The Role of Acyldihydroxyacetone Phosphate, Reduced Nicotinamide Adenine Dinucleotide, and Reduced Nicotinamide Adenine Dinucleotide Phosphate in the Biosynthesis of O-Alkyl Glycerolipids by Microsomal Enzymes of Ehrlich Ascites Tumor*

ROBERT L. WYKLE, CLAUDE PIANTADOSI,† AND FRED SNYDER

From the Medical Division, Oak Ridge Associated Universities, Oak Ridge, Tennessee 37830, and the Department of Medicinal Chemistry, School of Pharmacy, University of North Carolina, Chapel Hill, North Carolina 27514

SUMMARY

Palmitoyl dihydroxyacetone phosphate and [1-14C]hexadecanol were found to serve as precursors of O-alkyl lipids in a microsomal system from Ehrlich ascites tumor. Both acyldihydroxyacetone phosphate and dihydroxyacetone phosphate were tested. The system required no CoA when acyldihydroxyacetone phosphate was used as the glycerol source, and significantly lower concentrations of acyldihydroxyacetone phosphate than dihydroxyacetone phosphate were required for the optimal biosynthesis of O-alkyl lipids; a similar reaction was catalyzed by microsomal preparations from mouse preputial gland tumors. These findings indicated that acyldihydroxyacetone phosphate is a more efficient precursor of O-alkyl lipids than dihydroxyacetone phosphate. The CoA, ATP, and Mg++ that are required when dihydroxyacetone phosphate is the glycerol source are necessary for the formation of the acyldihydroxyacetone phosphate; the synthesis of acyldihydroxyacetone phosphate from [14C]dihydroxyacetone phosphate and palmitic acid was demonstrated in the microsomal system. The O-alkyldihydroxyacetone phosphate formed in the system was reduced by either NADPH or NADH to l-O-alkylglycerophosphate and subsequently acylated to form l-O-alkyl-2-acylglycerophosphate. The data also indicated that acyldihydroxyacetone phosphate was reduced to acylglycerophosphate by both NADH and NADPH. The organic synthesis of acyldihydroxyacetone phosphate is outlined as well as the identification of biosynthetic products.

Since the discovery that tumors have an unusually high content of O-alkylglycerolipids (1-4), we have been interested in the pathway by which the ether-linked lipids are biosynthesized in both normal and neoplastic cells. In our earlier studies of this problem using a microsomal enzyme system from preputial gland tumors of mice (5-8), we demonstrated that O-alkylglycerolipids are derived from fatty alcohols and DHAP. In addition, ATP, CoA, and Mg++ were required for the formation of the first detectable ether-containing member of the pathway, O-alkyl-DHAP. Similar observations have been made in enzyme systems from Ehrlich ascites cells (9), mouse brain and guinea pig liver (10), L-M cells (11), digestive glands and gonads of starfish (12), brain and livers of developing rats (13), and Tetrahywzena (14).

After the formation of O-alkyl-DHAP, NADPH was required to reduce the ketone group; however, NADPH inhibited the synthesis of the ether bond if present from the beginning of the incubations (5, 9, 10). These data and the CoA-ATP-Mg++ requirement led Hajra (15) to suspect that acyl-DHAP (16) could be involved in the biosynthesis of the ether bond in glycerolipids. Using a microsomal enzyme system from rat brain, Hajra (15) found that CoA and ATP are required in the system to form acyl-DHAP which then apparently exchanges with fatty alcohol to form O-alkyl-DHAP. Since NADPH reduces acyl-DHAP to acylglycerophosphate in the system, the inhibitory effect of NADPH on the formation of O-alkyl-DHAP is thus explained. The NADPH present at the beginning of the reaction can reduce the acyl-DHAP as it is formed, making it unavailable for exchange with the alcohol.

In the present study, we found that acyl-DHAP serves as a precursor of O-alkylglycerolipids in Ehrlich ascites tumor cells. Murooka et al. (17) recently reported that a similar pathway occurs in bacteria for the biosynthesis of O-alkylhomoserines from DHAP, dihydroxyacetone phosphate.
O-acetylhomoserine and alcohols such as methanol and ethanol. The importance of our results is highlighted by the recent findings by Agranoff and Hajra (18) that the acyl-DHAP pathway of glyceride synthesis is of major significance in Ehrlich ascites cells. This finding led them to suggest that the high levels of ether-linked lipids observed in tumors may be related to their ability to synthesize acyl-DHAP.

