TABLE V
Comparison of Sulfones, Sulfoxides, and Sulfides

R	No. of chain atoms	Melting point, °C.[a]			Long Spacing, Å		
		Sulfone	Sulfoxide	Sulfide	Sulfone	Sulfoxide	Sulfide
Methyl	13	98	87	46	30.50[b]	........[c]	28.65
n-Propyl	15	101	60	44	35.10	34.55[d]	........[c]
n-Butyl	16	104	76	55	37.15	35.55	35.65
n-Amyl	17	......[e]	....[e]	45	........[e]	........[e]	33.43
n-Hexyl	18	110	83	53	41.30	39.90	40.03
n-Heptyl	19	112	82	54	43.60	42.95	37.10
n-Octyl	20	114	88	60	45.90	44.30	44.25
n-Undecyl	23	119	94	68	52.35	51.40	44.30

[a] Determined with a micro hot stage.
[b] Polymorphic form from ethyl acetate, long spacing 28.2 Å.
[c] Weak pattern, long spacing uncertain.
[d] Polymorphic form from acetic acid, long spacing, 19.9 Å.
[e] Not prepared.

lecular layers. The corresponding angles of tilt are about 55° and 44° for the even and odd members, respectively. The large difference in long spacings of the even and odd members of the sulfide series indicates that the mode of packing of the aliphatic chains is quite different.

The methyl derivative of the series gave sharp and intense diffraction peaks unlike the weak pattern of the methyl sulfoxide derivative. Its long spacing however does not fall on the straight line produced by the other odd members of the series (Figure 3). The compound apparently crystallized in another manner which is also characteristic of methyl esters of long-chain aliphatic acids (1, 5).

The melting points of the sulfide derivatives are plotted in Figure 3. The melting points of the even and odd members show the expected alternation. It should be noted that the melting point of the butyl derivative in the even series and the melting point of the propyl derivative in the odd series are not in line with the other members of the series. Both exhibit melting points that appear to be much too high. This is in agreement with the x-ray data as discussed above. Attempts to observe visually a change in the appearance of the solid butyl derivative on slow heating were unsuccessful; only x-ray diffraction could detect that a change had taken place.

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Summary

X-ray diffraction powder data and melting points have been determined on three series of crystalline long-chain sulfur compounds, namely 11-(*n*-alkylsulfonyl)-undecanoic acids; 11-(*n*-alkylsulfinyl)undecanoic acids; and 11-(*n*-alkylthio)undecanoic acids; where R is a selected alkyl group from methyl through undecyl. In the sulfone series the long spacings increase regularly with the increase in the number of carbon atoms in R. In contrast to unsubstituted long-chain fatty acids the odd and even members fall on the same line in the plot of long spacings against carbon atoms in R. As expected, a nonalternation in melting point is observed. In both the sulfoxide and sulfide series two nonparallel straight lines are obtained, one for the even-membered and one for the odd-membered compounds, in the plot of long spacings against carbon atoms in R. As expected, the melting points of the sulfoxides and sulfides show an alternation. Polymorphism is more evident and complicates the interpretations most in the sulfide series and least in the sulfone series. All three series of compounds crystallized as tilted dimers.

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Reactions of Unsaturated Fatty Alcohols. VI. Guerbet Reaction of Soybean and Linseed Alcohols[1]

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THE CONDENSATION of alcohols under the influence of sodium metal to produce α-branched alcohols with twice as many carbon atoms was discovered by Guerbet about 1900. The reaction, as initially carried out, gave poor to moderate yields of Guerbet alcohol (I) while producing as by-products carboxylic acids, esters, carbonyl compounds, and resins. Further work on the reaction demonstrated that improved yields of (I) could be obtained by using certain additional catalysts and by removing water as it is formed (5, 3). Pratt and Kubler (6) and Bolle (2) studied the effect of reaction conditions on the type of products formed and were able to clarify the course of the reaction. According to Bolle, mechanism of the modified Guerbet reaction is illustrated as:

$$(1)\quad 2\,RCH_2CH_2OH \longrightarrow 2\,RCH_2CHO + 2\,H_2$$

$$(2)\quad 2\,RCH_2CHO \longrightarrow RCH_2CH = CRCHO + H_2O$$

$$(3)\quad RCH_2CH = CRCHO + RCH_2CH_2OH \longrightarrow RCH_2CH = CRCH_2OH + RCH_2CHO$$

$$(4)\quad RCH_2CH = CRCH_2OH \longrightarrow RCH_2CH_2CHRCHO$$

$$(5)\quad RCH_2CH_2CHRCHO + RCH_2CH_2OH \longrightarrow RCH_2CH_2CHRCH_2OH + RCH_2CHO$$

