**Mammary Carcinogenesis in Rats Fed Different Amounts and Types of Fat**

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**Abstract**

Rats fed 20% corn oil or lard showed increased 7,12-dimethylnbenzanthracene-induced mammary tumorigenesis and slightly increased growth rate compared to rats fed 5% fat; 20% corn oil accelerated sexual maturation, but 20% lard did not. In contrast, diets high in beef fat (30%) depressed tumor induction by 7,12-dimethylbenzanthracene or N-fluorenylacetamide compared to a diet containing 15% vegetable oil; dietary lipotrope content had no effect on tumorigenesis. Further studies are needed of the effects of type and amount of dietary fat on mammary tumorigenesis in several model systems.

**Introduction**

Increased dietary lipid enhances chemical carcinogenesis in the colon and mammary gland of experimental animals (1, 6). Since the dietary requirement for the lipotropic compounds is directly related to dietary lipid content (3) and since lipotrope deficiency enhances hepatocarcinogenicity of many chemicals (7, 8), it appeared possible that lipid enhancement of colon and mammary gland carcinogenesis might be the result of induction of relative lipotrope deficiency. 1,2-Dimethylhydrazine-treated rats fed a high-fat diet, marginally deficient in lipotropes, showed enhanced colon carcinogenesis compared to rats fed a nutritionally complete diet lower in fat (10). However, lipotrope supplementation of the deficient diet did not reduce tumor induction, and substitution of the fat content of the deficient diet into the control diet increased tumor induction to the level found in deficient rats although the control diet had a much greater lipotrope content (9). We concluded that increased susceptibility to colon carcinogenesis in rats fed high-fat diets was not the result of lipotrope deficiency.

Similar studies performed in female rats given DMBA or AAF to induce mammary gland tumors, previously reported in part (4), are reported here. In addition, experiments in progress to determine whether lipid enhancement of mammary carcinogenesis is associated with changes in growth rate, maturation, or serum prolactin content are discussed.

**Materials and Methods**

Female Sprague-Dawley rats (Charles River Laboratories, Wilmington, Mass.) were fed one of the experimental diets, Diets 1 to 3 (Table 1). Diet 1 is the nutritionally complete diet, and Diet 2 is the high-fat, marginally lipotrope-deficient diet used in earlier experiments. Diet 3 is Diet 1 with the fat content of Diet 2. The rats were given DMBA, 10 or 20 mg intragastrically, at age 55 days or fed AAF in the diet, 0.02% for 2 weeks and 0.0125% for 11 weeks, to induce mammary tumors. Rats were killed and necropsied 30 weeks after DMBA treatment or when they bore at least one mammary tumor greater than 1.0 cm in diameter. Cumulative probability of death with mammary tumor was calculated (11); results were compared statistically (5).

In studies in progress rats fed Diets 4 or 5 (Table 1) were given DMBA, 2.5 or 5.0 mg, at 55 days of age and are being necropsied as tumors develop. Nutrient content of the 2 diets is equivalent on a caloric basis. Growth, food intake, age at vaginal opening, and at first estrus have been measured. Serum prolactin is being measured using reagents kindly supplied by the National Institute of Arthritis, Metabolism, and Digestive Diseases Rat Pituitary Hormone Distribution Program, headed by Dr. A. F. Parlow.

**Results and Discussion**

**Effect of Lipotrope-deficient or Nutritionally Complete High-Fat Diets (Diets 2 and 3) on Mammary Carcinogenesis.** Diet 2 reduced tumor incidence in rats given 10 mg DMBA (48 versus 15%), but the difference was not significant (p < 0.1). In 2 experiments using AAF, mammary tumor development was slightly retarded by Diet 2, but final tumor incidence was not significantly affected by diet. Substitution of the fat content of Diet 2 into Diet 1 (Diet 3) significantly retarded tumor development (p = 0.01) (Chart 1).

Both mammary carcinogens, therefore, were somewhat less effective in rats fed Diet 2, and AAF was significantly less effective in rats fed Diet 3. These observations are contrary to the expected results in rats fed high-fat diets. There are many differences in composition between Diets 1 and 2, but the results in AAF-treated rats fed Diet 3 support the conclusion that retardation of mammary carcinogenesis by Diet 2 is due to its lipid content which is double the content of Diet 1 and predominantly saturated. There is no evidence that dietary lipotrope content has an effect in these 2 models; specific supplementation was not studied.

