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Antimicrobial Action of Esters of Polyhydric Alcohols

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A broth dilution method was used to determine the minimal inhibitory concentration of a series of fatty acid esters of polyhydric alcohols against gram-negative and gram-positive organisms. Gram-negative organisms were not affected. Gram-positive organisms were inhibited as follows. Of the monoglycerol esters, monoglycerol laurate was the most active. Esters of polyglycerols (tri-, hexa-, and decaglycerol esters) were generally active when the fatty acid had chain lengths of 8 to 12 carbon atoms. Sucrose esters, when active, except for laurate, are more active than the free fatty acid. The spectrum of antimicrobial action of esters of polyhydric alcohols is narrower when compared with the free acids.

In studies to delineate the structural relationships involved with antimicrobial activity of fatty acids and derivatives, a number of compounds had been screened (5, 5a, 6). Among those derivatives, esters of monohydric alcohols showed little or no inhibition; however, monoglycerol esters proved to be greatly inhibitory against gram-positive organisms. As a continuation, this report is a study of the antimicrobial action of an encompassing group of fatty acid derivatives, i.e., fatty acid esters of polyhydric alcohols. The esters studied were: methyl, glycerol, polyglycerol and sucrose.

MATERIALS AND METHODS

Source of compounds. Mono- and dilaurin and mono- and dicaprin were a gift from D. Rebello, Department of Chemical Technology, University of Bombay. The 2-monolaurin was the product of a special synthesis, obtained from Applied Science, State College, Pa. Trilaurin was obtained from Eastman Organic Chemicals, Rochester, N.Y. Lauric, capric, and oleic acids and monoolein were obtained from Sigma Chemicals, St. Louis, Mo. The polyglycerols were kindly supplied by V. K. Babayan, Stokely-Van Camp, Inc., Indianapolis, Ind. One group of sucrose esters, sucrose caprate, laurate, myristate, palmitate, oleate, elaidate, and linoleate, was the gift of Akiko Kato, Laboratory of Microbiology, Department of Agriculture Chemistry, University of Tokyo; another group of sucrose esters, sucrose laurate, myristate, palmitate, oleate, and linoleate, was obtained from T. Ishizuka, Dai-Ichi Kogyo Seiyaku Company, Ltd., Kyoto, Japan (Table 1).

The triglycerides, 1-palmitoyl-3-olein, 1,3-diolein, monomyristin, monostearin, and monolinolein were a gift from Robert Jensen, Department of Nutritional Sciences, University of Connecticut, Storrs, Conn. 1,3-Dilauroylolein, α-hydroxylaurate, and methyl-α-hydroxylaurate were obtained from Supelco Inc., Bellefonte, Pa.

All compounds used in this study were highly pure (>95%), except the sucrose esters. The difficulty in preparing these compounds and their subsequent purification have yielded products which are less satisfactory. However, the composition of the sucrose ester is known (Table 1).

Preparation of solutions. Standard suspensions (1,000 μg/ml) of fatty acids, polyglycerol esters, mono- and dilaurin, and mono- and dicaprin, and trilaurin (except for 2-monolaurin) were prepared as described previously (6).

Sucrose esters and 2-monolaurin suspensions were prepared by adding 200 ml of sterile Trypticase soy broth (TSB; BBL, 3%) to the weighed compounds (0.2 g dissolved in 1 ml of absolute methanol). This dilution of alcohol had no antimicrobial effect. These standard suspensions (1,000 μg/ml) were two-fold serially diluted with additional sterile broth to a concentration of 125 μg/ml. A 3.8-ml sample of each dilution was aseptically delivered into sterile, screw-capped culture tubes. All tubes were incubated overnight at 36 C to insure sterility. If a compound was found to have inhibitory activity at 125 μg/ml, further dilutions were made.