(I)

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Because olefinic double bonds are relatively stable to Meerwein-Ponndorf type of reductions, reaction 4 is preferred to a direct reduction of the unsaturated alcohol from 3 to product (I). According to this scheme reaction 1 is needed only to initiate the reaction; thereafter aldehyde needed in 2 can be supplied from reactions 3 and 5. The formation of acids probably results from the Dumas-Stas or Cannizzaro type of reactions shown by 6 and 7, respectively.

$$(6)\ RCH_2CH_2OH + H_2O \xrightarrow{NaOH} RCH_2COONa + 2H_2$$

$$(7)\ 2\,RCH_2CHO + H_2O \xrightarrow{NaOH} RCH_2COONa + RCH_2CH_2OH$$

Since water is necessary for these reactions, acid formation would be cut down by removing the water as it forms in reaction 2. Recently Sulzbacher (7, 8) achieved a high yield of Guerbet alcohols without simultaneous formation of acids by adding boron compounds to the charge. We have found that unsaturated fatty alcohols also react under these conditions to give high molecular weight product alcohols differing in composition from products usually obtained in the Guerbet reaction. This paper reports the preparation of condensed alcohols from soybean and linseed alcohols by using this method. The properties, particularly the film-forming properties, of these condensed alcohols are described.

Preparation and Properties of Condensed Alcohol

2-Hexadecyl Eicosanyl Alcohol. This material was prepared to obtain a sample of pure C_{36} α-branched alcohol for comparative purposes. A mixture of 135 g. (0.5 mole) of octadecanol, 8.4 g. (0.15 mole) of potassium hydroxide, and 5.2 g. (.075 mole) of boric anhydride was placed in a 500-ml. round-bottomed flask fitted with a stirrer, thermometer, nitrogen inlet tube, and large diameter exhaust tube. The contents were heated rapidlyy to 300°C. Evolution of water occurred at 120–150°C.; a rapid evolution of gas occurred at 170°C., after which no other products evolved except a small quantity of water occasionally. The reactants were held at 300–305°C. for 3 hrs.; then the contents were cooled, dissolved in toluene, and washed with water. Removal of the solvent yielded 116 g. of solid product containing 2% stearic acid. Distillation of this material gave a 50-g. fraction, b.p. 130–140°C./0.1 mm. and a 35-g. fraction, b.p. 265–275°C./0.1 mm. The residue amounted to 30 g. The first fraction was essentially unreacted octadecanol. The second fraction contained condensed alcohol, which was purified by recrystallization from 240 ml. of 95% ethanol-benzene mixture (10% benzene by volume). White crystals melting at 42°C. were collected.

Anal.: Calc. for $C_{36}H_{74}O$; C, 82.67%; H, 14.26%; OH, 3.25%; I.V., 0; Acid No., 0. Found: C, 82.78%; H, 14.10%; OH, 3.20%; I.V., 10.3; Acid No., 0.5.

Guerbet Reaction of Unsaturated Alcohols. A study of reaction conditions was made to reduce the amount of starting alcohol in the final product and thereby obtain a good yield of condensed alcohol. Soybean alcohol (Unadol 40)[2] was selected as the model compound.

