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The Synthesis of Taurine from Sulfate
VIII. A Constitutive Enzyme in Mammals[1] (38387)

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Studies in this laboratory have shown the presence of an enzyme system in chick (1) and rat (2) tissues which catalyzes the synthesis of taurine from serine and 3′- phosphoadenosine-5′- phosphosulfate (PAPS). The activity of this enzyme was shown to respond *in vitro* to intermediates of the transsulfuration pathway (3). The enzyme retains activity *in vivo* during a vitamin B_6 deficiency in the rat while the B_6-dependent hepatic cysteine sulfinic/cysteic acid (CSA/CA) decarboxylase activity is significantly reduced (4).

Since taurine is known to be present in high concentration in most animal tissues, and since certain metabolic conditions reduce its biosynthesis by transsulfuration, the presence of an alternate biosynthetic mechanism in animal tissues is beneficial (2). In the review by Jacobsen and Smith (5), it was stated that the incorporation of inorganic sulfate into taurine apparently is not a quantitatively significant means of synthesis in mammals. Since taurine appears to play a significant role in mammalian metabolism, especially in irritable cells such as muscle and nerve, a survey of mammalian genera was made to measure the activity of this enzyme system. The enzyme activity is a PAPS-sulfotransferase and is hereafter referred to as P_1.

Materials and Methods. Two strains of laboratory rats were tested for P_1 activity and found to be similar. Thereafter, rats were obtained from a colony maintained by the Agricultural Biochemistry faculty at W.V.U. or from Hilltop Laboratory Animals, Scottdale, Pa. Several tissues were sampled from rats and from sheep so that a ruminant–nonruminant comparison could be made. The P_1 activity was measured in the heart and liver only in the other animals, which included chick, cat, dog, guinea pig, hamster, monkey, mouse and rabbit.

These animals were sacrificed at varying dates during 1973 and 1974 and consequently different $PAP^{35}S$ preparations were used. So that these data may be comparative, the specific activity of each $PAP^{35}S$ preparation was determined from an aliquot after ion-exchange chromatography (6), and the PAPS concentration determined from a standard ATP curve at 259 nm. The specific activity of each $PAP^{35}S$ preparation varied due to the enzyme source, the $^{35}SO_4$ concentration, the ion-exchange column size, and the eluate volume collected for the PAPS peak. The PAPS concentration ranged from 8–40 μmoles/ml and the $PAP^{35}S$ spec act from 3000–70000 cpm/μg.

The enzyme assay was performed and the P_1 enzyme system was prepared from each source as previously described (1). The $PAP^{35}S$ was enzymatically synthesized and purified as reported earlier (7), and protein quantitated by the method of Lowry *et al.* (8).

Results. These data indicate that taurine biosynthesis from PAPS is uniformly distributed among a variety of mammalian species as well as the organs within each animal tested. Thus, P_1 may be a constitutive enzyme of animal cells since sulfate and taurine appear to be normal constituents of animal cells.

In Table I, the P_1 activity of heart and liver is shown in a number of mammals of different genera. In most instances the P_1 activity of liver and heart was similar and no trend of P_1 activity was observed between these tissues.

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TABLE I. The PAPS-Sulfotransferase (P_1) Activity of Heart and Liver of Mammals.

Animal	No. sampled	PAP^{35}S Spec act[b]	P_1 activity[a] Heart	Liver
Cat	2	37506	1802	1182
Chick	12	3194	1840	1314
Dog	2	2472	1517	2253
Guinea pig	3	2472	1672	1855
Hamster	3	5687	(c)	1567
Monkey	1	70512	1797	1535
Mouse	3	70512	(c)	1871
Rabbit	2	37506	1599	1857
Rat	6	2640	1021	1536
Sheep	12	70512	1244	1649

[a] Corrected spec act, due to different lots of PAP^{35}S, is the taurine -^{35}S formed/μg protein then multiplied by a factor equating that PAP^{35}S spec act to the highest, 70512.

[b] PAP^{35}S spec act was variable due to different preparations.

[c] Not determined.

In Table II, the P_1 activity of several tissues from a nonruminant animal and a ruminant animal is shown. In each tissue, the P_1 activity from the sheep was higher than that from the rat. Prior to slaughter, these sheep were grazing and were not supplemented with any other nutrients. The rats were fed a normal laboratory animal chow.

Discussion. The P_1 activity of the heart and liver from the animals tested (Table I) was similar, ranging from 1021 to 2253 cpm taurine-^{35}S formed/μg protein. No trend of activity between these two tissues was evident, in some instances heart activity was higher than liver (cat) and the reverse observed in the dog. Of significance, however, is the presence of the enzyme in each tissue tested.

The P_1 activity of the cat was similar to the other animals tested. It has been reported that cats do not have a requirement for sulfur amino acids (9), in which case the synthesis of taurine from sulfate would make a significant contribution to the tissue taurine. Cat liver contains high concentrations of taurine even though CSA/CA decarboxylase activity is limited (10). Horse tissue, not available for this study, should be assayed for P_1 activity since cat, horse, and man apparently lack the enzymes necessary for producing taurine from cysteine in the liver (5).

Sheep, which are herbivorous animals, excrete mainly glycine-conjugated bile acids and ingest no dietary taurine. Yet, the taurine concentration in sheep tissues is substantial (11), indicating *de novo* synthesis. Since the CSA/CA decarboxylase activity appears to be low in cow and calf liver (12), the P_1 activity may make a significant contribution to the tissue taurine. The P_1 activity of sheep tissues was higher in each tissue tested than for the rat (Table II). Regardless of diet or anatomical differences, this enzyme appears to be a component of all animal tissues.

It appears, therefore that this enzyme system which produces taurine from PAPS and serine may be a constitutive enzyme of animal cells. Since taurine appears in relatively high concentration in all animal cells and most organs lack the necessary enzymes for biosynthesis from cysteine (5), each cell would depend on absorption of taurine or its acidic precursor from plasma. Should a tissue lose its CSA/CA decarboxylase activity or become unable to actively absorb taurine, this alternate sulfotransferase (P_1) activity may make a significant contribution toward maintaining the cellular taurine concentration.

Summary. The enzyme system catalyzing the synthesis of taurine from sulfate and serine was assayed from a number of tissues of mammalian genera. This enzyme was present in the liver and heart of the cat, chick, dog, guinea pig, hamster, monkey, mouse, rabbit, rat, and sheep. The activity was higher in sheep liver, brain, heart, intestine, and kidney than in those tissues of rats. These data indicate that this mechanism for taurine biosynthesis is a constitutive animal enzyme which may be of significance when the transsulfuration pathway of taurine synthesis is impaired, or absent.

TABLE II. PAP ^{35}S-Sulfotransferase (P_1) Activity in Tissues from a Nonruminant (Rat) and a Ruminant (Sheep) Animal.[a]

Tissues	Rat[b]	Sheep[c]
Liver	1536	1649
Brain	1004	1376
Heart	1021	1244
Intestine	523	1656
Rumen epithelium	—	1444
Kidney	1163	1803

[a] P_1 spec act — Corrected as in Table I.

[b] Average of duplicate determinations from six animals.

[c] Average of duplicate determinations from 12 animals.

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