**MATERIALS AND METHODS**

**Preparation of Substrates**—We prepared acyl-DHAP by a sequence of reactions analogous to the one we used to synthesize alkyl-DHAP (19). The procedure is a modification of a series of reactions that Hartman (20) and Ballou and Fischer (21) used to synthesize halocetal phosphates and DHAP. The following sequence is an outline of the procedure we used; 3-O-benzyl glycerol + palmitoyl chloride → 1-O-palmitoyl-3-O-benzyl-2-hydroxypropylene → 1-O-palmitoyl-3-O-benzyl-2-propanone → 1-O-palmitoyl-2,2-dimethoxy-3-O-benzyl propylene → 1-O-palmitoyl-2,2-dimethoxy-2-propanone-3-phosphate → 1-O-palmitoyl-2,2-dimethoxy-3-phosphate → 1-O-palmitoyl-2-propanone-3-phosphate. Palmitoyl chloride was reacted with 3-O-benzyl glycerol (22) in the presence of pyridine at -20°, resulting in a crude mixture of the monoacyl and diacyl derivatives of 3-O-benzyl glycerol. The 1-O-palmitoyl-3-O-benzyl-2-hydroxypropylene, which was the predominant species present, was not isolated but was oxidized to the ketone in high yields with dimethylsulfuride and dicyclohexylcarbodiimide in the presence of trifluoroacetic acid (20, 23) in a manner similar to that used in the synthesis of 0-alkyl-DHAP (19). The 1-O-palmitoyl-3-O-benzyl-2-propanone was ketalized in the same manner as in the synthesis of alkyl-DHAP (19) then debenzylated by stirring with palladium black and H₂ at 20 p.s.i. at room temperature, and finally phosphorylated with diphenyl chlorophosphate. Platinum oxide was used to remove the phenyl groups of the diphenyl derivative; the 1-O-palmitoyl-2,2-dimethoxypropylene-3-phosphate released was subsequently treated with cyclohexylamine and isolated as the salt in 90% over-all yield. The complete details of the procedure and the analysis of the products will be given in a separate report (23a) (also see review by Piantadosi [24]).

The cyclohexylammonium and methylketal groups were removed from the cyclohexylammonium salt of 1-O-palmitoyl-2,2-dimethoxypropylene-3-phosphate to release acyl-DHAP by coating 15 mg of the salt from a chloroform solution on the inside surface of a 500-ml round evaporating flask; the flask was first filled with moist air, then filled with hydrogen chloride gas, stopped, and allowed to stand at room temperature for 3 hours. Next the flask was flushed with nitrogen and the acyl-DHAP dissolved in chloroform. The product was shown to be pure by thin layer chromatography in solvents (System I, see below) that separate acyl-DHAP (Rₚ 0.45) from the dimethylketone derivative of acyl-DHAP (Rₚ 0.66). The acyl-DHAP was placed in water (2 mg per ml) and dispersed sonically for use in incubations. Acdlyldihydroxycetone was prepared in a similar manner from 1-O-palmitoyl-2,2-dimethoxy-3-hydroxypropylene synthesized as described above.

Both alkyl-DHAP (19) and acyldihydroxycetone were prepared by the method of Piantadosi et al. (25). Unlabeled palmitic acid and cetyl alcohol, obtained from Applied Science Labs, were dispersed sonically in water for use in incubations. The [1-¹⁴C]palmitic acid was obtained from New England Nuclear and reduced by LiAlH₄ to obtain the [1-¹⁴C]hexadecanol. The labeled lipids were purified to >99% purity by thin layer chromatography prior to use.