Soybean alcohol (0.25 mole) was treated with potassium hydroxide (0.075 mole) and boric anhydride (0.037 mole) under the conditions shown in Table I. Heating at 300°C. for 1 hr. gave a product containing a considerable amount of unreacted soybean alcohol as shown by the high hydroxyl content and low molecular weight. As the reaction time was increased up to 4 hrs., the product approached the dimer stage as evidenced by hydroxyl content and an increase in viscosity. The molecular weight however increased beyond the theoretical value of 520 for the dimer alcohol. If the reaction continued for 6 hrs., as shown in Experiment 4 of Table I, the hydorxyl content fell below the theoretical value for the dimer (3.28%) and the viscosity and molecular weight of this product also decreased indicating possible degradation. When the reaction was carried out for 4 hrs. at 200°C. (Experiment 5), the product contained considerable unreacted soybean alcohol.

The loss of unsaturation during this reaction deserves some comment. Soybean alcohol (I.V., 118; conjugated diene, 31.6%) after 2 hrs. of heating at 300°C. had an iodine number of 83 and contained 11.2% conjugated diene. Heating this material for an additional 2 hrs. reduced the diene to 7% but left the iodine number unchanged. The iodine number at the end of 4 hrs. of reaction at 300°C. indicated approximately one double bond remaining for each alkyl side chain. The infrared spectra of the products from the 1-hr. through 6-hr. runs showed a gradual disappearance of *cis*- and *trans*-conjugated bonds (945 and 985 cm^{-1}, respectively) and an increase of isolated *trans* bonds (968 cm^{-1}) as the heating time at 300°C. was increased. A reaction that would consume diene and still leave one double bond per side chain can be illustrated as follows:

(8)

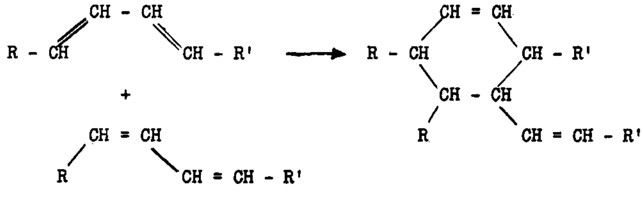

TABLE I

Condensed Alcohol Products from Unsaturated Fatty Alcohols

Experiment No.	Fatty alcohol	Amount of alcohol	React. temp.	Time	Amount of product	Product analyses							
						I.V.	OH[a]	Acid No.	Diene	Triene	Carbonyl O_2	Viscosity (Gardner)	Mol. wt.[b]
		g.	*°C.*	*hrs.*	*g.*		%		%	%	%		
1	Soybean	67	300	1	59	97	5.39	1.9	16.3	0	0	G	405
2	Soybean	67	300	2	57	83	3.45	6.1	11.2	0	0	T	595
3	Soybean	67	300	4	50	83	3.28	6.3	7.0	0	0	X	763
4	Soybean	67	300	6	55	89	2.60	5.7	1.0	0	0	W	645
5	Soybean	67	200	4	58.5	94	4.55	2.5	26.6	1.06	0.33	B	383
6	Linseed	65	300	3	50	92	3.14	6.1	1.0	0	0	Y	675

[a] Determination by infrared spectroscopy. Absorption measured at 3650 cm^{-1} in carbon disulfide solution. [b] Reference (4).

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[2] Supplied by Archer-Daniels-Midland, Minneapolis, Minn. The mention of firm names or trade products does not imply that they are endorsed or recommended by the U. S. Department of Agriculture over other firms or similar products not mentioned.

TABLE II

Analytical Data of Condensed Soybean Alcohols after Removal of Monomer by Distillation[a]

Experiment No.	Distillation data		Residue analyses					
	% Distilled	% Residue	Mol. wt.	Viscosity (Gardner)	I.V.	Acid No.	% Diene	% OH
1	53	47	849	X	89	5.6	12.4	3.72
2	15	85	718	V	86	7.5	11.6	2.94
3	0	100	859	X	78	10.7	2	2.52
4	4	96	793	X	78	7.8	>1	2.49

[a] Reaction product heated to 200°C./3 microns.

This reaction could occur among a) soybean alcohol molecules to produce dimers (mol. wt., 528; OH, 6.3%), b) soybean alcohol and Guerbet alcohol (mol. wt., 789; OH, 4.3%), c) Guerbet alcohol side chains intramolecularly to produce cyclic alcohols or intermolecularly to produce high molecular weight polyols (mol. wt., at least 520; OH, 3.28%), and d) mixtures of these types to produce high molecular weight polyols. Intermolecular reactions of type c) could explain the high molecular weight obtained in Experiment 3 even though the hydroxyl content indicates a dimer alcohol with a molecular weight of 520.

