Brain Aldehyde Dehydrogenase

LOCALIZATION, PURIFICATION, AND PROPERTIES*

(Received for publication, February 10, 1966)

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SUMMARY

Aldehyde-oxidizing capacity has been measured in rat, monkey, and bovine brain with the use of indole-3-acetaldehyde and nicotinamide adenine dinucleotide as substrates. The enzyme activity was found to be uniformly distributed in various areas of bovine brain.

Mitochondria, prepared by differential and density gradient centrifugation of rat brain homogenates, contained a major portion of the total aldehyde-oxidizing activity while smaller amounts were present in the supernatant fraction. The enzyme was purified from fresh bovine brain and also from frozen and thawed bovine and monkey brains. It has been separated from succinic semialdehyde dehydrogenase. The apparent pH optimum is 10, above which irreversible denaturation occurs.

A number of aliphatic aldehydes ranging from formaldehyde to palmitic aldehyde and aldehydes derived from serotonin, epinephrine, and dopamine (3,4-dihydroxyphenyl-ethyamine) were substrates for the enzyme. The rates of oxidation could be correlated with the electropositive nature of the carbonyl carbon atom. The $K_m$ values were exceptionally low and ranged from $2 \times 10^{-7}$ M to $7 \times 10^{-3}$ M. The enzyme was specific for NAD and NAD analogues. No activity was observed with NADP.

The effect of several sulphydryl-characterizing reagents on the monkey brain enzyme was determined. Tetraethylthiuram disulfide and p-chloromercuribenzoate produced 50% inhibition at approximately $5 \times 10^{-3}$ M while the enzyme was much less sensitive to $\gamma$-(p-arsenosophenyl)-n-butyrate.

This study provides direct evidence for the oxidation of aldehydes arising from biologically active amines in the brain. Brain aldehyde dehydrogenase may also be important in oxidizing toxic aldehydes derived from exogenous sources, e.g. acetaldehyde from ethanol.

It is known that a number of aldehydes occur in brain tissue. Blaschko, Richter, and Schlossmann (1) and Pugh and Quastel (2) first presented evidence that aldehydes arise in brain tissue by the oxidative deamination of monoamines. Since these early investigations, the presence of monoamine oxidase in brain has been well established (3) as is the production of aldehydes from amines by the enzyme (4-8). This information, coupled with the finding that the corresponding acids are produced from amines by isolated brain tissue (9, 10), shows by inference that the brain normally contains small amounts of various aldehydes and the enzymes necessary to oxidize these aldehydes to the corresponding acids. Brady and Koval (11) and Hoshishima, Vignais, and Zabin (12) have reported that palmitic aldehyde can arise in brain tissue from the reduction of palmitoyl coenzyme A, as a result of the action of a reversible nicotinamide adenine dinucleotide phosphate-linked aldehyde dehydrogenase.

Further, acetaldehyde has been found in brain tissue following ethanol administration (13).

It has been shown that succinic semialdehyde is a product of $\gamma$-aminobutyric acid metabolism in the brain (14). Albers and Salvador (15), Albers and Koval (16), and Pitts and Robins (17) have shown that this aldehyde is oxidized in the brain by a specific NAD-dependent succinic semialdehyde dehydrogenase.

The pathways involved in the oxidation of aldehydes have been studied in some tissues (18-21). Ridge (22) has presented indirect evidence that acetaldehyde is oxidized by brain tissue. Also, Brady, Formica, and Koval (23) have noted that palmitic aldehyde is oxidized by NAD and NADP in rat brain preparations. Lovenberg, Levine, and Sjoerdsmma (24) presented indirect evidence for the existence of aldehyde dehydrogenase in a number of tissues. Deitrich (25) found that a number of tissues including rat brain can oxidize indole-3-acetaldehyde. However, the enzyme systems in brain that catalyze aldehyde oxidation have not been well characterized as to the distribution in various areas, subcellular localization, substrate and cofactor specificities, or the nature of inhibitors. Therefore, this study was directed toward elucidation of some of these aspects.

Methods

Water used was deionized and double distilled in quartz. All reagents were of high quality. Aldehydes were distilled under nitrogen at atmospheric pressure whenever possible. The preparation and extraction of 3,4-dihydroxyphenylacetalde-

* Supported by the National Institute of Neurological Diseases and Blindness Grant NB-04551.

