International Congress Series 1304 (2007) 195–199

www.ics-elsevier.com

Dietary fat and peroxisome-proliferators affect production of quinolinate in rats, accompanied with suppression of gene expression of α-amino-β-carboxymuconate-ε-semialdehyde decarboxylase (ACMSD)

Yukari Egashira [a,*], Hiroyuki Hashimato [a], Kuniaki Saito [b], Hiroo Sanada [a]

[a] *Graduate School of Science and Technology, Chiba University, Matsudo 271-8510, Japan*
[b] *Gifu University Graduate School of Medicine, Gifu 501-1194, Japan*

Abstract. Hepatic α-amino-β-carboxymuconate-ε-semialdehyde decarboxylase (ACMSD) plays a key role in regulating NAD biosynthesis from tryptophan. ACMSD also seems to affect the generation of quinolinic acid (QA), a neurotoxin L-tryptophan metabolite. QA is also a potential endogenous toxin. The aim of this study was to evaluate QA concentration and ACMSD mRNA expression after dietary fat or peroxisome-proliferator ingestion. When male Sprague–Dawley rats were fed a clofibrate-free diet (control), or a clofibrate-containing diet for 8 days, hepatic ACMSD mRNA in rats consuming the clofibrate diet was strongly suppressed, as compared with that fed the control. Shifting from the control diet to a clofibrate diet suppressed ACMSD mRNA strongly at day 1 and continued through day 4. However, ACMSD activity decreased gradually. In rats fed with several kinds of peroxisome-proliferator-containing diets, the hepatic ACMSD mRNA was drastically decreased by all the peroxisome-proliferators we used. On the other hand, linoleic acid, clofibrate, bezafibrate and Wy-14,643 affected the serum QA levels. The change of serum QA concentration after peroxisome-proliferator ingestion is suggested to be, in part, due to a decreased ACMSD gene expression. These results suggest that the ingestion of peroxisome-proliferators affect serum QA concentration and that the transcription level of hepatic ACMSD is modulated by peroxisome-proliferators.

Keywords: Quinolinate; Aminocarboxymuconate-semialdehyde decarboxylase; Peroxisome-proliferator; Tryptophan

* Corresponding author. Laboratory of Food and Nutrition, Graduate School of Science and Technology, Chiba University, 648 Matsudo, Matsudo-shi, Chiba 271-8510, Japan. Tel.: +81 47 308 8861; fax: +81 47 308 8859.
E-mail address: egashira@faculty.chiba-u.jp (Y. Egashira).

0531-5131/
doi:10.1016/j.ics.2007.07.030

1. Introduction

Hepatic α-amino-β-carboxymuconate-ε-semialdehyde decarboxylase (ACMSD) [EC4.1.1.45] plays a key role in regulating NAD biosynthesis from tryptophan. ACMSD also seems to affect the generation of quinolinic acid (QA), a neurotoxin L-tryptophan metabolite. QA is also a potential endogenous toxin. Hepatic ACMSD activity is greatly affected by many factors such as nutrients, hormones and diseases. It was reported that ingestion of clofibrate, a hypolipidemic drug with peroxisome-proliferating activity, by rats leads to a decrease in their hepatic ACMSD activity [1]. Fukuwatari et al. also reported that phthalate esters, putative endocrine disrupters with a peroxisome-proliferating activity, inhibited the ACMSD activity [2]. In this study, we examined whether fatty acid and peroxisome-proliferators altered liver ACMSD gene expression and serum QA concentration.

2. Materials and methods

Animals. Male Sprague–Dawley rats (4-week-old) were allowed free access to food and water until being killed at the end of each experiment. Their livers were immediately perfused via the portal vein with ice cold physiological saline solution and excised. The liver samples were subjected to measurement of ACMSD activity and Northern blot analysis for determination of ACMSD mRNA expression. All rats were fed a 40% casein fat-free diet because a high protein fat-free diet increased ACMSD activity [3], facilitating the detection of hepatic ACMSD mRNA expression. The care and treatment of the rats were carried out according to the guidelines prescribed by the Faculty of Horticulture, Chiba

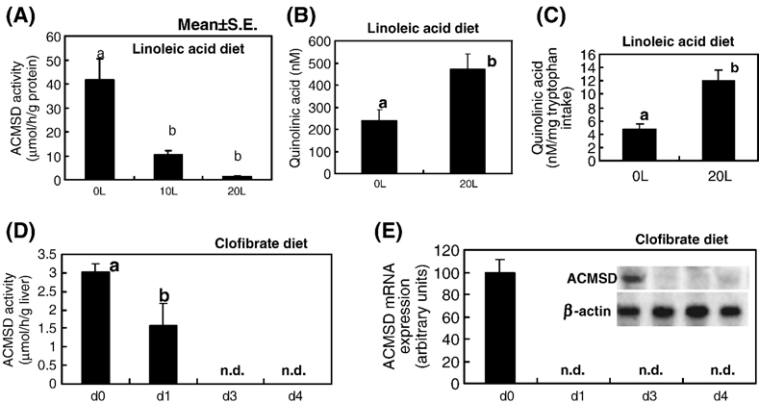

Fig. 1. (A) Hepatic α-amino-β-carboxymuconate-ε-semialdehyde decarboxylase (ACMSD) activity of rats fed diets containing 0–20% linoleic acid for 8 days. Values are means ± S.E, $n=5$. Different superscript letters in a dose response study indicate significant difference, $p<0.05$. (B,C) Effect of dietary 20% linoleic acid on serum quinolinic acid concentration under the condition of the approximately same calorie intake. (B) Serum quinolinic acid concentration (nM) (C) Serum quinolinic acid concentration (nM)/mg tryptophan intake. Values are means ± S.E, $n=6$. (D,E) Effect of the dietary shift to 0.24% clofibrate diet on hepatic ACMSD activity (D) and mRNA expression (E) in rats previously adapted to 0% clofibrate diet. Values are means ± S.E., $n=4$. Results obtained were normalized according to the signals from hybridization with β-actin and expressed in arbitrary units.