

Hui-chun Xie^{1,2}, Hong-Ping Han^{1,2}, Zhi Chen¹, Jian-Ping He^{2*}

¹The Key Laboratory of Education Ministry on Environments and Resources in Tibetan Plateau, Qinghai-Normal University, 38 West Wusi Road, Xining, 810008; ²Shaanxi Normal University, 199 South Chang'an Road, Xi'an, 710062

* **E-Mail:** ghxrt4219112@163.com

Abstract

Background: The content of resveratrol is relatively high in *Polygonum cuspidatum* Sieb. et Zucc., and the resveratrol has the effect of blood vessel dilating, microcirculation improving, platelet aggregation inhibiting and anti-cancer. The objective of this paper was to study the effect of resveratrol on lipid metabolism in hyperlipidemia mice.

Materials and Methods: Through the establishment of an experimental mouse model of hyperlipidemia, the effect of resveratrol on change in total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-c), and low-density lipoprotein cholesterol (LDL-c) levels in mouse serum were determined.

Results: Resveratrol group can apparently reduce TC, TG, LDL-c and AI of hyperlipidemic mice in a dose effect manner.

Conclusion: We concluded that resveratrol can effectively reduce blood lipid levels of hyperlipidemic mice.

Keywords: Resveratrol; hyperlipidemia; TC; TG; HDL-c; LDL-c

Introduction

Resveratrol is a polyphenolic compound widespread in liliaceous, polygonaceous, leguminous plants, as well as grape skins, peanuts, and a variety of medicinal plants. Its content is relatively high in *Polygonum cuspidatum* Sieb. et Zucc, a Chinese medicinal plant (Tyler, 1997; Jang et al., 1997). Modern pharmacological studies have revealed the apparent pharmacological effects of resveratrol on the cardio-cerebrovascular system, which has the blood vessel dilating, microcirculation improving, platelet aggregation inhibiting, anti-cancer, and anti-oxidant functions (Fauconneau et al., 1997; Wnag et al., 2002; Liang et al., 1996; Xu et al., 2006; Li et al., 2009; Hyun et al 2004) . Previous studies explored the lipid-lowering effect of resveratrol by treating mice with relatively high doses of resveratrol. In this study however, mice fed with a high fat diet were treated with relatively low doses of resveratrol in order to observe the effects of resveratrol on their serum and liver lipid levels.

Materials and methods

Instruments and reagents

Resveratrol was extracted from *Polygonum cuspidatum* Sieb. et Zucc. identified by Professor Jiang Hehua from Qinghai University, and the number is 2012-1001-05. During the experiment, the resveratrol was prepared to the suspensions of desired concentrations with distilled water. Serum total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) kits were purchased from the BioSino Bio-technology & Science Inc., Beijing. Optical microscope, ECOM-F6124 semi-automatic biochemical analyzer, high-speed tabletop centrifuge were also used.

Experimental animals

50 KM Mice, male (provided by the China Medical University), weighing 18-22 g, were fed ad libitum before the experiment. All experimental procedures were approved by the Animal Research Ethics Committee of Shanxi Medical College University.

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Preparation of high-fat diet

The formula of high-fat diet was 1% cholesterol, 0.3% sodium cholate, 10% lard, and 88.7% basal feed.

Grouping and processing

The mice were randomly divided into five groups, i.e., a basic control group and four experimental groups (n = 10). All mice were adaptively fed for 4 days ad libitum; temperature was controlled between 18-22°C. After adaptation, the high-fat group was fed with a high fat diet for 4 weeks, then 0.5 mL of venous blood was collected from the inner canthus, serum was separated, and TC level was determined. The mice were randomly divided into the high-fat group, resveratrol low-, medium- and high-dose groups according to the TC level. The basic control group was fed a normal diet, and the high-fat group was continued to be fed with a high fat diet. The resveratrol treatment groups (low-, medium- and high-dose groups) were intragastrically administered with 10, 20, and 40 mg/kg of resveratrol, respectively, and the basic control group and the high-fat control group were given an equal volume of 0.5% sodium carboxymethyl cellulose solution. Feeding was continued for 6 consecutive weeks.

