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Dietary regulation of hepatic enzymes in taurine biosynthesis in rats

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The effect of various dietary fibers, cholesterol, and bile acid on tissue taurine levels and the activity of hepatic enzymes in the taurine synthetic pathway was compared in rats. Compared with water-insoluble dietary fibers (10% in the diet, cellulose, and chitin), water-soluble dietary fibers (10% in the diet, pectin, and konjak mannan) decreased taurine levels in the liver and serum. A diet containing cholesterol (1%), sodium cholate (0.25%), and both of these steroids also reduced taurine levels in the liver and serum accompanying the decrease in urinary excretion of this compound. Cysteine dioxygenase activity was significantly lower in rats fed water-soluble fibers than in those fed water-insoluble fibers. Compared to water-insoluble dietary fibers, water-soluble fibers increased cysteinesulfinic acid decarboxylase activity. Compared with the steroid-free control diet, diets containing cholesterol, bile acid, and both of these steroids reduced cysteine dioxygenase activity. Dietary bile acid also reduced cysteinesulfinic acid decarboxylase activity, in contrast with cholesterol which increased it. Decarboxylase activity in rats fed a diet containing both of these steroids was comparable to that in animals fed a control diet. Aspartate aminotransferase activity was also modified by these dietary factors in some cases, but to a lesser extent. Fiber and steroids thus are dietary factors that demonstrably alter hepatic taurine synthesis in the rat. (J. Nutr. Biochem. 9:99–105, 1998) © *Elsevier Science Inc. 1998*

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Introduction

It has been demonstrated that tissue taurine concentration and the activity of enzymes involved in taurine synthesis in the liver, the major site of taurine synthesis, is easily modified by the sulfur amino acid nutritional status of rats.[1–9] Information on other dietary factors affecting hepatic enzyme activity in taurine synthesis, however, is scarce. We demonstrated previously[8,10–13] that diets containing water-soluble dietary fibers, when compared with those containing water-insoluble fibers or a fiber-free diet, decreased taurine concentration in the liver accompanying the increase in the bile acid glycine to taurine ratio. Water-soluble fiber increases biliary bile acid excretion[8,10–13] and hepatic cholesterol 7α-hydroxylase (EC 1.14.13.17) activity,[12] a rate-limiting enzyme in bile acid synthesis, so it is plausible that water-soluble dietary fiber increases the availability of bile acid for conjugation with taurine and thus decreases hepatic taurine concentration.[8,10–13] The observation that dietary cholesterol[10,13] and bile acid[13] elicited a decrease in hepatic taurine concentration accompanying an increase in the bile acid glycine to taurine ratio supports this consideration.

We found, however, that water-soluble dietary fiber decreased the activity of cysteine dioxygenase, an enzyme involved in the taurine synthetic pathway, and urinary taurine excretion.[12] This observation raises the possibility that water-soluble dietary fiber decreases hepatic taurine synthesis, and consequently lowers hepatic taurine concentration. The effect of water-soluble fiber on the activity of enzymes other than cysteine dioxygenase that are involved in the taurine synthetic pathway, however, remains to be studied. Information on the effects of dietary cholesterol and bile acid on the activity of enzymes in taurine biosynthesis is also scarce and, in this context, we studied the effects of dietary fiber, cholesterol, and bile acid on hepatic enzyme activity in taurine biosynthesis in the rat.

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Methods and materials

Animals and diets

Male Wistar rats obtained from a commercial breeder (Imamichi Institute of Animal Reproduction, Ibaraki, Japan) at 4 weeks of age were used in the present study. Animals were housed individually in stainless steel mesh cages in a room with controlled temperature (20 to 22°C), humidity (55 to 65%), and lighting (lights on from 0700 to 1900 hr), and fed a commercial nonpurified diet (Type NMF; Oriental Yeast, Tokyo, Japan). We followed the guide of our institute in the care and use of laboratory animals. In the first experiment (Experiment 1), after 5 days of acclimatization to housing conditions, rats were randomly divided into four groups of seven animals each and fed purified diets containing either 10% cellulose, chitin, citrus pectin, or konjak mannan for 22 days. In the second experiment (Experiment 2), four groups of seven rats each were fed one of the purified 5% cellulose diets containing 1% cholesterol, 0.25% sodium cholate, both 1% cholesterol and 0.25% sodium cholate or free of these steroids (controls) for 26 days. In Experiment 2, at 17 days in the feeding period, animals were transferred to metabolic cages and urine was collected for 2 days to measure taurine excretion. Animals were then again transferred to the usual stainless mesh cages for the rest of the experimental period. Body weight at the start of these experiments was 115 to 138 g for Experiment 1 and 89 to 103 g for Experiment 2. The basal composition of the experimental diet was (in weight %): casein, 20; corn oil, 5; corn starch, 15; mineral mixture,[14] 3.5; vitamin mixture,[14] 1.0, choline bitartrate, 0.2, and sucrose to 100. Dietary fibers and steroids were added to experimental diets at the expense of sucrose. At experiment termination, rats were anesthetized with diethyl ether and killed by bleeding from the abdominal aorta.

