The Synthesis of Taurine from Sulfate
IV. An Alternate Pathway for Taurine Synthesis by the Rat[1] (36839)

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The synthesis of taurine from cysteine by mammals is well documented, as in the synthesis of taurine from sulfate by the bird. It has been stated that the incorporation of inorganic sulfate into taurine is not a quantitatively significant means of taurine synthesis by the mammal (1). Yet, the enzyme system catalyzing the synthesis of taurine from L-serine and 3′-phosphoadenosine-5′-phosphosulfate (PAPS), recently demonstrated in chick liver (2), is also present in rat liver. This paper presents evidence for the *de novo* synthesis of taurine from L-serine and PAPS by the rat, a reaction which may be of significance under certain physiological conditions.

Materials and Methods. The rats used in these experiments were young males from an inbred colony maintained by the Agricultural Biochemistry faculty at WVU. This colony originated from Rockland albino rats in 1958.

The experimental animals weighed approximately 125 g initially and were fed a purified ration composed of (%): isolated soybean protein, 20; Wesson oil, 3; D-methionine, 0.3; complete vitamin premix, 4; complete mineral premix, 6; and glucose hydrate (Cerelose) to 100.

The data reported herein were obtained in two separate experiments. In the first, six rats were sacrificed after 7, 14, and 21 days on the experimental diet. On the day of sacrifice, each rat was given 20 μCi $^{35}SO_4^{2-}$ by stomach tube and the rats were sacrificed 6 hr after the isotopic dose. *In vivo* and *in vitro* taurine formation from sulfate were determined in this experiment. In the next experiment, livers were obtained from rats which had been fed the purified diet for 21 days, pooled, and the *in vitro* synthesis of taurine from serine and PAPS was determined and compared to that from chick liver.

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TABLE I. Rat Liver Total Taurine and Taurine Specific Activity.[a]

On diet (days)	Total taurine[b]	Taurine sp act[c]
7	103 ± 7.06[d]	1.43 ± 0.20
14	145 ± 16.09	1.66 ± 0.30
21	102 ± 7.67	1.93 ± 0.26

[a] Rats were sacrificed 6 hr after administration of $^{35}SO_4$ (20 μCi).
[b] Total taurine = μg taurine/g liver.
[c] Taurine sp act = cpm ^{35}S-taurine/μg taurine.
[d] Each value is the mean and the standard deviation of the mean of 6 rats.

The rats were sacrificed by stunning and bleeding, and the liver was excised and chilled. The liver homogenate, enzyme purification, and enzyme assays were identical to those previously described for the chick liver enzymes (2). The PAP^{35}S was prepared with chick liver enzymes as previously described (3). Protein was determined by the method of Lowry *et al.* (4), taurine by the method of Pentz *et al.* (5) and keto-acids by the method of Sayre and Greenberg (6).

Results. The results given in Table I indicate that rats have the enzymatic capability to synthesize taurine from sulfate. The diet furnished adequate quantities of sulfur amino acids, especially methionine. In 14-day-old chicks, supplemental methionine increased the specific activity of liver taurine from sulfate-^{35}S approximately 5-fold (7). Sanchez and Swendseid (8) reported significantly increased serine dehydrase activity in the livers of rats forcefed diets of increasing methionine levels. Should rat liver catalyze the synthesis of taurine from sulfate as do the chick liver enzymes (2), then the response to methionine would be due to the enhanced serine

TABLE II. Rat Liver PAPS-Sulfotransferase and L-Serine Dehydrase Activities.

On diet (days)	Transferase[a]	L-Serine dehydrase[b]
7	556	0.400
14	748	0.503
21	681	0.441

[a] PAPS-transferase activity = cpm ^{35}S-PAPS incorporated into ^{35}S-taurine/μg protein.

[b] L-Serine dehydrase activity = μmoles pyruvate formed/μg protein.

dehydrase activity. The specific activity of rat liver taurine did increase with time on this diet (Table I).

The *in vitro* synthesis of taurine from sulfate (PAP^{35}S) was also demonstrated with the enzymatic fraction from rat liver (Table II). The rat liver fraction isolated by the same procedure as previously described for chick liver (2) catalyzed the dehydration of L-serine and the transfer of the sulfate moiety of PAP^{35}S. The specific activity of PAP^{35}S-sulfotransferase from the liver of a 14-day-old chick was 19.8 cpm taurine-^{35}S formed/μg protein/5 min reaction, and from the liver of a 100 g male rat was 21.0. The PAPS-transferase activity of chick liver was observed to increase with fasting and this activity in rat liver increased from 5.08 to 7.13 when rats were fasted for 24 hr.

The concentration of PAPS in the *in vitro* reaction was the main factor determining the fate of the serine molecule. With increased PAPS, serine was converted into taurine with decreasing quantities of pyruvate formed by the chick liver system (2). Parallel studies with the rat liver system were made (Table III) and with increasing amounts of PAPS

TABLE III. Comparison of the PAP^{35}S-Sulfotransferase Activity[a] in Chick and Rat Liver as Affected by Concentration of PAP^{35}S.

PAP^{35}S concn[b]	Chick	Rat
0.1	15.8	20.1
0.3	51.3	85.0
0.5	96.2	150.7

[a] ^{35}S-Taurine formed (cpm/μg protein/5 min).

[b] PAP^{35}S vol/reaction mixture. This PAPS prepn contained 55,160 cpm/ml.

the increase in taurine specific activity was linear. The rat liver system was more active than the chick liver system.

It appears that the significance of this alternate pathway of taurine synthesis in the mammal may be its regulation by the tissue concentrations of sulfur amino acids. The availability of the substrates for this reaction, PAPS and serine (in its dehydrated form), has been directly linked to cysteine and methionine. Cysteine, when fed in higher levels to birds, depresses the level of taurine in the liver and minimizes the specific activity from sulfate-^{35}S (7).

The repression of this pathway by cysteine may be due to the effect of this compound on ATP-sulfurylase, the first enzyme required for the synthesis of PAPS (9). The increase in taurine due to the supplemental methionine did not enhance the production of PAPS in chick liver (10), thus it appeared to impose its effect by increasing the availability of the sulfo-acceptor, dehydrated serine.

Summary. The rat is capable of synthesizing taurine from sulfate. The enzymatic pathway appears to be similar to that in chick liver which utilizes L-serine and activated sulfate (PAPS). The enzymes which catalyze this reaction sequence appear to be the same as those for the chick liver system, serine dehydrase, PAPS-sulfotransferase, and cysteic acid decarboxylase.

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