Test indices

Before killing, the animals were fasted for 12 h. Blood was collected from the eyeballs and serum was separated. Then, the animals were killed, and livers were removed quickly and placed in a -70°C refrigerator for later use. Serum indices: serum total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-c), and low-density lipoprotein cholesterol (LDL-c) levels were determined in strict accordance with the kit instructions.

Statistical processing

Analysis of variance on experimental data was conducted using SPSS13 software. Test criterion $\alpha = 0.05$.

Results

Effect of resveratrol on body weight of hyperlipidemic model mice

There were no statistically significant differences in changes in body weight of the mice in each group before and after the experiment (Table 1).

Table 1: Effect of resveratrol on body weight of hyperlipidemic mice ($\bar{x} \pm s$, n=10)

Group	Dose (mg / kg)	Body weight before experiment	Body weight after experiment	Amount of change
Basic control group		42.2±2.3	50.3±3.2	8.1±1.8
High-fat Control group		42.5±3.1	50.9±3.5	8.4±0.9
Resveratrol group	10	43.2±3.4	52.3±4.5	9.1±2.3
	20	42.7±2.5	49.4±4.6	6.7±2.8
	40	41.9±3.6	49.8±3.9	7.9±2.4

Effect of resveratrol on pathological change of liver in mice

Macroscopically, the livers of mice in the high-fat group were greasy, yellowish, with prominent facets; the edges were not smooth, and grainy. The severity of hepatic steatosis in mice of the high-fat group was higher than that of each resveratrol treatment group. As can be seen from Figure 1, the pathological sections of mouse livers show that the liver cells of mice in each experimental group were basically normal, without occurrence of inflammatory cell infiltration, and fat vacuoles were present in only a small number of liver cells.

Effect of resveratrol on lipid levels in mice

Compared with the basic control group, serum TC, LDL-C levels significantly increased in the high-fat group. TC levels of each resveratrol treatment group were relatively low compared with the high-fat group, as shown in Figure 2 and Figure 3.

