Effects of Dietary Fat on the Uptake and Clearance of 7,12-Dimethylbenz(a)anthracene by Rat Mammary Tissue

Elias B. Gammal, Kenneth K. Carroll, and Earl R. Plunkett

The Department of Obstetrics and Gynecology and the Collip Medical Research Laboratory, University of Western Ontario, London, Canada

Summary. The concentration of 7,12-dimethylbenz(a)anthracene (DMBA) in mammary tissue was determined at different time intervals following its administration, in a single dose, to female Sprague-Dawley rats maintained on 3 different semisynthetic diets: low fat, high coconut oil, and high corn oil. In general, the rate of uptake and clearance of the carcinogen was similar in the 3 groups, with a peak concentration occurring 6 to 12 hours after its administration. At 6 hours the tissue level of DMBA in coconut oil fed rats was significantly lower than in the other 2 groups. However, the data obtained could not fully explain the effects of dietary fat upon DMBA mammary carcinogenesis.

Introduction. The influence of dietary fat upon 7,12-dimethylbenz(a)anthracene (DMBA)-induced mammary cancer in female rats was the subject of a recent study by the present authors (7). It was demonstrated that the observed enhancement of tumor formation depended on the nature as well as the amount of fat in the diet. Thus, coconut oil ingested by one group of animals did not exert the augmenting effect of an equally large amount of corn oil in another group. Moreover, parameters pertaining to tumor growth and development in the coconut oil-fed group were similar to those obtained in a group of rats fed a low fat diet. It was shown also that, at the time of cancer induction, definite changes had taken place in the fatty acid composition of mammary tissue, reflecting the three different dietary fat intakes. This pointed to a possible relationship between the nature of the fat in the immediate environment of the mammary gland and the carcinogenic process taking place in its epithelial cells.

Tannenbaum had suggested earlier that the amount of fat in the breasts of mice on a fat-enriched diet was a factor in carcinogenesis (13). Following a study of the levels of 3-methylcholanthrene (3-MC) in breast and fatty tissue after its administration to rats, Dao et al. (3) pointed to the role of mammary adipose tissue as a storage depot for this carcinogenic hydrocarbon. Later on, investigators using various methods of analysis showed that DMBA also concentrates in rat mammary tissue (1, 5, 6).

The present experiments were undertaken, therefore, to investigate whether the diet-altered composition of mammary fat would modify the uptake and clearance of DMBA by mammary tissue, in a manner which could account for the previously observed influence upon mammary carcinogenesis.

Materials and Methods. Groups of female, intact Sprague-Dawley rats of weaning age (21-23 days) were placed on 3 different semisynthetic diets. The first diet had a low fat content (0.5% corn oil, by weight); the second and third diets contained 20% by weight of coconut and corn oil, respectively. The detailed composition of these diets and the feeding schedule were described previously (7). At the age of 50-52 days the animals received 10 mg of DMBA intragastrically in 0.5 ml of sesame oil and were killed at various intervals thereafter.

Estimations of DMBA in mammary tissue were made separately for each animal, using the 4th pair of mammary glands. The assay method was described in detail elsewhere (6).

Results. Following administration of DMBA to the rats under study, its concentration was determined at intervals of 3, 6, 10, 12, 24, 72, and 120 hours. These data are presented in Table 1 where each value is the mean of 6 to 9 determinations.

There was a rapid rise of DMBA levels reaching a peak concentration 6 hours after its administration to rats fed low fat and high corn oil diets. In the high coconut oil group, however, the peak level was delayed to 12 hours after feeding the carcinogen and was lower than that of the other 2 groups. There followed a rapid drop in levels until 24 hours, when the decline became more gradual. At 5 days the concentration of the hydrocarbon averaged 0.08, 0.16, and 0.15 μg/gm of tissue in the low fat, high coconut oil, and high corn oil diet groups, respectively. Statistical analysis showed that, at the 6-hour interval, carcinogen concentration in the high coconut oil group was significantly less than in the other two groups.

