Intestinal absorption of selenite, selenate, and selenomethionine in the rat

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Regional characteristics of intestinal absorption of selenocompounds under conditions of dietary selenium deficiency, intraluminal glutathione (GSH), and GSH depletion by buthionine [S,R] sulfoximine (BSO) treatment were studied. Absorption of ^{75}Se from selenite, selenate, and selenomethionine (SeMet) was determined in ligated loops from duodena, jejuna, and ilea of selenium-deficient rats (0.009 ppm Se) or rats fed selenite-supplemented diets (0.20 ppm Se). Selenium deficiency had no effect on absorption of any selenocompound in any intestinal segment. SeMet was absorbed most rapidly from all segments. Selenate and selenite were most efficiently absorbed from the ileum. Substantial ^{75}Se was retained within ileal tissue during selenite and SeMet absorption but was readily transferred to the body during ileal selenate uptake. Luminal GSH (50 μmol/L) had no effect on mucosal GSH levels nor on selenite uptake. BSO treatment decreased tissue GSH levels to 37%–54% of controls depressing ^{75}Se-selenite uptake to 55%–64% and transfer to 29%–34% of controls. ^{75}Se-SeMet absorption was not altered by 1 mmol/L intraluminal GSH or by mucosal GSH depletion. No evidence for homeostatic regulation of selenium absorption was obtained. Intracellular GSH appears to be involved in transepithelial transport of ^{75}Se-selenite but not ^{75}Se-SeMet.

Keywords: selenite; selenate; selenomethionine; intestinal absorption; glutathione; buthionine sulfoximine

Introduction

The accumulation and retention of selenium in tissues depends on the form of selenium administered.[1–3] Both in vivo and in vitro studies have suggested that selenium is efficiently transported across the intestinal epithelium.[1] However, ^{75}Se from selenite and selenomethionine (SeMet), in contrast to selenate, appears to be extensively bound by mucosal tissue components[4,5] and may not be readily available for subsequent transfer into the body. The brush border membrane is one cellular component that can bind large quantities of selenite and SeMet-derived ^{75}Se.[6–8] Some evidence is available to indicate differential absorption of various selenium compounds in different parts of the digestive tract.[9] However, the relative efficiency of transepithelial transfer of different forms of selenium from various segments of the small intestine has not been determined.

Although no evidence for a specific transport system for selenite has been reported, tissue sulfhydryl groups including glutathione (GSH) are thought to be involved.[6,10,11] GSH has previously been shown to enhance the uptake of ^{75}Se from selenite in studies using everted gut sacs, isolated intestinal cells[11] and mucosal sheets from rats.[12] In addition, intraperitoneal administration of diethylmaleate, a sulfhydryl group reagent, depressed absorption from ligated loops of rat small intestine[11] but GSH levels were neither specifically manipulated nor measured. Buthionine-[S,R]-sulfoximine (BSO) is a specific inhibitor of GSH synthesis.[13] Intestinal selenite transport in BSO-treated animals has not previously been studied. No effect of dietary selenium on selenite absorption was observed in a balance study with the rat.[14] However, the influence of metabolism or binding of selenite by the intestinal tissue on lumen to blood transfer was not addressed. Although graded levels of dietary selenium did not

Published with the approval of Oregon State University Agricultural Experiment Station as Technical Paper #9067. This study was supported by Public Health Service Research Grant DK 38306 from National Institute of Diabetes and Digestive and Kidney Diseases.
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Received July 17, 1991; accepted October 21, 1991.

alter the transmural transport of either selenite-derived or selenomethionine-derived ^{75}Se across ligated loops of chick duodenum,[10] the effects of selenium deficiency were not studied in these animals. Selenate is thought to be absorbed by an active sodium-dependent process localized to the distal small intestine.[15,16] The possible modulation of this system by dietary selenium has not yet been explored.

The goals of the present work were to compare the relative efficiencies of absorption of selenium as selenite, selenate, and SeMet among various regions of the small intestine, to determine the influence of dietary selenium deficiency on selenium absorption, and to investigate the role of GSH in transepithelial selenium transport.

