Effect of Endocrine Organ Ablation on the Uptake and Clearance of 9, 10-Dimethyl-1, 2-benzanthracene-9-\(^{14}\)C by Mammary Parenchymal Cells of the Rat\(^{1}\)

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SUMMARY

Intact, ovariectomized, and hypophysectomized female Sprague-Dawley rats were sacrificed at various intervals after the administration of 9,10-dimethyl-1,2-benzanthracene-(DMBA)-9-\(^{14}\)C. The abdominal-inguinal mammary glands from the right side of the rat were used to determine the radioactivity contained within the mammary teat, fat pad, and vascular areas, while those from the left side were separated into parenchymal cell and fat cell fractions. The intracellular lipid of the parenchymal cells was extracted and quantitated. Although the pattern of carcinogen uptake and clearance by the parenchymal cell intracellular lipid was similar in all 3 groups, a greater concentration of DMBA was found in the fraction obtained from ovariectomized and hypophysectomized rats sacrificed at the later time periods. These data indicated that the intracellular lipid of the parenchymal cell is important in the uptake of carcinogen by either the body fat or mammary gland was unaffected by endocrine organ ablation. Recent studies, utilizing a procedure for the enzymatic separation of fat cells from the parenchymal tissue of the mammary gland, have indicated that the uptake of DMBA by the parenchymal cells and fat cells occurred simultaneously and independently (16). Thus, it appeared that the fat cells were of minor importance in the uptake of the carcinogen by the parenchymal cells. Furthermore, DMBA was concentrated in the intracellular lipid of the parenchymal cell and then released to other cellular constituents. The carcinogen released from the intracellular lipid was apparently bound by some cellular component, and the level of this bound carcinogen appeared to be maintained by the continual release of DMBA from the parenchymal cell intracellular lipid.

MATERIALS AND METHODS

Virgin female Sprague-Dawley rats were received from the dealer at 30 days of age. Ovariectomy was performed in our

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Laboratory when the animals were 35 days of age. Animals which had been hypophysectomized at 35 days of age were obtained from Hormone Assay Laboratory, Chicago, Ill. The animals were housed in groups of 5 in a room artificially illuminated 14 hr each day and maintained at a temperature of 75 ± 2°F. All animals received Wayne Lab Blox and tap water ad libitum. In addition to the standard laboratory diet, hypophysectomized rats received a high-protein canned dog food, oranges, and a 5% glucose solution instead of tap water. Immediately after autopsy, the sella turcica of each hypophysectomized animal was closely examined under a dissecting microscope, and any animal having remnants of pituitary tissue were not used in this study.

At 50 days of age, all animals received 20 mg of DMBA-9-14C (Nuclear-Chicago Corporation, Des Plaines, Ill.; specific activity, 0.58 mCi/mkmole) in 1 ml of sesame oil by gastric intubation. Animals were sacrificed at 3, 6, 16, 24, 48, and 72 hr after administration of the carcinogen. The abdominal-inguinal mammary glands on the right side of each rat were removed and used to determine the radioactivity contained within the mammary teat (parenchymal and adipose tissue), fat pad (adipose tissue only), and vascular areas (16). A portion of perirenal fat was also removed to determine the uptake of DMBA-9-14C by adipose tissue other than that associated with the mammary gland. The abdominal-inguinal mammary glands and fat pad from the left side were removed and enzymatically separated into intact parenchymal cells and fat cells (19), after which the parenchymal cells were further fractionated into dry, fat-free parenchymal cell residue and parenchymal cell intracellular lipid (16).

The mammary adipose tissue and parenchyma (teat), fat pad, vascular area, parenchymal cell intracellular lipid, dry, fat-free parenchymal cell residue, mammary fat cells, and perirenal fat were weighed and digested, and the radioactivity was determined in a Packard Tri-Carb Model 3002 liquid scintillation spectrometer as previously described (16). The thin-layer chromatographic and autoradiographic methods used in determining whether or not DMBA-9-14C was actually the compound being measured in the fat cell, parenchymal cell, and parenchymal cell intracellular lipid fractions have been reported (16).

