Available online at www.sciencedirect.com
ScienceDirect
ELSEVIER
Toxicology and Applied Pharmacology 216 (2006) 303 – 308
Toxicology and Applied Pharmacology
www.elsevier.com/locate/ytaap

Distribution and reuse of ^{76}Se-selenosugar in selenium-deficient rats

Kazuo T. Suzuki *, Layla Somekawa, Noriyuki Suzuki

Department of Toxicology and Environmental Health, Graduate School of Pharmaceutical Sciences, Chiba University, Chiba 260-8675, Japan

Received 21 April 2006; revised 17 May 2006; accepted 18 May 2006
Available online 27 May 2006

Abstract

Nutritional selenium compounds are transformed to the common intermediate selenide and then utilized for selenoprotein synthesis or excreted in urine mostly as 1β-methylseleno-*N*-acetyl-D-galactosamine (selenosugar). Since the biological significance of selenosugar formation is unknown, we investigated their role in the formation of selenoenzymes in selenium deficiency. Rats were depleted of endogenous natural abundance selenium with a single stable isotope (^{82}Se) and then made Se-deficient. ^{76}Se-Selenosugar was administered intravenously to the rats and their urine, serum, liver, kidneys and testes were subjected to speciation analysis with HPLC inductively coupled argon plasma mass spectrometry. Most ^{76}Se was recovered in its intact form (approximately 80% of dose) in urine within 1 h. Speciation analysis revealed that residual endogenous natural abundance selenium estimated by ^{77}Se and ^{78}Se was negligible and distinct distributions of the labeled ^{76}Se were detected in the body fluids and organs without interference from the endogenous natural abundance stable isotope. Namely, intact ^{76}Se-selenosugar was distributed to organs after the injection, and ^{76}Se was used for selenoprotein synthesis. Oxidation to methylseleninic acid and/or hydrolysis of the selenoacetal group to methylselenol were proposed to the transformation of selenosugar for the reuse. Effective use of an enriched stable isotope as an absolute label in hosts depleted of natural abundance isotopes was discussed for application in tracer experiments.
© 2006 Elsevier Inc. All rights reserved.

Keywords: Selenium; Selenosugar; Selenoprotein synthesis; Stable isotope; Speciation; Absolute label; Tracer experiment

Introduction

Selenium is an essential element for the normal function of the body. Nutritional selenium sources include both inorganic (selenite and selenate) and organic (selenoamino acid residues in proteins and free selenoamino acids) selenocompounds (Birringer et al., 2002; Ip, 1998; Suzuki, 2005). They are involved in the synthesis of selenoproteins (selenoenzymes) in which selenium is present as selenocysteinyl (SeCys) residues that participate in the redox reaction of selenoenzymes as the active center. Since nutritional selenium is incorporated into selenoenzymes according to the UGA codon for the SeCys residue (Chambers et al., 1986; Zinoni et al., 1986), diverse nutritional selenium sources have to be converted to the same intermediate, which is assumed to be selenide (Birringer et al., 2002; Ip, 1998; Suzuki, 2005).

Surplus selenium from a high dose of selenium and selenium liberated from degraded selenoproteins are excreted mostly in urine as 1β-methylseleno-*N*-acetyl-D-galactosamine (selenosugar) and in the case of excessive doses as selenosugar and trimethylselenonium (TMSe) (Francesconi and Pannier, 2004; Kobayashi et al., 2002; Suzuki, 2005; Suzuki et al., 2005). These observations suggest that nutritional selenocompounds and SeCys liberated from used selenoproteins are transformed to selenide and subsequently to the urinary metabolites (selenosugar and TMSe) for excretion.

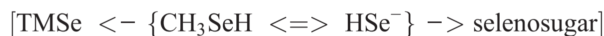
Selenosugar was the major urinary selenium metabolite within the normal to low-toxic range (Kobayashi et al., 2002). On the other hand, TMSe was found after higher doses, and it was thought to be a biological marker for excessive and toxic doses of selenium (Itoh and Suzuki, 1997). However, we showed that TMSe was excreted with dose beyond the low toxic range only in young rats but not in adults even though adults were more sensitive to higher doses (Suzuki et al., 2005). Therefore, TMSe cannot be a simple biological marker for excessive or toxic doses of selenium. Furthermore, selenium from methylseleninic acid (MSA^{IV}) [$CH_3Se(O)OH$] was

Abbreviations: eGPx, extracellular glutathione peroxidase; ICP MS, inductively coupled argon plasma mass spectrometry; MSA^{IV}, methylseleninic acid; selenosugar (Se-sugar), 1β-methylseleno-*N*-acetyl-D-galactosamine; SeCys, selenocysteine; Sel P, selenoprotein P; TMSe, trimethylselenonium.