**Incubations**—The incubations were carried out with microsomal preparations from Ehrlich ascites cells collected 7 days after transplantation. The microsomal preparation was made as reported earlier (9) and washed once. The [1-¹⁴C]hexadecanol and [1-¹⁴C]palmitic acid were added to the incubations in 10 µl of ethanol. The [U-¹⁴C]DHAP (34.5 mCi per mmole) was prepared enzymically in the incubation vials from [U-¹⁴C]fructose 1,6-diphosphate (72.4 mmoles, 5 µCi, Amersham-Searle) by adding 1 unit of aldolase to the complete incubation mixture. Specific conditions for each incubation are described in the legends to the tables. The incubations were stopped by extracting the lipids (26), and the distribution of radioactivity in the products was measured by area scraping or zonal scanning of thin layer chromatograms (27, 28). O-Alkylglycerols were measured in some experiments after reduction of the lipids by Vitrride [70% NaAlH₄(OCH₂CH₂OCH₃)₂, in benzene] from Eastman Organic Chemicals (29).

**Chemical and Chromatographic Procedures**—Other procedures, including LiAlH₄ reduction, mild saponification, hydrolysis by bacterial alkaline phosphatase, preparation of isopropylidene derivatives, periodate oxidation, extraction of lipids, and gas-liquid and thin layer chromatographic procedures were carried out as described earlier (7, 9). Unless otherwise specified, the sources of all cofactors, enzymes, and other materials were the same as reported earlier (6, 7, 9).

The following solvent systems were used for thin layer chromatography; I, chloroform-methanol-glacial acetic acid-water (50:25:5:2, v/v); II, chloroform-methanol-ammonium hydroxide (65:35:8, v/v); III, hexane-diethyl ether (40:60, v/v); IV, diethyl ether-water (100:0,5, v/v); V, hexane-diethyl ether-ethanol-glacial acetic acid (70:30:5:1, v/v); VI, hexane-diethyl ether-glacial acetic acid (80:20:1, v/v); and VII, hexane-dichloroethane (80:20, v/v). Silica Gel G layers were used with Systems III, IV, V, VI, and VII; Silica Gel HR was used with Systems I and II.

**RESULTS AND DISCUSSION**

The synthesis of ether-linked lipids from ¹³C-fatty alcohol and DHAP by the tumor microsomal system normally exhibits an absolute requirement for CoA, ATP, and Mg⁺⁺ (5, 9). However, the results in Table I show that when acyl-DHAP is used as a precursor, [¹³C]alcohol is incorporated into O-alkyl lipids in the absence of CoA. No ether-linked lipids were made from the [¹³C]alcohol in the absence of CoA when DHAP was used. These results indicate that acyl-DHAP is a precursor of O-alkyl lipids in Ehrlich ascites cells, and are in agreement with those Hajra (15) reported for microsomes from brain, mitochondria from guinea pig liver, and more recently for microsomes from ascites tumor cells (30). The data show that ATP increases the synthesis of O-alkyl bonds from acyl-DHAP. No requirement for Mg⁺⁺ was demonstrated, but the ascites microsomes may contain enough Mg⁺⁺ to mask a requirement as reported by Hajra (15). The effect of the concentration of acyl-DHAP on the biosynthesis of O-alkyl lipids is shown in Fig. 1. The optimal concentration of acyl-DHAP in the system was approximately
Table I

<table>
<thead>
<tr>
<th>Table I</th>
<th>Synthesis of O-alkyl lipids from DHAP and acyl-DHAP by microsomes of Ehrlich ascites cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>[1-14C]Hexadecanol incorporated into O-alkyl lipids*</td>
<td>Additions</td>
</tr>
<tr>
<td></td>
<td>DHAP</td>
</tr>
<tr>
<td>1. Complete</td>
<td>8.6; 8.6</td>
</tr>
<tr>
<td>2. Complete minus Mg++</td>
<td>1.7; 1.7</td>
</tr>
<tr>
<td>3. Complete minus CoA</td>
<td>0.2; 0.3</td>
</tr>
<tr>
<td>4. Complete minus ATP</td>
<td>0.3; 0.4</td>
</tr>
</tbody>
</table>

* O-Alkyl lipids were measured after reduction of the lipids by Vitride and separation of the products by thin layer chromatography in Solvent System IV.

The complete system in 3 ml contained ATP (10 mM), CoA (0.1 mM), MgCl2 (4.33 mM), potassium phosphate buffer (0.1 M, pH 7.1), [1-14C]hexadecanol (16 μM, 46 mCi per mmole), and microsomes from Ehrlich ascites cells (2 mg of protein); DHAP (1.66 mM) and acyl-DHAP (67 μM) were added as indicated. The incubation was carried out by shaking at 150 oscillations per min at 37°C for 1 hour.