Materials and methods

Animals and diets

Male Sprague-Dawley rats (Simonsen Laboratories, Gilroy, CA, USA) were given ad libitum access to tap water and either purified or commercial rat diets (Wayne Lab-blox, Allied Mills, Inc., Chicago, IL, USA). The basal diet[17] was composed of 30% torula yeast (Rhinelander Paper Co., Rhinelander, WI, USA), 51.5% sucrose, 9% purified cellulose (Solka Floc, Brown Co, Berlin, NH, USA), 5% corn oil, 3.5% AIN-76 mineral mix without sodium selenite,[18] 1% AIN-76 vitamin mix,[18] 0.3% DL-methionine, and 0.2% choline citrate. Selenium as sodium selenite was added to the basal diet. The diets were shown by analysis to contain selenium at the following levels (mg Se/kg diet): basal, 0.009; selenite-supplemented, 0.20; commercial rat diet, 0.46.

Procedures

In the first experiment, 48 weanling rats were divided into two groups and fed the purified diet with or without selenite supplementation for a period of 9–12 weeks. Selenite, SeMet, and selenate uptake measurements were performed at 9, 10, and 12 weeks, respectively. Animals were fasted overnight. Anesthesia was induced with sodium pentobarbital (80 mg/kg i.p.). In situ ^{75}Se absorption was measured using ligated loops made in the duodenum (D), mid-jejunum (J, 10 cm distal to the ligament of Treitz), and mid ileum (I, 10 cm proximal to the ileocecal valve) of each animal. The duodenal loops were 7–8 cm in length while the jejunal and ileal loops were 10 cm. A volume of 0.5 mL of 50 μmol/L sodium selenite; sodium selenate; or D,L-SeMet in 0.15 M NaCl, pH 7.4 was injected into the loops with tracer amounts of ^{75}Se (0.02 μCi $Na_2{}^{75}SeO_3$, $Na_2{}^{75}SeO_4$, or L-^{75}SeMet, Amersham Corp, Arlington Heights, IL, USA). Absorption was allowed to continue for 20 minutes when selenite or selenate was injected into the loops. However, because of the highly efficient uptake of SeMet, a shorter time period (8 minutes) was used. These time periods were based on prior work by others[10,15] and double perfusion studies in our laboratory. They were chosen to achieve a linear pattern of absorption in various regions of the small intestine in a system where the substrate absorbed from the lumen is not replenished. Following the absorption period, the loops were excised from the animal, blood was obtained by heart puncture and the animal was killed by exsanguination. The loops were drained and rinsed with 30 mL of ice-cold saline. Radioactivity in the loop contents, including the rinseouts and the empty loops, was determined in a gamma scintillation counter (Beckman Instruments Model 8000, Fullerton, CA, USA).

In a second experiment, the effects of luminal GSH or treatment with BSO on the absorption of ^{75}Se from selenite or SeMet were examined. Forty-two rats weighing approximately 300 g were fed commercially available rat diet for one week. BSO was administered by subcutaneous injection (2 mmol/kg body weight) to 14 animals 6 hours prior to surgery. Ligated loops 10 cm in length were made in the jejunum and ileum only. As before, a 50 μmol/L concentration of each selenium compound in 0.5 mL 0.9% NaCl, pH 7.4 was injected into the loops. When selenite was the substrate, 50 μmol/L GSH was added to the dosing solution and the absorption period was 20 min. This level of GSH was used because higher concentrations were shown to reduce selenite to elemental selenium under the experimental conditions. When selenomethionine was injected, 1 mmol/L GSH was present and an 8 min. absorption time was used. This higher level of GSH was used to mimic the normal intraluminal concentration and reduction of selenium did not occur. The intestinal loops were rinsed with ice-cold Earle's balanced salt solution[19] and the radioactivity was immediately determined. Mucosa was scraped from the underlying muscle layers with a glass microscope slide. The mucosal tissue was weighed and homogenized with a glass/teflon homogenizer in 10 volumes of ice-cold 100 mmol/L sodium phosphate buffer, pH 6.5. An aliquot representing approximately 2–3 mg protein was taken for measurement of GSH. GSH was determined by formation of the dinitrophenol derivative and analyzed by high pressure liquid chromatography (Spectra-Physics model 8000A, San Jose, CA, USA) according to the procedure of Fariss & Reed.[20] All solutions used in the derivatization were deaerated under nitrogen. Protein was analyzed by the Bio-Rad dye-binding method (Bio-Rad Laboratories, Richmond, CA, USA).

