An Investigation of the Oncogenic Activity of Two Representative Epoxy Resins*

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This study was undertaken to determine whether certain compounds containing two or more epoxy linkages possessed oncogenic activity. This possibility was suggested by the findings of Hendry and his co-workers (8) who produced sarcoma in rats—but not skin cancer in mice—with butadiene dioxide, and both types of tumor with vinyl cyclohexene dioxide.

Although the possibility that the epoxy resins would induce tumors seemed remote, many of them have industrial applications, and it was therefore deemed advisable to investigate them experimentally and to determine whether there was oncogenic activity and, if so, the degree of potency and type of tumor induced.

Over a period of 8 years, we have ascertained that the representative epoxy resins designated herein as A and B1 induced sarcoma in rats. Only Epoxy Resin A produced skin cancer in mice, and the potency was low. None of the seven compounds tested (Table 1) had any effect on the incidence of pulmonary adenoma in Heston A mice.

MATERIALS AND METHODS

In all experiments, mice were housed ten to a cage, rats in pairs, and rabbits singly. Rats and mice were fed our standard maintenance diet containing 21 per cent protein, 58 per cent carbohydrate, 6.97 per cent fat, 4.35 per cent fiber, 1.24 per cent calcium, 0.84 per cent phosphorus, and 6.66 per cent ash. Additives per pound of feed are 11,366 units vitamin A, 958 units vitamin D, 0.58 mg. riboflavin, 7.67 mg. pantothenic acid, 32.06 mg. niacin, and 577.58 mg. choline. Rabbits were fed on Rockland Rabbit Ration, supplemented twice weekly with fresh greens. All the animals were allowed feed and water ad libitum.

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Carcinoma production.—Two typical uncured epoxy resins of low molecular weight, designated as Epoxy Resin A (aliphatic) and Epoxy Resin B1 (aromatic), supplied by the Shell Development Company, were dissolved in acetone (reagent grade) to make solutions of 0.3 and 5.0 per cent. 20-Methylcholanthrene was dissolved in acetone to make a 0.3 per cent solution.

Male mice of the C57 strain (16—18 gm.) were divided at random into eight groups of 30 mice each and were housed in a room apart from all other experimental animals. The compounds were applied to the nape of the neck by a single stroke of a sable brush calibrated to deliver about 0.2 ml. Each solution was also applied to predesignated shaved areas on each of sixteen male albino rabbits, with brushes calibrated to deliver about 0.5 ml. in two strokes. The dosage schedule is given in Table 2.

A record was kept of the time when the neoplasms appeared. When dead animals were found to be in satisfactory condition for necropsy, this was performed, and sections of skin and internal organs were preserved in 10 per cent formalin for histologic examination. At the end of 24 months, survivors were sacrificed. All animals were carefully inspected for neoplastic or other visible pathologic change, external or internal. Skin samples from all sites of application, and sections of internal organs from all rabbits and alternate mice, were preserved in 10 per cent formalin for histologic study.

The TT50 (time at which 50 per cent of the animals would be expected to carry tumors) was calculated by plotting on log probit paper the tumor index against time. The tumor index at any given time is the number of animals that have developed tumors (whether dead or surviving) divided by the effective number of animals at that time. The effective number of animals is the initial number minus the number that have died without developing tumors. The tumor potency was also calcu-
TABLE 1
DESCRIPTION OF COMPOUNDS STUDIED

<table>
<thead>
<tr>
<th>Designation</th>
<th>Model formula</th>
<th>Physical state</th>
<th>Av. mol. wt.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epoxy Resin A</td>
<td>CH₂CH₂O−R−OCH₂CH₂</td>
<td>Liquid, ca. 300</td>
<td></td>
</tr>
<tr>
<td>Epoxy Resin B₁ B₂</td>
<td>CH₃CH₂O−R−OCH₂CH₂</td>
<td>Liquid, 350</td>
<td></td>
</tr>
<tr>
<td>Diglycidyl resorcinol ether</td>
<td>CH₃CH₂O−OCH₂CH₂</td>
<td>Liquid, 900</td>
<td></td>
</tr>
<tr>
<td>Poly(allyl glycidyl ether)</td>
<td></td>
<td>Liquid, 2000</td>
<td></td>
</tr>
<tr>
<td>Epoxodized soybean oil</td>
<td>CH₃(CH₂)₆H(CH₂)₅COOCH₂</td>
<td>Liquid, 900</td>
<td></td>
</tr>
</tbody>
</table>

* R represents aliphatic radicals, average molecular weight about 100.