Triglycerides, 1-palmitoyl-3-olein, 1,3-diolein (standard suspensions [1,500 μg/ml]), and monomyristin, monostearin, monoolein, and monolinolein (standard suspensions) were prepared by the method just described. Since only small quantities of compounds were available, less standard suspension was made and tests were necessarily conducted against fewer species. Compounds were compared on a molar

TABLE 1. *Analytical results of the samples: sucrose esters*

Sample	Sucrose ester (%)	Composition of SE (%)			Degree of substitution	Composition of fatty acid
		Mono-	Di-	Tri-		
Sucrose laurate	90.3	58.3	34.0	7.7	1.39	C_{12}, minimum 99%
Sucrose myristate	89.3	61.5	33.6	4.9	1.34	C_{14}, minimum 94%
Sucrose palmitate	87.1	52.4	36.4	11.1	1.45	C_{16}, minimum 93%
Sucrose oleate	67.9	60.2	32.8	7.0	1.35	$C_{18:1}$, 75.5% $C_{18:2}$, 11.5% C_{18}, 7.3% C_{16}, 5.2% C_{14}, 0.5%
Sucrose linoleate	72.0	48.7	36.0	15.4	1.51	$C_{18:2}$, 52.6% $C_{18:1}$, 24.9% $C_{18:3}$, 7.9% C_{18}, 5.3% C_{16}, 8.2% C_{20}, 0.9%

(micromoles per milliliter) basis.

Microorganisms. The microorganisms used in this study are those previously used (6) and continuously maintained in our laboratory. They are *Staphylococcus aureus*, *S. epidermidis*, *Streptococcus pyogenes* group A, *S. faecalis* group D, *Sarcina lutea* ATCC-9341. *Micrococcus* sp., *Nocardia asteroides* ATCC-3308, *Corynebacterium* sp. ATCC 10700, *S. pneumoniae* ATCC-6301, *Proteus vulgaris*, *P. mirabilis* ATCC-14273, *P. rettgeri* ATCC-9250, *Escherichia coli*, *Serratia marcescens* ATCC-13880, *Pseudomonas aeruginosa* ATCC-10145, *Klebsiella-Enterobacter* sp., and *Salmonella typhimurium*.

The inoculum (0.05 ml of an 18- to 24-h TSB culture [approximately 10^9 organisms per ml]) was aseptically delivered into all dilutions of the compounds, mixed well, and incubated at 36 C. A tube of inoculated broth without compound served as a positive control, and an uninoculated set of dilutions incubated with the test dilutions served as a negative control.

After 18 h of incubation, the minimal inhibitory concentration (MIC) of each compound was determined for the organisms tested. The MIC is defined as the lowest concentration of compound at which no macroscopic evidence of growth was observed after 18 h of incubation when turbidity of the inoculated broth dilutions was compared with uninoculated control tubes.

In those cases in which the test compound itself caused turbidity so that the MIC could not accurately be determined, a sample (0.015 ml) of the mixed broth in question was inoculated onto a Trypticase soy agar plate containing 5% defibrinated sheep blood, incubated at 36 C, and examined after 18 h for bactericidal end points. There was usually only a one-tube difference between cidal and static concentrations. However, compound turbidity did not confuse the readings. Either compounds were inhibitory at low concentrations where solubility was almost complete or comparison of the dilutions in question with uninoculated controls was sufficient to determine whether growth had occurred.

Controls. Those procedures previously used are applicable in this study. Lauric, capric, and oleic acids were used as internal controls and for comparison with our previous report (6). These included (i) confirmation of the stability of those compounds which were autoclaved (fatty acids, polyglycerol esters, mono- and dilaurin, mono- and dicaprin, and trilaurin), (ii) confirmation that dispersed or suspended compound material contributes to the effectiveness of the compound, and (iii) confirmation that added protein (0.1% albumin) has no effect on the determination of the MIC under the conditions of these experiments. (6).

RESULTS

The MIC for the compounds studied are given in Tables 2–7. No inhibition was found against the gram-negative organisms *P. rettgeri*, *P. vulgaris*, *P. mirabilis*, *Klebsiella-Enterobacter* sp., *E. coli*, *P. aeruginosa*, *S. typhimurium*, and *S. marcescens*.