Selenium levels in diets and whole blood were measured fluorometrically according to the semi-automated method of Brown and Watkinson,[21] using an Alpchem II system (Alpchem Corp., Milwaukie, OR, USA). Whole blood glutathione peroxidase (GSHPx, EC 1.11.1.9) activity was determined by the coupled enzyme procedure of Paglia and Valentine[22] as modified by Black et al.[23]

Intestinal transport of selenium was evaluated as three components. The amount of the total ^{75}Se missing from the lumen was considered to be "absorbed." The amount present in the loop tissue after rinsing was referred to as "intestinal retention." The percent "transferred to the body" was obtained by difference between absorption and retention.

Statistical analyses were performed with the Student-Newman-Keuls test.[24] A value of $P < 0.05$ was considered statistically significant.

Results

The overall weight gains for the animals fed the purified diets for 9 weeks were 16.5 ± 0.5 g/wk and 16.2 ± 1.4 g/wk (mean ± SEM) for the selenite-supplemented and -deficient groups, respectively. These animals were used for the measurement of selenite absorption. There was an 18% depression in weight gain for the deficient rats as compared with the supplemented animals (15.3 ± 0.8 g/wk versus 12.6 ± 0.9 g/wk) in the rats fed the diets for 10 weeks. These animals were used to study SeMet absorption. However, there were no differences between the two groups

of animals fed for 12 weeks (13.3 g/wk ± 0.6 versus 13.2 g/wk ± 0.5) and used to measure selenate uptake.

The selenium status of the rats was confirmed by whole blood selenium levels and whole blood GSHPx activity *(Table 1)*. Whole blood selenium levels in deficient animals averaged only 12% of those achieved by the supplemented rats. GSHPx activity in deficient animals was depressed to approximately 7% of values obtained for the supplemented groups. The whole blood selenium and GSHPx values (means ± SEM) for the animals fed the commercial diet were 0.490 ± 0.006 μg/mL and 494 ± 8 nmol NADPH oxidized/(min × mg Hb), respectively.

Figure 1 shows the extent of ^{75}Se absorption from ligated loops in each segment of the small intestine using selenite, selenate and SeMet. The percentage of the total dose removed from the lumen varied from 10%–80%. There were no differences in ^{75}Se absorption from selenite, selenate, or SeMet between the supplemented and deficient groups in any segment of the small intestine.

SeMet was very rapidly absorbed in each segment studied. Significantly more SeMet than selenite or selenate was absorbed from all three gut segments. Although the magnitude of selenate absorption in the ilea appears slightly greater than SeMet uptake, there was nearly a four-fold difference in absorption time. The uptake of SeMet is so rapid that shorter absorption times were used (8 min.) as compared to the absorption period when inorganic forms of selenium were used (20 min.).

The overall magnitude of uptake was greater for selenate than selenite by approximately 40%, but regional differences in efficiency were observed. Selenite absorption in the duodena was 60% higher than selenate uptake ($P < 0.01$). However, selenate absorption exceeded selenite uptake in the jejuna by 54% ($P < 0.01$) and in the ilea by 2.7-fold ($P < 0.01$). The absorptive efficiency of both inorganic selenium compounds increased with progression down the gut. Selenate uptake exhibited a far steeper gradient between proximal and distal segments than did selenite.

The retention in the loop tissue and transfer to the body of ^{75}Se as a percentage of the total dose of ^{75}Se-selenite absorbed is illustrated in *Figure 2*. The partitioning of absorbed ^{75}Se between retention and transfer was similar in the duodenum and jejunum. However, a greater percentage of the absorbed dose was retained

Table 1 Whole blood selenium and glutathione peroxidase levels

	Selenium (μg/mL)		GSHPx (nmoles NADPH oxidized/min × mg Hb)	
Selenium in loop dose	Supplemented	Deficient	Supplemented	Deficient
^{75}Selenite	0.465 ± 0.018[a]	0.051 ± 0.001[b]	535 ± 12	41.4 ± 3.5[b]
^{75}Selenate	0.497 ± 0.020	0.056 ± 0.003[b]	466 ± 14	28.3 ± 1.7[b]
^{75}SeMet	0.505 ± 0.021	0.075 ± 0.005[b]	478 ± 12	40.0 ± 2.1[b]

[a]Values are means ± SEM; $n = 8$ animals per group.
[b]All deficient groups significantly lower than supplemented $P < 0.01$.