Student's t test was used to determine the difference between the means of any 2 fractions obtained at the same time, the difference between the means of a specific fraction obtained at any 2 time intervals, or the difference between the means of a specific fraction obtained at the same time from different groups of animals. Any stated difference (increase or decrease) between the values reported herein is understood to be statistically significant at a level of confidence of 95% or greater.

RESULTS

Samples of a benzene solution of DMBA, DMBA-9-14C, fat cell, parenchymal cell, and parenchymal cell intracellular lipid fractions obtained from intact, ovariectomized, or hypophysectomized animals fed DMBA-9-14C were subjected to thin-layer chromatography on glass plates coated with Silica Gel G. In every trial, single spots migrated in a solvent system of Skellysolve B:diethyl ether:glacial acetic acid (80:20:1) to positions with the same Rf values (0.80). Autoradiography of the thin-layer chromatograms indicated that the radioactivity measured in these fractions obtained from all 3 groups of animals was associated with DMBA-9-14C. No demonstrable difference was found in the chromatograms and autoradiographs of fractions collected at the various hr after carcinogen feeding. Neither DMBA nor DMBA-9-14C could be detected on thin-layer chromatograms or autoradiographs of samples of various lipid solvent (benzene, chloroform, ether, acetone, and hot ethanol) extracts of the dry, fat-free parenchymal cell residue from intact, ovariectomized, or hypophysectomized animals. Thus, the radioactivity associated with these fractions was not soluble in lipid solvents.

A comparison of the specific activity of either perirenal fat or mammary fat pad from intact (Table 1), ovariectomized (Table 2), and hypophysectomized (Table 3) rats indicated that the patterns of DMBA-9-14C uptake and clearance by these tissues were similar in all 3 groups of animals. However, the concentration of DMBA in the fat pad of hypophysectomized rats was significantly greater than that in the fat pad of either intact or ovariectomized animals sacrificed 48 hr after carcinogen administration. The patterns of concentration and clearance of DMBA observed for the fat cell fraction obtained from either intact or ovariectomized rats were not significantly different (Chart 1). During the first 24

Chart 1. Comparison of the uptake and clearance of DMBA-9-14C by the fat cell fraction of intact (*), ovariectomized (•), or hypophysectomized (•) rats. All animals received 20 mg of DMBA-9-14C and were sacrificed at various intervals after feeding, and the radioactivity of the specific tissue fraction was determined. Each point represents the mean specific activity of fat cell fractions obtained from at least 10 (no treatment) or 5 (ovariectomized or hypophysectomized) rats.
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Table 1

The specific activity of mammary gland components and perirenal fat of intact rats receiving DMBA-9-14C

At least 10 animals were used in determining the specific activity of each tissue fraction at each time interval. All values are means ± S.E.

