STUDIES *in vivo* ON THE METHIONINE–SPARING EFFECT OF CYSTEINE IN RATS

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SUMMARY

This investigation was conducted to clarify the role of cysteine on its methionine-sparing effect by studying *in vivo* the various parameters that are directly related to the metabolism of the methionine carbon, such as conversion to CO_2, and incorporation of the methionine carbon into proteins, phospholipids and nucleic acids. At low (0.4%) dietary level of methionine, cysteine had a depressive effect on the oxidation of the methionine carbon to carbon dioxide, and with 0.51% cysteine in the diet the oxidation of the methyl or carboxyl carbon of methionine to CO_2 was depressed by 29 and 20%, respectively. The amount of the label in urine samples was unaltered by the level of cysteine in the diet, and the body retention of either the methyl or carboxyl carbon of methionine was greater at low methionine intake when cysteine in the diet was increased. Under these conditions, rat growth was enhanced by feeding increasing amounts of cysteine. The incorporation of methionine methyl carbon into tissue nucleic acids and phospho-

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lipids was depressed by high (0.51%) levels of cysteine in the diet, at a low (0.4%) methionine intake. Under these conditions there was an increased incorporation of the methionine methyl or carboxyl carbon into tissue proteins. In addition, it appears that the resynthesis of methionine from homocysteine is enhanced by increasing the amounts of cysteine in the diet. All of these findings suggest that the addition of cysteine increases the availability of methionine for protein synthesis and, hence, growth.

INTRODUCTION

As is widely known, the metabolism of methionine and cysteine are closely interrelated. The major metabolic functions of methionine are: a) its utilization for protein synthesis (1); b) its conversion to S-adenosylmethionine (2), the dominant biological methyl group donor, and c) the transfer of sulfur to serine for cysteine formation (3, 4) with further metabolism of the α-ketobutyrate carbon to CO_2 (5). Cystine can spare from one-third (6) to two-thirds (7) of the methionine required for growth of the rat. In studies not specifically designed to investigate the cysteine-methionine relationship, Aguilar[2] observed that three-fifths of the sulfur-containing amino acids requirements for maximum growth can be met by cysteine. The methionine-sparing effect of cysteine appears to involve inhibition of ATP: L-methionine-S-adenosyltransferase, EC 2.5.1.6 (8) and of cystathionine synthetase[3] (8) by cysteine. In addition, it has been reported that cystine may increase the choline requirement by inhibiting transmethylation from methionine (9), possibly through a decrease of S-adenosyl-methionine formation (8). It has been postulated, however, that there exists an antagonism of cysteine on methionine utilization when the dietary level of methionine is suboptimal (10), and that the methionine-sparing effect of cysteine is not due to a depression in the activity of cystathionine synthetase and subsequently on methionine oxidation (11).

As the mechanism of the methionine-sparing effect of

2 Aguilar, T.S. Efficiency of utilization of essential amino acids by the rat for growth. M. S. Thesis, University of Wisconsin, Madison, 1970.

3 Shannon, B.M., J.M. Howe and H.E. Clark. Interrelationships between dietary methionine and cysteine as reflected by growth and certain hepatic enzymes. *Fed. Proc., 30:* 234, 1971 (Abstr).

cysteine has not been defined as yet, and in view of the above information related to *in vitro* enzymatic studies, this study was carried out in order to clarify the role of cysteine on the metabolism of methionine. This was done by studying *in vivo* the various parameters directly related to the metabolism of the methionine carbon, such as conversion to CO_2, and incorporation of the methionine carbon into proteins, phospholipids and nucleic acids.