Monoglycerols. The monoglycerol laurate was the most active compound in this series (Table 2 and Fig. 1). The monoglycerol 2-laurate, although slightly less active than the 1-mono derivative(s), is still considered to be highly active. The shorter fatty acid chain length monoglycerols, acetate and butyrate, were inactive as was the stearate. The C_{18} monoglycerols containing unsaturated fatty acids, oleate and linoleate, showed slight activity. Of the gram-positive organisms, *S. pyogenes* was the most susceptible organism and *S. faecalis* group D was the least susceptible.

Polyglycerols. For each polyhydric alcohol, tri-, hexa, and deca-glycerol, seven esters were examined. Individual MICs are given in Tables 3 to 5. The acetate and butyrate esters were inactive, except that *S. pyogenes* was inhibited by decaglycerol butyrate. The *S. faecalis* group

TABLE 2. *Monoglycerol esters: MICs*

Esters	MIC (μmol/ml)						
	Streptococcus pyogenes	*Corynebacterium* sp.	*Nocardia asteroides*	*Micrococcus* sp.	*Staphylococcus aureus*	*Staphylococcus epidermidis*	*Streptococcus faecalis*
Glycerol acetate	No inhibition (>7.46)[a]						
Glycerol butyrate	No inhibition (>6.17)[a]						
Glycerol caproate	2.63	>5.26[a]	>5.26[a]	5.26	>5.26[a]	[b]	>5.26[a]
Glycerol caprylate	2.29	>4.59[a]	>4.59[a]	>4.59[a]	>4.59[a]	[b]	>4.59[a]
Glycerol pelargonate	2.16	2.16	2.16	2.16	>4.31[a]	[b]	>4.31[a]
Glycerol caprate	0.20	0.20	0.50	0.10	1.00	1.00	2.00
Glycerol laurate	0.05	0.05	0.09	0.09	0.09	0.09	>3.63[a]
Glycerol myristate	0.17	0.17	>3.31[a]	[b]	>3.31[a]	[b]	[b]
Glycerol stearate	No inhibition (>2.79)[a]						
Glycerol oleate	>2.81[a]	1.40	>2.81[a]	[b]	>2.81[a]	[b]	[b]
Glycerol linoleate	1.41	0.14	>2.82[a]	[b]	>2.82[a]	[b]	[b]
Glycerol-2-laurate	0.09	0.19	0.19	0.09	0.19	0.09	>3.63[a]

[a] No inhibition, maximum concentration tested listed.
[b] Test not performed.

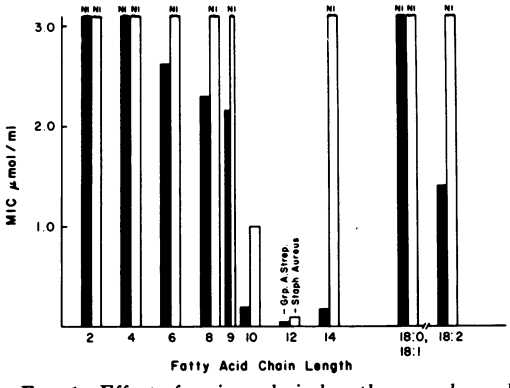

FIG. 1. *Effect of various chain length monoglycerol esters on Staphylococcus aureus and Streptococcus pyogenes. NI, No inhibition; dark bars, Streptococcus pyogenes; light bars, Staphylococcus aureus.*

D and *S. aureus* strains were not inhibited by any of the polyglycerol esters. Figure 2 illustrates the trends in polyglycerol inhibition against a susceptible organism, *S. pyogenes*. The decaglycerol is the only glycerol polymer which gives inhibition for fatty acid chain length less than six. From chain length 8 to 12 the polyglycerol inhibition is relatively constant, except for decaglycerol caproate.

One higher-chain length polyglycerol, triglycerol oleate, was tested. This compound was found to be non-inhibitory at the concentration tested (1.98 μmol/ml).

Sucrose esters. Table 6 lists the MICs of sucrose esters against susceptible gram-positive organisms. Sucrose palmitate is the only sucrose ester which inhibits the growth of *S. epidermidis* and *S. lutea*.

In general, sucrose esters, except for laurate, are more active than the free fatty acids. Contrary to previous experience, both *cis* and *trans* 18:1 isomers were active. Concomitant with the increase of activity of these esters compared with the free acids for individual organisms, there is a decrease in the spectrum of antimicrobial action. None of the sucrose esters tested inhibits *Bacillus subtilis*, *S. aureus*, or *S. faecalis* group D.