<table>
<thead>
<tr>
<th>Tissue fraction</th>
<th>1 hr a</th>
<th>3 hr</th>
<th>6 hr</th>
<th>16 hr</th>
<th>24 hr</th>
<th>48 hr</th>
<th>72 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teat</td>
<td>21.9 ± 1.9</td>
<td>132.3 ± 14.4</td>
<td>250.4 ± 12.0</td>
<td>316.4 ± 25.2</td>
<td>153.7 ± 16.7</td>
<td>38.3 ± 5.8</td>
<td>13.1 ± 2.5</td>
</tr>
<tr>
<td>Fat pad</td>
<td>17.9 ± 2.0</td>
<td>112.4 ± 12.4</td>
<td>246.1 ± 15.7</td>
<td>309.9 ± 23.2</td>
<td>182.4 ± 19.9</td>
<td>70.3 ± 11.5</td>
<td>50.5 ± 5.0</td>
</tr>
<tr>
<td>Vascular</td>
<td>25.6 ± 2.4</td>
<td>105.1 ± 12.9</td>
<td>207.0 ± 14.2</td>
<td>213.7 ± 23.1</td>
<td>115.9 ± 14.8</td>
<td>29.2 ± 8.0</td>
<td>12.2 ± 2.1</td>
</tr>
<tr>
<td>Collagenase-treated Parenchymal cells</td>
<td>0.5 ± 0.1</td>
<td>2.5 ± 0.3</td>
<td>5.8 ± 0.5</td>
<td>2.7 ± 0.2</td>
<td>1.6 ± 0.1</td>
<td>1.0 ± 0.1</td>
<td>0.6 ± 0.1</td>
</tr>
<tr>
<td>Parenchymal cells, dry, fat-free</td>
<td>24.7 ± 1.9</td>
<td>30.9 ± 4.0</td>
<td>48.5 ± 3.3</td>
<td>35.4 ± 1.6</td>
<td>30.0 ± 2.9</td>
<td>29.0 ± 4.2</td>
<td></td>
</tr>
<tr>
<td>Parenchymal cell lipid</td>
<td>290.6 ± 15.6</td>
<td>530.5 ± 61.0</td>
<td>214.3 ± 12.3</td>
<td>128.4 ± 11.2</td>
<td>61.7 ± 9.3</td>
<td>53.5 ± 4.0</td>
<td></td>
</tr>
<tr>
<td>Fat cells</td>
<td>24.9 ± 1.4</td>
<td>185.1 ± 21.0</td>
<td>323.2 ± 24.9</td>
<td>416.4 ± 29.5</td>
<td>210.5 ± 16.1</td>
<td>92.0 ± 16.9</td>
<td>52.6 ± 7.8</td>
</tr>
<tr>
<td>Perirenal fat</td>
<td>41.2 ± 6.1</td>
<td>224.5 ± 27.1</td>
<td>471.3 ± 25.8</td>
<td>554.9 ± 33.5</td>
<td>331.3 ± 29.0</td>
<td>93.0 ± 10.3</td>
<td>39.5 ± 3.4</td>
</tr>
</tbody>
</table>

a Hr after the p.o. administration of 20 mg of DMBA-9-14C (50 μCi) in 1 ml of sesame oil.

Table 2

The specific activity of mammary gland components and perirenal fat of ovariectomized rats receiving DMBA-9-14C

At least 5 animals were used in determining the specific activity of each tissue fraction at each time interval. All values are means ± S.E.