TABLE 2
CARCINOMA PRODUCTION

<table>
<thead>
<tr>
<th>Species</th>
<th>Compound</th>
<th>PERCENT</th>
<th>APPLICATIONS*</th>
<th>ANIMALS (month)</th>
<th>TUMOR INDEX†</th>
<th>TUMOR POTENCY‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouse</td>
<td>Acetone</td>
<td>100</td>
<td>3</td>
<td>0, 18, 18, 84</td>
<td>All</td>
<td>Malignant</td>
</tr>
<tr>
<td></td>
<td>Epoxy Resin A</td>
<td>5.0</td>
<td>1</td>
<td>1, 0, 0, 0</td>
<td>1/20</td>
<td>1/20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0</td>
<td>3</td>
<td>0, 0, 0, 1</td>
<td>4/13</td>
<td>4/13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0</td>
<td>3</td>
<td>0, 1, 2, 4</td>
<td>157#</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>20-Methylcholanthrene</td>
<td>0.5</td>
<td>1</td>
<td>0, 0, 0, 0</td>
<td>20/20</td>
<td>19/20</td>
</tr>
<tr>
<td>Rabbit</td>
<td>Acetone</td>
<td>100</td>
<td>3</td>
<td>0, 0, 0, 0</td>
<td>5.4</td>
<td>264</td>
</tr>
<tr>
<td></td>
<td>Epoxy Resin A</td>
<td>0.5</td>
<td>1</td>
<td>0, 0, 0, 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0</td>
<td>3</td>
<td>0, 0, 0, 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Epoxy Resin B₁</td>
<td>0.5</td>
<td>1</td>
<td>0, 0, 0, 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0</td>
<td>3</td>
<td>0, 0, 0, 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>20-Methylcholanthrene</td>
<td>0.5</td>
<td>1</td>
<td>1, 2, 10, 14, 15</td>
<td>15/15</td>
<td>14/15</td>
</tr>
</tbody>
</table>

* Groups of 30 mice received 0.2 ml.; sixteen rabbits received 0.5 ml. of each compound.
† No. animals with tumors + effective number of animals at the time when the last tumor appeared.
‡ Time at which 50 per cent of the animals would be expected to carry tumors, expressed in weeks.
§ 10,000 ÷ TT₅₀ in days.
# Extrapolated.
lated, where possible, by dividing 10,000 by the TT50 in days (9).

Sarcoma production.—The test animals were male rats (80—100 gm.) of the Long-Evans strain. These were randomized into four groups of 30 rats each and given three injections (once a week) in the nape of the neck. The test compounds were Epoxy Resins A and B1, and the total amount administered was equal to the LD50; that is, 0.41 gm/kg of Epoxy Resin A, 10 per cent in propylene glycol, and 2.58 gm/kg of Epoxy Resin B1, 50 per cent in propylene glycol. The positive control was 1,2,5,6-dibenzanthracene, and the negative control was propylene glycol.

The rats were examined weekly and their necks palpated for signs of tumor formation. When a definite tumor was discovered, the time lapse in weeks since the start of the experiment was recorded. Twenty-four months after the initial injection, surviving animals were decapitated. Sections from each area of injection, as well as from viscera of all animals, were fixed in 10 per cent formalin for histologic examination. When possible, the TT50 and tumor potency were calculated.

Incidence of pulmonary adenoma.—A series of three experiments was undertaken to determine whether injection of various compounds would affect the incidence of pulmonary adenoma in male mice of the Heston A strain. The positive control in all experiments was 0.6 per cent 20-methylcholanthrene in propylene glycol. The resin diluents were used as negative control. There were 30 mice in each group, and each was given a series of three injections. The total dose of each test compound approximated its LD50, as follows:

Experiment I: Epoxy Resin A, 0.3 gm/kg, 5 per cent in propylene glycol; Epoxy Resin B1, 4.0 gm/kg, 95 per cent in acetone. Injections were made intraperitoneally, every other day.

Experiment II: Epoxy Resins B1 and B2, 1.85 and 1.32 gm/kg, respectively, 25 per cent in acetone. Injections were made subcutaneously in the scapular region, every other day.