MATERIALS AND METHODS

Animals, Diets and Isotopes

Six groups of weanling male rats of the Holtzman strain were fed *ad libitum* individually for five days, an amino acid diet (12) in gel form containing 0.4% L-methionine and 0, 0.17, 0.34 or 0.51% L-cysteine. This was done so that the molar ratio methionine:cysteine for the cysteine supplemented diets was: 1.91, 0.96 or 0.64, respectively, for the last three. The other two diets contained 0.8% methionine, with (0.34%) or without cysteine. Table 1 shows the percentage composition of the basic experimental amino acid diet. The diets were prepared as gels by mixing them in dry form with an approximately equal quantity of a boiling 3% agar solution. Food was removed at 9:00 p.m. on day five, 10 and a half hours prior to feeding radioactive diets, and each treatment group was divided into two subgroups of three. The rats of each subgroup were individually placed in air-tight glass metabolic chambers and received 5 g of the experimental diet in gel form labeled with 3 μ Ci of L-(methyl-^{14}C)-methionine[4] (three rats) or L-(1-^{14}C)-methionine[5] (three rats). Preparation of the labeled diet in gel form was as described above, but in disposable syringes, containing the 5 g diet plus the labeled dose.

Collection of CO_2, Sample Preparation and Radioactivity Determination

Samples of CO_2 were collected at hourly intervals during the first 12 hours of the experiment, and as a single sample during the

4 New England Nuclear, Boston, Massachusetts.

5 Schwarz BioResearch, Orangeburg, New York.

TABLE 1

PERCENTAGE COMPOSITION OF THE BASIC EXPERIMENTAL DIET [a]

Ingredients	Amino acid diet
L-amino acid mixture[a]	18.52
Salt mixture[b]	5.0
Vitamin mixture[b]	0.5
Choline chloride	0.2
Corn oil	10.0
Glucose monohydrate	32.89
Cornstarch	32.89

a Dry weight basis, taken from Aguilar, Harper and Benevenga (12). The basic L-amino acid mixture contained: (%/o of the diet) Arg. HCl, 1.35; his, HCl H_2O, 0.4; ile, 0.8; leu, 1.08; lys HCl, 1.76; met, 0.8; phe, 1.14; thr, 0.8; tryp, 0.17; val, 0.8; ala, 0.34; asp, 0.34; glu, 3.41; gly, 2.28; pro, 0.34; cys, 0.34; ser, 0.34; tyr, 0.34; asp (NH_2), 0.6; and sodium acetate, 1.09. The percentages of met and/or cys in the present experimental diets were changed for each group trial as indicated in the text.

b Taken from Rogers and Harper (13), for a diet intended to promote maximal growth.

second 12 hours of the experiment. The procedures used for trapping and counting the CO_2 were described earlier (14). At 24 hours all rats were anesthetized with ether and heparinized blood samples were withdrawn by heart puncture, and centrifuged; the plasma thus obtained was stored at −20°C for further analysis. Liver and muscle *(longissimus dorsi)* tissues were also taken, and immediately frozen until use. The gastrointestinal contents were rinsed out with distilled water, combined with the feces and spilled food, and homogenized with a Polytron homogenizer.[6] An aliquot of sample containing less than 300 mg of dry matter was freeze-dried and then combusted to CO_2 by a modified Van

6 Kinematica GMBH, Luzern, Schweiz.

Slyke's wet combustion method.[7] The radioactivity in aliquots of the carbon dioxide collected in 1:2 ethanolamine-methylcellosolve mixture was determined using the techniques developed for respired CO_2 (14); this value was then used to calculate the net