<table>
<thead>
<tr>
<th>Tissue fraction</th>
<th>3 hr a</th>
<th>6 hr</th>
<th>16 hr</th>
<th>24 hr</th>
<th>48 hr</th>
<th>72 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teat</td>
<td>120.6 ± 25.5</td>
<td>203.1 ± 30.1</td>
<td>209.3 ± 35.7</td>
<td>122.3 ± 34.3</td>
<td>19.5 ± 5.7</td>
<td>11.6 ± 1.8</td>
</tr>
<tr>
<td>Fat pad</td>
<td>86.3 ± 14.5</td>
<td>155.2 ± 17.3</td>
<td>243.6 ± 61.9</td>
<td>183.6 ± 34.0</td>
<td>67.4 ± 20.1</td>
<td>37.3 ± 11.5</td>
</tr>
<tr>
<td>Vascular</td>
<td>88.1 ± 15.6</td>
<td>172.4 ± 28.2</td>
<td>133.1 ± 35.7</td>
<td>106.7 ± 13.9</td>
<td>11.7 ± 1.7</td>
<td>7.7 ± 0.8</td>
</tr>
<tr>
<td>Collagenase-treated Parenchymal cells</td>
<td>2.3 ± 0.2</td>
<td>2.6 ± 0.2</td>
<td>2.3 ± 0.2</td>
<td>2.2 ± 0.2</td>
<td>0.8 ± 0.1</td>
<td>0.6 ± 0.03</td>
</tr>
<tr>
<td>Parenchymal cells, dry, fat-free</td>
<td>17.1 ± 2.7</td>
<td>21.7 ± 1.8</td>
<td>35.5 ± 3.1</td>
<td>39.0 ± 1.5</td>
<td>22.8 ± 1.5</td>
<td>16.4 ± 0.7</td>
</tr>
<tr>
<td>Parenchymal cell lipid</td>
<td>192.7 ± 19.1</td>
<td>281.6 ± 27.9</td>
<td>247.4 ± 36.8</td>
<td>187.9 ± 25.4</td>
<td>68.3 ± 11.3</td>
<td>69.6 ± 5.8</td>
</tr>
<tr>
<td>Fat cells</td>
<td>154.0 ± 43.5</td>
<td>258.4 ± 41.4</td>
<td>399.7 ± 97.5</td>
<td>240.2 ± 35.9</td>
<td>77.0 ± 19.1</td>
<td>51.4 ± 10.5</td>
</tr>
<tr>
<td>Perirenal fat</td>
<td>166.1 ± 37.4</td>
<td>292.8 ± 46.6</td>
<td>406.0 ± 79.5</td>
<td>269.8 ± 59.6</td>
<td>82.6 ± 25.4</td>
<td>41.2 ± 8.2</td>
</tr>
</tbody>
</table>

a Hr after the p.o. administration of 20 mg of DMBA-9-14C (50 μCi) in 1 ml of sesame oil.

Table 3

The specific activity of mammary gland components and perirenal fat of hypophysectomized rats receiving DMBA-9-14C

At least 5 animals were used in determining the specific activity of each tissue fraction at each time interval. All values are means ± S.E.

<table>
<thead>
<tr>
<th>Tissue fraction</th>
<th>3 hr a</th>
<th>6 hr</th>
<th>16 hr</th>
<th>24 hr</th>
<th>48 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teat</td>
<td>104.6 ± 14.4</td>
<td>210.4 ± 25.6</td>
<td>393.6 ± 24.0</td>
<td>273.8 ± 23.1</td>
<td>113.8 ± 13.5</td>
</tr>
<tr>
<td>Fat pad</td>
<td>93.2 ± 17.1</td>
<td>181.6 ± 27.2</td>
<td>338.3 ± 31.4</td>
<td>237.4 ± 26.2</td>
<td>118.1 ± 19.8</td>
</tr>
<tr>
<td>Vascular</td>
<td>79.2 ± 16.4</td>
<td>219.0 ± 21.2</td>
<td>207.2 ± 22.9</td>
<td>164.7 ± 15.4</td>
<td>67.6 ± 9.1</td>
</tr>
<tr>
<td>Collagenase-treated Parenchymal cells</td>
<td>1.7 ± 0.2</td>
<td>4.5 ± 0.3</td>
<td>3.5 ± 0.4</td>
<td>2.0 ± 0.5</td>
<td>1.2 ± 0.1</td>
</tr>
<tr>
<td>Parenchymal cells, dry, fat-free</td>
<td>12.3 ± 0.8</td>
<td>21.9 ± 1.1</td>
<td>35.8 ± 3.2</td>
<td>23.4 ± 1.9</td>
<td>21.7 ± 1.8</td>
</tr>
<tr>
<td>Parenchymal cell lipid</td>
<td>263.7 ± 23.6</td>
<td>332.2 ± 13.7</td>
<td>301.8 ± 49.3</td>
<td>173.1 ± 11.6</td>
<td>87.7 ± 8.8</td>
</tr>
<tr>
<td>Fat cells</td>
<td>102.5 ± 22.6</td>
<td>263.9 ± 47.6</td>
<td>393.1 ± 38.7</td>
<td>277.0 ± 26.7</td>
<td>150.3 ± 12.0</td>
</tr>
<tr>
<td>Perirenal fat</td>
<td>263.0 ± 59.8</td>
<td>410.6 ± 45.9</td>
<td>373.3 ± 64.9</td>
<td>274.1 ± 56.3</td>
<td>155.7 ± 30.5</td>
</tr>
</tbody>
</table>

a Hr after the p.o. administration of 20 mg of DMBA-9-14C (50 μCi) in 1 ml of sesame oil.