Experiment III: Diglycidyl resorcinol ether, 0.075 gm/kg, 1 per cent in propylene glycol; poly(allyl glycidyl ether), 0.125 gm/kg, 2 per cent in propylene glycol; epoxodized soybean oil, 2.15 gm/kg, 50 per cent in propylene glycol. Injections were made intraperitoneally, once a week.

In all experiments, the mice were sacrificed 16 weeks after the first injection. After careful gross inspection, various tissues were taken from one-third of the animals for microscopic study. The lungs of all mice were fixed in 10 per cent formalin and examined under a dissection microscope for signs of pulmonary adenoma. The number of single and multiple tumors was recorded. Sections of lung were then examined histologically.

In addition to the above, two feeding experiments were run, to determine the effects of Epoxy Resins A and B1 on the incidence of tumors induced by a potent carcinogen and on the incidence of spontaneous tumors. The resins were carefully mixed in amounts of 2 per cent into our standard feed, which was then made up into pellets. The daily intake of each mouse was 5—6 mg. of resin, on the basis of food consumption records.

a) Induced tumors: Three groups of mice of the Heston A strain were given injections intraperitoneally of 0.03 gm/kg of 20-methylcholanthrene, and two of these were fed the resinous diets. The third group and a fourth (uninjected) were fed standard uncontaminated feed.

b) Spontaneous tumors: To ascertain the influence of the resinous diets on the spontaneous generation of pulmonary adenomas, three similar groups of mice were fed on the two resin diets and the normal diet, without injection of a carcinogen. These animals were maintained on their respective diets for a period of 11 months.

RESULTS

CARCINOMA PRODUCTION

A summary of the incidence of skin tumors in mice and rabbits is given in Table 2.

Mice.—Of the original 240 mice, only 104 survived for the entire experimental period of 2 years. Survivors in the positive control group were sacrificed at 6 months.

The negative control group, receiving acetone, showed no changes at the end of 1 year. At 18 months, depilation and whitening of the hair at the site of application had appeared. At the end of 2 years there were no visible tumors, and the pathologist reported all sites normal with the exception of three that showed small eschars. No gross lesions were observed except those attributable to age.

Three groups received Epoxy Resin A. The group receiving 0.3 per cent once weekly did not differ appreciably in appearance from the controls during the experimental period. The group receiving 5 per cent once weekly also showed depilation and whitened fur during the 2d year, and one mouse developed a fibrosarcoma at the site of application after 22 months. The nineteen survivors were in poor condition, with unkempt fur and decreased activity. The mice receiving 5 per cent thrice weekly showed depilation and dry scaly skin, as well as whitened fur, by the end of the 1st year. The eleven survivors were in poor condition at the end of 2 years. Four tumors appeared at the
site of application in this group: squamous-cell carcinomas appeared at 10, 16, and 22 months, and a sarcoma at 23 months. Most of the mice in this group also showed skin ulceration and eschar or dermal thickening and inflammation at the site, on microscopic examination.

Among the three groups receiving Epoxy Resin B1, there were no visible changes at 1 year. At 18 months, some mice showed thinning of hair and whitening of fur at the site, but at 2 years all sites appeared normal and no gross tumors had appeared.

All the mice painted with 20-methylcholanthrene (0.3 per cent once weekly) developed a characteristic depilated reddish brown area at the site after two or three applications. Definite tumors appeared in six mice by the 4th week, and the last tumor appeared at 12 weeks. Physical deterioration made sacrifice advisable between the 21st and 28th weeks, by which time nineteen of twenty mice had developed malignant neoplasms at the site. There were sixteen squamous-cell carcinomas, five of them invading skeletal muscle; three subcutaneous fibrosarcomas; and one papilloma. There was one apparent metastasis from the application site, a squamous-cell carcinoma of the lungs.

Rabbits.—Of the original sixteen rabbits, thirteen survived for the 2-year experimental period. Two which were sacrificed because of physical deterioration had papillary squamous-cell carcinomas at the site of application of 20-methylcholanthrene. A third rabbit which died at 11 months had hyperkeratosis at the site of application of 20-methylcholanthrene, but no sign of malignancy. Among the surviving rabbits, all but one developed papillary squamous-cell carcinomas at the site of 20-methylcholanthrene application, varying from superficial to very invasive. None of the sites painted with epoxy resins or with acetone developed tumors, although there were flaky or erythematous areas from time to time. The internal organs showed no relevant abnormalities.

