Biodynamics of radioactive trace elements in Se-deficient rats: application of the multitracer technique

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The uptake and the distribution of radioactive trace elements in Se-deficient rats were examined by the multitracer technique, which can be used to evaluate the behavior of many elements under the same experimental condition. The uptake of Se was larger in the brain, spleen, and testicles of the Se-deficient rats than in those of the normal ones. The uptake of As, Fe, and Sc was larger in the liver of Se-deficient rats than in that of normal ones. In the bone, the uptake of Zr of Se-deficient rats was larger than that of normal ones. Selenium is known to be in a competitive or synergetic relationship with several metals. From the present result on Sc and Zr, it was newly elucidated that there is also some interaction between those elements and Se.

Introduction

A number of studies on the role of Se in biochemistry are found in literature.[1-3] Selenium is one of the essential trace elements and is known as the central ion in glutathione peroxidase. Thirteen Se-containing proteins (molecular weights from 12100 to 75400) have been found in organs of rat.[4] The binding of selenite to plasma proteins and the role of erythrocytes have been studied.[5,6] In rats and humans, at least two Se-binding proteins are present in plasma, although they cannot incorporate selenite. It is well known that fishes with high concentration of Hg in their body have also high concentration of Se, and that Hg poisoning is inactivated by action of Se. It is also reported that Se is in a competitive or synergetic relationship with several metals such as Mn, Fe, Co, Zn, and As. Therefore, it is very interesting and important to clarify the distribution of trace elements in various organs of Se-deficient rats. However, no systematic study has been reported on the behavior of trace elements in Se-deficient rats. This paper describes the uptake and the distribution of radioactive trace elements in Se-deficient rats examined by the multitracer technique, which can be used to evaluate the behavior of many elements under the same experimental condition.

Experimental

Preparation of multitracer solutions

Multitracer solutions containing various radionuclides were prepared from Ag target irradiated with ^{12}C, ^{14}N or ^{16}O 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 a reduced pressure. The residue was finally dissolved in a physiological saline solution.

The behavior of Ca, Sc, Fe, As, Se, Sr, Y, and Zr was examined.

Animals and treatment

Mother (Wistar) rats had been fed with Se-deficient diet (produced by Oriental Yeast Co., LTD.) since their 14th day of pregnancy until the weanling period of their baby rats. The weanling male rats were separated from their mothers, and were fed with Se-deficient diet until the age of 12 weeks. These 12-week-old Se-deficient rats and normal male Wistar rats of the same age were used for experiment.

Determination of Se concentration by instrumental neutron activation analysis

The samples of each organ was lyophilized, and pulverized with an agate mortar. Two samples for each organ (about 100mg of each powdered organ was weighed accurately) were sealed independently in polyethylene and irradiated for 24h with the standard samples of bovine liver (NBS SRM 1577) by the thermal neutron flux of 1.5×10^{12}n $cm^{-2}s^{-1}$ at F-24C in TRIGA II nuclear reactor of Rikkyo University. The criterion of photopeak identification on γ-ray spectra were 3σ above the back ground level.

Measurement of radioactivity in the various organs

A tenth ml of saline containing the multitracer was injected intravenously into each rat. The Se-deficient and normal rats were sacrificed at 3, 12, 24 and 72 hours after injection, and the radioactivities of their organs, tissues and blood were determined by γ-ray spectrometry. The observed γ-rays were assigned to tracers of different elements on the basis of their energies and half-lives.

Results and Discussion

Se concentration in various organs by neutron activation analysis

The values in Table 1 show the Se content in various organs and As for the normal and the Se-deficient rats, a small amount of Se was found only in the kidney and testicles and no Se was detected in all the other organs. Thus, the 'Se-deficient rats' used in the present experiment were proven to be really deficient in Se.

Distribution of trace elements in various organs

The characteristic results obtained on some of the elements (Se, As, Sc, Fe and Zr) are shown in Fig. 1.

Uptake of Se in the liver of Se-deficient rats was decreased with the elapse of time while the uptake of

Table 1. Selenium concentration (ppm) in various organs of normal and Se-deficient rats

	Bone	Brain	Kidney	Liver	Spleen	Testicles
Normal rats	—	1.0	6.6 ± 0.4	4.3 ± 0.3	2.6 ± 0.3	8.3 ± 0.6
Se-deficient rats	—	0.6	0.8 ± 0.1	0.07	0.3	3.5 ± 0.2

— : not detectable. Normal and Se-deficient rats determined by neutron activation analysis.