Di- and tri-glycerides. Listed in Table 7 are the di- and tri-glycerides tested. In general, these compounds were inactive. However, the E-O-O and Tri 18:2 were found to be active at 1.70 and 1.19 μmol/ml, respectively, against *S. pyogenes*. Also 12-O-12 was found to be active at 1.78 μmol/ml against the *S. pyogenes* and *S. aureus*.

Two other C_{12} derivatives were tested against six organisms. α-Hydroxylaurate was active against *S. pyogenes* (0.23 μmol/ml) and *N. asteroides* (4.63 μmol/ml). Methyl-α-hydroxylaurate was inhibitory to *S. aureus*, *S. pyogenes*, and *S. cerevisiae* (0.54 μmol/ml) and *N. asteroides* (4.34 μmol/ml). Neither compound was inhibitory for *S. faecalis* group D.

DISCUSSION

The biological properties of certain fatty acid esters have been studied (4). Methyl and certain polyoxyethylene esters are known to render certain fatty acids nontoxic. However, polyoxyethylene and sorbitan esters have been the only fatty acid esters of polyhydric alcohols studied previously (4).

With derivatives of lauric acid (C_{12}) as a model, the structural relationships of esters to

TABLE 3. *Triglycerol esters: MICs*

Esters	MIC (μmol/ml)						
	Streptococcus pyogenes	*Corynebacterium* sp.	*Nocardia asteroides*	*Micrococcus* sp.	*Staphylococcus aureus*	*Staphylococcus epidermidis*	*Streptococcus faecalis*
Triglycerol acetate	No inhibition (>3.55)[a]						
Triglycerol butyrate	No inhibition (>3.23)[a]						
Triglycerol caproate	1.47	2.96	2.96	2.96	>2.96[a]	[b]	>2.96[a]
Triglycerol caprylate	0.27	1.37	1.37	0.27	>2.73[a]	[b]	>2.73[a]
Triglycerol pelargonate	0.26	1.32	1.32	0.26	>2.63[a]	[b]	>2.63[a]
Triglycerol caprate	0.15	0.32	[b]	1.26	>2.50[a]	>2.50[a]	>2.50[a]
Triglycerol laurate	0.29	0.24	[b]	0.29	>2.36[a]	>2.36[a]	>2.36[a]

[a] No inhibition, maximum concentration tested listed.
[b] Test not performed.

TABLE 4. *Hexaglycerol esters: MICs*

Esters	MIC (μmol/ml)						
	Streptococcus pyogenes	*Corynebacterium* sp.	*Nocardia asteroides*	*Micrococcus* sp.	*Staphylococcus aureus*	*Staphylococcus epidermidis*	*Streptococcus faecalis*
Hexaglycerol acetate	No inhibition (>1.98)[a]						
Hexaglycerol butyrate	No inhibition (>1.88)[a]						
Hexaglycerol caproate	0.89	>1.79[a]	1.79	1.79	>1.79[a]	[b]	>1.79[a]
Hexaglycerol caprylate	0.17	0.85	0.85	0.17	>1.70[a]	[b]	>1.70[a]
Hexaglycerol pelargonate	0.17	0.83	0.83	0.17	>1.66[a]	[b]	>1.66[a]
Hexaglycerol caprate	0.19	0.39	[b]	0.79	>1.58[a]	>1.58[a]	>1.58[a]
Hexaglycerol laurate	0.19	0.38	[b]	0.38	>1.52[a]	>1.52[a]	>1.52[a]

[a] No inhibition, maximum concentration tested listed.
[b] Test not performed.