Fig. 1. The effect of concentration of acyl-DHAP on the biosynthesis of O-alkyl lipids from [1-14C]hexadecanol. The complete system and conditions were the same as those listed for Table I. CoA and DHAP were not present. The incorporation of [1-14C]hexadecanol into O-alkyl lipids was linear with time under these conditions at all concentrations of acyl-DHAP shown.

60 μM. Levels of acyl-DHAP greater than 60 μM inhibited the synthesis of O-alkyl lipids. In contrast, when lower concentrations of DHAP (67 μM) were used with the complete system shown in Table I, only 2 to 3 nmoles of the [14C]hexadecanol were incorporated into O-alkyl lipids. The microsomal preparations used in these studies contained sufficient endogenous fatty acid for the synthesis of acyl-DHAP from DHAP; thus, the system is able to make alkyl-DHAP via acyl-DHAP when CoA, ATP, and Mg++ are present. When microsomal preparations (6) from preputial gland tumors were substituted for microsomes from ascites cells in the complete system, alkylglycerolipids were also synthesized.

The distribution of 14C in the products (O-alkyl-DHAP, O-alkyldihydroxyacetone, alcohol, and wax esters) formed from [1-14C]hexadecanol and DHAP (Table I, No. 1) or acyl-DHAP (Table I, No. 3) was the same as on thin layer chromatograms developed in Solvent Systems I or V. The ether-linked lipid formed from acyl-DHAP and [1-14C]hexadecanol in the absence of CoA was reduced by LiAlH4 and the [14C]O-alkylglycerol was isolated by thin layer chromatography. A portion of the [14C]-O-alkylglycerol was treated to form an isopropylidene derivative (31); thin layer chromatographic analysis of the 14C products revealed that 90% of the activity migrated with an authentic isopropylidene derivative of O-hexadecylglycerol in Solvent System VII. Gas liquid chromatography of the isolated isopropylidene derivative (7) demonstrated that 84% of the 14C activity was associated with the O-hexadecylglycerol isopropylidene. The isolated alkylglycerol was also identified by periodate oxidation; the product had an RF identical to that of standard O-alkylglycolic aldehyde in Solvent System IV.

In order to show that the tumor microsomal preparation synthesizes acyl-DHAP when furnished with ATP, CoA, Mg++, and DHAP, we incubated unlabeled palmitic acid (150 nmoles/3 ml) with [1-14C]DHAP (see "Materials and Methods") in the presence of NaF (20 mM) and examined the products as described below. In a parallel experiment, unlabeled hexadecanol (150 nmoles/3 ml) was used instead of palmitic acid for comparison. The phospholipid fraction formed by incubating palmitic acid and [14C]DHAP (86% of the 14C-lipids synthesized, representing 13.5 nmoles [14C]DHAP) contained a single labeled product which migrated with authentic acyl-DHAP in both acidic (System I) and basic (System II) solvent systems. The Rf values in the two systems were 0.45 and 0.12, respectively. A portion (100,000 cpm) of the fraction identified as [14C]acyl-DHAP was subjected to saponification at room temperature (9). Most of the radioactivity (93%) remained in the water phase after extracting the lipids from the saponification mixture. This finding indicated that the [14C]DHAP moiety was bound to the lipid by an ester linkage. The [14C]acyl-DHAP was further identified by removing the phosphate group with bacterial alkaline phosphatase (9, 32) to form acyldihydroxyacetone. The [14C]acyldihydroxyacetone chromatographed with authentic acyldihydroxyacetone in Solvent System III, a system that separates acyl- and alkylidihydroxyacetone from each other and from monoglycerides. Acyldihydroxyacetone (5% of 14C-lipids synthesized) was also formed during the incubation of palmitic acid and [14C]DHAP to synthesize acyl-DHAP; this was shown by chromatography of the untreated neutral lipid fraction in Solvent System III. In addition, the products contained small amounts of [14C]alkylidihydroxyacetone (6% of 14C-lipids synthesized) even though no fatty alcohol had been added to the system.