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Succinic semialdehyde was prepared from diethylformylsucinate (kindly supplied by Dr. Albers\(^2\)), by a modification of the method of Deitrich, Helleman, and Wein (26). The method of Slater and Bonner (33) and imidazooamine oxidase of Health, Bethesda, Maryland.

12,000 X

eactivity was assayed by the method of Weissbach and figures. Monkey brains were obtained frozen from Asiatic Imports, Inc., San Francisco, California.

The aldehyde-oxidizing activity of the various preparations was determined in duplicate by measuring the amount of indole-3-acetic acid formed in 10 min at 300 with indole-3-acetaldehyde. The indole-3-acetic acid formed was determined in duplicate by measuring the amount of indole-3-acetaldehyde and figures. Monkey brains were obtained frozen from Asiatic Imports, Inc., San Francisco, California.

The aldehyde-oxidizing activity of the various preparations was determined in duplicate by measuring the amount of indole-3-acetic acid formed in 10 min at 30\(^\circ\) with indole-3-acetaldehyde or its sodium bisulfite compound as the substrate in the presence of NAD and tissue. The indole-3-acetic acid formed was determined by a modification of the fluorometric method of Weissbach et al. (32) and is described in greater detail elsewhere.\(^1\)

Assay conditions are described in the respective tables and figures. Recovery of added indole-3-acetic acid from reaction mixtures was approximately 90\%. Unless otherwise indicated, protein was determined by the biuret method with bovine serum albumin as the standard.

Succinate dehydrogenase activity was measured spectrophoto-
metrictochemically or fluorometrically. Spectrophotometric measurements were made with a Gilford model 2000 attachment for the Beckman DU monochromator. Fluorometric determinations of the rate of NADH formation were performed with a Turner model 110 fluorometer with primary and secondary filters No. 7-60 and No. 8, respectively. The increase in fluorescence was determined at 1-min intervals for 5 min. The increase in the 1st min was used as the initial rate. The fluorescence of NADH was linear with concentration and the minimum quantity that could be determined was 0.2 mpmole. The authenticity of NADH was checked by a complete disappearance of fluorescence (measured as above) and absorbance at 340 m\(\nu\) upon adjusting the pH of the system to 1.0 or by addition of crystalline horse liver alcohol dehydrogenase (Sigma) to the reaction mixture.

**RESULTS**

**Localization**—Aldehyde-oxidizing activity was present in all areas of bovine brain studied. The specific activity with indole-3-acetaldelyde bisulfite and NAD ranged from a low of 1.8 in the cerebellum to a high of 4.9 in the caudate nucleus (Table 1).

Table II shows the aldehyde-oxidizing activity in various subcellular fractions of rat brain. The mitochondrial fraction contained 60% of the total activity, while 20% was found in the 20,000 X g supernatant fluid. These values fluctuate somewhat depending on individual techniques used in isolation of the mitochondria. The percentage recovery of aldehyde-oxidating activity in the mitochondrial fraction, the hyposmotically shocked mitochondrial fraction, and the density gradient pellet
was similar to the percentage recovery of succinate dehydrogenase and monamine oxidase. Aldehyde-oxidizing activity was released from the mitochondrial fraction by freezing and thawing or by sonically treating this fraction. From these data it was concluded that a major portion of rat brain aldehyde-oxidizing activity is associated with the mitochondria. However, the possibility of a second enzyme localized in the 20,000 × g supernatant fluid cannot be ruled out.

The NAD requirement for aldehyde oxidation by aged or dialyzed rat brain homogenates was investigated. The aged homogenate was stimulated 3-fold by 1.2 mM NAD. The dialyzed homogenate, which possessed little activity in the absence of NAD, was stimulated 11-fold by addition of this coenzyme. These results suggest that the major aldehyde-oxidizing system of brain homogenates is an NAD-linked dehydrogenase. Addition of NADP instead of NAD to whole undialyzed homogenates resulted in some stimulation of indole-3-acetic acid production but this was not additive with the stimulation of activity afforded by NAD.

**Purification from Mitochondria**—Aldehyde-oxidizing activity was purified approximately 9-fold from the supernatant fraction of sonically treated bovine brain mitochondria by treatment with solid (NH₄)₂SO₄. The material precipitated by 0.5 to 0.8 saturation of (NH₄)₂SO₄ contained most of the enzymatic activity. A second experiment gave similar results but somewhat less purification. The best preparation obtained had an activity of 230 mmoles of indole-3-acetic acid formed per mg of protein in 10 min. (This represented a 191-fold increase over the whole bovine brain.) The preparations were free of NADH oxidase and alcohol dehydrogenase, and were NAD-dependent. NADP was ineffective as a cofactor for this system.