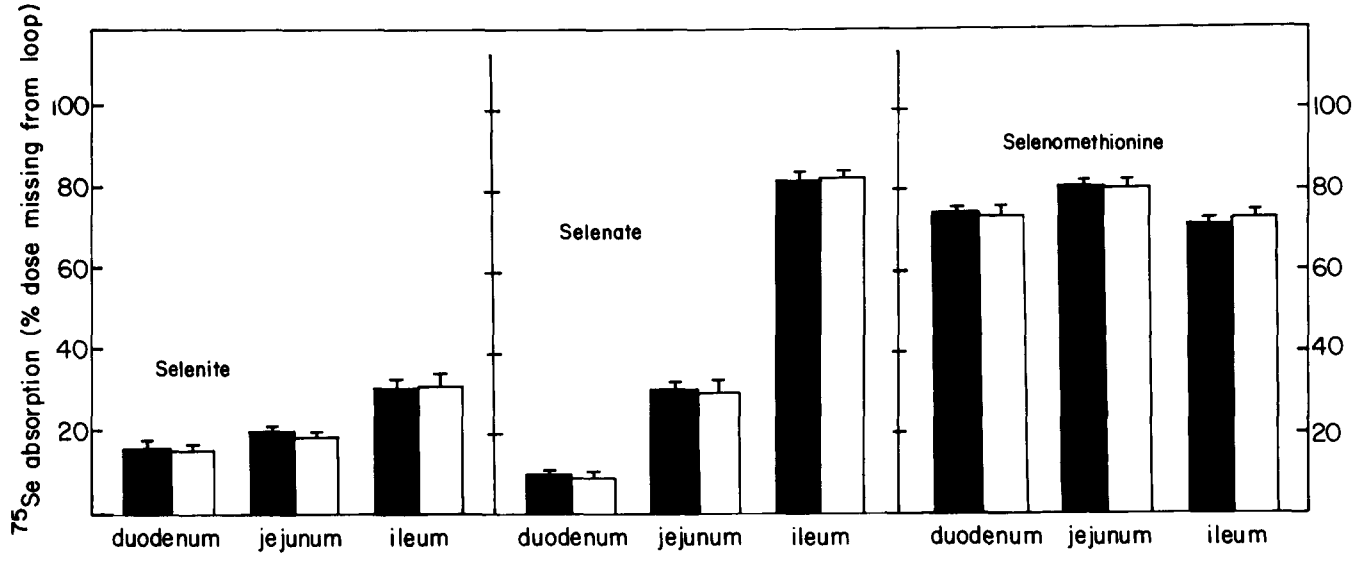

Figure 1 Absorption of ^{75}Se from selenite (left), selenate (middle), and selenomethionine (right) from ligated loops of rat duodenum, jejunum, and ileum of animals fed selenite-supplemented or Se-deficient diets. Closed bars: selenium-deficient animals; open bars: selenium-supplemented rats. Values are means ± SEM of 6–8 animals.

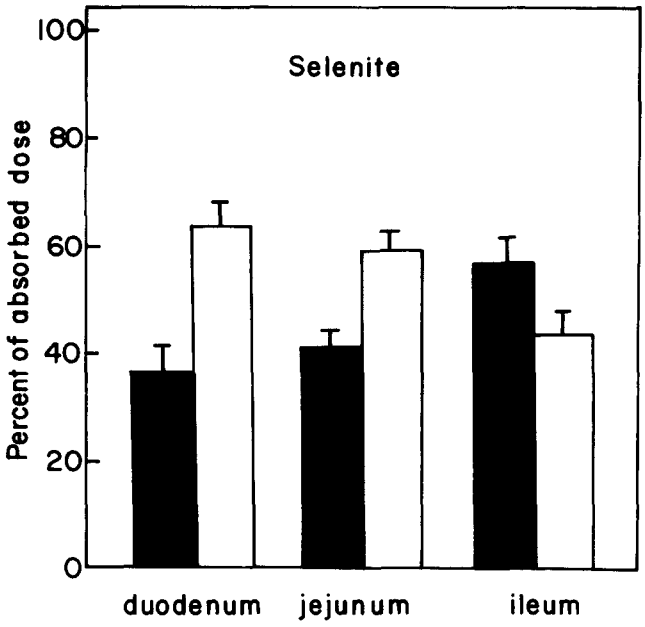

Figure 2 Retention in loop tissue and transfer to the body of ^{75}Se as a percentage of the total dose of ^{75}Se-selenite absorbed from ligated loops of rat duodenum, jejunum, and ileum. Closed bars: retained in loop tissue; open bars: transferred to body. Values are means ± SEM of 6–8 animals.