TABLE 5. *Decaglycerol esters: MICs*

Esters	MIC (μmol/ml)					
	Streptococcus pyogenes	*Corynebacterium* sp.	*Nocardia asteroides*	*Micrococcus* sp.	*Staphylococcus aureus*	*Streptococcus faecalis*
Decaglycerol acetate	No inhibition (>1.25)[a]					
Decaglycerol butyrate	0.12	>1.21[a]	>1.21[a]	>1.21[a]	>1.21[a]	>1.21[a]
Decaglycerol caproate	>1.17[a]	>1.17[a]	>1.17[a]	1.17	>1.17[a]	>1.17[a]
Decaglycerol caprylate	0.11	1.13	0.56	0.11	>1.13[a]	>1.13[a]
Decaglycerol pelargonate	0.56	1.11	0.56	0.56	>1.11[a]	>1.11[a]
Decaglycerol caprate	0.11	1.10	0.55	0.55	>1.10[a]	>1.10[a]
Decaglycerol laurate	0.26	0.53	[b]	0.53	>1.06[a]	>1.06[a]

[a] No inhibition, maximum concentration tested listed.
[b] Test not performed.

antimicrobial activity can be illustrated. Methyl-laurate is usually inactive or at best, weakly active. However, the hydroxylated ester (α-hydroxymethyl laurate) had activity. Thus, finding a single free functional group to be important, we examined the actions of compounds esterified to polyhydric rather than monohydric alcohols. Among the glycerol compounds studied were mono- and di-glycerides and polyglycerol esters. Although use of these compounds as emulsifiers and additives in edible food-stuffs has been documented (1, 12), this antimicrobial screen answers the question concerning the intrinsic preservative properties of polyglycerol esters (1).

Studies concerning the biological properties of monoglycerides are relatively recent (7, 8). In these studies only the antitumor effect was studied or the microbial screen was limited (8, 11). Kato et al. (7, 8) tested monoglycerides (a

mixture of C_{16}, C_{18}, and $C_{18:1}$) isolated from fungal mycelia for activity against Ehrlich ascites tumor. This mixture of monoglycerides proved negative in activity when screened against *Sarcina lutea*. Our results confirm that monostearin is inactive, although the monolein was slightly inhibitory for one organism. A report on sterilizing conditions of injectable oils (13) shows the intrinsic sporicidal character of an oil which was a mixture of mono-, di-, and triglycerides of C_8 and C_{10} fatty acids. In comparison with our results, only the C_8 and C_{10} monoglycerides could be implicated as the active structures. Additional studies by Kato et al. (9, 10) also show monoglycerides to have a wide range of biological activity, cytotoxicity, and hemolytic activity. In regard to other biochemical effects, Coutelle and Schewe (3) found 50% depression of nicotinamide adenine dinucleotide (reduced form) (NADH) oxidase system with 0.14 nmol of mono-glyceride per μg of protein, with the monoglyceride acting only on the O_2 side of flavine of NADH dehydrogenase.

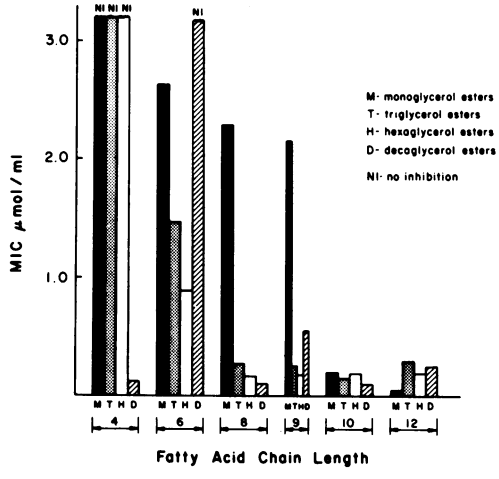

FIG. 2. *Comparison of chain lengths and glycerol number on inhibition of Streptococcus pyogenes.*

In our study other glycerides (di-, tri-) did not display the antimicrobial activity indicated for monoglycerides (table 7). The activity against *S. pyogenes* of E-O-O and trilinolein at high concentration may be due to impurities outside our limits of detection.

