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Title of research project	Bioavailability and hazard assessment of nine naturally occurring selenium compounds
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【Abstract】

Selenium (Se) shows biologically ambivalent characteristics in animals. It is an essential element but becomes severely toxic when the amount ingested exceeds the adequate intake level. Its biological, nutritional, and toxicological effects are strongly dependent on its chemical form. In this study, we evaluated the toxicity and bioavailability of nine naturally occurring Se compounds, or the so-called bioselenocompounds including selenite, selenate, selenocyanate, selenomethionine, selenocystine, *Se*-methylselenocysteine, selenohomolanthionine, *N*-acetylgalactosamine-type selenosugar, and trimethylselenonium ion, *in vivo* and *in vitro*. Selenite and selenocystine showed higher toxicity than the other bioselenocompounds *in vitro*. In an *in vitro* membrane permeability study using Caco-2 cells, selenomethionine and Se-methylselenocysteine were more efficiently transported than the other bioselenocompounds. The effect of bioselenocompounds on nutritional availability was quantitatively determined from the recovery of serum selenoproteins in Se-deficient rats by speciation analysis. In contrast to the *in vitro* study, there were no significant differences in the assimilation of Se into serum selenoproteins among the bioselenocompounds, including selenoamino acids, selenosugar, and inorganic Se species, such as selenite, selenate, and selenocyanate, except trimethylselenonium ion. These results indicate that animals can equally assimilate both inorganic and organic naturally occurring selenocompounds except trimethylselenonium ion, which is the urinary metabolite of excess Se. We confirmed that the bioselenocompounds except trimethylselenonium ion had equivalent nutritional availabilities. In addition, the mutagenicity of nine bioselenocompounds was evaluated by using the Ames test. *Salmonella* typhimurium TA98, TA100, and TA1535 were used for the mutagenicity evaluation in the presence or absence of S9 mix, a metabolic activator. Only selenate showed weak mutagenicity even in the absence of S9 mix. None of the bioselenocompounds except selenate exhibited mutagenicity in all the strains tested in the presence or absence of S9 mix. Selenomethionine and selenocystine reduced the number of colonies in all the strains although no other selenoamino acids exerted the same effect. These results indicate that selenate directly or indirectly injures genome. Among the bioselenocompounds tested, selenomethionine and selenocystine show antibacterial activity, but the mechanism is unclear. Further, we observed that gut micro flora can transform the bioselenocompounds into selenomethionine, suggesting that gut microflora contribute to efficient absorption of bioselenocompounds in various foods and feeds. Consequently, the disruption of micro flora by selenocompounds affects the nutritional availability of the selenocompounds.