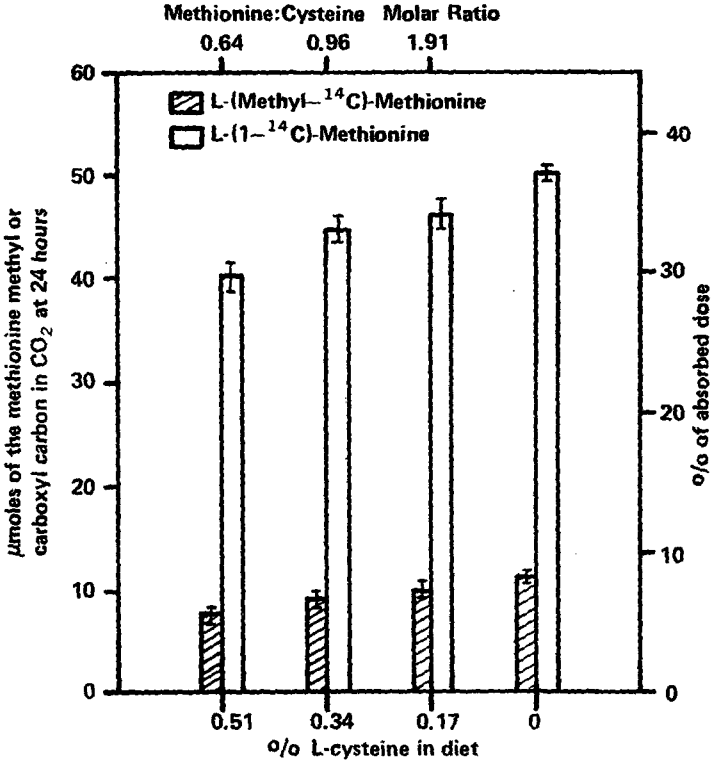

FIGURE 1

Molar conversion of the methionine methyl or caboxyl carbon to carbon dioxide expired over 24 hours by rats consuming diets with various levels of cysteine

7 Aguilar, T.S., N.J. Benevenga and A.E. Harper, unpublished results.

"absorbed dose" by subtracting it from the amount of radioactivity fed. Radioactivity in the urine samples collected over the 24-hr period, after centrifuging to eliminate contaminating feces or any solid material, was determined using the scintillation fluid described by Bruno and Christian (15). The procedures for the extraction and determination of tissue phospholipids, RNA, DNA and proteins were described earlier (16).

As observed in Figure 1 on previous page, all values are the average of three. The vertical lines represent standard deviation of the mean. All rats consumed 5 g of the labeled diet containing 134 μmoles (0.4%) methionine and 0 (0%), 70 (0.17%), 140 (0.34%) or 210 (0.51%) μmoles cysteine. All diets contained 0.2% choline. Less than 3% of the ingested label was recovered in the feces, gastrointestinal contents and spilled food. The molar conversion of the methionine carbon to carbon dioxide was calculated by the following relationship:

$$= \frac{(\mu\text{moles of methionine consumed})\,(\text{dpm in } CO_2 \text{ at 24 hours})}{(\text{Absorbed dose in dpm})}$$

RESULTS

Figure 1 shows the effect of dietary cysteine level on the molar conversion of the methionine methyl or carboxyl carbon to carbon dioxide expired over 24 hours by rats consuming diets which contained 0.4% methionine. At low methionine levels (0.4%), cysteine had a depressive effect on the oxidation of methionine carbon to carbon dioxide only at high cysteine levels (e.g., 0.51%, or a ratio of 0.64 moles met/mole cys). At the highest cysteine level (0.51%) the oxidation of the methyl and carboxyl carbon of methionine to CO_2 was depressed by 29 or 20%, respectively, of that observed with the cysteine-free diet. It should be noted, however, that this depressive effect is not seen at the 0.8% methionine level (Table 2) where the met/cys molar ratio is 1.91. Apparently, cysteine exerts its effect only in diets low in methionine and with very high cys/met molar ratios (e.g., 1.56).

As seen in Table 2, the urine radioactivity over 24 hours was not altered by the level of cysteine in the diet. Therefore, the retention of either the methyl or carboxyl carbon of methionine is greater in a low methionine intake when cysteine in the diet is

