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Characterization of tryptophan–niacin metabolism in rats fed with an excessive tryptophan diet

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Abstract. We investigated tryptophan–niacin metabolism in rats when fed with an excessive tryptophan diet. Male rat of the Wistar strain (3 weeks old) were divided into the four groups of five rats each, and one of the group was fed with a 20% casein diet added with 0, 0.5, 1, 2, and 5% tryptophan for 30 days. The last day urine samples (24-h urine) were collected for analyses for the metabolites of tryptophan such as kynurenic acid (KA), xanthurenic acid (XA), 3-hydroxyanthranilic acid (3-HA), quinolinic acid (QA), nicotinamide (Nam), N^1-methylnicotinamide (MNA), N^1-methyl-4-pyridone-3-carboxamide(4-Py), and N^1-methyl-2-pyridone-5-carboxamide (2-Py). The urinary excretion of KA, XA, and 3-HA were increased according to the intake of tryptophan. However, the excretion of QA was almost the same in the groups between the groups of 2 and 5% tryptophan diets. The sum metabolites of Nam+MNA+2-Py+4-Py were almost the same in the 1–5% tryptophan diets. The value of (2-Py+4-Py)/MNA decreased sharply in the 0.5 and 1% Trp diets. Therefore the adverse effects of dietary Trp were observed from the diet containing 0.5% Trp, which was calculated as 0.45 g/kg of rat body weight. © 2007 Published by Elsevier B.V.

Keywords: Quinolinic acid; N^1-methylnicotinamide; N^1-methyl-2-pyridone-5-carboxamide; Tryptophan; Niacin; N^1-methyl-4-pyridone-3-carboxamide

1. Introduction

Niacin, serotonin and melatonin are very important bioactive compounds, which derive from an essential amino acid, tryptophan. Niacin is concerned with various metabolisms as a vitamin. Serotonin is involved in relieving pain, hypnosis, and tranquilizes as a

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neurotransmitter. Melatonin is a pineal hormone which works the rhythm of sleep. Based on these facts, tryptophan is widely found on the market as supplement. The adverse effects of tryptophan are not well known. We started to research the metabolism change of tryptophan by an excessive intake of tryptophan.

2. Materials and methods

2.1. Chemicals

Vitamin-free milk casein, sucrose, L-methionine, Gelatinized cornstarch, L-tryptophan (Trp), nicotinamide (Nam), and quinolinic acid (QA) were purchased from Wako Pure Chemical Industries (Osaka, Japan). Kynurenic acid (KA), xanthurenic acid (XA), 3-hydroxyanthranilic acid (3-HA), and N^1-methylnicotinamide (MNA) chloride were purchased from Tokyo Kasei Kogyo (Tokyo, Japan). N^1-Methyl-2-pyridone-5-carboxamide (2-Py) and N^1-methyl-4-pyridone-3-carboxamide (4-Py) were synthesized by the methods of Pullman and Colowick [1] and Shibata et al. [2], respectively. The mineral (AIN-93-G-MX) and niacin-free vitamin (AIN-93-VX) mixtures were obtained from Oriental Yeast Kogyo (Tokyo, Japan). All other chemicals used were the highest purity available from commercial sources.

2.2. Animal and diet

The care and treatment of the experimental animals conformed to the University of Shiga Prefecture guidelines for the ethical treatment of laboratory animals. Twenty male rats of the Wistar strain (3 weeks old obtained from Clea, Japan) were divided into four groups of five each, and placed in an individual metabolic cage (CT-10 for rats; Clea Japan). One of the groups was fed with a 20% casein diet as a control group and others were fed with test diets which added the 20% casein diet to 0.5, 1, 2, and 5% Trp (Table 1), and allowed free access to food and water. The animal room was maintained at the temperature of around 20 °C with 60% humidity and a 12 h light/12 h dark cycle (light onset at 6:00 a.m.). Body weight and food intake were measured daily at around 9:00 a.m., and food and water were

Table 1

	Ctrl diet (%)	Test diet (Ctrl diet+Trp) (%)			
		+0.5% Trp	+1.0% Trp	+2.0% Trp	+5.0% Trp
Casein	20	20	20	20	20
L-Methionin	0.2	0.2	0.2	0.2	0.2
Gelatinized cornstarch	45.9	45.4	44.9	43.9	40.9
Sucrose	24.4	24.4	24.4	24.4	24.4
Corn oil	5	5	5	5	5
Mineral mixture (AIN-93-G-MX)	3.5	3.5	3.5	3.5	3.5
Vitamin mixture (AIN-93-VX niacin free)	1	1	1	1	1
Trp	0	0.5	1	2	5