Babayan and McIntyre (2) have shown that polyglycerol esters encompass a wide range of hydrophilic to lipophilic natures, dependent on fatty acid chain length and glycerol polymer length. Longer fatty acid chains decrease water solubility, whereas greater glycerol polymerization tend to increase water solubility (2). With exceptions, the trends in inhibition for medium-length fatty acid polyglycerol esters tend to follow the solubility properties. Caproic and caprylic acids (C_6 and C_8) are inactive (6). Their corresponding polyglycerol esters are inhibitory. The exception is decaglycerol caproate. The MICs for the longer-chain polyglycerol esters (C_{10} and C_{12}) are close to the MICs for the corresponding fatty acid. The decrease in antimicrobial spectrum of higher-molecular-weight polyglycerol esters is probably related to their specific physical or structural properties, or both. The larger the molecular structure, the more limited the inhibition. The reason for this specificity is not obvious.

Because of their water solubility, sucrose esters were among the most interesting com-

TABLE 6. *Sucrose esters: MICs*

Esters	MIC (μmol/ml)						
	Streptococcus pneumoniae	*Streptococcus pyogenes*	*Corynebacterium* sp.	*Nocardia asteroides*	*Micrococcus* sp.	*Sarcina lutea*	*Staphylococcus epidermidis*
Capric acid	1.45	1.45	1.45	1.45	2.9	2.9	2.9
Sucrose caprate	0.06	0.06	0.25	0.25	1.00	>2.00[a]	>2.00[a]
Lauric acid	0.06	0.12	0.12	0.12	0.62	1.24	2.49
Sucrose laurate	0.12	0.03 (0.12)[b]	0.47 (0.23)	0.47 (1.90)	1.90	>1.90[a]	>1.90[a]
Sucrose myristate	0.23	0.05 (0.11)	0.11 (0.11)	0.23 (0.11)	0.23	>1.84[a]	>1.84[a]
Sucrose palmitate	0.05	0.10 (0.20)	0.43 (0.26)	0.43 (>1.72[a])	0.26	0.43	0.86
Sucrose elaidate	0.20	0.20	1.64	0.20	0.82	>1.64[a]	>1.64[a]
Oleic acid	>3.55[a]	1.77	>3.55[a]	>3.55[a]	>3.55[a]	>3.55[a]	>3.55[a]
Sucrose oleate	0.05	>1.64[a] (0.41)	1.64[a] (>1.64[a])	0.41 (0.21)	0.21	>1.64[a]	>1.64[a]
Sucrose linoleate	0.05	0.41 (0.82)	>1.66[a] (1.66)	0.41 (1.66)	0.82	>1.66[a]	>1.66[a]

[a] No inhibition, maximum concentration tested listed.

[b] Values in parentheses represent a second set of sucrose esters. Gram-positive organisms not inhibited by sucrose esters: *Staphylococcus aureus*, *B. subtilis*, *Streptococcus faecalis* group D.

TABLE 7. *Compounds tested*

Diglycerides		
1,2-Dilaurin		
1,3-Dilaurin		
1-Palmitoyl-3-olein		
1,3-Diolein		
Triglycerides[a]		
12-12-12	O-O-O	P-O-P
O-12-12	O-O-16:1	S-O-B
E-12-12	O-O-S	P-O-S
12- E-12	O-O-P	E-E-12
12-O-12 (1.78 μmol/ml)[b]		
O-O-E (1.70 μmol/ml)		
18:2-18:2-18:2 (1.14 μmol/ml)		

[a] Shorthand designations: O, oleate; P, palmitate; E, elaidate; S, stearate; 16:1, palmitoleate; 18:2, linoleate; B, butyrate.

[b] MICs listed for *Streptococcus pyogenes*.

pounds studied. Esterification to sucrose formed an active compound from a non-inhibitory free fatty acid. Examples are the $C_{18:1}$ isomers. Elaidic (*trans*) and Oleic (*cis*) acids are inactive, whereas their sucrose esters have activity. Unless isomerization has occurred, this is the first example of a (*trans*) fatty acid derivative with antimicrobial activity. The variations in results obtained with two sets of sucrose esters from two sources may be explained by the fact that these derivatives are mixed (Table 1).

Kato et al. (10) found sucrose laurate to be most active against Ehrlich ascites tumor. Sucrose laurate was shown to be more active than lauric acid in inhibiting the growth of *E. coli* (11). Using the same source for our derivative, we found no inhibition of *E. coli* or other gram-negative organisms by lauric acid or its sucrose esters. This difference may be explainable by strain difference or media. Kato (11) used a defined minimal medium, whereas ours was TSB.