* Corresponding author. Fax: +81 43 226 2865.
E-mail address: ktsuzuki@p.chiba-u.ac.jp (K.T. Suzuki).

0041-008X/$ - see front matter © 2006 Elsevier Inc. All rights reserved.
doi:10.1016/j.taap.2006.05.016

incorporated into selenoenzymes and selenosugar through methylselenol [CH_3SeH] followed by selenide [HS^-], where TMSe was more effectively produced and excreted into urine from MSA^{IV} than from selenite (Suzuki et al., in press). Therefore, methylselenol was the precursor for TMSe, and TMSe was produced when excess methylselenol was present. In other words, the formation of TMSe depended on the dose, selenium sources, and metabolic balance of the transformation between methylselenol and selenide including further transformation to TMSe and selenosugar (Suzuki et al., in press).


[TMSe <− {CH_3SeH <=> HSe^-} −> selenosugar]

Thus, while selenosugar is the major metabolite for the excretion of selenium, we do not know why selenium is excreted in the form of selenosugar or how selenium is synthesized to selenosugar, including the source of the sugar moiety. The source of the sugar moiety of selenosugar was suggested to be not of direct dietary origin but of endogenous origin (Suzuki et al., 2005), and the excretion of selenium in the form of selenosugar is not economical from the viewpoints of biological energy. There may be some additional biological significance for the excretion of selenium in the form of selenosugar rather than simple excretion of a urinary metabolite. For example, selenosugar excreted from organs/tissues may be redistributed and reused for the synthesis of selenoenzymes, especially in selenium deficiency.

The present study was conducted to examine if selenosugar can be used for the synthesis of selenoenzymes, especially in selenium deficiency. Selenosugar labeled with an enriched selenium isotope was synthesized to trace the labeled selenium. After tracing the label with HPLC-ICP MS, we could determine if intact selenosugar was redistributed and used after appropriate transformation to selenide, for the synthesis of selenoproteins.

Although several stable isotopes can be used as tracers for selenium, their natural abundance ratios are rather high, except for ^{74}Se (0.89%), i.e., ^{76}Se (9.37), ^{77}Se (7.63), ^{78}Se (23.77), ^{80}Se (49.61) and ^{82}Se (8.73%). A stable isotope with a higher natural abundance ratio reduces our ability to detect the label due to a lower enrichment effect relative to the corresponding endogenous natural abundance stable isotope. However, an enriched stable isotope of lower natural abundance ratios is more expensive. Therefore, we lowered the endogenous natural abundance ratios to increase the ratio of labeled to the corresponding natural abundance stable isotope. This was accomplished by depleting rats of endogenous selenium (natural abundance selenium stable isotopes) with a single selenium isotope (^{82}Se) after giving them a selenium-deficient diet and drinking water containing an excessive dose of ^{82}Se-enriched selenite. In the current depletion procedure, endogenous selenium of natural abundance ratios was reduced to a negligible level as can be seen in the profiles of residual ^{78}Se after the depletion. Thus, although an enriched stable isotope can be a relative tracer by comparing with the endogenous natural abundance isotope, the present ^{76}Se-selenosugar was traced as an absolute tracer by neglecting endogenous natural abundance isotope (residual isotope after the depletion). As a result, even if labeled selenium was not efficiently incorporated, it could be traced as an absolute label. Therefore, incorporation and transformation were more easily and clearly traced than in rats with normal natural abundance selenium.

Materials and methods

Reagents. Hydrogen peroxide and nitric acid were purchased from Wako Pure Chemicals Co. (Osaka, Japan). A standard selenium solution for atomic absorption spectrophotometry (1000 μg/ml; Kanto Chemicals Co., Tokyo, Japan) was used after appropriate dilution with 0.1 M nitric acid for calibration of selenium concentration. Trimethylselenonium (TMSe) iodide was purchased from Tri Chemicals Inc. (Yamanashi, Japan).