hr, the specific activities of the fat cell fraction from intact, ovariectomized, and hypophysectomized animals did not differ. Thereafter, the specific activity of the fat cell fraction of hypophysectomized animals was significantly greater than the specific activity of this fraction obtained from either the intact or the ovariectomized animals. During the 1st 16 hr following carcinogen feeding, a similar pattern of DMBA uptake by the teat and vascular areas obtained from all 3 groups was observed (Tables 1 to 3). Following this period, the DMBA content of the teat and vascular areas obtained from hypophysectomized rats was significantly greater than that from either the intact or ovariectomized animals.

Depicted in Chart 2 are the specific activity patterns of the mammary parenchymal cells obtained from all 3 experimental
Carcinogen Uptake by Mammary Parenchymal Cells

Chart 2. Comparison of the uptake and clearance of DMBA-9-14C by parenchymal cell fraction of intact (●), ovariectomized (○), or hypophysectomized (▲) rats. Experimental conditions and procedures were the same as those described in the legend of Chart 1.

Groups. Parenchymal cells of both the intact and the hypophysectomized animals exhibited a maximum specific activity at 6 hr after feeding, while the specific activity of parenchymal cells isolated from ovariectomized rats was maintained at a constant level from 3 to 24 hr after DMBA. Thereafter, the pattern of carcinogen clearance from the parenchymal cells was similar in all 3 groups. The specific activity of the parenchymal cell intracellular lipid of intact animals reached a peak at 6 hr after DMBA feeding which was significantly greater than that of either ovariectomized or hypophysectomized animals (Chart 3). The radioactivity associated with the parenchymal cell intracellular lipid of intact rats declined rapidly from 6 to 48 hr after the administration of the carcinogen. Thereafter, a more gradual clearance of DMBA was observed. Maximum uptake of the carcinogen by the parenchymal cell intracellular lipid of ovariectomized or hypophysectomized animals appeared to occur between 6 and 16 hr after DMBA feeding. The clearance of DMBA from the parenchymal cell intracellular lipid of ovariectomized rats was similar to that of the intact animals. Although the concentration of DMBA within the parenchymal cell intracellular lipid of hypophysectomized rats was greater than that of intact animals at 24 and 48 hr after feeding, the pattern of clearance of DMBA was similar to that of both intact and ovariectomized rats.

The patterns of carcinogen uptake and clearance by the dry, fat-free parenchymal cell residue of intact, ovariectomized, and hypophysectomized animals are shown on Chart 4. Parenchymal cell dry, fat-free residue specific activity of intact rats reached a peak value of 48.5 dpm/mg at 16 hr after DMBA-9-14C administration. A small decrease in DMBA concentration occurred between 16 and 24 hr after feeding; but, thereafter, a statistically significant change in specific activity was not evident. The dry, fat-free parenchymal cell residue of animals ovariectomized prior to DMBA feeding exhibited a maximum uptake between 16 and 24 hr after administration of the carcinogen. Thereafter, the specific activity declined to values significantly less than those of intact rats at the 48- and 72-hr intervals. The pattern of
indicated that ovariectomy did not alter the intracellular lipid concentration and binding of carcinogens. This higher specific activity might be correlated with the observed differences in the specific activity of the parenchymal cell intracellular lipid fraction and the observed differences in the specific activity of the parenchymal cell may be of importance in the maintenance of a high specific activity within the parenchymal cell intracellular lipid fraction of intact animals but all values were significantly lower. Since the binding of DMBA to parenchymal cell DNA and protein in vivo has been reported (18), it is possible that the specific activity of the dry, fat-free parenchymal component represents DMBA which may be bound to nucleic acids and/or cellular proteins in all 3 groups of rats.