The activity of the enzyme was essentially linear with protein concentration. In addition, the reaction was stoichiometric with kynuramine according to the method of Weissbach and Bonner (33).

### Table I
**Distribution of aldehyde-oxidizing capacity in various areas of bovine brain**

<table>
<thead>
<tr>
<th>Area</th>
<th>Mean (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebellum</td>
<td>1.8 (1.4–2.1)</td>
</tr>
<tr>
<td>Cerebral cortex</td>
<td>3.5 (3.2–3.8)</td>
</tr>
<tr>
<td>Pons-medulla</td>
<td>3.8 (3.2–4.4)</td>
</tr>
<tr>
<td>Caudate nucleus</td>
<td>4.9 (4.4–5.5)</td>
</tr>
<tr>
<td>Thalamus</td>
<td>3.4 (3.1–3.8)</td>
</tr>
<tr>
<td>Lentiform nucleus</td>
<td>2.9 (2.4–3.4)</td>
</tr>
<tr>
<td>Midbrain-hypothalamus</td>
<td>3.2 (3.1–3.4)</td>
</tr>
<tr>
<td>Pineal gland</td>
<td>2.0</td>
</tr>
</tbody>
</table>

* Values represent millimicromoles of indole-3-acetic acid formed per 10 min per mg of protein.
* Head of the caudate nucleus.
* Medial nuclei of the thalamus.
* Includes internal capsule and lateral thalamic nuclei along with globus pallidus and putamen.

### Table II
**Subcellular localization of aldehyde-oxidizing activity of rat brain**

The mitochondrial fraction was hypsosmotically shocked with distilled water to rupture the nerve ending particles as described by De Robertis et al. (30), or was centrifuged through a discontinuous sucrose gradient as described by Whittaker et al. (31) consisting of 1-nil layers of 1.4 M, 1.2 M, 1.0 M, and 0.8 M sucrose in tubes for the SW-39 rotor of a Spinco model L centrifuge. The tubes were centrifuged at 100,000 × g for 45 min. After centrifugation each fraction was removed by suction and resuspended in water to the original volume of mitochondrial suspension. This table is a composite of nine separate experiments.

| Fraction           | Aldehyde-oxidizing activity | Recovery
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mg protein x brain</td>
<td>%</td>
</tr>
<tr>
<td>Homogenate</td>
<td>1.45</td>
<td>194</td>
</tr>
<tr>
<td>Supernatant, 20,000</td>
<td>× g for 20 min</td>
<td>0.80</td>
</tr>
<tr>
<td>Mitochondria</td>
<td>3.04</td>
<td>118</td>
</tr>
<tr>
<td>Mitochondria (hyperosmotic)</td>
<td>4.00</td>
<td>103</td>
</tr>
<tr>
<td>Density gradient</td>
<td>supernatant</td>
<td>7.30</td>
</tr>
<tr>
<td></td>
<td>pellet, 1.4 M sucrose</td>
<td></td>
</tr>
</tbody>
</table>

* Aldehyde-oxidizing activity was determined as described in Table I and is given as millimicromoles of indole-3-acetic acid formed per 10 min per mg of protein or per g of brain, wet weight.
* Succinate dehydrogenase activity was measured spectrophotometrically with K₃[Fe(CN)₆] according to the method of Slater and Bonner (32).
* Monoamine oxidase activity was measured spectrophotometrically with kynuramine according to the method of Weissbach et al. (34).

The apparent optimal pH for the reaction was 10; however, the decrease in enzyme activity above pH 10 was not reversed by adjusting the pH to 9.0. At pH 10 irreversible denaturation occurs, necessitating a rapid determination of initial rates. At pH 9.6 the reaction rate was linear for several minutes. As a result, subsequent experiments with the partially purified enzyme system were performed at pH 9.6.

Results presented in Table III show that aldehyde dehydrogenase from bovine brain mitochondria is nonspecific and oxidizes a number of aliphatic aldehydes ranging from formaldehyde to pimelic aldehyde. Also, glycolaldehyde and betaine aldehyde as well as aldehydes derived from the biologically active amines, namely 5-hydroxindole-3-acetaldehyde, 3,4-dihydroxyphenylglycolaldehyde, and 3,4-dihydroxyphenylacetaldehyde were oxidized by this enzyme system. The Michaelis constants for the various aldehydes are exceptionally low. If, indeed, the enzyme behaves in vivo as it does in vitro, these results could explain the inability to detect these aldehydes in normal brain tissue. This preparation also catalyzes the oxidation of succinic semialdehyde. However, the rates of oxidation

* Downloaded from http://www.jbc.org/
The rate of the reaction was determined by dehydrogenase purified from bovine brain mitochondria, see Table IV and the text.