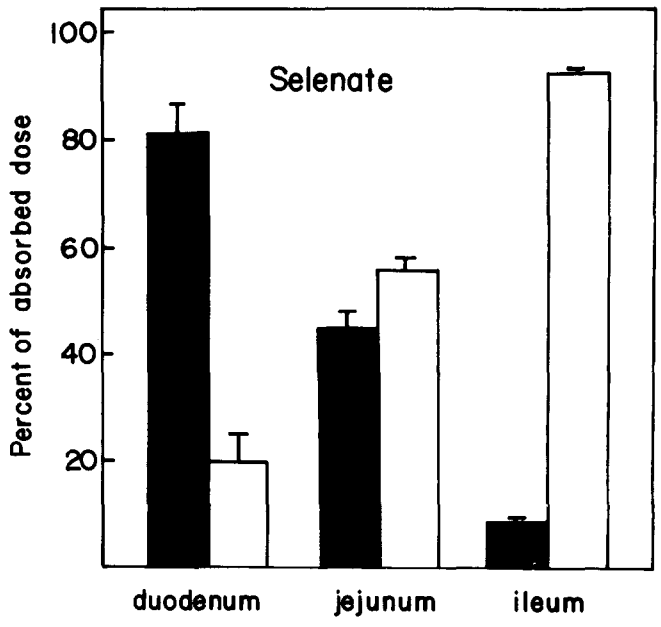

Figure 3 Retention in loop tissue and transfer to the body of ^{75}Se as a percentage of the total dose of ^{75}Se-selenate absorbed from ligated loops of rat duodenum, jejunum, and ileum. Closed bars: retained in loop tissue; open bars: transferred to body. Values are means ± SEM of 6–8 animals.

by the ileal tissue (I versus D, $P < 0.01$; I versus J, $P < 0.05$). The apparent increase in absorption for this segment can be accounted for by a higher tissue retention. Radioselenium retention by the tissue varied among segments from 5%–17% of the total dose originally injected into the loops. The total quantity of selenite-derived ^{75}Se transferred to the body was not different among the segments.

The ability of the small intestine to transport absorbed ^{75}Se-selenate into the body increased dramatically with progression down the gut *(Figure 3)*. Whereas the duodenum and jejunum transferred 20% and 55%, respectively, 92% of the dose absorbed by the ileum was transported out of the intestinal tissue (I versus D, I versus J, and J versus D, $P < 0.01$). Tissue retention of radioselenium ranged from 6%–14% of the total dose administered. The ileum is clearly the most active intestinal segment in transepithelial selenate transport.

The distribution of ^{75}Se uptake between retention and transfer during SeMet absorption is illustrated in *Figure 4*. Retention of ^{75}Se by the loop tissue varied from 19%–27% of the total dose injected. The ability of the ileum to transfer the absorbed radioselenium out of the intestinal tissue was significantly less than for the duodenum or jejunum ($P < 0.01$).

GSH levels of mucosal tissue from excised loops of rats fed the commercial diet are presented in *Table 2*. There were no differences between the controls and the animals exposed to intraluminal GSH during the absorption of selenite (50 μmol/L GSH) or SeMet (1 mmol/L GSH) in either the jejunum or the ileum. BSO treatment significantly lowered tissue GSH levels