SARCOMA PRODUCTION

Table 3 summarizes the results. Of the original 120 rats, 45 survived the 2-year experimental period: seventeen in the negative control group (propylene glycol); ten with Epoxy Resin A; fourteen with Epoxy Resin B1; and four in the positive control group (1,2,5,6-dibenzanthracene).

In total, 47 malignant tumors were noted in the animals, 30 at the site of injection. There were seventeen in the positive control, none in the negative control, nine with Epoxy Resin A, and four with Epoxy Resin B1. There were also two nonmalignant tumors appearing at the site of injection, both with Epoxy Resin A. There were seventeen malignant tumors appearing elsewhere: five in the negative control, three in the positive control (including two metastases), two with Epoxy Resin A, and seven with Epoxy Resin B1. These were not considered to be relevant to the experiment.

Grossly, the survivors were in good health but showed general signs of aging. At necropsy, lymphosarcoma of the lung was the most common lesion. There were also foreign-body reactions at the site of injection, fibromas, pneumonia, bronchiectasis, lung abscess, hyperplasia of the spleen, liver degeneration, parasitic infestation of the liver and urinary bladder, and mild pyelonephritis, scattered through the groups.

Among rats injected with Epoxy Resin A, two of ten survivors and nine of twenty that died had tumors at the site of injection: eight sarcomas or fibrosarcomas, two fibromas, and one unidentifiable because of its condition, which was arbitrarily classified as malignant. A squamous-cell carcinoma appeared behind the left ear of one rat.

Four fibrosarcomas appeared at the site of injection of Epoxy Resin B1, all in rats that survived the experimental period.

Among rats injected with 1,2,5,6-dibenzanthracene, there were seventeen tumors at the site of injection of epoxy resins or with acetone.

### Table 3

<table>
<thead>
<tr>
<th>Compound</th>
<th>No. with Tumors</th>
<th>Time for Tumor Production</th>
<th>Tumor Index*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Survival Ratio</td>
<td>Range (days)</td>
<td>Mean</td>
</tr>
<tr>
<td>Propylene glycol</td>
<td>17/50</td>
<td>154-660</td>
<td>402</td>
</tr>
<tr>
<td>Epoxy Resin A</td>
<td>10/50</td>
<td>210-630</td>
<td>405</td>
</tr>
<tr>
<td>Epoxy Resin B1</td>
<td>14/50</td>
<td>108-510</td>
<td>337</td>
</tr>
<tr>
<td>1,2,5,6-Dibenzanthracene</td>
<td>4/50</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Tumor index = number of animals with tumors + effective number of animals at the time when the last tumor appeared
† Time at which 50 per cent of the animals would be expected to carry tumors, expressed in weeks.
‡ Extrapolated.

<table>
<thead>
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<td>1,2,5,6-Dibenzanthracene</td>
<td>4/50</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
application, eight fibrosarcomas, six sarcomas, and three not identifiable because of autolysis, which were arbitrarily classed as malignant. There were two cases of metastasis from the site of injection to the lung. The rats carrying tumors all died during the experimental period. None of the survivors had neoplasms at the site, although all of them had foreign-body reactions.

INCIDENCE OF PULMONARY ADENOMA

The three groups of positive control mice (20-methylcholanthrene) showed almost 100 per cent tumor response (twenty of 22; 24 of 24; and eighteen of eighteen) in 16 weeks. Only two of these mice had single adenomas.

In contrast, the incidence in mice injected with Epoxy Resins A, B, and B1; diglycidyl resorcinol ether; poly(allyl glycidyl ether); and epoxidized soybean oil was from 0 to seven single tumors, with no multiple tumors. Eight of 27 mice given Epoxy Resin B1 carried pulmonary adenomas, and two of these were double. However, there was no statistical difference between the incidence with any of the test compounds and that in the negative control groups. There were six mice with tumors in the acetone group, none multiple, and a total of six in the two propylene glycol groups, one multiple. Both of the feeding experiments also gave negative results.