TABLE 2

DISTRIBUTION OF THE ^{14}C ACTIVITY AT 24 HOURS IN SAMPLES FROM RATS FED DIETS NORMAL OR LOW IN METHIONINE WITH VARIOUS LEVELS OF CYSTEINE[a]

o/o of diet		o/o of the absorbed dose[b]					
		L-(methyl-^{14}C)-methionine			L-(1-^{14}C)-methionine		
Met	Cys	CO_2	Urine	Body[c]	CO_2	Urine	Body
0.8	—	16.2 ±0.9[d]	4.6 ±0.3	79.2	○52.7 ±0.6	2.9 ±0.3	44.4
0.8	0.34	17.2 ±0.3	4.1 ±0.1	78.7	○50.5 ±0.5	2.9 ±0.1	46.6
0.4	—	● 8.2 ±0.2	5.4 ±0.3	86.4	● 37.4 ±0.6	● 3.3 ±0.2	59.3
0.4	0.17	7.3 ±0.6	5.8 ±0.4	86.9	△ ● 33.7 ±0.8	2.8 ±0.3	63.5
0.4	0.34	● 6.8 ±0.5	5.0 ±0.2	88.2	□ ● 33.2 ±0.9	□● 2.4 ±0.1	64.4
0.4	0.51	● 5.8 ±0.6	5.1 ±0.6	89.1	□△ ● 29.9 ±0.9	□3.0 ±0.2	67.1

a The average weight gain over a 4-day period for the rats consuming the diets which contained 0.4o/o methionine and 0, 0.17, 0.34 or 0.51o/o cysteine was of 17.5, 18.8, 20.0 or 21.8 g, respectively.

b More than 97o/o of the methionine consumed was absorbed.

c By difference: absorbed dose–(CO_2 +urine).

d Average of three ± standard deviation of the mean.

Limits of significance of the Student distribution for the 0.4o/o methionine level, were $P < 0.05$, ● for the 0o/o cysteine to the others, △ for the 0.17o/o cysteine to the others, □ for the 0.34o/o cysteine to the others, and ○ for the 0.8o/o met level.

increased, thus suggesting that the addition of cysteine increases the methionine availability for protein synthesis and, hence, growth. The weight gain in this study supports this notion since the 4-day weight gain for the rats that consumed diets containing 0.4% methionine and 0, 0.17, 0.34 or 0.51% cysteine, was of 17.5, 18.8, 20.0 or 21.9 g, respectively.

The results on the incorporation of the methionine methyl carbon into tissue RNA and DNA of rats fed the diets containing 0.4% of L-methionine and various levels of L-cysteine, are shown in Figure 2. It is apparent that the incorporation of methyl carbon into liver and muscle RNA was depressed only by relatively high levels of cysteine at low levels of methionine. The effect on liver DNA was clearly evident when cysteine addition was of only 0.17%. In contrast, cysteine appeared to enhance the incorporation of the methionine methyl carbon into muscle DNA when the methionine intake was 0.4% of the diet, but not at higher (0.8%) methionine levels (16).

Table 3 shows the extent of incorporation of the methionine methyl carbon into liver, muscle or plasma phospholipids of rats fed various levels of cysteine and methionine. Increasing amounts of cysteine consumed tended to lower the incorporation of methyl carbon into tissue phospholipids only at the 0.4% methionine level with the highest cysteine intake (met/cys, 0.64). This was not observed in hepatic tissue at 0.8% methionine where the ratio methionine:cysteine was 1.91. Again, it is clear that cysteine affects methionine metabolism at high cys/met ratios (e.g., 1.56).

The incorporation of the methionine methyl or carboxyl carbon into the tissue proteins of rats fed diets containing different quantities of cysteine at 0.8 or 0.4% methionine, is shown in Table 4. The effect of cysteine on the incorporation of methionine carbon into tissue proteins was evident only at the 0.4% dietary methionine level and again at high cysteine levels (e.g., cys/met, 1.04 or 1.56).

The radioactivity ratios from the methyl to carboxyl carbons of methionine incorporated into liver protein as affected by the concentration of cysteine in the diet are shown in Table 5. A decrease in the value of this ratio is interpreted as an indication of the extent of remethylation of the homocysteine produced by demethylation of methionine with endogenous (unlabeled) methyl groups. Again, cysteine had an effect only at low methionine levels when cysteine in the diet was 0.51%. This tendency did hold in muscle and plasma proteins where these ratios decreased

as the concentration of cysteine in the diet was increased, thus indicating an enhancement of methionine resynthesis at high levels of cysteine.

