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Effect of melatonin on serum cholesterol status with formation of alpha-naphthylisothiocyanate-induced liver injury in rats

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Abstract. Liver injury with cholestasis appeared 24 h, but not 12 h, after treatment of rats with alpha-naphthylisotiocyanate (ANIT) (75 mg/kg, i.p.). Serum total, free, and estrified cholesterol levels were unchanged at 12 h after ANIT treatment but increases in serum total and free cholesterol levels occurred at 24 h. Melatonin (100 mg/kg, p.o.) administered at 12 h after ANIT treatment significantly attenuated these increases at 24 h after the treatment. Thus, melatonin attenuates the disruption of serum cholesterol status with liver injury formation in rats treated with ANIT.

Keywords: Alpha-naphthylisothiocyanate; Liver injury (rat); Melatonin; Serum cholesterol status

1. Introduction

Aberrations in lipid and lipoprotein metabolism have been reported in rats and mice with alpha-naphthylisothiocyanate (ANIT)-induced acute liver injury with cholestasis [1–6]. In ANIT-treated rats, increases in total cholesterol (T-Chol) and free cholesterol (F-Chol) concentrations as well as phospholipid concentration and a decrease in the ratio of esterified cholesterol (E-Chol) concentration to F-Chol concentration (E-Chol/F-Chol) in the plasma or serum occur with the appearance of cholestasis [1–5].

It has been reported that prolonged administration of melatonin (MT) attenuates increased serum T-Chol concentration in rats fed a hypercholesterolemic diet [7]. It is

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Table 1
Effect of MT on serum T-Chol, F-Chol, and E-Chol levels and the E-Chol/F-Chol ratio in ANIT-treated rats

Group	T-Chol (mg/100 ml)	F-Chol (mg/ml)	E-Chol (mg/100 ml)	E-Chol/F-Chol (%)
12 h after ANIT				
Control	65.5±2.7	21.0±1.3	44.5±1.7	2.13±0.08
MT	64.0±1.6	20.9±1.7	43.1±1.6	2.14±0.02
24 h after ANIT				
Control	61.7±4.3	14.5±0.7	47.3±3.9	3.27±0.25
MT	75.1±5.3	19.2±1.3*	55.9±4.2	2.91±0.11*
ANIT	133.0±5.8*	77.1±4.4*	55.9±5.9	0.75±0.10*
ANIT+MT	87.6±3.2*#	38.8±3.0*#	48.8±2.7	1.31±0.13*#

Each value is a mean±S.E. (n=5–7). * $p<0.05$ (vs. control); # $p<0.05$ (vs. ANIT).

known that MT protects against ANIT-induced acute liver injury with cholestasis in rats by exerting its antioxidant and anti-inflammatory actions [5,8]. It is also known that orally administered MT reduces an increase in serum T-Chol concentration in rats with ANIT-induced acute liver injury with cholestasis [5]. However, it is still unknown whether orally administered MT attenuates the disruption of serum cholesterol status in rats treated once with ANIT.

In the present study, therefore, we examined whether orally administered MT attenuates the disruption of serum cholesterol status in rats treated once with ANIT.

2. Materials and methods

Male Wistar rats (7-week old) fasted for 15 h received a single injection of either ANIT (75 mg/kg. i.p.) dissolved in olive oil. All rats were fasted and received water ad libitum during experiments. At 12 h after ANIT injection, ANIT-treated and untreated rats received MT (100 mg/kg, p.o.) suspended in 1 ml of 0.25% CMC and 0.25% CMC, respectively. Each rat was sacrificed under ether anesthesia at 12 or 24 h after ANIT injection at which time blood was collected from the inferior vena cava. Serum alanine aminotransferase and aspartate aminotransferase (liver cell damage markers), gamma-glutamyl transpeptidase, total bilirubin, and total bile acid (biliary damage markers), T-Chol, and F-Chol were assayed using commercial test kits. Serum E-Chol was determined by the difference between the T-Chol and F-Chol concentrations. All values obtained are expressed as the mean±S.E. All data were statistically analyzed by ANOVA (StatView). The level of significance was set at $p<0.05$.

3. Results

The levels of all serum marker enzymes and components studied, increased 24 h, but not 12 h, after ANIT treatment (data not shown). There were no differences in serum T-Chol, F-Chol, and E-Chol concentrations and the E-Chol/F-Chol ratio between ANIT-treated and control rats at 12 h after the treatment (Table 1). ANIT-treated rats had significantly higher serum T-Chol and F-Chol concentrations and a significantly lower serum E-Chol/F-Chol ratio than control rats at 24 h after the treatment, although the serum E-Chol concentration