The antimicrobial activity of polyglycerol esters is impressive. Acetate and butyrate polyglycerol esters are generally inactive. Inhibition increases for the esters as the fatty acid chain length increases. Caprate and laurate polyglycerol esters are the most active. For monoglycerol esters, caprate and laurate are the most active. Di- and triglycerides are generally inactive. Except for laurate, sucrose esters are more active than the corresponding fatty acid. For all these active esters of polyhydric alcohols, the spectrum of antimicrobial activity is narrower. However limited in their activity, these compounds have a diversity of physical properties which could increase their applicability. A particular ester or set of esters can be selected on the basis of their solubility to "fit a formulation." Since these compounds represent various structures, selection can also include consideration of chemical compatibility. The full potential of these and related active lipid derivatives needs to be explored.

LITERATURE CITED

1. Babayan, V. K., T. G. Kaufmann, H. Lehman, and R. J. Tkaczuk. 1964. Some uses and applications of polyglycerol esters in cosmetics are pharmaceutical preparations. J. Soc. Cos. Chem., 473-483.
2. Babayan, V. K., and R. T. McIntyre. 1971. Preparation and properties of some polyglycerol esters of short and medium chain length fatty acids. J. Amer. Oil Chem. Soc., **48**:307-309.
3. Coutelle, C. H., and T. Schewe. 1970. Fattsauren und Monoglyzeride aus Homogenaten von Froscheiern und Kaulquappere als Hemmstoffe der Atmungskette. Acta. Biol. Med. Germ. **25**:47-63.
4. Dubos, R. J. 1947. The effect of lipids and serum albumin on bacterial growth. J. Exp. Med. **85**:9-22.
5. Kabara, J. J., A. J. Conley, and J. P. Truant. 1972. Relationship of Chemical Structure and antimicrobial activity of alkyl amides and amines. Antimicrob. Ag. and Chemother. **2**:492-498.

5a. Kabara, J. J., A J. Conley, D. J. Swieczkowski, I. A. Ismail, M. Lie Ken Jie, and F. D. Gunstone. 1973. Unsaturation in fatty acids as a factor for antimicrobial action. J. Med. Chem. **16**:1060.

6. Kabara, J. J., D. M. Swieczkowski, A. J. Conley, and J. P. Truant. 1972. Fatty acids and derivatives as antimicrobial agents. Antimicrob. Ag. and Chemother. **2**:23-28.
7. Kato, A., K. Ando, K. Kodama, S. Suzuki, K. Suzuki, G. Tamura, and K. Arima. 1969. Production, isolation and purification of antitumor active monoglycerides and other antibiotics from *Sepedonium Ampullosporum*. J. Antibiot. XXII, 71-76.
8. Kato, A., K. Ando, K. Kodama, G. Tamura, and K. Arima. 1969. Identification and chemical properties of antitumor active monoglycerides from fungal mycelia. Studies on antiviral and antitumor antibiotics. X. J. Antibiot. XXII:77-82.
9. Kato, A., K. Ando, G. Tamura, and K. Arima. 1971. Effects of some fatty acid esters on the viability and transplantability of Ehrlich ascites tumor cells. Cancer Res. **31**:501-504.
10. Kato, A., K. Ando, S. Suzuki, G. Tamura, and K. Arima. Antitumor activity of fatty acids and their esters II—activity of monoglycerides and other esters. Prog. in Antimicrob. and Antican. Chemother. Proc. of 6th Int. Congr. Chemother., p. 142-145.
11. Kato, A. and K. Arima. 1971. Inhibitory effect of sucrose ester of lauric acid on the growth of *Escherichia coli*. Biochem. Biophys. Res. Commun. **42**:596-601.
12. Nash, N. H., and L. M. Brickman. 1972. Food emulsifiers—science and art. J. Amer. Oil Chem. Soc. **49**:457-461.
13. Pasquale, D. D., D. Jaconia, P. Eisman, and L. Lachman. 1964. A study of sterilizing conditions for injectable oils. Bull. Parenteral Drug Ass. **18**:1-11.