However, in the parallel experiment containing unlabeled fatty alcohol and [14C]DHAP, a larger amount (18% of 14C-lipids formed) of O-alkyldihydroxyacetone was recovered in the neutral lipid fraction but no detectable acyldihydroxyacetone. The phospholipid fraction contained mostly [14C]O-alkyl-DHAP. These studies indicated that acyl-DHAP was formed in the system used to synthesize O-alkyl lipids. During the course of
this investigation, Agranoff and Hajra (18) reported that the acyl-DHAP pathway is the dominant one for glycerolipid synthesis in homogenates of Ehrlich ascites cells.

One or more phosphatases are present in the microsomal preparation that can remove the phosphate group from both acyl- and alkyl-DHAP. Our results suggest that the ether-containing ketolipids are more stable than the acyl analogs in this system, and thus make it possible to detect the small amount of alkylidihydroxyacetone produced in the absence of exogenous fatty alcohol. Mild saponification of the neutral lipids formed from palmitic acid resulted in a complete loss of the peak corresponding to [4C]acylidihydroxyacetone while the [4C]alkylidihydroxyacetone was unchanged.

Both NADH and NADPH, when added to the ether-synthesizing system at the beginning of the incubation, inhibited the synthesis of O-alkyl ethers from [1-14C]hexadecanol and DHAP (Table II). Similar inhibition was observed in earlier studies using NADPH (5, 9, 10); NADH was found to partly inhibit the reaction in mitochondria of guinea pig liver and microsomes of mouse brain (10). In a later study, Hajra (15) proposed that the inhibition by NADPH resulted from the reduction of acyl-DHAP to acylglycerophosphate, thereby making acyl-DHAP unavailable for the formation of alkyl-DHAP by an exchange with fatty alcohol. Earlier evidence (5, 9, 10) indicated that NADPH can reduce both O-acyl-DHAP and O-alkylidihydroxyacetone, but suggested that neither of these compounds is reduced by NADH. In the present study using Ehrlich ascites microsomes, NADH reduced O-alkyl-DHAP to O-alkylglycerophosphate which was subsequently acylated by the system using endogenous fatty acids to form O-alkylacylglycerophosphate (Table III) as observed earlier when NADPH was used (9, 10). The O-alkylidihydroxyacetone was reduced much more slowly by NADH than by NADPH.

Since NADH and NADPH reduced O-alkyl-DHAP and since both NADH and NADPH inhibited the synthesis of O-alkyl lipids if present at the beginning of the reaction, it seemed probable that NADH reduces acyl-DHAP in the Ehrlich ascites system. Therefore, we carried out the experiment reported in Table IV to determine if NADH reduces acyl-DHAP to acylglycerophosphate in the Ehrlich ascites system. The results indicate that NADH is more effective than NADPH for the reduction and leads to the formation of phosphatidic acid in the system. The [14C]phosphatidic acid formed chromatographed with authentic phosphatidic acid in Solvent Systems I and II; it was also treated with snake venom phospholipase A (9) and yielded a product that chromatographed with authentic lysophosphatidic acid in Solvent System I. Alkaline methanolysis (9) of the phosphatidic acid resulted in the complete loss of 14C from the phospholipid fraction and recovery of the 14C label in fatty acids and in methyl esters of fatty acids. Identification of the phosphatidic acid was based on these findings. No glycerophosphate dehydrogenase could be detected in the washed microsomes (8). Similar studies in our laboratory have also shown that the synthesis of phosphatidic acid from DHAP by micro-

### Table II

| Additions | [1-14C]Hexadecanol incorporated into O-alkyl lipids
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>12; 12</td>
</tr>
<tr>
<td>Plus NADPH</td>
<td>2.1; 2.2</td>
</tr>
<tr>
<td>Plus NADH</td>
<td>2.2; 2.1</td>
</tr>
</tbody>
</table>

* The system and conditions were the same as listed for Table I, except in this experiment DHAP (1.66 mM) was added to all tubes and no acyl-DHAP was added. NADH (1.66 mM) and NADPH (1.66 mM) were added at the beginning of the incubation.