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Km (M)</th>
<th>Vmax (mnmoles/min/mg protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formaldehyde</td>
<td>7.0 x 10^-3</td>
<td>218</td>
</tr>
<tr>
<td>Acetaldehyde</td>
<td>3 x 10^-2</td>
<td>192 and 132</td>
</tr>
<tr>
<td>Propionaldehyde</td>
<td>2.0 x 10^-7</td>
<td>182</td>
</tr>
<tr>
<td>Butyraldehyde</td>
<td>2.3 x 10^-7</td>
<td>166</td>
</tr>
<tr>
<td>Isobutyraldehyde-NaHSO₃</td>
<td>1.6 x 10^-7</td>
<td>130</td>
</tr>
<tr>
<td>Heptaldehyde</td>
<td>3.5 x 10^-10</td>
<td>200</td>
</tr>
<tr>
<td>Decylaldehyde</td>
<td>1.3 x 10^-3</td>
<td>357</td>
</tr>
<tr>
<td>Palmitic aldehyde-NaHSO₃</td>
<td>1.3 x 10^-4</td>
<td>122</td>
</tr>
<tr>
<td>Glycolaldehyde</td>
<td>1.1 x 10^-2</td>
<td>296</td>
</tr>
<tr>
<td>Trimethylacetaldehyde</td>
<td>2.0 x 10^-3</td>
<td>123</td>
</tr>
<tr>
<td>Monochloroacetaldehyde</td>
<td>6.0 x 10^-6</td>
<td>385</td>
</tr>
<tr>
<td>Phenylacetaldehyde</td>
<td>4.0 x 10^-7</td>
<td>294</td>
</tr>
<tr>
<td>5-Hydroxyindoleacetaldehyde</td>
<td>2.5 x 10^-6</td>
<td>84</td>
</tr>
<tr>
<td>3,4-Dihydroxyphenylacetaldehyde</td>
<td>1.0 x 10^-5</td>
<td>150</td>
</tr>
<tr>
<td>3,4-Dihydroxyphenylglycolaldehyde</td>
<td>3.0 x 10^-4</td>
<td>101</td>
</tr>
<tr>
<td>Betaine aldehyde</td>
<td>2.0 x 10^-5</td>
<td>77</td>
</tr>
<tr>
<td>Succinic semialdehyde*</td>
<td>2.0 x 10^-5</td>
<td>161</td>
</tr>
</tbody>
</table>

*Although this preparation does catalyze the oxidation of succinic semialdehyde, see Table IV and the text.

Assay for indole-3-acetic acid formation was performed as described in the text and Table I. NADH formation was measured spectrophotometrically at 30°C at 340 nm with either 0.5 mM acetaldehyde or 0.5 mM succinic semialdehyde as substrate. The aldehydes were added to quartz cuvettes containing a final concentration of 10 mM sodium pyrophosphate buffer, pH 9.6; 1 mM NAD; and sufficient water to give 1 ml. Protein concentration of the DEAE-cellulose fraction was determined by the method of Murphy and Kies (36).

<table>
<thead>
<tr>
<th>Fraction</th>
<th>Specific activity</th>
<th>Yield</th>
<th>Amount of NADH formed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homogenate</td>
<td>0.61</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Supernatant</td>
<td>2.97</td>
<td>79</td>
<td></td>
</tr>
<tr>
<td>(NH₄)₂SO₄ (0.4-0.6 saturation)</td>
<td>6.75</td>
<td>53</td>
<td>2.7  4.9</td>
</tr>
<tr>
<td>DEAE-cellulose</td>
<td>68.86</td>
<td>59</td>
<td>31</td>
</tr>
</tbody>
</table>

