Bioassay for carcinogenic activity of a number of epoxides, lactones, hydroperoxides, and peroxides was reported from the laboratory at New York University (2, 3). The compounds were tested by skin application on mice, s.c. injection in mice and rats, and feeding and intratracheal instillation in rats.

Another series of related compounds was more recently tested at Fels Research Institute by s.c. injection in mice (1). Included in this series were compounds such as stearic acid and γ-stearalactone which, on the basis of known structure-biological activity relationships and the known occurrence of some of these compounds as normal constituents of mammalian tissues, were not expected to be carcinogenic. Nevertheless, several of these compounds resulted in the induction of sarcomas at the injection site.

Because the results were difficult to evaluate, a meeting of investigators from the 2 laboratories was held in 1967. It was decided to repeat the bioassays of some of these compounds in 2 laboratories with the use of similar protocols and the same highly purified chemicals. We are communicating the results of this joint study.

Five compounds were selected: stearic acid, methyl stearate, γ-stearalactone, p-nitroperbenzoic acid, and glycidyl stearate.

The same chemical samples and the same batch of tricaprylin as vehicle were used in both laboratories. The chemicals were given s.c. to mice once weekly for 26 weeks. The conditions of the experiments, as described in the full reports (1, 3) were as identical as possible. The only known difference was that the New York University experiments were with ICR/Ha Swiss Millerton female mice, whereas the Fels experiments used CFW (Swiss Webster) female mice.

The results are summarized in Table 1. The replication of results in terms of s.c. sarcoma induction is remarkably similar in the 2 laboratories. Four of the 5 compounds induced sarcomas in less than 10% of the animals. One compound was negative in both laboratories.

Data on pulmonary and mammary tumors, as well as a few other tumors distant to the injection site, did not contribute further evidence of carcinogenic activity. Various neoplastic lesions were found in 20% of the group receiving glycidyl stearate and in 6 to 10% of all other groups.

Of the 4 compounds that induced sarcomas in mice, only 2 were expected to be active on the basis of known
structure-activity relationships (4); these are glycidyl stearate and p-nitroperbenzoic acid. The former is a monofunctional alkylating agent and the latter is a peracid. Both types of agents have been shown in earlier studies to be carcinogenic (1, 2). The findings with methyl stearate and γ-stearolactone were surprising, since both of these compounds are relatively unreactive and their conversion in vivo to reactive species is difficult to envision. We considered the possibility that “solid-state” carcinogenesis was involved with some of these compounds, but they were lipid-soluble and gave clear solutions in tricaprylin at the concentrations used.

Low-level carcinogenic activity for the s.c. tissue of mice has been replicated in 2 laboratories for methyl stearate, γ-stearolactone, p-nitroperbenzoic acid, and glycidyl stearate, but interpretation of the data remains moot. It will therefore be desirable to test these compounds further, with other routes and additional species.

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REFERENCES


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