Enzyme assays

The liver was homogenized in 7 volumes of 0.25 mol/L sucrose. Homogenates were centrifuged at 1000 × *g* for 10 min and supernatants recentrifuged at 8000 × *g* for 10 min. The 8000 × *g* supernatant fraction thus obtained was used as the enzyme source for the measurement of enzyme activity in sulfur amino acid metabolism. The activity of cystathionine synthase (EC 4.2.1.22)[15] and γ-glutamylcysteine synthetase (EC 6.3.2.2)[16] was assayed radiochemically. Two different assay conditions, one NAD-dependent and the other NAD-independent, were used to measure cysteine dioxygenase (EC 1.13.11.20) activity as described by Yamaguchi and Hosokawa.[17] Incubation mixture for the NAD-dependent assay contained 10 mmol/L cysteine, 4 mmol/L NAD, 0.5 mmol/L $Fe_2(NH_4)(SO_4)_2$, 10 mmol/L hydroxylamine, and 2.0 to 3.0 mg of enzyme protein in 100 mmol/L potassium phosphate buffer (pH 6.8) in a final volume of 2 mL. NAD-independent assay (final volume 1 mL) was conducted in the presence of 10 mmol/L cysteine and 1.0 to 1.5 mg enzyme protein in 100 mmol/L glycine buffer (pH 9.0) after anaerobic activation as described previously.[12] Cysteine dioxygenase enzyme product, cysteinesulfinic acid, was purified using Dowex 50W-X8 column chromatography, reacted with o-phthalaldehyde, and determined by reversed-phase HPLC using a 4.6 × 150 mm Capsel Pack AG 120A C_{18} column (Shiseido Co., Tokyo, Japan) with a mobile phase of acetonitrile:water (30:70, vol/vol) containing 25 mmol/L sodium phosphate buffer (pH 6.0) at a flow rate of 0.4 mL/min and detected with a fluorometer at 395 nm (excitation) and 455 nm (emission).[12,17] Cysteinesulfinic acid decarboxylase (EC 4.1.1.29) activity was assayed as detailed previously.[9] Aspartate aminotransferase (EC 2.6.1.1) activity was measured spectrophotometrically using either 10 mmol/L aspartate or 15 mmol/L cysteinesulfinate as the substrate.[18] Aspartate aminotransferase is located in both cytosols and mitochondria,[18] so the supernatant obtained after centrifugation at 1000 × *g* of liver homogenate was used as an enzyme source.

Tissue taurine and glutathione analysis

Taurine concentrations in the liver, serum, and urine were determined by HPLC as described previously.[11,19] Glutathione concentrations in the liver and serum were determined enzymatically by the method of Griffith.[20]

Statistical analysis

The examination of significant differences of means with a pooled estimated variance was established according to the methods of Snedecor and Cochran[21] for one-way classification as detailed previously.[13]

Results

Average food intake (21.5 to 22.6 g/day) and animal growth (155 to 167 g/22 day) were comparable among rats fed various dietary fibers (Experiment 1). No significant difference was seen in liver weight among rats fed various fibers (5.27 to 5.51 g/100 g body weight). In the experiment in which rats were fed diets containing cholesterol and bile acid or free of these steroids (Experiment 2), no significant differences were seen in average daily food intake (19.4 to 20.3 g/day) or animal growth (209 to 232 g/26 day). Liver weight was significantly higher in rats fed a diet containing 1% cholesterol alone (6.20 ± 0.40 g/100 g body weight) or one containing both 1% cholesterol and 0.25% sodium cholate (6.90 ± 0.82 g/100 g body weight) than in animals fed a steroid-free control diet (5.41 ± 0.79 g/100 g body weight). A diet containing 0.25% sodium cholate alone, however, did not affect this parameter (5.90 ± 0.45 g/100 g body weight).

