Behavior of various elements in selenium-deficient rats using the multitracer technique

Rieko HIRUNUMA and Shuichi ENOMOTO The Institute of Physical and Chemical Research (RIKEN) 2-1, Hirosawa, Wako-shi, Saitama 351-0198, Japan

Abstract

Uptake and distribution of various trace elements in the Se-deficient rats (I) and (II) were examined by the multitracer technique, which can be used to evaluate the behavior of many elements under the same experimental condition. Wistar male rats born to Se-deficient darm were fed with Se-deficient diet for 12 weeks after birth to make them Se-deficient rats (I). And male rats were fed with Sedeficient diet for 8 weeks to make them Se-deficient rats (II). The multitracer solution was injected intravenously into each rat. These rats were sacrificed at several times after injection, and the radioactivity in their organs was measured using high-purity Ge detectors. The uptake of Se was higher in the brain of the Se-deficient rats (I) and (II) than in that of the control ones. The uptake of Se was higher in the testicles of the Se-deficient rats (II) than in that of the control ones. The uptake of As, Fe, and Sc was larger in the liver of the Se-deficient rats (I) than in that of the Sedeficient (II) and control ones.

1 Introduction

Selenium is an essential and a poisonous element to mammals, which means administration of Se compounds has a narrow margin of safety between therapeutic and toxic doses [1]. A number of studies on the role of Se in biochemistry are found in literature: selenium is known as the central element of glutathione peroxidase [2]. Thirteen Se-containing proteins (molecular weights from 12,100 to 75,400) have been found in organs of rats [1]. The binding of selenite to plasma proteins and the role of erythrocytes have been studied [3,4]. In rats and human, at least two Sebinding proteins, in which selenite is not incorporated, are present in plasma. It is well known that Hg poisoning is inactivated by some effect of Se [5]. Other than this, it is reported that Se is in a competitive or synergetic relationship with several elements such as Cd, Zn, Co, Ag, and Au [6-8]. Therefore, it is expected that distributions of other trace elements in various organs are also influenced by the amount of Se fed to the mammals. However, no systematic study has been reported on the behavior of trace elements in Se-deficient rats. This paper describes the uptake and distribution of trace elements in two types of Sedeficient rats examined by the multitracer technique. This technique is useful to evaluate the behavior of many elements under the identical experimental condition [9]. In this investigation, rats bred on Se-deficient diet from the fetal period were used as Se-deficient rats (I). Se-deficient rats (II) were fed on Se-deficient diet from the weanling period.

2 Experimental

2.1 Preparation of a multitracer solution

Multitracer solutions containing various kinds of radionuclides were prepared from an Ag target irradiated with ¹²C, ¹⁴N, or ¹⁶O beam of 135 MeV/nucleon from RIKEN Ring Cyclotron. The irradiated Ag target was dissolved in (1:1) HNO₃. Then Ag was precipitated as AgCl with conc. HCl and the AgCl was filtered out. The solution was evaporated to dryness under reduced pressure. The residue was dissolved in a physiological saline solution.

2.2 Animals

Wistar male rats of 12-week-old were used in the present study.

Se-deficient rats (I): Wistar dam rats had been fed with Se-deficient diet (produced by Oriental Yeast Co., LTD., Japan) since their 14th day of pregnancy until the weaning period of their baby rats. The male rats were ablactated from their dams, and were fed with Se-deficient diet until the age of 12 weeks. These male rats were used as Sedeficient rats (I).

Se-deficient rats (II): Wistar male rats (4 weeks old) were fed with Se-deficient diet for 8 weeks to make them Se-deficient rats (II).

Control rats: Four-week-old male rats were fed with Sedeficient diet added with 0.2 ppm of Se (adequate level of Se for normal growth) for 8 weeks and used as control rats.

2.3 Administration of the multitracer

A tenth ml of saline solution containing the multitracer was injected intravenously into each rat. The Se-deficient (I), (II), and control rats were sacrificed at 72 hours after injection, and the radioactivity of their organs, tissues and blood was measured using high-purity Ge detectors. The observed γ -rays were assigned to each nuclide on the basis of its energy and half-life. The behavior of Be, Na, Ca, Sc, V, Cr, Mn, Fe, Co, Zn, Ga, As, Se, Rb, Sr, Y, Zr, Tc, Ru, and Rh was examined.

