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Effects of Selenium Supplementation on the Diabetic Condition Depend on the Baseline Selenium Status in KKAY Mice

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Abstract Oxidative stress in obesity leads to insulin resistance in type 2 diabetes. Some selenoproteins possess antioxidant properties, suggesting that selenium (Se) may protect against type 2 diabetes; however, evidence from epidemiological studies is contradictory. We hypothesized that Se status before supplementation (baseline) contributes to the supplementation outcome. This study aimed to clarify the influence of baseline Se status on the effect of Se supplementation on the diabetic condition. Six-week-old KKAY mice were fed a diet without supplemental Se or with 0.1 ppm Se in the form of L-selenomethionine (SeM) for 2 weeks to create low-Se and sufficient-Se baseline statuses, respectively. For the next 4 weeks, low-Se mice were given a SeM (0.5 ppm Se)-supplemented diet, and sufficient-Se mice were given either a SeM (0.5 ppm Se)- or sodium selenite (0.5 ppm Se)-supplemented diet; control groups continued on baseline diets. Serum Se concentrations, glutathione peroxidase (GPx) activities, adiponectin levels, glucose tolerance, and insulin sensitivity were analyzed. All mice became diabetic during the 2-

week baseline induction period. At the end of the supplementation period, Se-receiving groups demonstrated significantly higher Se concentrations and GPx activities than their respective controls. Sufficient-Se mice receiving SeM had lower blood glucose levels and better insulin sensitivity than control and sodium selenite-receiving mice, whereas low-Se mice receiving SeM showed no such improvements compared with their controls. Our results suggest that Se supplementation in the form of SeM may help prevent type 2 diabetes aggravation in people taking the 55 µg/day Se recommended dietary allowance.

Keywords Type 2 diabetes · Selenium · Selenomethionine · Glucose tolerance · Glutathione peroxidase · Insulin sensitivity

Abbreviations

AUC	Area under the curve
DAN	2,3-Diaminonaphthalene
GPx	Glutathione peroxidase
GSH	Reduced glutathione
GR	Glutathione reductase
HFD	High-fat diet
HOMA-IR	Homeostasis Model Assessment of Insulin Resistance
OGTT	Oral glucose tolerance test
PB	Phosphate buffer
QUICKI	Quantitative Insulin Sensitivity Check Index
ROS	Reactive oxygen species
SeM	L-Selenomethionine
SeS	Sodium selenite
Low-Con	Low-Se control
Low-SeM	Low-Se mice receiving SeM
Suf-Con	Sufficient-Se control
Suf-SeM	Sufficient-Se mice receiving SeM

Novian Febiyanto and Chiho Yamazaki contributed equally to this work.

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