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Original Article

Effect of red yeast rice on toxicity of oxidized cholesterol and oxidized fish oil in rats

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SUMMARY

Background & aims: A study was undertaken to investigate the effect of red yeast rice on oxidized cholesterol and oxidized fish oil-induced toxicity in male Wistar rats.
Methods: The rats were divided into five groups, 30 male Wistar rats were fed with diets supplemented with 1% red yeast rice, 2% oxidized cholesterol or 3% oxidized fish oil for 6 weeks.
Results: Red yeast rice increase the levels of high-density lipoprotein cholesterol (HDL-C) in plasma, and glutathione (GSH) level in plasma, and decrease the activities of alkaline phosphatase (ALP), alanine transaminase (ALT) and aspartate transaminase (AST) in plasma, and the levels of low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), triacylglycerols and total cholesterol in plasma, and relative ratios of liver weight to body weight and thiobarbituric acid-reactive substances (TBARS) level in the liver of rats caused by oxidized cholesterol and oxidized fish oil. That red yeast rice might reduce the biochemical parameters characteristic in the plasma and liver of rats caused by oxidized cholesterol and oxidized fish oil.
Conclusions: It was also found that red yeast rice may play an important role in suppressing and a good recovering on short-term preventing effect from the toxicity of oxidized cholesterol and oxidized fish oil-induced toxicity in rats.
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1. Introduction

Red yeast rice (RYR) is a common food item found in China, used for many centuries to enhance the color and flavor of food, as well as a traditional medicine for digestive and vascular functions.[1–4] In the late 1990s, dietary supplement companies commercialized RYR extracts able to reduce cholesterol as efficiently as statin drugs, but were only able to sell it until 2001.[2,4,5–10] In the spring of 2001, the US Food and Drug Administration (FDA) banned the sale of any dietary supplements containing RYR or xuezhikang.[11] This product has been used in food, as a preservative or to maintain taste and color in fish and meat or for its medicinal properties.[12] RYR is a dietary staple in many Asian countries with typical consumption ranging from 0.5 to 2 oz/person/day.[13] The medicinal properties of RYR were described by pharmacologists of the Ming Dynasty (1368–1644) as cited by Ma et al.[3] Increased levels of cholesterol and triglycerides are known to be risk factors for developing coronary artery diseases. Lipid-lowering agents that inhibit HMG coenzyme A reductase are now prominent among the drugs of choice for treating hypercholesterolemia.

It is well known that marine fish are rich in *n*-3 PUFAs.[14] We have found that PUFAs inhibited the acute induction of hypertriglyceridemia and liver enlargement by a single mega dose of retinyl palmitate in rats.[15] On the other hand, these PUFAs are easily oxidized when fish livers are cooked in the air. The oxidized fish oil is a hazardous substance to human beings and animals.[16–18]

Recently, Wei et al.[19] reported that RYR played an important role in reducing the toxic effect of lipid peroxidation in rats. The marine food, usually contain amounts of cholesterol and PUFAs. Cholesterol and PUFAs oxidized during cooking, when people intake of these kinds of marine foods, the oxidized of cholesterol and fish oil were not usually prevented. The oxidized cholesterol and oxidized fish oil are harmful for human health. Therefore, the aim of the present study was to evaluate the effect of RYR on oxidized cholesterol and oxidized fish oil-induced toxicity in male Wistar rats.

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2. Materials and methods

2.1. Preparation of RYR

RYR is described as the fermented product of rice on which red yeast (*Monascus purpureus*) has been grown. *M. purpureus* strain BCRC 31498 was purchased from the Bioresources Collection and Research Center (Food Industry Research and Development Institute, Taiwan, R.O.C.). The fungus was maintained on malt extract broth (MEB) agar, containing 4 g yeast extract/l, 20 g malt extract/l, 20 g glucose/l, and 20 g agar (pH 7.0)/l. Freshly inoculated cultures were incubated at 28 °C for 5 days, after which stock cultures were kept at 4 °C and transferred to fresh medium monthly.

M. purpureus strain BCRC 31498 was grown in liquid medium by inoculating one loop of stock culture into a 500-ml Erlenmeyer flask containing 50 ml of malt extract agar I (Blakeslee's formula) growth medium (containing (1) malt extract 20.0 g, (2) glucose 20.0 g, (3) peptone 1.0 g, (4) distilled water 1.0 l, (5) agar 20.0 g, pH 4.7) and incubating the culture at 30 °C on a rotary shaker at 220 rpm. Lovastatin esterase activity was induced by the addition of lovastatin ammonium salt (LAS) to each flask to a final concentration of 0.5 mg/ml. The culture was then allowed to incubate for another day before it was harvested.

Table 1
Composition of the experimental diet for animal test of RYR, oxidized fish oil and oxidized cholesterol.