In this study, the level of nonlipid-extractable DMBA within the parenchymal cell was maintained at higher levels in intact animals than in either the ovariectomized or hypophysectomized rats. Therefore, not only might there be decreased lipolysis, increased lipogenesis, and decreased release of DMBA from the parenchymal lipid of ovariectomized and hypophysectomized rats, but also other cellular metabolic processes which these hormonal alterations are known to influence (1, 21) might be responsible for diminished binding of the carcinogen. Altered metabolic activity cannot definitely be ruled out. Although lipid metabolism within parenchymal cells of ovariectomized and hypophysectomized rats may be the result of a decreased rate of lipolysis coupled with an increased rate of lipogenesis.

Maximum DMBA-9-14C uptake by the dry, fat-free parenchymal cell residue from ovariectomized rats was found to occur later than that of intact rats, and, thereafter, the carcinogen content declined to levels significantly lower than those of intact animals. The pattern of DMBA-9-14C uptake and clearance of hypophysectomized rats was parallel to that of intact animals but all values were significantly lower. Since the binding of DMBA to parenchymal cell DNA and protein in vivo has been reported (18), it is possible that the specific activity of the dry, fat-free parenchymal component represents DMBA which may be bound to nucleic acids and/or cellular proteins in all 3 groups of rats.

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Analysis of these data indicated that ovariectomy or hypophysectomy might not have appreciably altered the uptake and clearance of DMBA by the parenchymal cells. However, these procedures resulted in distinct changes in the parenchymal cell intracellular lipid uptake and clearance of DMBA. Furthermore, the importance of the intracellular lipid of the parenchymal cell in the exposure of the parenchymal cell to DMBA has been reported (16). In this study, the initial concentration of DMBA within the parenchymal cell intracellular lipid was less in ovariectomized rats than in intact rats. Although the clearance of DMBA from the intracellular lipid in ovariectomized rats was similar to that in intact rats, a significantly greater specific activity was observed in this lipid fraction in ovariectomized animals sacrificed at 72 hr after carcinogen feeding. This higher specific activity might represent a decreased release of DMBA and/or might result from an increased lipid content. Since an earlier investigation indicated that ovariectomy did not alter the intracellular lipid content of parenchymal cells when compared to that of intact animals (17), this finding cannot be explained in terms of the lipid content of the parenchymal cell. The pattern of DMBA uptake and clearance from the parenchymal cell intracellular lipid of hypophysectomized rats was similar to that of ovariectomized rats. In addition, a greater amount of DMBA was retained within the intracellular lipid of hypophysectomized animals than that retained in this component of intact animals sacrificed at 24 and 48 hr after feeding. The increased level of carcinogen within the parenchymal cell intracellular lipid may possibly represent a decreased release of DMBA and/or an increased intracellular lipid content. Hypophysectomy resulted in a significant elevation of the intracellular lipid content of the parenchymal cells (17). Thus, maintenance of a high specific activity within the parenchymal cell intracellular lipid fraction of hypophysectomized rats probably results from an increased lipid level. However, the possible influence of decreased metabolic activity and/or decreased release of DMBA cannot be ruled out. Although lipid metabolism within parenchymal cells has not been studied, Hilf et al. (9–12) have examined lipid metabolism within the mammary gland fat pad of rats following ovariectomy and hypophysectomy. These investigators have reported a decrease in lipolytic activity and an increase in lipogenesis within the mammary gland of ovariectomized and hypophysectomized rats. The decreased clearance of DMBA-9-14C from the intracellular lipid of parenchymal cells of ovariectomized and hypophysectomized rats may be the result of a decreased rate of lipolysis coupled with an increased rate of lipogenesis.