Compared with water-insoluble dietary fibers, water-soluble fibers reduced taurine concentrations in the liver and serum (*Table 1*). Hepatic taurine contents expressed in mmol/100 g body weight were also lower in rats fed water-soluble fibers than in animals fed water-insoluble fibers. Hepatic glutathione concentration and content among groups were comparable.

Compared with a steroid-free control, diets containing either 1% cholesterol or 0.25% sodium cholate and a diet containing both of these steroids significantly reduced taurine levels in the liver and serum (*Table 2*). Although differences were not necessarily statistically significant, values were lower in rats fed a diet containing both of steroids than in animals fed diets containing either cholesterol or sodium cholate alone. Dietary steroids both as cholesterol and bile acid significantly reduced urinary taurine excretion. Values were, however, comparable among the three groups of rats fed diets containing steroids. Hepatic but not serum concentration of glutathione was lower in rats fed a diet containing both cholesterol and bile acid than in other groups. No such difference in the liver glutathione level was confirmed, however, when expressed in terms of content.

Hepatic enzyme activity in sulfur amino acid metabolism in rats fed various dietary fibers are summarized in *Table 3*. Enzyme activity was expressed both in specific activity

Table 1 Effect of dietary fibers on taurine and glutathione levels in the liver and serum

	Dietary fiber			
	Cellulose	Chitin	Pectin	Konjak mannan
Taurine				
Liver				
(μmol/g)	2.60 ± 1.43—a	2.56 ± 0.82—a	0.728 ± 0.140—b	0.825 ± 0.283—b
(μmol/100 g bw)	13.9 ± 7.9—a	13.9 ± 4.8—a	3.95 ± 0.820—b	4.52 ± 1.43—b
Serum (μmol/L)	370 ± 56—a	321 ± 53—a	228 ± 63—b	236 ± 58—b
Glutathione				
Liver				
(μmol/g)	6.87 ± 0.69—a	6.37 ± 0.21—a	6.48 ± 0.71—a	6.68 ± 1.24—a
(μmol/100 g bw)	36.1 ± 3.17—a	34.3 ± 1.6—a	34.9 ± 4.0—a	37.0 ± 8.2—a

n = 7 animals/group.
Values are mean ± SD. Values in a line with different letters are significantly different at $P < 0.05$.

(nmol/min per mg protein) and total activity (μmol/min per 100 g body weight). Both specific and total activity of hepatic cystathionine synthase was the same in all groups. No significant dietary fiber-dependent changes were seen in the specific activity of γ-glutamylcysteine synthetase in the liver. Total activity was, however, slightly but significantly lower in rats fed cellulose than in those fed other fibers. Pectin and konjak mannan in relation to cellulose and chitin profoundly reduced specific and total activity of cysteine dioxygenase in the liver under both NAD-independent and NAD-dependent assay conditions. In contrast, compared to water-insoluble fibers, water-soluble fibers significantly increased hepatic cysteinesulfinic acid decarboxylase activity regardless of value expression. Compared with water-insoluble fibers, water-soluble fibers significantly decreased specific activity of hepatic aspartate aminotransferase irrespective of the substrate (aspartate or cysteinesulfinate). Although differences were not necessarily significant, total enzyme activity measured with aspartic acid and cysteinesulfinic acid substrates was also lower in rats fed water-soluble fibers than in those fed water-insoluble fibers.

Dietary cholesterol and bile acid reduced specific and total activity of cysteine dioxygenase in the liver under both NAD-independent and NAD-dependent assay conditions (*Table 4*). Bile acid was more effective than cholesterol in reducing enzyme activity. Value observed in rats fed a diet containing both cholesterol and bile acid was comparable to that in those fed a diet containing bile acid alone. Cholesterol feeding significantly increased specific and total activity of cysteinesulfinic acid decarboxylase in the liver. In contrast, dietary bile acid decreased enzyme activity to half that obtained with a steroid-free control diet. Value in animals fed a diet containing both of these steroids was comparable to that in controls. Specific and total activity of aspartate aminotransferase were highest in rats fed a diet containing cholesterol alone, irrespective of the type of substrate. Differences were not always statistically significant, however.