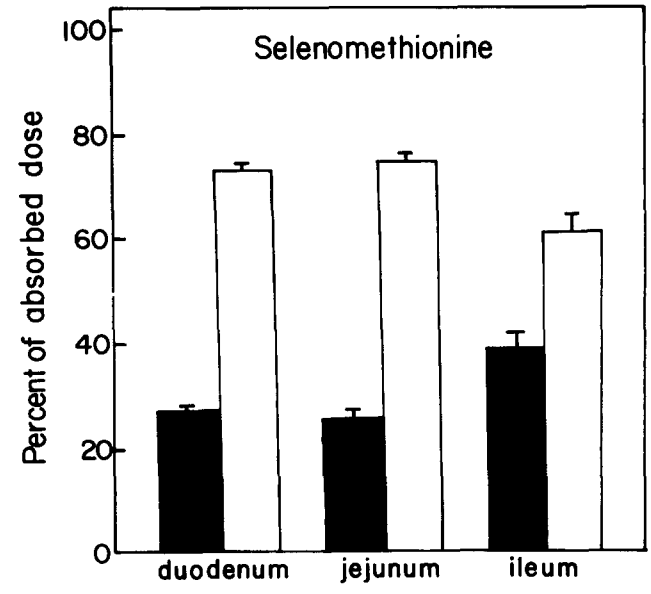

Figure 4 Retention in loop tissue and transfer to the body of ^{75}Se as a percentage of the total dose of ^{75}Se-selenomethionine absorbed from ligated loops of rat duodenum, jejunum, and ileum. Closed bars: retained in loop tissue; open bars: transferred to body. Values are means ± SEM of 6–8 animals.

to 54% of control values in the jejunum and 37% of controls in the ileum during selenite uptake ($P < 0.01$). In addition, GSH levels were significantly higher in jejunal mucosa than in ileal tissue ($P < 0.01$) in animals treated with BSO. GSH was depressed to 51% and 43% of control values in jejunum and ileum, respec-

Table 2 Effect of luminal GSH and BSO on mucosal GSH levels during absorption of selenite & selenomethionine (DL-SeMet).

	nmoles GSH/mg protein			
	50 μmol luminal selenite		50 μm luminal SeMet	
Group	Jejunum	Ileum	Jejunum	Ileum
Control	13.6 ± 1.6[a]	11.8 ± 1.0	11.0 ± 0.8	11.4 ± 0.7
GSH[b]	12.5 ± 0.7	11.4 ± 0.7	10.4 ± 0.8	12.4 ± 0.9
BSO	7.28 ± 0.40[c]	4.40 ± 0.26[c,d]	5.58 ± 0.34[c]	4.95 ± 0.31[c]

[a]Values are means ± SEM. $n = 5$ or 6 animals.
[b]50 μmol/L intraluminal GSH during selenite absorption; 1 mmol/L during selenomethionine uptake.
[c]Significantly different from controls $P < 0.01$.
[d]Significantly different than jejunum $P < 0.01$.

tively, during SeMet absorption ($P < 0.01$). The pattern of absorption, retention in loop tissue, and transfer to the body of ^{75}Se during selenite uptake from the jejunum and ileum in animals exposed to intraluminal GSH or parenteral BSO is illustrated in *Figure 5*. No changes in selenite uptake in either the jejunum or ileum were observed in response to the presence of 50 μmol/L intraluminal GSH. However, BSO treatment decreased jejunal absorption to 55% ($P < 0.01$) and transfer to 29% ($P < 0.01$) of controls. Absorption from the ileal loop was depressed to 64% ($P < 0.05$) and transfer to 34% of control values ($P < 0.01$). There were no significant differences in the percentages of the total dose retained by the loop tissue in either the jejunum or the ileum. The ileum was approximately twice as effective as the jejunum in removing luminal ^{75}Se and retaining it in the loop tissue for all three groups ($P < 0.01$). Although the ileum was more active than the jejunum in transferring ^{75}Se into the body for the control ($P < 0.05$) and GSH groups ($P < 0.01$), there were no significant differences between the segments when animals were treated with BSO.

No effects of 1 mmol/L intraluminal GSH or BSO treatment on transmural transport of ^{75}Se-SeMet in jejunal or ileal loops were observed *(Figure 6)*. There were slight, but significant, differences in absorption between the jejunum and ileum. In agreement with the first experiment, the ileal segment bound a greater proportion of the absorbed dose than the jejunum for all three groups ($P < 0.01$).