The product from the 6-hr. reaction at 300°C. showed a lower viscosity and hydroxy content and a higher iodine number than the product from Experiment 3. These data suggest that the product from Experiment 4 was partially dehydrated to hydrocarbons. Infrared spectra of the product from Experiment 4 did not appear to confirm the presence of terminally unsaturated hydrocarbons characterized by a strong band in the 880–910 cm^{-1} region (1). Infrared evidence for materials, where the double bond is other than terminal, would be complicated by absorption of double bonds present in the soybean side chains.

To obtain direct evidence for monomeric alcohol in the materials shown in Table I, reaction products 1-4 were distilled at 3 microns of pressure while the pot temperature was slowly raised to 200°C. In this manner the reaction products were separated into a distillate and residue, as shown in Table II. Products from the 1-hr. and 2-hr. runs contained unreacted soybean alcohol, but the 4-hr. run had no distillate, indicating complete conversion to high molecular weight products. Possible degradation of the 6-hr. product has been suggested earlier, and support for this view was obtained when 4% of the product was distilled under the conditions used to remove monomer alcohol. Examination of this distillate in the infrared indicated a hydroxy-compound rather than an olefinic hydrocarbon. Poorly resolved bands at 696 and 750 cm^{-1} and weak bands at 1612, 1500, and 1470 cm^{-1} in the spectra of the reaction product from Experiment 4 before distillation were either clearly resolved or intensified in the distillate. These bands are associated with substituted benzene compounds. Additional evidence for aromatic compounds in this distillate from the 6-hr. reaction was obtained from an examination of the ultraviolet spectra. Bands of medium intensity at 262, 265, 268, and 272 mμ were observed. These bands are associated with benzene compounds.

The residue fractions shown in Table II when compared with the undistilled fractions are characterized by lower hydroxyl content, increased molecular weights, approximately the same or slightly lower iodine numbers, less diene conjugation, and higher viscosities. The increase in viscosity and molecular weight, as well as the decrease in hydroxyl content in residues from Experiments 1 and 2, can be accounted for in part by distillation of monomer alcohol. Since the residue from the 1-hr. reaction at 300°C. has a hydroxyl content greater than theory for dimer alcohol, it must be presumed that a portion of soybean alcohols in this residue was dimerized by a reaction similar to reaction 8. Dimer material of this type would not distill under the conditions used but would contribute to high hydroxyl content.

A significant drop in hydroxyl content was noted when the product from Experiment 3 was heated under conditions necessary to distill monomer alcohol. Since no distillate was obtained, the disappearance of hydroxyl and increase in viscosity of the residue suggest formation of ethers by loss of water between two alcohol molecules. Examination of the infrared spectra failed to reveal a band characteristic of a C–O linkage in the 1070–1150 cm^{-1} region.

It appears that the best conditions for carrying out the Guerbet reaction with soybean alcohol to produce a product containing no unreacted starting alcohol is exemplified by Experiment 3, Table I. To establish whether these reaction conditions would give a product low in monomeric alcohol and to establish whether multiple condensations of the Guerbet type were occurring, octadecanol (1 mole) was treated with boric anhydride (0.15 mole) and potassium hydroxide (0.3 mole) at 300°C. for 4 hrs. The resulting product was dissolved in hexane, washed free of alkali, dried, and stripped free of solvent to yield a white solid, m.p. 39–41°C.

Anal.: I.V., 4.9; Acid No., 2.7; diene, 1.6%; triene, 0%; M.W., 526 (theory 523); OH, 3.28% (theory 3.25%).