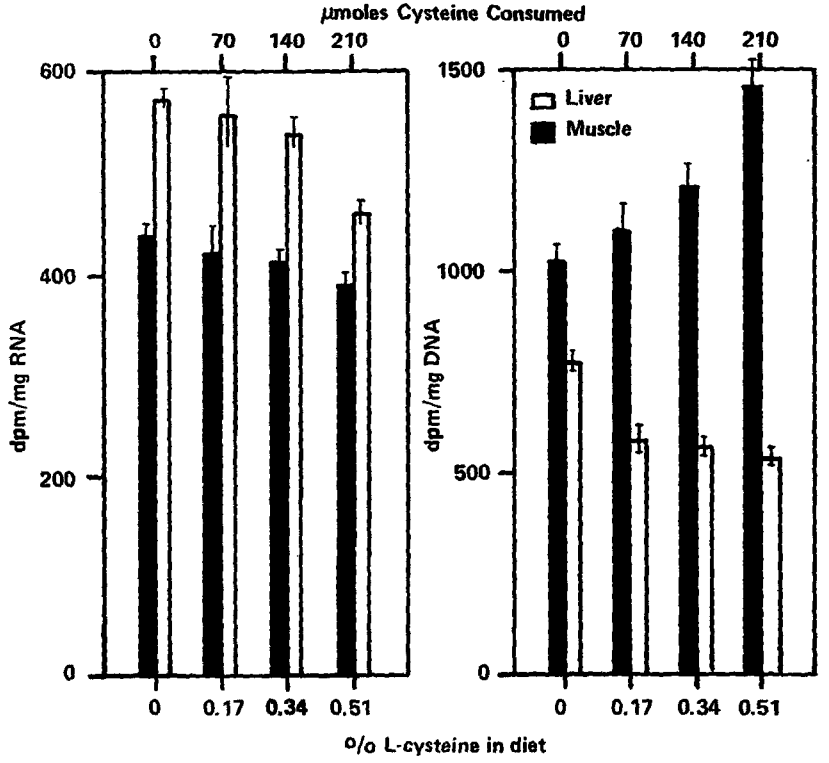

FIGURE 2

Incorporation of the methyl carbon of methionine into tissue RNA and DNA of rats fed diets containing 0.4% of L-methionine with various levels of L-cysteine

The bars and vertical lines represent the average of three, and standard deviation of the mean, respectively. The relative specific activities were obtained by correcting the determined specific activities for tissue, for the size of the methionine pool and meth-

TABLE 3

RELATIVE SPECIFIC ACTIVITY[a] OF LIVER, MUSCLE *(longissimus dorsi)* AND BLOOD PLASMA PHOSPHOLIPIDS FROM RATS FED VARIOUS LEVELS OF CYSTEINE AT TWO LEVELS OF METHIONINE AND INJECTED WITH L-(METHYL-^{14}C)-METHIONINE

o/o of diet		dpm/mg phospholipids		
Met	Cys	Liver	Muscle	Plasma
0.8	—	4,351 ±135[b]	○522 ± 30	6,875[c]
0.8	0.34	4,578 ±185	○450 ± 10	7,372
0.4	—	●3,045 ±149	●333 ± 8	4,812
0.4	0.17	2,787 ± 29	△●293 ± 5	4,016
0.4	0.34	2,723 ±118	●280 ± 9	3,823
0.4	0.51	●2,653 ±140	△●246 ± 20	3,629

a Obtained as described in Figure 2.

b Average of three ± standard deviation of the mean.

c Pooled samples of three rats.

d Limits of significance of the Student distribution for the 0.4o/o methionine level, were $P < 0.05$, ● for the 0o/o cysteine to the others, △ for the 0.17o/o cysteine to the others, □ for the 0.34o/o cysteine to the others, and ○ for the 0.8o/o met level.

ionine consumption. The pool size of liver-free methionine (0.14 μmoles/g tissue) was calculated from data of Daniel and Waissman (17) for nonfasted 55 g male rats. The pool size of skeletal muscle free methionine (0.054 μmoles/g tissue) was calculated from data presented by Ryan and Carver (18) for 90 g male rats. The total skeletal muscle (22 g) was estimated using the data of Miller (19) on the relative proportion of skeletal muscle in the rat as a function of body weight. The methionine consumed in five g diet was 134 μmoles. To obtain the relative specific activities shown in this Figure, the determined specific activity was multiplied by the "correction factor" of 0.5, as this factor was equaled to 1.0 when methionine in the diet was 0.8o/o. The concentration of cysteine in per cent of the diet is given at the bottom of the graph, and its consumption in μmoles at the top of same.