Selenium-deficient diet. A commercially available selenium-deficient diet (Oriental Yeast, Tokyo) was used with the following constituents: Torula yeast 30%, sucrose 55.7%, lard 5%, liver oil 3%, mineral mixture (g per 100 g of mixture: $CaHPO_4$ 14.56, KH_2PO_4 25.72, NaH_2PO_4 9.35, NaCl 4.66, Ca-lactate 35.09, Fe-citrate 3.18, $MgSO_4$ 7.17, $ZnCO_3$ 0.11, $MnSO_4 \cdot 4–5\ H_2O$ 0.12, $CuSO_4 \cdot 5\ H_2O$ 0.03 and KI 0.01) 5%, vitamin mixture (per 100 g of mixture: vitamin A 46600 IU, vitamin D_3 23300 IU, vitamin E 1.2 g, vitamin K_3 6.0 mg, vitamin B_{12} 0.20 mg, vitamin C 588 mg, biotin 1.0 mg, folic acid 2.0 mg, calcium panthothenate 235 mg, nicotinic acid 294 mg and inositol 1.176 g, adjusted to 100 g with lactose) 1%, and DL-methionine 0.3%.

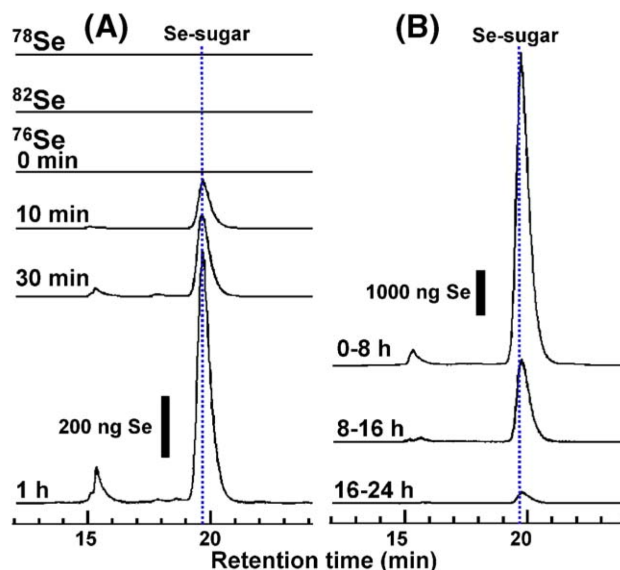


Fig. 1. Time-related changes in the distributions of ^{76}Se in the urine of rats after a single intravenous injection of ^{76}Se-selenosugar. Rats were depleted of natural abundance selenium as described in Materials and methods. ^{76}Se-Selenosugar (Se-sugar) was injected intravenously as a single dose of 25 μg Se/kg body weight, and (A) urine was collected at each time point by direct sampling from the bladder of each rat before sacrifice, and (B) 8-h urine was collected using a metabolic cage from three rats that were sacrifice 24 h later. The collected urine in each group was combined and centrifuged at 1600×*g* for 10 min to remove non-soluble matters. The urine specimen was subjected to speciation analysis on a GS 320 column by HPLC-ICP MS. ^{78}Se profile is presented to show the residual selenium after the depletion with ^{82}Se, while ^{82}Se profile shows the endogenous selenium profile after the depletion with ^{82}Se. Elution profiles of ^{76}Se show the distributions of ^{76}Se in the urine at 0 (before injection of the labeled selenosugar), 10, 30 and 60 min obtained from the bladder, and 8-h urine collected after an intravenous injection of ^{76}Se-selenosugar. Each ^{76}Se profile was presented after normalization to selenium content per urine remaining in the bladder at each time point (A) and 8-h urine (B). Although authentic TMSe was eluted at 24.0 min, TMSe was not detected in the present urine specimens. The vertical bar shows the detection level of selenium by HPLC-ICP MS.

Download English Version:

https://daneshyari.com/en/article/2571794

Download Persian Version:

https://daneshyari.com/article/2571794

Daneshyari.com