### Table III

| Additions | [1-14C]Hexadecanol in products from incubation
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>10; 11</td>
</tr>
<tr>
<td>Plus NADPH</td>
<td>1.5; 1.7</td>
</tr>
<tr>
<td>Plus NADH</td>
<td>1.4; 1.6</td>
</tr>
</tbody>
</table>

### Table IV

| System | [1-14C]Palmitic acid in products from incubation
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyl-DHAP</td>
<td>Phosphatidic acid</td>
</tr>
<tr>
<td>Complete</td>
<td>17; 21</td>
</tr>
<tr>
<td>Complete plus NADPH</td>
<td>1.2; 1.3</td>
</tr>
<tr>
<td>Complete plus NADH</td>
<td>2.1; 3.5</td>
</tr>
<tr>
<td>Complete minus DHAP</td>
<td>3.6; 2.0</td>
</tr>
<tr>
<td>Complete plus NADPH minus DHAP</td>
<td>1.1; 1.4</td>
</tr>
</tbody>
</table>

* Based on radioassay of products after separation in Solvent Systems I and II. Values are given for duplicate incubations.

The NADH (1.66 mM) and NADPH (1.66 mM) were added after the incubation had been in progress for 1 hour and the incubation was then continued for 30 min. All other components were added at the beginning of the incubation. The system contained NaF (20 mM), DHAP (1.66 mM), and no acyl-DHAP. All other components and conditions were the same as listed for Table I.

Based on radioassay of products after separation in Solvent Systems I and II. Values are given for duplicate incubations.

* The NADH (1.66 mM) and NADPH (1.66 mM) were added at the beginning of the incubation. The system contained NaF (20 mM), DHAP (1.66 mM), and no acyl-DHAP. All other components and conditions were the same as listed for Table I.

Based on radioassay of products after separation in Solvent Systems I and II. Values are given for duplicate samples.

The complete system contained ATP (10 mM), CoA (0.1 mM), MgCl2 (4.33 mM), NaF (20 mM), potassium phosphate buffer (0.1 M, pH 7.1), DHAP (1.66 mM), [1-14C]palmitic acid (23 μM, 10 μCi per amole), and microsomes from Ehrlich ascites cells (2 mg of protein). In the samples indicated, NADH (1.66 mM) or NADPH (1.66 mM) was added at the beginning of the incubation. The incubation was carried out at 37°C for 30 min in a total volume of 3 ml.
some from mouse preputial gland tumors is stimulated by both NADH and NADPH. These results agree with the findings of Puleo et al. (33) who found that acyl-DHAP is reduced by NADH with microsomes from hamster intestinal mucosa, and with those of Rao et al. (34) who found that with microsomes from rat liver, NADH was more effective than NADPH for the formation of phosphatidic acid. In their studies they also found that the washed microsomes did not contain glycerophosphate dehydrogenase. Agranoff and Hajra (18) reported that they were unable to detect any interconversion of NADPH and NADH in homogenates of Ehrlich ascites cells.

The inhibition of the synthesis of O-alkyl lipids by NADH and NADPH (Table II) is thus best explained as resulting from the reduction of acyl-DHAP. The nonspecificity of pyridine nucleotides for the reduction of acyl-DHAP suggests that the acyl-DHAP pathway may contribute even more to glycerolipid synthesis in Ehrlich ascites cells than was estimated by Agranoff and Hajra (18) since they used [3H]NADH for measuring the reduction of acyl-DHAP. The nonspecificity of pyridine nucleotides for the reduction of acyl-DHAP suggests that the requirement for reduced nucleotides may be more specific. Our studies indicate that acyl-DHAP is a precursor of O-alkylglycerolipids in Ehrlich ascites cells. Hajra (30) has suggested that acyl-DHAP may also react directly with fatty aldehydes to form the O-alk-1-enyl bond of plasmalogens in Ehrlich cells, and therefore are formed via the same pathway as the plasmalogens are formed directly from O-alkyl lipids in these cells, and brain. However, our recent studies (29, 35, 36) with a cell-free system from Ehrlich ascites cells indicate that plasmalogens are formed directly from O-alkyl lipids in these cells, and therefore are formed via the same pathway as the O-alkyl glycerolipids.

REFERENCES

M. R. Grigor, personal communication.
The Role of Acyldihydroxyacetone Phosphate, Reduced Nicotinamide Adenine Dinucleotide, and Reduced Nicotinamide Adenine Dinucleotide Phosphate in the Biosynthesis of O-Alkyl Glycerolipids by Microsomal Enzymes of Ehrlich Ascites Tumor

Robert L. Wykle, Claude Piantadosi and Fred Snyder