–203.
3. Bayliss, M., J. Bacteriol. 31:489 (1936).
4. Kodicek, E., Soc. Exp. Biol. Symp. 3:217 (1949).
5. Nieman, C., Bacteriol. Rev. 18:147 (1954).
6. Chattaway, F.W., C.C. Thompson and A.J.E. Barlow, Biochem. J. 63:648 (1956).
7. Glassman, H.N., Bacteriol. Rev. 12:105 (1948).
8. Prince, H.N., J. Bacteriol. 78:788 (1959).
9. Stock, C.C., and T. Francis, Jr., J. Exp. Med. 71:661 (1940).
10. Stock, C.C., and T. Francis, Jr., Ibid. 77:323 (1943).
11. Stock, C.C., and T. Francis, Jr., J. Immunol. 47:303 (1943).
12. Sands, J.A., Antimicrob. Agents Chemother. 12:523 (1977).
13. Kabara, J.J., in *The Pharmacological Effects of Lipids*, edited by J.J. Kabara, American Oil Chemists' Society, Champaign, IL, 1978, p. 1.
14. Kabara, J.J., JAOCS 56:760 (1979).
15. Kabara, J.J., J. Food Prot. 44:633 (1981).
16. Kabara, J.J., J. Food Safety 4:13 (1982).
17. Kabara, J.J., A.J. Conley, D.M. Swieczkowski, I.A. Ismail, M.S.F. Lie Ken Jie and F.D. Gunstone, J. Med. Chem. 16:1060 (1973).
18. Kabara, J.J., R. Vrable and M.S.F. Lie Ken Jie, Lipids 12:753 (1977).
19. Kabara, J.J., (ed.) The *Pharmocological Effect of Lipids*, American Oil Chemists' Society, Champaign, IL, 1978.
20. Kabara, J.J., D.M. Swieczkowski, A.J. Conley and J.P. Truant, Antimicrob. Agents Chemother. 2:23 (1972).
21. Conley, A.J., and J.J. Kabara, Ibid. 4:501 (1973).
22. Kato, N., and I. Shibasaki, J. Ferment. Technol. 53:793 (1975).
23. Beuchat, L.R., Appl. Environ. Microbiol. 39:1178 (1980).
24. Shibasaki, I., J. Food Safety 4:35 (1982).
25. Lampen, J.O,, and A. von Leeuwenhoek, J. Microbial. Seiol. 34:1 (1968).
26. Hierholzer, J., and J.J. Kabara, Ibid. 4:1 (1982).
27. Kenney, D., Cosmet. Toiletries 97:71 (1982).
28. Kabara, J.J., and C.M. Wernette, Ibid. 97:77 (1982).