Ingredient (%)	Diets[a]				
	A	B	C	D	E
Casein	20	20	20	20	20
Methionine	0.3	0.3	0.3	0.3	0.3
Cellulose	10	10	10	10	10
Corn oil	3	0	0	0	0
Oxidized fish oil	0	3	3	3	3
Cholesterol	2	2	2	0	0
Oxidized cholesterol	0	0	0	2	2
Choline	0.2	0.2	0.2	0.2	0.2
AIN mineral	3.5	3.5	3.5	3.5	3.5
AIN vitamin	1	1	1	1	1
RYR	0	0	1	0	1
Corn starch	25	25	20	25	20
Surcose	35	35	35	35	35

[a] Group A = received the basal or control diet. All other groups were fed the basal diet with the addition of the following: Group B = oxidized fish oil + cholesterol diet (3% oxidized fish oil + 2% cholesterol), Group C = oxidized fish oil + cholesterol + taurine diet (3% oxidized fish oil + 2% cholesterol + 1% RYR), Group D = oxidized fish oil + oxidized cholesterol diet (3% oxidized fish oil + 2% oxidized cholesterol), Group E = oxidized fish oil + oxidized cholesterol + taurine diet (3% oxidized fish oil + 2% oxidized cholesterol + 1% RYR).

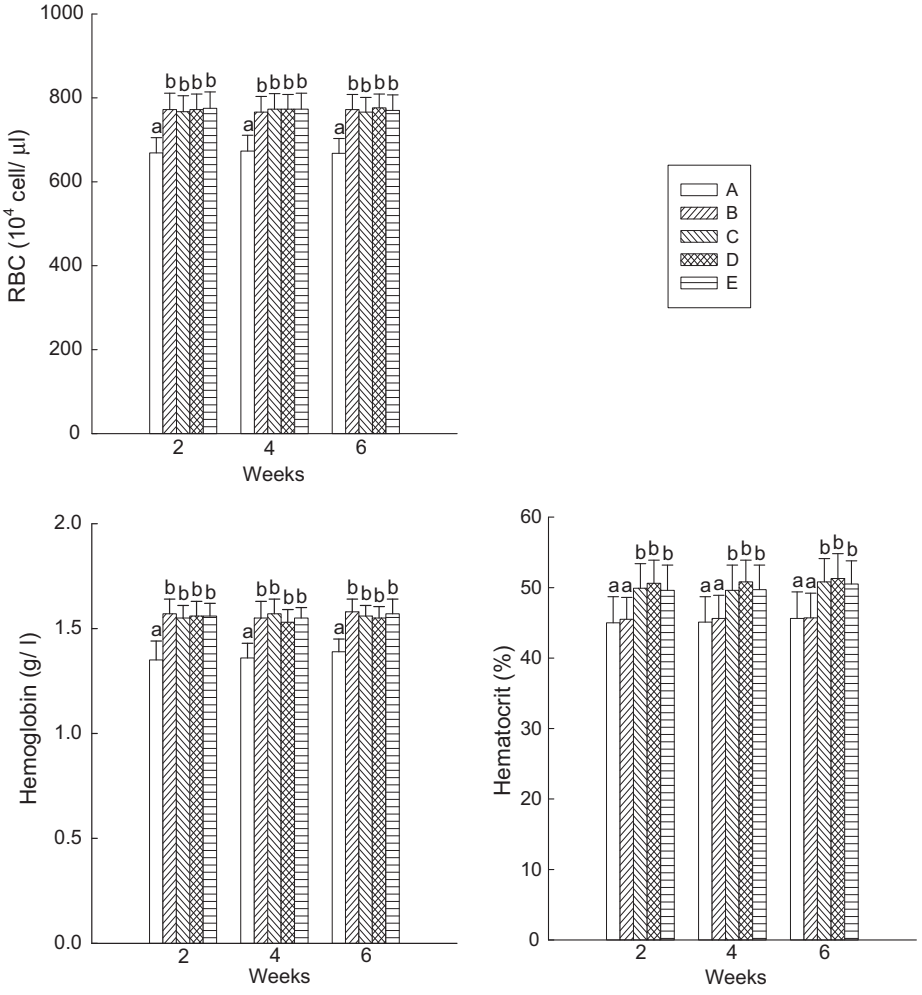

Fig. 1. Effects of RYR, oxidized fish oil and oxidized cholesterol on the RBC, Hgb and Hct of rats fed on diet after 6 weeks. (a–b) Values in the figure with different letters are significantly different at $P < 0.05$. Group A = received the basal or control diet. All other groups were fed the basal diet with the addition of the following: Group B = oxidized fish oil + cholesterol diet (3% oxidized fish oil + 2% cholesterol), Group C = oxidized fish oil + cholesterol + RYR diet (3% oxidized fish oil + 2% cholesterol + 1% RYR), Group D = oxidized fish oil + oxidized cholesterol diet (3% oxidized fish oil + 2% oxidized cholesterol), Group E = oxidized fish oil + oxidized cholesterol + RYR diet (3% oxidized fish oil + 2% oxidized cholesterol + 1% RYR).

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