Discussion. Our results revealed once more that the peak concentration of DMBA in rat breast tissue occurred within the first 12 hours following its administration, concurring with earlier studies in animals maintained on standard commercial diet (6, 12) and with those reported by Hoshino and Bernet.
concerning 3-MC levels in mice (10). It was also interesting to note that, except for a delayed peak concentration in the coconut oil-fed rats, the rate of uptake and clearance of DMBA by mammary tissue was similar in the 3 different diet groups. The most appreciable difference, however, occurred 6 hours after DMBA feeding, when its tissue concentration in coconut oil-fed rats was significantly lower than in both low fat and high corn oil groups. Also, statistical analysis of the average peak levels in the high corn oil and coconut oil groups (6-hour and 12-hour values, respectively) showed a difference which was close to significance (P = 0.05 < 0.1). Whether this could account for the lower carcinogenic response previously elicited in coconut oil-fed animals (7) is not certain and any interpretation of these differences should be considered with caution, since the optimal tissue level of DMBA for the carcinogenic process is not known. However, the observation that DMBA was equally present in the mammary tissue of low fat and high corn oil-fed rats, whereas tumorigenesis was significantly more pronounced in the latter, strongly suggests that factors other than DMBA tissue concentration were probably involved.

Thus, further investigation is required to clarify the mechanism by which dietary fat affects mammary carcinogenesis. In such studies, it would be important to consider, among other aspects, the effects of diet upon lipids in both the structure of the mammary parenchymal cells and their environment. Experimental results of various investigators lend significant support to this consideration. At the tissue level, Hoshino has demonstrated that fatty tissue provides an essential environment for the growth of mammary parenchyma (8, 9). Therefore, it is conceivable that an altered environment, as achieved by diet in our study (7), may modify the carcinogenic response of the epithelial cells. On the other hand, different studies reviewed by van Deenen (4) have shown that, in a number of mammals, the fatty acid composition of cell membrane phospholipids is significantly modified by the type of fat ingested. Indeed, in one of these studies (11), an interesting relationship was observed between such an effect and membrane permeability. More recently, it was shown that the fatty acids characteristic of ingested fat became prominent components of microsomes and mitochondria in the mammary glands of lactating rats (2). These observations should be taken into account in future studies, due to their possible implications in cellular metabolism and permeability.

Table 1

<table>
<thead>
<tr>
<th>Time after DMBA feeding (hr)</th>
<th>Low fat (0.5% corn oil)</th>
<th>High coconut oil (30%)</th>
<th>High corn oil</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>11.4 ± 3.14</td>
<td>9.4 ± 1.83</td>
<td>13.8 ± 2.72</td>
</tr>
<tr>
<td>6</td>
<td>16.1 ± 1.99</td>
<td>9.0 ± 2.06</td>
<td>19.5 ± 2.74</td>
</tr>
<tr>
<td>12</td>
<td>15.5 ± 3.45</td>
<td>11.3 ± 2.01</td>
<td>16.5 ± 3.60</td>
</tr>
<tr>
<td>24</td>
<td>12.9 ± 2.10</td>
<td>12.0 ± 2.29</td>
<td>13.3 ± 2.46</td>
</tr>
<tr>
<td>72</td>
<td>5.6 ± 1.42</td>
<td>3.9 ± 0.97</td>
<td>4.7 ± 0.81</td>
</tr>
<tr>
<td>120</td>
<td>0.6 ± 0.13</td>
<td>0.9 ± 0.24</td>
<td>0.8 ± 0.17</td>
</tr>
</tbody>
</table>

Concentration (mean ± S.E.) of 7,12-dimethylbenz(a)anthracene (DMBA) in µg/gm mammary tissue of rats on different dietary fats. Each rat received 10 mg of DMBA/0.5 ml of sesame oil by stomach tube at 0 hour. At 6 hours, the P value for low fat and high coconut oil groups was <0.05 and for high corn oil and coconut oil groups <0.01.

Dietary Fat and DMBA Concentration in Mammary Tissue

REFERENCES


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