Distillation of this product under the conditions used in the soybean alcohol experiments (Table II) gave a distillate of octadecanol (12%). A mixture of octadecanol (12%) and dimer alcohol (88%) would have a molecular weight of 492.5 and contain 3.62% hydroxyl. Comparison of these values with the data actually obtained reveals that the product is low in hydroxyl and has a higher molecular weight than expected. Because thermal condensations shown by (8) cannot occur, this product must contain some trimer and higher molecular weight alcohols resulting from multiple Guerbet condensations. The high molecular weight of the soybean products listed in Tables I and II could therefore be caused in part by multiple Guerbet condensations as well as by the condensation reactions examplified by reaction (8).

In the Guerbet reaction with soybean alcohol the presence of dimer alcohol derived from saturated and oleyl alcohols was established by distillation of a preparation (50 g.) similar to that obtained in Experiment 3. No unreacted soybean alcohol was obtained, and the first fraction was distilled at 255–265°C./.07 mm. to yield 15 g. of yellow oil with a Gardner viscosity of D.

Anal.: Calc. for $C_{36}H_{70}O$; C, 83.3%; H, 13.59%; OH, 3.28%; I.V., 97.7 (assuming 2 double bonds/mole); Acid No., 0; % carbonyl oxygen, 0; Mol. Wt., 519. Found: C, 83.1%; H, 13.29%; OH, 3.28%; I.V., 72.4; Acid No., 9.4; carbonyl oxygen, 0%; Mol. Wt., 524.

The residue material from this distillation (35 g.) was a viscous oil with a molecular weight of 1500. These results show that at least 30% of the product from the reaction of soybean alcohol is present as the dimer form. Probably more of the product is dimer because the molecular weight obtained by recombining the volatile fraction and residue from this distillation would be 1256. The value is considerably higher than the molecular weight of a typical product obtained from the Guerbet reaction before distillation (750–800). Thermal polymerization of the product probably results from high pot temperatures (approx. 300°C.) necessary for distillation of dimer alcohol. An increase in molecular weight occurred but to a smaller extent when a similar product from soybean alcohol obtained in Experiment 3 (Tables I and II) was heated to remove monomeric alcohol.

Linseed alcohol (I.V., 166; diene, 25%; triene, 1.5%) was treated with potassium hydroxide and boric anhydride for 3 hrs. at 300°C. The product was similar to the soybean product obtained under these conditions except that viscosity and iodine number are slightly higher. Analyses on the product from linseed alcohol are shown in Table I.

Several esters of soybean and linseed condensed alcohols were prepared by refluxing the alcohols with the appropriate acid and p-toluene sulfonic acid in toluene. After 3 hrs. of reflux the esters were washed with water, sodium carbonate, and finally with water until neutral. Acid values on the esters were:

Ester	Soybean	Linseed
Acrylic	6.3	1.2
Sorbic	4.8	2.0
Maleic	13.0	13.3
Soybean	10.7	1.1

Film Properties of Unsaturated Condensed Alcohols and Their Esters

Films of soybean and linseed condensed alcohols and their sorbic, acrylic, maleic, and soybean esters were prepared by dissolving 1 g. of material in 3 g. of toluene. Cobalt naphthenate (0.1%) was used as a drier. Films were cast on slides (for hardness tests) or on small soft-glass test tubes (for solvent resistance) and baked in an electric oven. Baking cycles were: 1 hr. at 150°C. or 20 min. at 200°C. Films baked for 10 min. at 200°C. were not sufficiently tack-free to warrant testing. Air-dried films of condensed alcohols with cobalt drier did not form tack-free films in 4 days. Table III lists the results of test performed on baked soybean and linseed condensed alcohols. Films baked at 150°C. for 1 hr. were harder than those baked at 200°C. for 20 min. Alkali resistance of the 150°C. linseed films was superior to soybean films under these conditions. Linseed condensed alcohol films baked for 1 hr. appear to have better solvent resistance than all other films tested.

Table IV lists alkali resistance and hardness of films from certain esters of soybean and linseed condensed alcohols. Esterification of soybean condensed alcohols appears to improve hardness and alkali resistance of films made from them although films from the sorbic ester show only slightly more alkali resistance than those from the unesterified alcohols. A possible explanation for the superior alkali resistance of the condensed alcohol esters over the alcohols themselves may be that oxidation of the free alcohol group to an acid occurs during the baking cycle. An improvement in hardness upon esterification was not observed with condensed alcohol films although their alkali resistance was improved. The soybean fatty acid ester of soybean condensed alcohol air-dried to a soft film in 3 days.