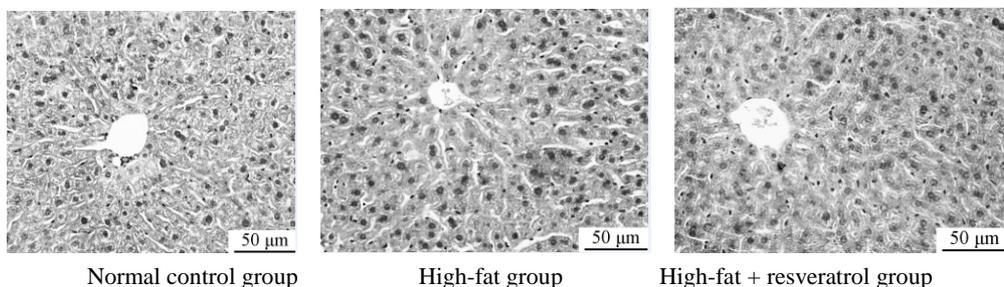


Figure 1: Pathological sections of livers of mice in each experimental group

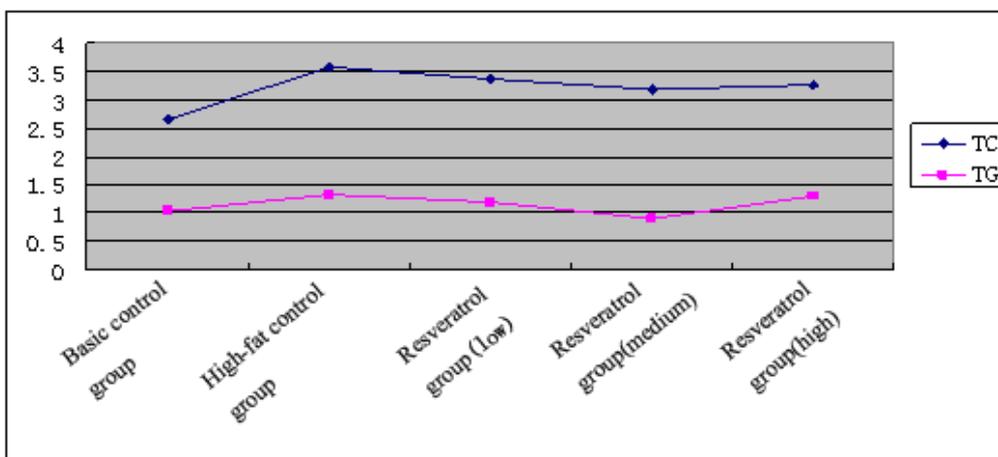


Figure 2: Changes in lipid levels (TC, TG) in mice of each group

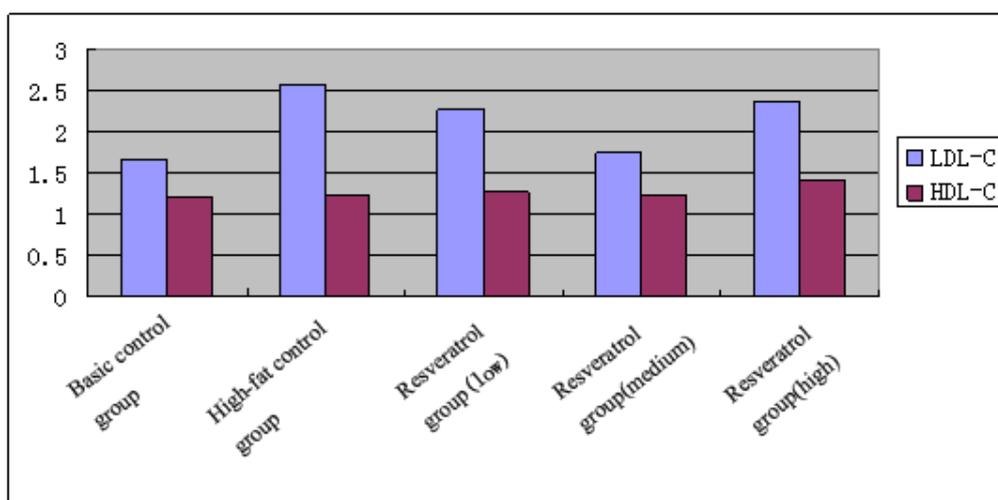


Figure 3: Changes in lipid levels (LDL-C, HDL-C) in mice of each group

Discussion

Hyperlipidemia is crucial for the induction of atherosclerosis and cardio-cerebrovascular diseases. Clinically, arteriosclerosis index (AI) and TG level are often used as important criteria for the diagnosis of coronary artery disease. Plasma LDL combines with the proteoglycans in the

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arterial wall to produce insoluble precipitate, stimulating the proliferation of fibrous tissue, and thus causes the atherosclerotic plaque. Serum total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-c), and low-density lipoprotein cholesterol (LDL-c) are commonly used indices, reflecting the body's lipid metabolism. *Polygonum cuspidatum* Sieb. et Zucc, Radix Polygoni Multiflori and other Chinese medicines rich in resveratrol have long been used in folk medicine for the treatment and prevention of hyperlipidemia and arteriosclerosis. Studies have found that resveratrol can lower the liver lipid levels in rats, and reduce triglyceride synthesis in mouse liver (Garcia-Garcia et al., 1999; Gronbaek et al., 2000; Doeherty et al., 1999).

In this experiment, mouse model of hyperlipidemia has been successfully established using a high-fat diet. Compared with the normal control group, serum TG, TC levels, as well as TG level in liver tissue were significantly increased in mice of the model group. The resveratrol group can significantly reduce the TC, TG, LDL-c and AI in hyperlipidemic mice in a dose effect manner. This may be due to the phenolic hydroxyls contained in resveratrol, through oxidation. Cholesterol is suppressed and unsaturated fatty acids are oxidized. Platelet aggregation is suppressed, accumulation of cholesterol and fat in the blood is prevented, and peripheral blood circulation is improved, thus exerting the hyperlipidemia preventing and atherosclerosis inhibiting effects.

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