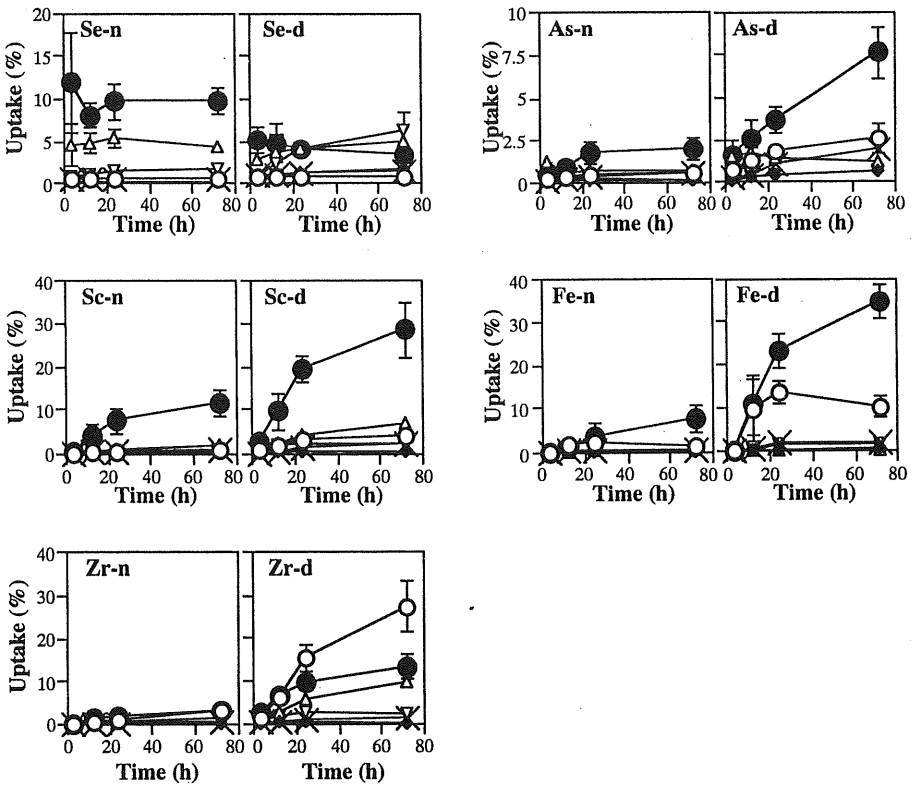

Fig. 1. Time dependence of the uptake of Se, As, Sc, Fe and Zr in various organs of normal and Se-deficient rats.
n: Normal rats; d: Se-deficient rats.

Se in brain and testicles was increased at 72 h of post injection. It has been reported that, with inadequate Se intake there was a priority supply of the element to the brain, the reproductive and the endocrine organs rather than the liver, and at a molecular level to Se-containing proteins other than glutathione peroxidase.[4] Similar results were obtained in our experiment (Fig. 1) , suggesting that the organs such as brain, and testicles need Se only in a small amount but Se has a very important and acute role in these organs.

The radioactivity of As in the liver of normal rats was increased only marginally but in case of

Se-deficient rats it was increased conspicuously with time. The following twin reasons are suggested for this accumulation of As in the liver of Se-deficient rats. First reason: It has been reported that As was in a competitive relationship with Se and also that Se poisoning was preventable by As.[7,8] Inorganic As, which is especially toxic to animals in this form, is detoxicated by methylation in the liver, and this methylated As is excreted through urine. Since the chemical form of As is AsO_3^- in our multitracer, the accumulation of As in the liver of Se-deficient rats can be interpreted as a result of the decrease in effectiveness of the As methylation. Second reason: Arsenic enhances Se excretion to bile, while Se also enhances As excretion to bile.[9,10] The observed accumulation of As in Se-deficient rats suggests that bile excretion of As was decreased by Se-deficiency.

The accumulation of Sc and Fe in the liver was increased with time in normal and Se-deficient rats. Interestingly, the uptake behavior of Sc and Fe was similar in the liver of normal and Se-deficient rats. Iron is of course one of the essential elements in living organisms, whereas for Sc no beneficial role has been reported. The reason for the similar uptake behavior between Sc and Fe is considered to be due to their same ionic valence (Sc^{3+} and Fe^{3+}) and the similarity of their ionic radii (0.73Å for Sc^{3+} and 0.64Å for Fe^{3+}).[11]

No difference was observed in the uptake behavior of most of bone seeking elements such as Ca, Sr, and Y between normal and Se-deficient rats. On the contrary, bone uptake of Zr was clearly different between Se-deficient rats and normal ones. Although Zr is classified into bone seeking elements, there are not so many reports yet on behavior of Zr in animals. The uptake different from other bone seeking elements might be due to its unique chemical form of ZrO^{2+} in the aqueous medium. The present experiment showed that Zr behaves in a characteristic way different from that of other bone seeking elements.

Conclusions

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

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