a) Feeding strain A mice for 16 weeks on diets containing 0.2 per cent Epoxy Resin A or B1 did not influence the incidence of pulmonary adenoma induced by previous injection with 20-methylcholanthrene. The number of mice with lung tumors was, respectively, eighteen of eighteen, and 24 of 24; all these tumors were multiple. The incidence did not differ from that in injected mice fed a normal diet; in this group twenty of 25 developed tumors, all multiple. In contrast, un.injected control mice, fed the normal diet, showed only four tumors among twenty mice, and none of these was multiple.

b) Diets containing 0.2 per cent of Epoxy Resin A or B1 did not affect the incidence of pulmonary adenoma in mice over a period of 11 months. In mice fed Epoxy Resin A, seventeen of 29 survivors carried lung adenomas, and in eight of these the tumors were multiple. The number of tumors per mouse ranged from two to four. Twelve of the 25 surviving mice fed Epoxy Resin B1 had lung tumors, one of which was multiple (two tumors). Two of the mice in this group died only 1 month earlier, at 10 months, without tumors. Fifteen of the 29 surviving control mice, fed a normal diet, had tumors, four of which were multiple (two to five per mouse). The difference was not significant, according to the $x^2$ test.

DISCUSSION

The inadvisability of extrapolating data on carcinogenicity from one species to another warrants repeating. The route of administration within the species is important. Studies by Andervont and Shimkin (1, 15) showed no complete parallel between the ability to produce pulmonary tumors in mice of Strain A and sarcogenicity following subcutaneous injection, or carcinogenicity following cutaneous application. Badger et al. (2) and Kenaway et al. (11) likewise pointed out a number of polycyclic hydrocarbons of low but positive carcinogenicity when applied to mice, which did not produce sarcoma when injected subcutaneously. Conclusions drawn must be qualified by a consideration of species, strain, sex, dose, route of administration, frequency of administration, and vehicle. Results are valid only within the particular experimental milieu. A compound that produces skin cancer in mice in 10 weeks may take 3 or 4 years to produce such tumors in monkeys, and may not produce any tumors in rats or guinea pigs (16).

The negative results of skin application to rabbits suggest that the carcinogenicity of these resins, if present, is probably not high. Rabbits are usually more refractory to carcinogens than the inbred C57 mice, and even 20-methylcholanthrene was slow to produce tumors, the TTI 53 weeks in rabbits as compared with 5.4 weeks in mice.

The positive results in the sarcogenesis experiment are not inconsistent with low oncogenicity, since rats are unusually susceptible to subcutaneous implantations, and sarcomas may be produced in this manner by compounds which are hard to conceive of as hazardous—e.g., 25 per cent solutions of sodium chloride or glucose (7).

In further support of the suggestion of a low degree of oncogenicity are the results of the final experiments. Neither the resins nor the other epoxy compounds tested by injection had any effect on the incidence of pulmonary adenoma in mice of Strain A, although the control carcinogen regularly produced almost 100 per cent tumor response. Epoxy Resins A and B1 also had no effect when fed for as long as 11 months to such mice, at a level of 0.8 per cent of the diet.

Hendry (8) used repeated administration for the experimental production of sarcoma with butadiene dioxide and vinyl cyclohexene dioxide; however, from our observations, it is quite likely that repeated injection would not have been necessary.
Since the epoxy linkage is relatively active chemically, it probably does not survive long in a biologically active medium. In aqueous media, the bond is usually opened by the addition of a chlorine or hydroxy group, both of which are readily available in body tissue. Moreover, since the linkage is also readily reactive with primary and secondary amines, it might combine with amino acids, proteins, peptides, or other nitrogen-containing compounds present in the tissues.

In the case of the water-soluble Epoxy Resin A, there must have been some almost immediate reaction with cellular constituents, since without some chemical combination the compound would not be expected to remain in the area of injection. Epoxy Resin B may have been confined in the area by its very low solubility.

Haddow (6) pointed out that the monoepoxides are not biologically active and that even among the diepoxides there is a threshold of activity below which the compounds are not biologically effective. In a series of homologs of butadiene dioxide, the activity was inversely related to the molecular weight.

