[S4-1] [4/18/2003(Fri) 09:30-10:10/Maple Hall]

Nutritional Source and Metabolism of an Essential Element Selenium

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Selenium is an ultra trace essential element for the normal functioning body because of forming the active center of redox enzymes such as four kinds of glutathione peroxidases (GPx), thioredoxin reductase (TR) and 5'-iodothyronine deiodinase. However, the adequate range between deficient and excessive levels is very narrow.

Inorganic (selenite and selenate) and organic (selenocysteine (SeCys) and selenomethionine (SeMet)) selenium can be utilized as the nutritional source. Inorganic selenium compounds are reduced to the assumed intermediate, selenide (HSe^-), while organic seleno amino acids are transformed to the same intermediate, selenide by the cleavage of C-Se bond (lyase). The common intermediate, selenide is incorporated into selenoproteins in the form of SeCys residue by the UGA codon for SeCys. Surplus selenium is methylated, and then excreted into urine in the form of methylated metabolites, i.e., monomethylated selenium (MMSe) within nutritional range and trimethylated selenium (TMSe) in toxic range, as shown in Figure 1.

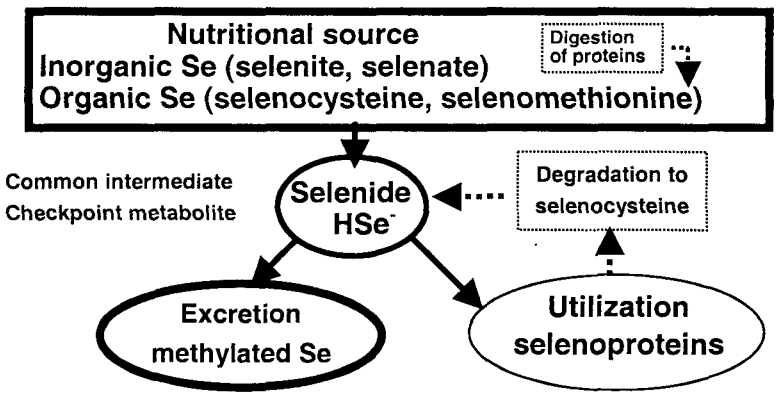

Figure 1. Proposed mechanism for Se metabolism.

Recently, we identified that MMSe is a new type of natural selenium compound, selenosugar (1beta-methylseleno-N-acetyl-D-galactosamine). The urinary selenosugar was the major selenium metabolite within the nutritional demand, and it was also present in the liver immediately after an intravenous injection of selenite as one of the two seleno metabolites. Inhibition of methylation in vivo produced a preferential production of the other seleno metabolite, which was identified as glutathione (GSH)-conjugated selenosugar, as shown in Figure 2. Thus, the intermediate and checkpoint metabolite, selenide is assumed to be transformed to GSH-conjugated selenosugar, and then methylated to the urinary selenosugar. Seleno metabolites in urine can be used as a biomarker for the nutritional demand of selenium.

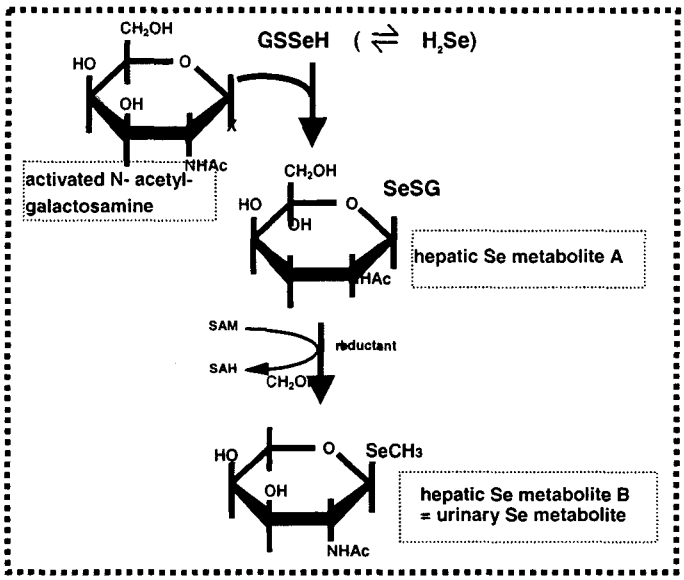

Figure 2. Proposed mechanism for selenosugar metabolism.

Selenium present in the body is mostly present in the form of SeCys and SeMet, the former one being the active center of seleno enzymes, while the latter one being a non-active form. Selenium compounds have to be transformed to the common intermediate, selenide before being utilized for selenoprotein synthesis, and then selenium is incorporated into selenoproteins in the form of SeCys. Selenium in seleno compounds has to be recognized as selenium to follow the metabolic pathway of selenium. SeMet is transformed to SeCys, and then to selenide in the regulated pathway (recognized as selenium). However, there is an

additional pathway for SeMet; SeMet can be utilized as Met without being discriminated from Met. In this case, selenium in SeMet is not recognized as selenium. Excessive SeMet was demonstrated to be incorporated without being recognized as selenium (without discriminated from Met). In our recent experiment, we further demonstrated that not only SeMet, but also selenohomocysteine is utilized in the non-regulated manner.