3 Results and Discussion

Influences exerted by Se-deficiency were observed on the behavior of Se, As, Fe, and Sc in various organs. Figure 1 shows the uptake of Se in the brain, the testicles, and the liver of the Se-deficient (I), (II), and control rats. The uptake of Se was higher in the brain of the Se-deficient rats (I) and (II) than in that of the control ones. On the other hand, the uptake of Se in the testicles was higher for the Sedeficient rats (II) only compared with that for the control



Fig. 1 Uptake of Se in the brain, testicles, and liver of the Se-deficient (I), (II), and control rats.

ones. And, there was almost no influence on the uptake of Se in the testicles of the Se-deficient rats (I). In the liver, the uptake of Se in the control rats was the highest among the three types, and that in the Se-deficient rats (I) was the lowest. For control rats, the uptake of Se in the liver was much larger than that in the brain and the testicles (Fig.1). For Se-deficient rats (II), the uptake in the brain and the testicles was larger than that in the liver. It is reported that Se fed to Se-deficient rats is absorbed preferentially in organs such as the brain and the testicles. It is considered that the results described above are attributed to this reason. Against this idea, however, the uptake in the testicles of Sedeficient rats (I) was smaller than that of Se-deficient rats (II), while almost comparative uptake was observed for the brain. Only a limited number of investigations, in which rats in so severe Se-deficient state as Se-deficient rats (I) were used, has been reported. The spermatozoa formation is the only one function, to our knowledge, which is so sensitive that Se-deficient state from the early stage of pregnancy makes the development of the function impossible. The decrease of the uptake of Se in the testicle of rats (I) is, therefore, considered to be related to this fact.

Larger uptake was observed for As, Fe, and Sc in Sedeficient rats (I) compared with that in Se-deficient rats (II) and control rats (Fig. 2). Selenium is known to enhance As excretion into the bile in rats [10-12]. The observed increase in As uptake suggests that the bile excretion of As



Fig. 2 Uptake of As, Fe, and Sc in the liver of the Sedeficient (I), (II), and control rats.

was decreased by the severe Se-deficiency. The increase of Fe uptake in the liver suggests an increase of Fe-binding proteins, such as ferritin or catalase in the liver. One of the reasons for the similar behavior between Sc and Fe is presumably the similarity of their ionic valence and of their ionic radii (0.73Å for Sc³⁺ and 0.64Å for Fe³⁺ [13]).

4 Conclusion

Using the multitracer technique, we have revealed characteristic effects of Se-deficiency on the uptake behavior of several trace elements. Uptake of As, Fe, and Sc in the liver of Se-deficient rats (I) was increased with time. Selenium is known to be in a competitive or synergetic relationship with several metals. From the present result on Sc, it was newly elucidated that there is also some interaction between those elements and Se.

Acknowledgement

We thank Professor H. SAKURAI of Kyoto Pharmaceutical University and Professor K. ENDO of Showa College of Pharmaceutical Sciences. We are grateful to Dr. T. OZAKI, and the staff of the RIKEN Accelerator Research Facility for cooperation in the heavyion irradiation.

References

- [1] D. Behne et al.: Evidence for specific selenium target tissues and new biologically important selenoproteins. Biochim. Biophys. Acta, **966**, 12 (1988).
- [2] R. F. Burk (ed.), Selenium in biology and human health, Springer-Verlag, New York (1994).
- [3] A. Mas et al.: Selenite metabolism in rat and human blood., Biol. Trace Elem. Res. **15**, 97 (1988).
- [4] A. Mas et al.: Role of glutathione in selenite binding by human plasma, Biol. Trace Elem. Res. **20**, 95 (1989).
- [5] T. Urano et al.: Inhibitory effect of selenium on biliary secretion of methyl mercury in rats. Biochem. Biophys. Res. Commun., 239, 862 (1997).
- [6] J. Gambhir and R. Nath: Effect of cadmium on tissue glutathione and glutathione peroxidase in rats: influence of selenium supplementation. Indian J. Exp. Biol., 30, 597 (1992).
- [7] R. S. Bedwal and A. Bahuguna: Zinc, copper and selenium in reproduction. Experientia, **50**, 626 (1994).
- [8] J. P. Berry et al.: Interaction of selenium with copper, silver, and gold salts. Electron microprobe study., J. Submicrosc. Cytol. Pathol., 27, 21 (1995).
- [9] S. Ambe et al.: "Multitracer" a new tracer technique Its principle, features, and application., J. Radioanal. Nucl. Chem. 195, 297 (1995).
- [10] O. A. Levander and C. A. Baumann: Selenium metabolism V. Studies on the distribution of selenium in rats given arsenic. Toxicol. Appl. Pharmacol., 9, 98 (1966).
- [11] O. A. Levander and C. A. Baumann: Selenium metabolism VI. Effect of arsenic on the excretion of selenium in the bile. Toxicol. Appl. Pharmacol., 9, 106 (1966).
- [12] E. Glattre et al.: Study of distribution and interaction of arsenic and selenium in rat thyroid., Biol. Trace Elem. Res. 49, 177 (1995).
- [13] R. C. Weast (ed.): CRC Handbook of Chemistry and Physics, 70th ed., pp. F-187, CRC Press, Inc., Boca Raton, Florida (1989-1990).

-360 -