Table IV

Purification of NAD-dependent aldehyde dehydrogenase from frozen bovine brain

Comparison of Enzyme Preparations—Several experiments were undertaken in order to determine whether or not the enzyme purified from brain mitochondria was the same as that purified from frozen and thawed brain. These experiments also serve to define further the enzymatic properties of the preparations. Fig. 2 is a plot of the log of the ratio of the maximal velocity with various substrates compared to the maximal velocity with propionaldehyde (taken as 100) as a function of the Taft sigma values (40) for the corresponding substituent groups. The higher the sigma values, the greater the electron withdrawal from the carbonyl carbon atom. It can be seen that the relative velocities obtained with the mitochondrial enzyme are virtually identical with those obtained with the use of the enzyme from...
Fig. 2. Illustration of the maximal rate of oxidation of various aliphatic aldehydes as correlated with the Taft sigma values (σ*). Rates are calculated as a percentage of the maximal rate obtained with propionaldehyde and plotted as a log versus Taft's σ* values (40). (■), aldehyde dehydrogenase purified from bovine brain mitochondria; the rate of NADH formation was measured fluorometrically. (○), aldehyde dehydrogenase purified from frozen-thawed bovine brain supernatant fluid; the rate of formation of NADH was measured spectrophotometrically.

**Table V**

**Cofactor specificity of bovine brain aldehyde dehydrogenase**

Rates were measured spectrophotometrically as described in the text. Acetaldehyde, final concentration of 1 mM, was added to quartz cuvettes containing a final concentration of 10 mM sodium pyrophosphate buffer, pH 9.6; various concentrations of NAD or NAD analogues; enzyme and water to give 1 ml. Molar extinction coefficients and (λ) used for NAD, deamino-NAD, and 3-acetylpyridine-NAD were 6220 (340 mμ), 6220 (340 mμ), and 9100 (363 mμ), respectively.

<table>
<thead>
<tr>
<th>NAD analogue</th>
<th>From frozen brain</th>
<th>From mitochondria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>K&lt;sub&gt;m&lt;/sub&gt;</td>
<td>V&lt;sub&gt;max&lt;/sub&gt;</td>
</tr>
<tr>
<td>NADP</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>NAD</td>
<td>1 × 10&lt;sup&gt;-3&lt;/sup&gt;</td>
<td>32</td>
</tr>
<tr>
<td>Deamino-NAD</td>
<td>3 × 10&lt;sup&gt;-4&lt;/sup&gt;</td>
<td>23</td>
</tr>
<tr>
<td>3-Acetylpyridine-NAD</td>
<td>1 × 10&lt;sup&gt;-4&lt;/sup&gt;</td>
<td>32</td>
</tr>
</tbody>
</table>

a Aldehyde dehydrogenase was purified by the methods described in the text and Table IV.
b Expressed as millimicromoles of NADH or NADH analogue formed per min per mg of protein.

differ to any significant degree for the two enzyme preparations. Since the two enzyme preparations are purified by different procedures, it is likely that different contaminating proteins are present. This might serve to explain the differences noted between the two preparations as shown in Table V.

**Effect of Inhibitors**—Table VI gives the concentration of several compounds which inhibit aldehyde dehydrogenase iso-
lated from frozen and thawed monkey brain. The sulfhydryl-characterizing reagents, p-chloromercuribenzoate and \( \gamma \)-(p-arsenophenyl)-n-butyrate, produced 50\% inhibition at 6 \times 10^{-4} \text{M} \) and 1 \times 10^{-4} \text{M}, respectively. These results suggest that sulfhydryl groups are important for the activity of the enzyme. Tetraethylthiuram disulfide and chloral hydrate produced a 50\% inhibition at 5 \times 10^{-4} \text{M}.

**DISCUSSION**

The aldehyde-oxidizing activity of brain tissue observed, at least 1 \text{mumole} per hour per g of tissue, wet weight, is in great excess of the amount required to oxidize the aldehydes derived from the biologically active amines in normal brain tissue. Specter, Melmon, and Sjoerdsma (41) and Udenfriend and Weissbach (42) have estimated that the half-life of norepinephrine in the rat is approximately 1 to 2 hours while the half-life of 5-hydroxytryptamine is less than 1 hour. The normal levels of these amines are 3 to 4 \text{mumoles} per g of brain, wet weight (43). Thus, a maximum of 1 to 2 \text{mumoles} of the aldehydes from these amines normally would be formed per hour per g of brain. The above data indicate that under optimal conditions, brain tissue has the capacity to metabolize aldehydes derived from exogenous sources as well as those arising endogenously. Other factors such as compartmentalization of the aldehydes may be important, but no information is currently available.