TABLE III

Film Properties of Baked Unsaturated Fatty Condensed Alcohols Containing Cobalt Drier

Test reagent	Condensed alcohol			
	Soybean		Linseed	
	150°C.[a]	200°C.[b]	150°C.[a]	200°C.[b]
Hardness	3 [c]	2	3	2
18% HCl	S. 15 min.[d]	(........)[d]	F, 8 hrs.[d]	F, 8 hrs.
5% NaOH	D, 15 min.[d]	S, 1½ hrs.	F, 1 hr. D, 8 hrs.	F, 1¼ hrs.
2% "Tide"	S, 3 hrs.	S, 24 hrs.	F, 4 hrs.	F, 6 hrs.
95% Ethanol	(........)	(........)	(........)	F, 8 hrs.
White gas	(........)	(........)	(........)	(........)
Ethyl acetate	F, 8 hrs.	F, 8 hrs.	(........)	(........)
Acetone	(........)	(........)	(........)	F, 24 hrs.
Chloroform	F, 15 min.	F, 15 min.	(........)	F, 24 hrs.
Benzene	F, 1 hr.	F, 1¼ hr.	(........)	(........)
Water	F, 24 hrs.	F, 8 hrs.	(........)	F, 8 hrs.

[a] Baked for 1 hr. [b] Baked for 20 min. [c] Pencil-hardness test. [d] S = Swells, F = Frosting, D = Dissolving, (........) No attack in 24 hrs.

TABLE IV

Alkali Resistance and Hardness of Films from Unsaturated Condensed Alcohol Esters Baked for 1 hr. at 150°C. (Cobalt drier)

Compound	Film hardness[a]	5% NaOH[b]
Soybean condensed alcohol	3	D, 15 min.[c]
Sorbic ester	4	D, 20 min.
Maleic ester	4	S, 45 min.[c]
Soybean ester	3	S, 30 min.
Acrylic ester	4	S, 4 hrs.
Linseed condensed alcohol	3	D, 8 hrs.
Sorbic ester	2	S, 6 hrs.
Maleic ester	2	S, 22 hrs.
Soybean ester	2	S, 4 hrs.
Acrylic ester	2	S, 22 hrs.

[a] Pencil-hardness test. [b] Immersed for 24 hrs. [c] D = Dissolving, S = Swelling.

Baked films of the esters listed in Table IV were immersed for 24 hrs. in 95% ethanol, benzene, butanol, mineral oil, hexane, and acetone, respectively. In all these solvent tests the films were unaffected by this treatment. Chloroform caused swelling of acrylic, maleic, and sorbic ester films within 1 hr. Soybean ester films showed some evidence of swelling in 2 hrs.

Summary

Both soybean and linseed alcohols were heated with potassium hydroxide and boric anhydride at 300°C. for 3 to 4 hrs. Products obtained under these conditions contained no unreacted starting alcohol, and each one appeared to be a mixture of condensed alcohols with average molecular weights of 720–860.

Infrared spectroscopic studies and chemical analyses indicate that little or no ethers, esters, or carbonyl compounds were present in the final product from either alcohol. Such reactions as thermal cross-linking of the unsaturated side chains probably account for higher molecular weight products than those obtained in the Guerbet reaction of stearyl alcohol.

Condensed alcohols from soybean and linseed alco-

hol were esterified with acrylic, sorbic, maleic, and soybean fatty acids to yield products with low acid numbers. Preliminary experiments demonstrated that these alcohols and their esters showed promise as materials for protective coatings. Films from these alcohols and esters were cast from toluene containing a cobalt naphthenate drier and were baked at 150°C. for 1 hr. or at 200°C. for 20 min. All of the baked films were hard to moderately hard and showed good resistance to aqueous alkali and organic solvents. In general, films from soybean condensed alcohol and its esters were harder than those from linseed condensed alcohols, but the linseed films were superior in alkali and solvent resistance. A soybean fatty acid ester of soybean condensed alcohol air-dried to a soft film in 3 days.