Discussion

One of the important physiological function of taurine is conjugation of bile acid. Non-mammalian species conjugate bile acid exclusively with taurine, whereas mammalian species can synthesize both glycine- and taurine-conjugated bile acids. The bile acid glycine to taurine ratio, however, considerably varies among mammalian species.[22–24] Conjugation with both glycine and taurine occurs in man, and the glycine conjugates are predominant under the most condition. It has long been recognized, in contrast, that rat

Table 2 Effect of dietary steroid on taurine and glutathione levels in the liver and serum and urinary taurine excretion

	Dietary steroid			
	Control	Cholesterol	Bile acid	Cholesterol + bile acid
Taurine				
Liver				
(μmol/g)	2.63 ± 1.67—a	0.830 ± 0.159—b	0.846 ± 0.095—b	0.588 ± 0.148—b
(μmol/100 g bw)	14.6 ± 10.1—a	5.14 ± 0.95—b	5.19 ± 0.79—b	4.00 ± 0.77—b
Serum (μmol/L)	363 ± 50—a	283 ± 58—b	227 ± 48—c	206 ± 61—c
Urinary excretion				
(μmol/day per 100 g bw)	0.637 ± 0.138—a	0.314 ± 0.050—b	0.332 ± 0.048—b	0.272 ± 0.056—b
Glutathione				
Liver				
(μmol/g)	6.39 ± 0.42—a	6.24 ± 0.98—a	6.54 ± 0.87—a	4.95 ± 0.34—b
(μmol/100 g bw)	34.5 ± 2.6—a	38.7 ± 6.9—a	38.6 ± 5.6—a	34.1 ± 4.0—a
Serum (μmol/L)	7.15 ± 1.80—a	9.58 ± 6.43—a	7.64 ± 1.51—a	9.96 ± 5.93—a

n = 7 animals/group.
Values are mean ± SD. Values in a line with different letters are significantly different at $P < 0.05$.

Table 3 Effect of dietary fiber on the activities of enzymes in sulfur amino acid metabolism in rat liver

Enzyme	Dietary fibers			
	Cellulose	Chitin	Pectin	Konjak mannan
Cystathionine synthase				
(nmol/min per mg)	5.62 ± 0.56—a	6.16 ± 1.91—a	6.10 ± 0.87—a	6.03 ± 1.14—a
(μmol/min per 100 g bw)	4.40 ± 0.34—a	5.13 ± 1.67—a	5.15 ± 0.85—a	5.04 ± 1.22—a
γ-Glutamylcysteine synthetase				
(nmol/min per mg)	1.23 ± 0.16—a	1.47 ± 0.13—a	1.67 ± 0.24—a	1.57 ± 0.32—a
(μmol/min per 100 g bw)	0.962 ± 0.143—a	1.22 ± 0.10—b	1.40 ± 0.16—b	1.30 ± 0.29—b
Cysteine dioxygenase				
NAD-independent assay				
(nmol/min per mg)	5.60 ± 1.75—a	5.66 ± 1.43—a	2.02 ± 1.35—b	1.32 ± 1.00—b
(μmol/min per 100 g bw)	4.33 ± 1.19—a	4.73 ± 1.32—a	1.70 ± 1.14—b	1.09 ± 0.82—b
NAD-dependent assay				
(nmol/min per mg)	1.06 ± 0.37—a	1.01 ± 0.08—a	0.535 ± 0.331—b	0.550 ± 0.278—b
(μmol/min per 100 g bw)	0.805 ± 0.198—a	0.845 ± 0.185—a	0.457 ± 0.296—b	0.468 ± 0.251—b
Cystenesulfinic acid decarboxylase				
(nmol/min per mg)	29.2 ± 6.1—a	33.0 ± 3.7—a	46.1 ± 2.9—b	44.8 ± 5.3—b
(μmol/min per 100 g bw)	22.6 ± 2.9—a	27.3 ± 2.9—b	38.8 ± 2.9—c	37.1 ± 3.4—c
Aspartate aminotransferase				
Aspartic acid substrate				
(nmol/min per mg)	169 ± 16—a	169 ± 11—a	132 ± 13—b	145 ± 19—b
(μmol/min per 100 g bw)	140 ± 13—ab	144 ± 13—a	109 ± 13—c	127 ± 21—bc
Cysteinesulfinic acid substrate				
(nmol/min per mg)	164 ± 13—a	167 ± 16—a	138 ± 19—b	147 ± 13—b
(μmol/min per 100 g bw)	136 ± 13—a	140 ± 13—a	114 ± 19—a	130 ± 26—a