TABLE 4

RELATIVE SPECIFIC ACTIVITY[a] OF LIVER, MUSCLE *(longissimus dorsi)* AND BLOOD PLASMA PROTEINS FROM RATS FED DIETS CONTAINING VARIOUS LEVELS OF CYSTEINE AT TWO LEVELS OF METHIONINE

o/o of diet		dpm/mg protein					
		Liver		Muscle		Plasma	
Met	Cys	M[b]	C[b]	M	C	M	C
0.8	—	963± 48[c]	863 ± 38	○321 ± 18	○ 324 ± 11	791[d]	590
0.8	0.34	1,002± 17	865 ± 14	○390 ± 12	○ 378 ± 24	791	617
0.4	—	● 409± 14	● 591 ± 31	● 196 ± 11	● 206 ± 10	285	352
0.4	0.17	△ ● 456± 14	△ 630 ± 18	△ 215 ± 12	△ 238 ± 19	302	431
0.4	0.34	● 503± 29	△ ● 680 ± 16	□ ● 236 ± 11	□ ● 274 ± 15	302	434
0.4	0.51	△ ● 549± 25	△ ● 728 ± 21	□ △ ● 270 ± 8	□ △ ● 339 ± 18	319	443

a Obtained as described in Figure 2.

b Methyl (M) or carboxyl (C) labeled methionine.

c Average of three ± standard deviation of the mean.

d Pooled samples of three rats.

e Limits of significance of the Student distribution for the 0.4o/o methionine level, were $P < 0.05$, ● for the 0o/o cys, to the others, △ for the 0.17o/o cys to the others, □ for the 0.34o/o cys to the others, and ○ for the 0.8o/o met level.

TABLE 5

RATIOS OF RADIOACTIVITY[a,b] FROM THE METHYL TO CARBOXYL CARBONS OF METHIONINE INCORPORATED INTO TISSUE PROTEIN AT VARIOUS LEVELS OF CYSTEINE INTAKE, AT TWO DIETARY LEVELS OF METHIONINE

o/o of diet				
Met	Cys	Liver	Muscle	Plasma
0.8	—	1.11	0.99	1.34
0.8	0.34	1.16	1.03	1.38
0.4	—	0.69	0.95	0.81
0.4	0.17	0.72	0.90	0.70
0.4	0.34	0.74	0.86	0.70
0.4	0.51	0.76	0.80	0.72

a Calculated from Table 4.

b This ratio equal to one when the labeled methionine was consumed by the rat.

DISCUSION

Effect of Cysteine on Transmethylation of Methionine

It has been reported that at low levels of methionine intake the activity of ATP:L-methionine-S-adenosyltransferase, EC 2.5.1.6, is decreased by the addition of cystine to the diet (8). Therefore, if the depressive effect of cysteine on the activity of this enzyme is sufficient to provoke a substantial decrease in the formation of S-adenosylmethionine, one would expect to have more "intact methionine" available for protein synthesis, which would result in a concomitant decrease in the incorporation of the methyl carbon of methionine into tissue RNA and phospholipids and also in its conversion to CO_2. In fact, Table 3 and Figure 2, respectively, show that at 0.4o/o of methionine, cysteine at a 0.51o/o level depresses significantly the incorporation of the methyl carbon of methionine into phospholipids and RNA; Table 2 shows that the conversion of the methyl carbon to CO_2 is significantly depressed when the addition of cysteine to the diet

amounts to 0.51o/o. In addition, Table 4 demonstrates that the incorporation of the methyl group into proteins is increased particularly at the 0.51o/o level.