Few epoxy compounds with lower molecular weight than Epoxy Resin A can be used for building epoxy polymers. The proportion of epoxy groups in this resin is therefore higher than in most of the epoxy resins. As the molecular weight increases, the number of reactive groups per unit of weight decreases. Thus, the epoxy equivalent for Epoxy Resin A is 140—160 and that of Epoxy Resin B is similar, 190—210, while that of Epoxy Resin B may exceed 2000 (17). It should be appreciated that cured resins have still fewer free epoxy linkages. The conversion varies with the conditions of cure, and in the series studied by Dannenberg and Harp (4) ranged from 69.8 to 97.7 per cent.

Hueper (10) suspects the following of being carcinogenic: mitotic poisons; compounds producing aplasia or hyperplasia, congenital defects in offspring, or disturbances of endocrine function; and compounds with cross-linking properties (which would include all compounds capable of polymerization). In this regard, the work of Oppenheimer (13, 14) is of interest. He produced malignant tumors in rodents by the subcutaneous embedding of various polymers, among them cellophane, silk, and nylon.

Oppenheimer (14) considered that the carcinogenic activity was inherent in the polymer rather than in the monomer or related to impurities that might be present. In reviewing possible modes of action, he stated: "Since normal polymer breakdown in various aging processes proceeds via a free radical mechanism, it is reasonable to assume that some of the biological breakdown products may also be of a free radical nature. Free radicals are known to effect depolymerization of nucleic acids and to a certain extent to produce tumors." This hypothesis was strengthened by the finding that polymers in a finely divided physical state or in perforated sheets (conditions which retard free-radical formation) are less actively oncogenic than the same polymers in a plain film.

It is possible that the epoxy resins polymerized when injected at the pH of the biological medium into a relatively confined space, forming planar surfaces and subsequently giving rise to free-radical formation. No formed plastic was visible microscopically, however.

In 1955, Kotin (12) reported that he was able to produce skin tumors in mice with an atmospheric extract free of aromatic polycyclic hydrocarbons. The samples were stated to contain oxidation products of aliphatic hydrocarbons formed in the air in accordance with the theory developed by Haagen-Smit (3). Kotin postulated that epoxides were present (although evidence of their positive identification was not furnished) which resulted from the interaction of peracids and unsaturated hydrocarbons. Along with these epoxides, Kotin has listed ozonides, peroxides, and peracids as suspected carcinogens.

In our opinion, the failure in our experiment to affect the incidence of pulmonary adenoma in mice neither confirms nor refutes the possibility that these compounds could cause cancer of epithelial cells of the human respiratory tract. It is, however, an indication of the relatively low degree of carcinogenic activity of these compounds, since active carcinogens readily produce multiple adenoma in mice of this strain.

Practically speaking, any hazard due to epoxy resins would stem from contact with the skin. Cancers of the skin are rarely if ever produced by single contact, and there is invariably a considerable latent period. As judged from the few authenticated cases of skin cancer of environmental origin, prolonged contact and relatively poor industrial hygienic practices would also be required for the development of such tumors. Precautions have already been developed for the safe handling of epoxy resins; these eliminate in large measure the skin-irritating effects and should be sufficient in their scope to protect against any more far-reaching effects.

**SUMMARY**

An evaluation has been made of the oncogenic activity of two uncured epoxy resins. A liquid...
bisphenol-based epoxy resin produced no carcinomas in C3H mice when applied thrice weekly for 2 years in a concentration of 5 per cent. Carcinomas were produced by a liquid aliphatic epoxy resin at this level, but with a tumor potency of only 9 as compared with 264 for the positive control, 20-methylcholanthrene. The resins by subcutaneous injection in rats showed TT50 (time at which 50 per cent of the animals would be expected to carry tumors) of 100 and 157 weeks, and tumor potencies (10,000 divided by TT50 in days) of 14 and 9, respectively, as compared with a TT50 of 53 weeks and a tumor potency of 44 for 1,2,5,6-dibenzanthracene. Injection of either of these resins, two solid bisphenol-based epoxy resins of higher molecular weight, or of diglycidyl resorcinol, poly(allyl glycidyl ether), or epoxodized soybean oil did not alter the incidence of pulmonary adenoma in strain A mice over a period of 16 weeks. Feeding 0.1 per cent of either liquid resin in the diet for 11 months also did not alter the incidence, nor did similar feeding for 16 weeks alter the incidence of induced tumors in mice pretreated with 20-methylcholanthrene.

On the basis of this study, the potential hazard of skin irritation or carcinogenesis would seem to be obviated by the ordinary good industrial hygiene practices.

REFERENCES
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