$n = 7$ animals/group.
Values are mean ± SD. Values in a line with different letters are significantly different at $P < 0.05$.

conjugates bile acids almost exclusively with taurine. Considerable species to species differences in the bile acid glycine to taurine ratio has been explained by the difference in the substrate specificity of hepatic bile acid-CoA:amino acid *N*-acyltransferase (EC 2.3.1), which catalyses condensation of bile acid-CoA with amino acid to form taurine- or glycine-conjugated bile acid.[25–29] The bile acid conjugation enzyme purified from rat liver cytosols has a much higher affinity for taurine than for glycine,[26,29] thus accounting for the predominance of taurine-conjugated bile acid in this animal species. We demonstrated, however, the glycine-conjugated bile acid became to be abundant in the bile of rats fed water-soluble fibers,[8,10–13] cholesterol,[10,13] and bile acid.[13] Our previous study[13] excluded the possibility that these dietary factors induce bile acid-conjugation enzyme specific for glycine which is distinct from the enzyme-specific for taurine. These nutritional conditions were all accompanied by the decrease in hepatic taurine concentra-

Table 4 Effect of dietary steroid on the activities of enzymes in sulfur amino acid metabolism in rat liver

Enzyme	Dietary steroid			
	Control	Cholesterol	Bile acid	Cholesterol + bile acid
Cysteine dioxygenase				
NAD-independent assay				
(nmol/min per mg)	4.37 ± 1.40—a	1.40 ± 0.66—b	0.253 ± 0.151—c	0.252 ± 0.151—c
(μmol/min per 100 g bw)	2.68 ± 1.03—a	0.896 ± 0.444—b	0.155 ± 0.079—c	0.159 ± 0.090—c
NAD-dependent assay				
(nmol/min per mg)	0.842 ± 0.304—a	0.420 ± 0.185—b	0.126 ± 0.042—c	0.086 ± 0.026—c
(μmol/min per 100 g bw)	0.515 ± 0.214—a	0.269 ± 0.124—b	0.080 ± 0.024—c	0.056 ± 0.019—c
Cysteinesulfinic acid decarboxylase				
(nmol/min per mg)	31.1 ± 8.7—a	43.7 ± 4.0—b	14.5 ± 5.0—c	29.1 ± 2.6—a
(μmol/min per 100 g bw)	18.5 ± 4.5—a	27.7 ± 2.1—b	9.49 ± 3.2—c	18.8 ± 1.3—a
Aspartate aminotransferase				
Aspartic acid substrate				
(nmol/min per mg)	234 ± 61—ab	283 ± 58—b	212 ± 32—a	223 ± 29—a
(μmol/min per 100 g bw)	159 ± 40—a	193 ± 29—a	147 ± 26—a	185 ± 34—a
Cysteinesulfinic acid substrate				
(nmol/min per mg)	228 ± 45—ab	283 ± 58—b	213 ± 32—a	211 ± 29—a
(μmol/min per 100 g bw)	155 ± 29—a	193 ± 29—b	147 ± 26—a	175 ± 37—ab

$n = 7$ animals/group.
Values are mean ± SD. Values in a line with different letters are significantly different at $P < 0.05$.

tion,[8,10–13] and therefore the reduction in hepatic concentration of this compound was regarded as the primary factor to cause the enrichment of glycine-conjugated bile acid. With regard to the mechanism by which these dietary factors decreased hepatic taurine concentration, we previously demonstrated that at least water-soluble fibers decreased hepatic cysteine dioxygenase activity.[12] However, the detailed information on the responses to these nutritional conditions of key enzymes in taurine biosynthetic pathway has been lacking. This study clearly demonstrated that these dietary factors profoundly modify the activity of hepatic enzymes in taurine biosynthesis in the rats.