**Effects of a High-Fat Diet (Diet 5) on Growth, Maturation, Serum Prolactin Content, and DMBA Carcinogenesis in Female Rats.** In a preliminary experiment comparison was made of mammary tumor development in rats fed Diets 4 and 5, purified diets similar to Diet 1 containing 5% corn oil (Diet 4) or 20% corn oil substituted isocalorically for carbohydrate (Diet 5). Diet 5 enhanced tumor development (Chart 2) as expected from earlier reports (1).

In a larger study in progress, rats are fed Diets 4 or 5 or the same diets containing lard in place of corn oil and given 2.5 mg DMBA. Preliminary results, based on gross tumor diagnosis, show enhanced tumor development in both groups fed 20% fat compared to the corresponding low-fat group. Other
Table 1

Composition of experimental diets fed to rats treated with AAF or DMBA

<table>
<thead>
<tr>
<th>Component</th>
<th>Diet 1</th>
<th>Diet 2</th>
<th>Diet 3</th>
<th>Diet 4</th>
<th>Diet 5</th>
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<tbody>
<tr>
<td>Casein</td>
<td>22</td>
<td>3</td>
<td>22</td>
<td>20</td>
<td>23</td>
</tr>
<tr>
<td>Peanut meal</td>
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<td>0</td>
<td>0</td>
<td>0</td>
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<td>Gelatin</td>
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<td>6</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Fibrin</td>
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<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>L-Cystine</td>
<td>0</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Vegetable oil(^a)</td>
<td>15</td>
<td>2</td>
<td>2</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>Beef tallow</td>
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<td>30</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Carbohydrate</td>
<td>55.7</td>
<td>36.3</td>
<td>38.7</td>
<td>67.6</td>
<td>48.2</td>
</tr>
<tr>
<td>Cellulose</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Vitamins(^b)</td>
<td>2.3</td>
<td>2.2</td>
<td>2.3</td>
<td>2.4</td>
<td>2.8</td>
</tr>
<tr>
<td>Minerals(^c)</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

\(^a\) When lard is fed in Diets 4 and 5, the diets contain, respectively, corn oil, 1 and 1.1%, and lard, 4 and 18.9%.

\(^b\) Content recommended for rats (3) except Diet 2, which contains no folate and is low in niacin.

\(^c\) Rogers-Harpers salt mix supplemented to supply recommended amounts (3).

ruts fed 5% corn oil through DMBA treatment and then fed one of the other 3 diets show increased tumorigenesis if fed 20% corn oil, as reported by others (1), but no effect of a change to 5 or 20% lard (Table 2). Weight gain has been slightly (5 to 10%) greater in animals fed the high-fat diets; food utilization has not been affected by dietary fat content. Age at vaginal opening was significantly earlier in rats fed 20% corn oil [29.9 ± 3.1 (S.E.) days] than in any other group (5% corn oil, 31 ± 3.4 days; 20% lard, 31.1 ± 3.8 days; 5% lard, 31.7 ± 3.6 days). Earlier maturation in rats fed high-fat diets has been reported (2) and may be a mechanism by which dietary fat influences carcinogenesis. The preliminary data in lard-fed rats are not consistent with that hypothesis.

Serum prolactin content after 3 or 10 weeks of dietary treatment is approximately the same in all groups. Later studies of serum estrogen are in progress.

In summary, a nutritionally complete diet containing 20% corn oil or lard enhanced DMBA mammary tumorigenesis compared to the same diet containing 5% lipid. A similar diet (Diet 3) containing 30% tallow and 2% vegetable oil depressed AAF mammary tumorigenesis compared to the same diet containing 15% oil. Since different types and quantities of fat and different carcinogens were used, firm conclusions cannot be drawn, but the results suggest that the effect of dietary lipid on mammary carcinogenesis may depend on the model system used and on the quantity and quality of fats compared.

References


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Cancer Res 1981;41:3735-3737.

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