According to the above data, however, the extent of inhibition of methionine activating enzymes (EC 2.5.1.6) by cysteine (0.51o/o) at a low methionine (0.4o/o) intake, is not such that may seriously affect the production of homocysteine for remethylation, the accumulation of which would be relatively enhanced by the depression of cystathionine formation by cysteine (8, 20). Nevertheless, the inhibitory effect of cysteine on methionine activating enzyme would account for the aggravating effect of cysteine (cystine) on the conditions of fatty liver degeneration seen in choline or methionine deficiency (21, 22).

The Methionine-Sparing Effect of Cysteine: A Probable Mechanism of Action

The mechanism of the methionine-sparing effect of cysteine has not yet been defined. None the less, it appears to be accomplished through an inhibitory action of cysteine on the ATP:L-methionine-S-adenosyltransferase, EC 2.5.1.6 (8), and on the cystathionine synthetase[8] (8) in the liver tissue. This inhibitory effect by cystine on these enzymes was evident at subnormal levels of methionine intake[8] (8); in the case of cystathionine synthetase, the decrease in enzyme activity was not pronounced at normal (0.7 to 0.8o/o) levels of dietary methionine,[8] although it was comparable to the depression of conversion of the methionine carboxyl carbon to expired carbon dioxide due to cysteine (16).

At a low methionine intake one would still expect a demand for methionine in protein synthesis. A greater fraction of methionine available would be used for this purpose; hence, if cysteine is supplied, any methionine-sparing effect of cysteine should be magnified, and changes in the metabolism of the methionine carbon should be evident. Therefore, the use of carboxyl-labeled methionine in concert with a supply of cysteine should result in a decreased conversion of the carboxyl carbon to CO_2, which was the case (Figure 1). This, in turn, should result in an increased

8 See footnote 3.

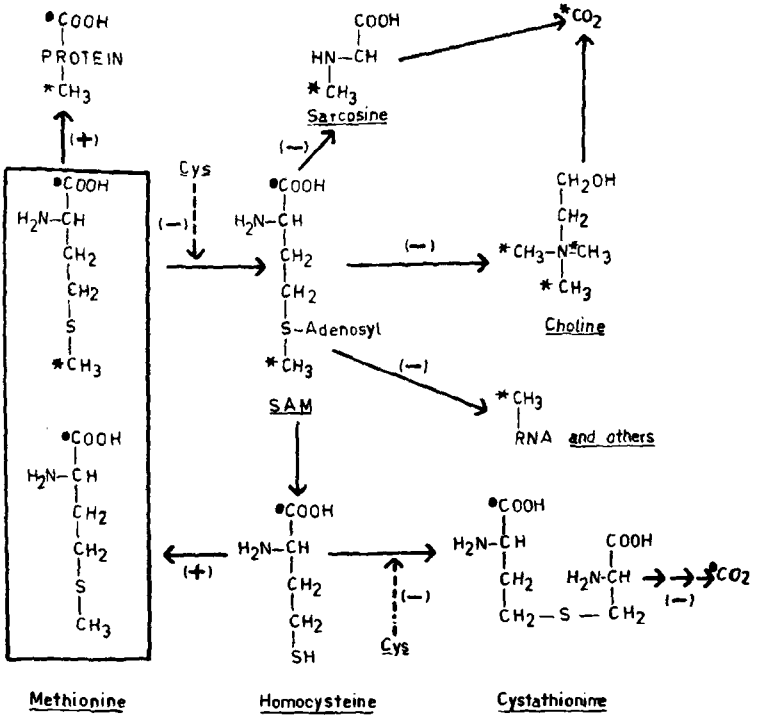

FIGURE 3

Possible scheme for the action of the methionine-sparing effect of cysteine

Cysteine, by depressing the formation of SAM and cystathionine, increases the availability of methionine for protein synthesis and, hence, growth. This is concomitant with a decreased catabolism of homocysteine to CO_2 that results in an increased resynthesis of methionine and, also, with a decrease in the transmethylations from methionine (i.e., of RNA, phospholipids, etc.). (+) Indicates enhancement. (−) Indicates depression.