A number of compounds, thought to inhibit aldehyde dehydrogenase in vivo (see references in Reference 38), cause a marked increase in blood acetaldehyde concentration after ethanol administration. Under these conditions, brain aldehyde dehydrogenase may be inhibited by such compounds and could thus be saturated with acetaldehyde; hence, the rate of oxidation of aldehydes derived from the biologically active amines would be much lower. It is possible that aldehydes derived from these amines are involved in the physiological response to aldehyde dehydrogenase inhibitors.

The ability of the various regions of the brain to oxidize aldehydes is in keeping with the observations of Weiner (44) and Bogdanski, Weissbach, and Udenfriend (45) that monoamine oxidase is present in all areas of the brain. One would expect aldehyde-oxidizing activity to have a distribution similar to monoamine oxidase; otherwise, oxidative deamination of amines would result in the accumulation of aldehydes which are known to inhibit various metabolic processes (46, 47).

A major portion of the aldehyde-oxidizing activity was associated with the mitochondrial fraction, while the 20,000 \( \times g \) supernatant fluid contained a substantial amount of the total activity. The possibility that more than one enzyme is present has been considered. After homogenization of frozen and thawed bovine brain, all of the activity in the 30,000 \( \times g \) supernatant fluid indicating that the mitochondrial enzyme was released by this procedure. If more than one enzyme is present in the 30,000 \( \times g \) supernatant fluid and these enzymes are purified together, one might expect this preparation to have different kinetic properties from the bovine brain mitochondrial enzyme preparation. However, these values for the enzyme systems were similar, suggesting that the same enzyme system was purified from both sources. The question of the presence of a separate enzyme in the soluble portion of brain homogenates is unanswered by these experiments.

The data obtained with various aldehydes indicate that the maximal velocity of the enzyme reaction is related to the elec-
tropositive nature of the carbonyl carbon atom. Greater rates are obtained as this carbon atom becomes more positive. This concept is in agreement with the results of Deitrich, Hellerman, and Wein (26) with respect to the correlation of the rates of oxidation of substituted benzaldehydes with Hammett's sigma values. Several other investigators have made use of Hammett's equation as applied to enzymatic reactions (48, 49). The investigation of d-amino acid oxidase by Neims, De Luca, and Hellerman (49) is of particular interest because of the very large effect noted as the electronic nature of the carbon atom was altered. The present study shows that the Taft equation may be useful for this type of correlation.

The fact that succinic semialdehyde was not oxidized by the enzyme preparations purified by DEAE-cellulose column chromatography indicates that aldehyde dehydrogenase is distinct from succinic semialdehyde dehydrogenase. The presence of succinic semialdehyde dehydrogenase activity in the 9-fold purified preparation from bovine brain mitochondria is in keeping with the results obtained by Salganicoff and De Robertis (50). These investigators found that succinic semialdehyde dehydrogenase is a mitochondrial enzyme which is easily solubilized by various mechanical procedures. Other workers have found succinic semialdehyde dehydrogenase to be virtually specific for succinic semialdehyde (16, 17).

The relationship between enzyme activity and pH is similar to that found for aldehyde dehydrogenase from bovine liver (18, 26). In addition, the broad substrate specificity is comparable to the bovine liver enzyme.

Recently, in a study of succinic semialdehyde dehydrogenase, Pitts and Quick (51) have found that small amounts (0.1 \mu g, dry weight) of brain do not catalyze the oxidation of several aldehydes by NAD. Calculation from our data show that such small amounts of tissue do not contain sufficient nonspecific aldehyde-oxidizing capacity to be measurable, even with the sensitive techniques used by these workers.

Previous reports of isolation of an aldehyde dehydrogenase from brain are those of Brady and Koval (11) and Brady et al. (23). These investigators observed the presence of a reversible NADP-linked palmitic aldehyde dehydrogenase in particles (presumably microsomes) from brain. Particles, sedimented between 20,000 and 100,000 \( \times g \), also contained an NADP-linked palmitic aldehyde dehydrogenase. The enzyme described in this report is certainly distinct from the NADP-linked enzyme described by Brady et al. but the relationship to the NAD-linked enzyme is not clear.

Although the enzyme from monkey brain is inhibited by a number of sulfhydryl-characterizing reagents, the preparation is relatively crude and as such may not reveal the full sensitivity of the preparation to these compounds.

**Acknowledgment**—The authors would like to thank Dr. Leslie Hellerman for his helpful criticism and suggestions in the preparation of the manuscript.

**REFERENCES**

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