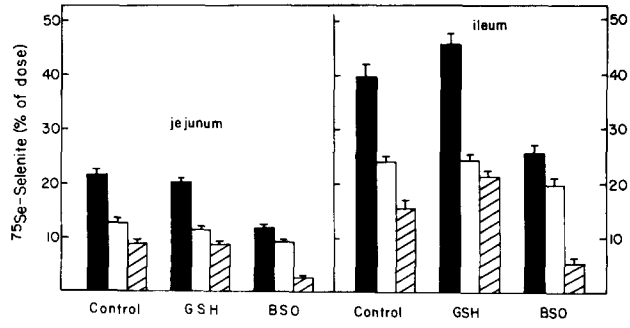

Figure 5 Absorption, retention in loop tissue, and transfer to the body of ^{75}Se as a percentage of the total dose of ^{75}Se-selenite injected into ligated loops of jejunum (left) and ileum (right) from rats exposed to 50 μmol/L intraluminal GSH or parenteral BSO. Closed bars: absorbed from lumen; open bars: retained in loop tissue; hatched bars: transferred to body. Values are means ± SEM of 6–7 animals.

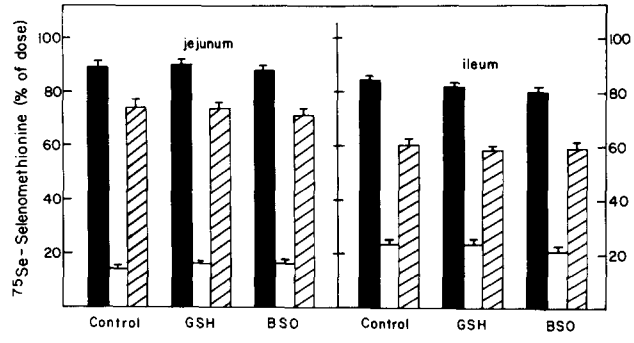

Figure 6 Absorption, retention in loop tissue, and transfer to the body of ^{75}Se as a percentage of the total dose of ^{75}Se-selenomethionine injected into ligated loops of jejunum (left) and ileum (right) from rats exposed to 1mmol/L intraluminal GSH or parenteral BSO. Closed bars: absorbed from lumen; open bars: retained in loop tissue; hatched bars: transferred to body. Values are means ± SEM of 6–7 animals.

Discussion

The present studies indicate that the selenium status has no effect on the regulation of intestinal transport of selenium compounds by dietary selenium level. This is consistent with previous investigators who demonstrated no effect of selenium deficiency on selenite absorption using a balance study with the rat.[14] These data are also in agreement with studies using ligated loops of chick duodenum where the uptake of selenite and SeMet was not altered in response to graded levels of dietary selenite.[10] In marked contrast, the absorption of zinc has been shown to be homeostatically regulated.[25,26] The retention of selenium has been shown to be inversely related to selenium status,[1] but the present results and those of others[10,14] indicate that this regulation is not at the intestinal level.

In retrospect, the use of L-SeMet may have been preferable to DL-SeMet, but this is not considered a major problem for a number of reasons. D- and L-

isomers of methionine, the most widely studied essential amino acid, are utilized with equal efficiency in the rat and other species.[27] Studies have demonstrated that the selenium analog displays parallel metabolic behavior. Both D- and L- isomers of SeMet have been shown to be equally effective in restoring hepatic GSH-Px activity in rats and the rates of selenium accumulation in muscle were very similar.[28] Furthermore, both enantiomorphs of SeMet were found to be equally toxic to rats.[29] Intestinal transport, as a component of utilization, is unlikely to be vastly different for the two stereoisomers. Even with the assumption that D-SeMet is unavailable, the rate (nmol/min) of L-SeMet absorption is still nearly three-fold greater than that of selenite even when selenite uptake is facilitated by GSH. It should be noted that DL-SeMet has been used with L-SeMet in absorption studies from ligated segments in the chick and the authors did not note any difficulties with this approach.[10]

These studies clearly demonstrate that SeMet is the most rapidly absorbed of the selenocompounds studied and is very efficiently taken up from all segments of the small intestine. Previous investigators using everted gut sacs of hamsters have observed that approximately 35%–45% of SeMet-derived ^{75}Se retained by the tissue is protein-bound.[4,5] Presumably, some proportion will be substituted for methionine in protein synthesis. Recent evidence suggests that the brush border membrane may provide at least some of the binding sites.[8] However, the present data indicate that neither selenium status nor GSH are involved in the tissue retention of SeMet-derived ^{75}Se.