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A Note on the Toxicities of Methyl Oleate Peroxide and Ethyl Linoleate Peroxide[1]

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IN A PREVIOUS REPORT oral supplements of ethyl linoleate hydroperoxide given to rats fed a fat-free diet resulted in intensification of the dermal symptoms of EFA deficiency and decreased the tetraenoic acid contents of the rats, suggesting that the peroxide may have some toxic effect (1). It therefore seemed logical to test the toxicity of hydroperoxides of oleate and linoleate given by oral and intraperitoneal routes.

Methyl oleate peroxide and ethyl linoleate peroxide were prepared from methyl oleate and ethyl linoleate *via* autoxidation of the former and lipoxidase oxidation of the latter (1). The peroxides were separated from the unreacted substrates by countercurrent distribution and stored in evacuated ampoules below −15°C. until used. The methyl oleate peroxide had a peroxide value of 5420, 89% of theoretical for the pure substance. Ethyl linoleate peroxide had a peroxide value of 4770, 81% of the theoretical value of the pure peroxide. Both preparations were predominantly hydroperoxides.

The peroxides were diluted 1:25 in hydrogenated coconut oil for the intraperitoneal injections into normal mice. Those mice which survived 48 hrs. were counted as alive although some died later. For oral administration the undiluted peroxides were used. Unfortunately the limited amounts of the peroxides did not allow the use of large numbers of mice to fix the intraperitoneal LD_{50} accurately or the use of high oral doses to approach the toxic level. The survival data are given in Table I.

The data indicate that methyl oleate peroxide is more toxic (LD_{50} = 6 mg.) than ethyl linoleate peroxide (LD_{50} = 12 mg.) when administered intraperitoneally. However 200-mg. doses of either peroxide did not kill mice within 48 hrs. when fed orally. Daily doses of 75 mg. per rat likewise did not kill rats within 6 weeks (1). It thus appears that the peroxide is either not absorbed from the intestine or is inactivated by the intestinal contents.

TABLE I
Toxicities of Methyl Oleate Peroxide and Ethyl Linoleate Peroxide

Substance	Route	Dose (mg.)	No. mice	Survivors
Methyl oleate peroxide........	Intraperitoneal	2	2	2
Methyl oleate peroxide........	Intraperitoneal	6	10	5
Methyl oleate peroxide........	Intraperitoneal	8	6	2
Methyl oleate peroxide........	Intraperitoneal	10	2	0
Methyl oleate peroxide........	Oral	100	5	5
Methyl oleate peroxide........	Oral	200	2	2
Ethyl linoleate peroxide......	Intraperitoneal	2	2	2
Ethyl linoleate peroxide......	Intraperitoneal	6	3	2
Ethyl linoleate peroxide......	Intraperitoneal	10	3	3
Ethyl linoleate peroxide......	Intraperitoneal	12	13	5
Ethyl linoleate peroxide......	Intraperitoneal	14	8	3
Ethyl linoleate peroxide......	Intraperitoneal	16	10	3
Ethyl linoleate peroxide......	Intraperitoneal	20	3	1
Ethyl linoleate peroxide......	Oral	100	4	4
Ethyl linoleate peroxide......	Oral	200	2	2

It should be pointed out that the failure to determine the acute oral toxicity of these peroxides does not imply that they are nontoxic. Linoleate peroxide and its thermal decomposition products, for example, have been observed to intensify symptoms of EFA deficiency (1), and it is known that oxidized fats have adverse effects upon growth and metabolism which are observable in long-range experiments.

The mechanism of the toxicity of fatty peroxides is not indicated by these experiments. Pure ethyl linoleate was administered intraperitoneally in doses as large as 1 g. in mice or 5 g. in rats without adverse effect so the long-chain unsaturated ester itself is not toxic. The toxicity must be related to the peroxide function of the molecules. Measurement of the polyunsaturated acid contents of the carcasses of the mice revealed no relationship between dose levels of peroxide and polyunsaturated fatty acid contents.

REFERENCE

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