Analysis of these data indicated that ovariectomy or hypophysectomy might not have appreciably altered the uptake and clearance of DMBA by the parenchymal cells. However, these procedures resulted in distinct changes in the parenchymal cell intracellular lipid uptake and clearance of DMBA. Furthermore, the importance of the intracellular lipid of the parenchymal cell in the exposure of the parenchymal cell to DMBA has been reported (16). In this study, the initial concentration of DMBA within the parenchymal cell intracellular lipid was less in ovariectomized rats than in intact rats. Although the clearance of DMBA from the intracellular lipid in ovariectomized rats was similar to that in intact rats, a significantly greater specific activity was observed in this lipid fraction in ovariectomized animals sacrificed at 72 hr after carcinogen feeding. This higher specific activity might represent a decreased release of DMBA and/or might result from an increased lipid content. Since an earlier investigation indicated that ovariectomy did not alter the intracellular lipid content of parenchymal cells when compared to that of intact animals (17), this finding cannot be explained in terms of the lipid content of the parenchymal cell. The pattern of DMBA uptake and clearance from the parenchymal cell intracellular lipid of hypophysectomized rats was similar to that of ovariectomized rats. In addition, a greater amount of DMBA was retained within the intracellular lipid of hypophysectomized animals than that retained in this component of intact animals sacrificed at 24 and 48 hr after feeding. The increased level of carcinogen within the parenchymal cell intracellular lipid may possibly represent a decreased release of DMBA and/or an increased intracellular lipid content. Hypophysectomy resulted in a significant elevation of the intracellular lipid content of the parenchymal cells (17). Thus, maintenance of a high specific activity within the parenchymal cell intracellular lipid fraction of hypophysectomized rats probably results from an increased lipid level. However, the possible influence of decreased metabolic activity and/or decreased release of DMBA cannot be ruled out. Although lipid metabolism within parenchymal cells has not been studied, Hilf et al. (9–12) have examined lipid metabolism within the mammary gland fat pad of rats following ovariectomy and hypophysectomy. These investigators have reported a decrease in lipolytic activity and an increase in lipogenesis within the mammary gland of ovariectomized and hypophysectomized rats. The decreased clearance of DMBA-9-14C from the intracellular lipid of parenchymal cells of ovariectomized and hypophysectomized rats may be the result of a decreased rate of lipolysis coupled with an increased rate of lipogenesis.

Maximum DMBA-9-14C uptake by the dry, fat-free parenchymal cell residue from ovariectomized rats was found to occur later than that of intact rats, and, thereafter, the carcinogen content declined to levels significantly lower than those of intact animals. The pattern of DMBA-9-14C uptake and clearance of hypophysectomized rats was parallel to that of intact animals but all values were significantly lower. Since the binding of DMBA to parenchymal cell DNA and protein in vivo has been reported (18), it is possible that the specific activity of the dry, fat-free parenchymal component represents DMBA which may be bound to nucleic acids and/or cellular proteins in all 3 groups of rats.

In this study, the level of nonlipid-extractable DMBA within the parenchymal cell was maintained at higher levels in intact animals than in either the ovariectomized or hypophysectomized rats. Therefore, not only might there be decreased lipolysis, increased lipogenesis, and decreased release of DMBA from the intracellular lipid of ovariectomized and hypophysectomized rats, but also other cellular metabolic processes which these hormonal alterations are known to influence (1, 21) might be responsible for diminished binding of the carcinogen. Altered metabolic activity cannot definitely be correlated with the observed differences in the specific activity of the parenchymal cell intracellular lipid fraction and dry, fat-free parenchymal cell residue obtained from either intact, ovariectomized, or hypophysectomized animals. However, these studies do appear to suggest that the metabolic activity of the parenchymal cell may be of importance in concentrating and binding of carcinogens.
REFERENCES


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