resynthesis of methionine[9] due to an increased availability of homocysteine for remethylation (23). If cysteine had a depressive effect on the formation of S-adenosylmethionine one would expect incorporation of the label into the compounds normally methylated by S-adenosylmethionine to be decreased. The fact that the incorporation of methyl carbon from methionine into phospholipids (Table 3), RNA (Figure 2) and conversion to carbon dioxide (Table 2) was decreased when cysteine was added to the diet at a level of 0.51%, supports this motion. The reduction of methionine used for methylation and increase in the proportion of homocysteine remethylated, results in an increased availability of methionine for protein synthesis (Table 4) and, hence, growth (see footnote, Table 2). The increase in incorporation of the methyl carbon into protein due to cysteine can be attributed in part to inhibition of cysteine on the ATP:L-methionine-S-adenosyltransferase and also to reutilization of labeled methyl through remethylation of homocysteine, and that of the carboxyl carbon to an increased resynthesis of methionine as a result of inhibition of cystathionine synthetase by cysteine.

On this basis, a scheme for the action of the methionine-sparing effect of cysteine is presented in Figure 3, which supports and clarifies the hypothesis of Finkelstein (24) in that methionine metabolism is a cycle with a unidirectional outlet: the transulfuration pathway, in which cysteine regulates the synthesis of cystathionine. When cysteine is ingested in sufficient quantities the transulfuration is decreased, resulting in the return of a greater fraction of homocysteine to the methionine pool. However, this is evident only at subnormal levels of methionine intake; at higher levels (0.8%)cysteine does not affect the flow of carbon through these enzymes, possibly due to a build-up of the substrates for these two enzymes so that the rate of reaction is maintained.

9 Aguilar, T. S. Studies on the effect of dietary levels of methionine, cysteine and choline on the metabolism of methionine carbon in the growing rat. *Diss. Abstr. International, 32:* 6491-B, 1972.

RESUMEN

ESTUDIOS *in vivo* DEL EFECTO AHORRATIVO DE LA CISTEINA EN EL METABOLISMO DE LA METIONINA EN RATAS

Esta investigación se llevó a cabo con el propósito de esclarecer el rol de la cisteína en su efecto economizador de la metionina, estudiando *in vivo* los varios parámetros directamente relacionados al metabolismo del carbono de la metionina, tales como conversión a CO_2, e incorporación del carbono de la metionina en las proteínas, fosfolípidos y ácidos nucleicos. A bajos (0.4%) niveles de metionina en la dieta, la cisteína tuvo un efecto depresivo en la oxidación del carbono de metionina a anhídrido carbónico, y con 0.51% de cisteína en la dieta, la oxidación del carbono metilo o carbono carboxilo de la metionina a CO_2 disminuyó en 29 y 20%, respectivamente. La cantidad del marcador en muestras de orina no se vio alterada por el nivel de cisteína en la dieta, y la retención corporal de los carbonos metilo o carboxilo de la metionina fue mayor a ingestas bajas de metionina al incrementar la cisteína de la dieta. Bajo estas condiciones, el crecimiento de las ratas aumentaba al alimentárseles con cantidades crecientes de cisteína. La incorporación del carbono metilo de la metionina en los ácidos nucleicos y fosfolípidos disminuyó a altos (0.51%) niveles de cisteína en la dieta y a una baja (0.4%) ingesta de metionina. En estas circunstancias hubo una mayor incorporación del carbono metilo o carboxilo de la metionina en las proteínas tisulares. Además, parece ser que la resíntesis de la metionina a partir de la homocisteína aumenta al incrementar los niveles de cisteína. Estos hallazgos sugieren que la adición de cisteína aumenta la disponibilidad de metionina para la síntesis proteínica y, por consiguiente, el crecimiento.

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