As previously reported, selenate absorption is clearly most efficient in the more distal regions of the small intestine.[15,16] Selenate-derived ^{75}Se is very rapidly transferred into the body and does not appear to interact with intestinal components to an appreciable extent. These results are in agreement with those of others who have further demonstrated an electroneutral Na^+-anion cotransport system shared by sulfate in the distal gut.[7,15,16] The brush border membrane displays little tendency to bind selenium during selenate absorption.[7]

Although selenite is removed from the lumen most efficiently in the ileum, the ^{75}Se-selenite may interact with tissue components most readily in this segment. McConnell and Cho[5] indicated that 90% or more of tissue radioselenium was protein-bound during everted gut sac studies using selenite or selenocysteine. Although direct evidence for specific cellular binding sites is lacking, isolated brush border membrane vesicles accumulate large quantities of bound selenium.[6,7]

Several mechanisms for tissue selenium retention and its influence on transepithelial transport can be suggested. Selenite may react nonenzymatically with both soluble and membrane-bound protein sulfhydryl groups and free thiols, predominantly GSH, to form RSSeSR and GSSeSG.[6,7,10] The selenium bound at fixed sites in the cell may potentially be available for transport by exchange with soluble thiols. The action of glutathione reductase might reduce the selenotrisulfide of GSH to elemental selenium forming an insoluble precipitate within the cell.[30,31] However, cellular GSH appeared to facilitate selenium transfer in the present studies. GSSeSG may be reduced first to the intermediate, selenopersulfide, GSSeH, which may be further reduced to hydrogen selenide[30,31] and subsequently incorporated into amino acids.

BSO is a potent inhibitor of gamma glutamylcysteine synthetase.[13] Inhibition of GSH synthesis and reduced availability from biliary and vascular sources lowered mucosal GSH content.[32] Decreased GSH levels impaired the ability of the intestine to transport selenite-derived ^{75}Se across the epithelium. Because the tissue radioselenium content was only slightly lowered, GSH appears to assist with transfer into the blood. Administration of diethylmaleate, a thiol depleting agent, inhibited luminal selenite uptake from loops made in proximal rat small intestine,[11] further suggesting a role for sulfhydryl groups in selenite absorption.

Thiols, especially GSH, appear to be required for selenium metabolism in a number of cell types. The binding of intravenously administered selenite to plasma proteins is thought to depend on the prior metabolism by erythrocytes to form a GSH complex.[33] The excretion of ^{75}Se following uptake of selenite by erythrocytes is reduced by sulfhydryl inhibitors.[34] Uptake of selenite by lymphocytes is dependent on the presence of sulfhydryl groups and may involve the formation of the selenotrisulfide of GSH.[34] Recent findings support a role for GSH in the metabolism of selenite but not SeMet by chick plasma.[35] The addition of GSH and glutathione reductase to plasma simulated the function of the erythrocyte in facilitating the binding of selenite-derived ^{75}Se to plasma proteins.[35] It seems likely that the enterocyte may share this requirement for GSH in metabolizing dietary selenite.

These findings underscore the importance of the distal small intestine in the absorption of inorganic selenium, particularly when the effect of residence time is considered. The distribution of SeMet uptake follows that described for methionine and other neutral amino acids, although these results and those of others[4,8] indicate that subsequent metabolism may affect ultimate transepithelial transfer. Similar retention of ^{75}Se by the loops during uptake of selenite and SeMet suggests that components of the mucosal tissue may be involved in binding a common metabolite. Selenocysteine is a likely candidate. Metabolic pathways for the conversion of both selenium compounds to selenocysteine have been outlined by others.[35,36]

A high bioavailability of selenium from the commonly ingested forms has been assumed based on indirect absorption measurements in both animals and humans.[14,37,38] These studies, however, do not account for metabolism or binding by the intestinal cell. Parenterally administered selenium compounds, particularly SeMet and selenite, are probably not the forms of selenium ultimately secreted into the blood by the intestine. Fecal ^{75}Se as a measure of endogenous loss following i.v. or i.p. injection may not accurately rep-

resent plasma-to-lumen flux of selenium compounds, although this method is considered appropriate for other minerals, such as calcium, copper, and zinc. Further studies are needed to determine the metabolism of dietary selenium compounds by the intestinal cell during the process of absorption.

Acknowledgments

The authors wish to thank Dr. Darren Warren, Department of Biochemistry and Biophysics, for the gift of BSO and for the glutathione analyses; and Dr. Kenneth Rowe, Department of Statistics, for his assistance with the statistical analysis.

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