Influence of selenium deficiency and sulforaphane on lipid metabolism in growing rats

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Introduction

In recent years the trace element selenium (Se) was subject to a critical discussion regarding its role in lipid metabolism and diabetes. Some studies with animal models have shown positive effects of Se in the treatment of obesity, diabetes and hyperlipidemia. However, only high supranutritive selenate concentrations were effective [1, 2]. More recent studies in humans have shown that a high selenium status is associated with hyperlipidemia, including both increased cholesterol (Chol) and increased triglycerides (TG) [3, 4]. In contrast, data of our group revealed that feeding a Se deficient diet to rats reduced liver TG and Chol compared to their companions fed diets with adequate or slightly supranutritive Se [5, 6].

One very recent investigation suggested beneficial effects of sulforaphane (SFN), the main isothiocyanate in broccoli, on cholesterol metabolism in hamsters [7]. Furthermore, the transcription factor nuclear factor erythroid
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2-related factor 2 (Nrf2), which can be activated via SFN, seems to be a negative regulator of lipid synthesis [8].

Consequently the aim of our study was to investigate if SFN can counteract negative effects of Se supplementation on lipid metabolism in a similar manner like Se deficiency.

Materials and Methods

Rats and diets

28 weaned albino rats (initial body weight: 63.1 ± 1.25 g) were divided into 4 groups of 7. The basal diet was a high fat diet (20% lard, 0.15% cholesterol) with 1.5% methionine. The rats of the positive control group (PC) were fed a Se deficient diet. The diets of the other 3 groups (NC = negative control, SFN50, SFN100) contained 150 µg Se/kg. The rats of groups SFN50 and SFN100 received 2 single oral SFN doses of 50 µmol SFN and 100 µmol SFN 2 days before the end of the experiment. After 6 weeks of feeding, the animals were decapitated under CO₂ anesthesia for blood and organ sampling.

TG and Chol concentration in liver and plasma

TG and Chol concentration in liver and plasma were analyzed photometrically using commercial test kits (DiaSys Diagnostic Systems GmbH, Germany).

Relative mRNA concentration of ABCG8 and LDLR

Liver RNA was extracted using the acid guanidinium thiocyanate-phenol-chloroform extraction method [9]. Reverse transcription of 1.2 µg of total RNA and real-time RT-PCR of ABCG8 and LDLR were performed as described previously [10]. Amplification data were analysed with the Rotor-Gene 6000™ series software using the ΔΔCt method [11].
normalization the mean value of β-Actin and Rpl13a expression was used. Relative mRNA expression levels are expressed as x-fold changes relative to group PC = 1.0.

Statistical analysis

The data were analysed by one-way ANOVA using the SPSS Statistics Package 19.0 for Windows.

Results

Liver TG were significantly lower in Se deficient PC rats than in the Se sufficient NC group and in group SFN50 (Figure 1A). Liver Chol was reduced in Se deficient rats (PC) compared to all other groups (Figure 1B). SFN administration did not influence liver Chol concentration compared to the Se-sufficient control group NC. Plasma TG concentration was significantly reduced in group SFN100 compared to all other groups (Figure 1C). Plasma Chol was lower in tendency in SFN50 rats and in SFN100 rats than in both control groups (Figure 1D).
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Figure 1 (A-D): Total Chol and TG concentrations in liver (A, B) and plasma (C, D). Values are means ± SEM. Different small letters indicate significant differences between means (p ≤ 0.05).

SFN treatment at both concentrations increased relative liver LDLR mRNA concentration about 1.5-fold compared to PC and NC rats (Figure 2). Liver ABCG8 mRNA expression was about 2 to 4-fold higher in groups PC, SFN50 and SFN100 than in NC rats.

Figure 2: Relative mRNA concentrations of LDLR and ABCG8 in the liver. Values are means ± SEM. Different small letters indicate significant differences between means (p ≤ 0.05).
Discussion

The aim of our study was to investigate if SFN can counteract negative effects of Se supplementation on lipid metabolism in a similar manner like Se deficiency. Our results confirmed the findings of previous studies that Se deficiency decreases TG [6] and Chol [5] in the liver. In contrast to Se deficiency, SFN efficiently reduced TG and Chol in the plasma but not in the liver. A reason for the missing effect of Se deficiency on plasma TG and Chol could be the lower mRNA level of LDLR and the subsequent lowered import of Chol into the liver. Simultaneously the export of Chol from the liver by ABCG8 was similar between the Se deficient rats and the SFN supplemented groups. To explain the strong effect of SFN on plasma TG further analysis are needed.

References


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