Cysteine dioxygenase and cysteinesulfinic acid decarboxylase are involved in the conversion of cysteine to taurine. Cysteine is converted to cysteinesulfinic acid by a reaction catalyzed by cysteine dioxygenase. The reaction catalyzed by cysteinesulfinic acid decarboxylase in turn converts cysteinesulfinic acid to hypotaurine. Cysteinesulfinic acid is located at a metabolic branch point in cysteine metabolism. The reaction catalyzed by aspartate aminotransferase transaminate cysteinesulfinic acid to form β-sulfinylpyruvate thus diverts sulfinic acid from taurine synthesis.[30] Cysteine dioxygenase, cysteinesulfinic acid decarboxylase and aspartate aminotransferase are, therefore, regarded as enzymes that regulate the taurine synthesis rate from cysteine. It has been reported that hepatic cysteine dioxygenase and cysteinesulfinic acid decarboxylase activity are easily modified by physiological conditions and protein nutritional status of rats. Cysteine dioxygenase activity is low at birth but progressively increases to an adult level 1 month after birth.[31] The injection of hydrocortison increased enzyme activity,[32] but glucagon and dibutyryl cyclic AMP decreased it.[32] Adrenalectomy[5] and hyperthyroidism, induced in rats by injecting triiodothyronine, depressed cysteinesulfinic acid decarboxylase activity in the rat liver.[33] Higher levels of dietary protein and sulfur amino acids increased cysteine dioxygenase activity and lowered cysteinesulfinic acid decarboxylase activity in the liver accompanying an increase in tissue levels and urinary taurine excretion.[1–9] Our results demonstrate that type of dietary fiber and cholesterol and bile acid plus protein nutrition are dietary factors regulating hepatic cysteine dioxygenase and cysteinesulfinic acid decarboxylase. Information on regulation by physiological and nutritional conditions of aspartate aminotransferase are scarce. Daniels and Stipanuk[2] reported that the addition of 2.6% cystcine to 20% casein diet caused cysteine dioxygenase activity to increase and cysteinesulfinic acid decarboxylase activity to decrease without influencing aspartate aminotransferase activity in the rat liver. In the present study, aspartate aminotransferase activity was also modified by dietary fiber and steroids in some cases but to a lesser extent than cysteine dioxygenase and cysteinesulfinic acid decarboxylase activity. Thus, aspartate aminotransferase may play a minor role in regulating hepatic taurine biosynthesis. The activity of cystathionine synthase, the enzyme involved in the pathway to convert methionine to cysteine,[15,30] was not modified by the type of dietary fiber. Thus, it is possible that alteration in the rate of methionine conversion to cysteine is not a factor in determining taurine biosynthesis and content in the liver of rats fed various fibers. Compared with other fibers, cellulose significantly reduced total, but not specific activity of γ-glutamylcysteine synthetase, a rate-limiting enzyme in glutathione biosynthesis,[16] without influencing the hepatic concentration of glutathione. The physiological significance of this change is thus uncertain at present.

In the present study, two different assay conditions one NAD-dependent and the other NAD-independent were used to measure hepatic cysteine dioxygenase activity. Assay condition essentially the same to NAD-dependent assay employed in the present study has been employed by many investigators (see Methods and materials).[2,6,7] Yamaguchi et al.[17] have reported an alternative assay condition that they called NAD-independent assay and further showed that anaerobic pre-incubation in the presence of cysteine increased enzyme activity assayed under this condition. Although it is probable that both assay conditions measure the same enzyme activity, some criticism[34] has been made for the NAD-independent assay because it uses rather high pH value (9.0) and of the fact that physiological significance of the anaerobic activation is totally uncertain. We observed previously that water-soluble dietary fiber decreased hepatic cysteine dioxygenase activity assayed under NAD-independent condition.[12] Present study showed that water-soluble fibers decreased not only NAD-independent but also NAD-dependent cysteine dioxygenase activity in rat liver. It is, therefore, intelligible that water-soluble fibers have a potency to lower cysteine dioxygenase activity in rat liver. We also demonstrated, in the present study, that cholesterol and bile acid decreased the hepatic activity of this enzyme irrespective of assay conditions. Yamaguchi et al.[17,35,36] have presented evidence indicating that cysteine dioxygenase regulates the rate of hepatic taurine synthesis. Thus, these dietary factors may reduce hepatic synthesis of taurine. Decreased hepatic taurine synthesis reported to be accompanied by reduced urinary taurine excretion.[2,7,37] We demonstrated previously that water-soluble fibers reduced urinary taurine excretion.[12] It was further demonstrated, in the present study, that cholesterol and bile acid also reduced this parameter (*Table 2*). Although these observations obtained using cell-free homogenates strongly support the consideration that these dietary factors reduced hepatic taurine synthesis, an examination of the metabolic fate of physiological concentration of cysteine substrate in intact hepatocytes will be required to draw a more definite conclusion regarding dietary regulation of hepatic taurine synthesis.

