

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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### REFERENCES

1. Bellamy, L. J., "Infrared Spectra of Complex Molecules," p. 44, New York, John Wiley and Sons, 1954.
2. Bolle, J., *Compt. rend.*, **233**, 1628-1629 (1951).
3. Bolle, J., and Bourgeois, L., *Compt. rend.*, **233**, 1466-1467 (1951).
4. Gast, L. E., Schneider, W. J., and Teeter, H. M., *J. Am. Oil Chemists' Soc.*, **34**, 307-310 (1957).
5. Miller, R. E., and Bennett, G. E. (Monsanto Chemical Co.), U. S. Patent 2,762,847 (Sept. 11, 1956).
6. Pratt, E. F., and Kubler, D. G., *J. Am. Chem. Soc.*, **76**, 52-56 (1954).
7. Sulzbacher, M., British Patent 655,864 (August 1, 1951).
8. Sulzbacher, M., *J. Applied Chem.*, **5**, 637-641 (1955).

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## A Note on the Toxicities of Methyl Oleate Peroxide and Ethyl Linoleate Peroxide<sup>1</sup>

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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<sub>50</sub> 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<sub>50</sub> = 6 mg.) than ethyl linoleate peroxide (LD<sub>50</sub> = 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

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	3
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

either not absorbed from the intestine or is inactivated by the intestinal contents.

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

1. Holman, Ralph T., and Greenberg, Sheldon I., *Archives Biochem. Biophys.*, **49**, 49 (1954).

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