Water-soluble dietary fibers and cholesterol, but not cholic acid, increased hepatic cysteinesulfinic acid decarboxylase activity. This reciprocal response of cysteine dioxygenase and cysteinesulfinic acid decarboxylase has been demonstrated in rats fed diets differing in protein or sulfur amino acid content.[1–9] In the present study, however, dietary cholic acid decreased both cysteine dioxygenase and cysteinesulfinic acid decarboxylase activity in the liver. We also reported that guanidinoethane sulfonic acid, a taurine-lowering agent, decreased both cysteine dioxygenase and cysteinesulfinic acid decarboxylase activity in the rat liver.[38] This reciprocal response is therefore not a general feature of the regulation of these enzymes in the taurine synthetic pathway.

It is possible that water-soluble dietary fiber impaired the

digestion and absorption of dietary protein in the intestinal lumen and thus limited the availability of sulfur amino acid. These changes may alter enzyme activity in taurine biosynthesis as observed in the current study. Changes by water-soluble dietary fibers in the hepatic activity of cysteine dioxygenase and cysteinesulfinic decarboxylase resembled those observed in rats fed a diet low in sulfur amino acid.[1–9] It is unlikely, however, that alteration in the process of digestion and absorption of dietary protein is responsible for changes in the activity of enzymes in taurine biosynthesis, at least in rats fed cholesterol and bile acid. Alternatively, the present observation that dietary steroids modify hepatic cysteine dioxygenase and cysteinesulfinic decarboxylase activity raised the possibility that alterations by dietary fiber of cholesterol and (or) bile acid metabolism may in some way influence the activity of these enzymes in taurine biosynthesis. It has been demonstrated that dietary water-soluble dietary fiber and cholesterol increase the rate of bile acid synthesis in the liver, whereas bile acid inhibits it.[12,24,39] In the present study, dietary fiber, cholesterol, and bile acid all decreased hepatic cysteine dioxygenase activity. In contrast, dietary fiber and cholesterol increased hepatic cysteine sulfinic acid decarboxylase activity, but cholic acid decreased it. We observed previously that cholestyramine feeding increased cholesterol 7α-hydroxylase activity without affecting cysteine dioxygenase activity.[12] Therefore, there is the possibility that cysteine sulfinic acid decarboxylase (but not cysteine dioxygenase) and bile acid synthesis are coordinately regulated each other. Further studies to examine the effects of various nutritional and physiological conditions on the activity of hepatic enzymes in bile acid and taurine synthesis are required to clarify this point. It has been demonstrated that hepatic taurine synthetic activity is considerably different among animal species.[40,41] Also, responsiveness to nutritional conditions of lipoprotein and bile acid metabolism is different according as the differences in the animal species used.[42,43] Therefore, examination of the effects of various dietary factors on the metabolism of taurine and bile acid in animal species other than rats may provide valuable information regarding the relationship between taurine and bile acid metabolism.

This study clearly demonstrated that dietary water-soluble fibers and steroids are dietary factors to modulate the activity of enzymes in taurine synthesis. It is difficult, however, to understand an underlying physiological basis that would favor the changes observed in the present study. Dietary water-soluble fibers, cholesterol and bile acid all increase the availability of bile acid in the liver,[8,11–13,39] so these dietary factors should conceivably augment the demand for taurine to conjugate bile acid. It is therefore reasonable to expect that these nutritional conditions increase hepatic taurine synthesis. Present observation indicates, however, that these nutritional conditions reduce hepatic taurine synthesis. Consequent reduction in the availability of taurine increase glycine-conjugation but decrease taurine-conjugation of bile acid in rats.[8,10–13] Taurine is synthesized from essential sulfur amino acids, so augmented increase in hepatic taurine synthesis without an increased dietary supply of sulfur amino acids may causes some untoward effects in animals through depletion of essential sulfur amino acids. Thus, the failure to induce hepatic taurine synthesis in response to dietary water-soluble fibers and steroids may represent a physiological response to conserve essential sulfur amino acids. If this consideration is correct, responses to these dietary factors of parameters for taurine synthesis may be modified according as the differences in sulfur amino acid nutritional status of animals. Further studies are required to clarify this point.

In conclusion, we demonstrated that the type of fiber and cholesterol and bile acid are dietary factors that alter the activity of hepatic enzymes in taurine synthesis. An underlying physiological basis that would favor the observed changes remained to be clarified, however. Taurine is believed to be concerned in maintaining various physiological activity in organisms,[44] so further study is needed to clarify the mechanism by which these dietary factors influence hepatic enzymes in taurine biosynthesis.

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