

Antihyperlipidemic Activities of Common Garden Peony (*Paeonia lactiflora* Pall.)

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Abstract

Key words: anti-hyperlipidemic activity, simvastatin, total cholesterol, triglyceride, lipoprotein.

Article information:
Received: 07 Jun. 2013
Accepted: 18 Apr. 2014
Published: 20 Apr. 2014

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We studied different extracts of aboveground and underground parts of *Paeonia lactiflora* Pall. in experiment. For doing so this research needs to start up with total cholesterol. Total cholesterol is a direct cholesterol measurement that measures all cholesterol molecules in the blood, including low density lipoproteins (LDL), high density lipoproteins (HDL), and very low density lipoproteins (VLDL). The serum total cholesterol (TC) and low density lipoproteins (LDL) levels were significantly different in the experimentally-induced hypercholesterolemia rats. Effect on serum triglyceride (TG) level compared to control group, simvastatin and hypercholesterolemia diet (HD), but almost all were similar with simvastatin. Effect on serum high density lipoproteins (HDL) level compared between those. Extracts (PL1, PL2) were lower, almost the same with hypercholesterolemia diet (HD).

Cite this paper as:

Tserendejid, Ts., Zhaorigety, S., Gerelty, B. & Sukhdolgor, J. 2014. Antihyperlipidemic activities of Common garden peony (*Paeonia lactiflora* Pall.). *Mong. J. Biol. Sci.*, 11(1-2): 63-66.

Introduction

Paeonia lactiflora Pall. is a very popular plant used for traditional medicine in eastern countries. Mostly its root is used as a crude drug in traditional prescriptions in China, Japan, Korea and Mongolia as well as in some European countries (Ligaa, 2006). It is commonly used in nourishing blood, activating circulation, alleviating pain, regulating menstruation, treating liver disease and cancer. In recent years scientists from Korea and China are intensively investigated the antioxidant, cytotoxic, anti mutagenic, anti allergic, liver protective, anti arthritis and anticancer activities of roots and some pure substances of *P. lactiflora* and determined its positive effects. The 10 extracts of aboveground and underground parts of *P. lactiflora* showed a lowering effect of all level in the experimentally induced hyper lipidemic rats.

Hyperlipidemia is an abnormally high level of fatty substances, which called lipids and largely cholesterol and triglycerides contained in the blood. These fatty substances travel in the blood by attaching to proteins forming large molecules called lipoproteins. A subcategory of hyperlipidemia is hypercholesterolemia in which there is high level of total cholesterol (<http://www.americanheart.org>.2005). Hyperlipidemia is major risk factor for the atherosclerosis. Other complications are coronary heart disease, ischemic cerebra vascular disease, hypertension, obesity and diabetes mellitus (Chattopadhyaya *et al.*, 1996). It has been well established that nutrition plays an important role in the etiology of hyperlipidemias, atherosclerosis and other coronary heart disease (CHD) complications like

myocardial infarction (Zulet *et al.*, 1999).

The etiology and pathogen city of coronary heart diseases lie in the casual relationship between the development atherosclerosis elevated plasma lipid percentage cholesterol levels in blood and plasma, genetic make up, endocrinological aberration, immunologic and autonomic factors, blood flow and coagulation (Chattopadhyaya *et al.*, 1996).

Lipids. The biological molecules that are insoluble in aqueous solutions and soluble in organic solvents are classified as lipids (King, 2005).

The herbal hypolipidemics have gained importance to file the lacunae created by the allopathic drugs. A number of plants have been found to be useful in hyperlipidemia. Contents like garlic, onion and coriander used in day to day preparation of food in Indian kitchens. High intake of saturated fat and cholesterol increases serum LDL-C, probably by decreasing the amount of and/or activity of LDL receptors in the liver. Elevated and modified LDL is one of the principal factors in the development of atherosclerosis. Feeding the high fat diets causes fatty liver with accumulation (Zulet *et al.*, 1999).

The aim of the present study is to examine the possible antihyperlipidemic activity of 10 extracts of aboveground and underground parts of *P. lactiflora*. The type of dietary fat as well as the amount of cholesterol occurring in the diet has been associated with several metabolic disorders. Thus, the other aim of the present study was to investigate the influence of a hypercholesterolemia

diet enriched with pig oil and cholesterol on lipid metabolism in a rat model.

Material and Methods

Plants. The aboveground and underground parts of *P. lactiflora* were collected from the Dadal district of Khentii province, Mongolia in September 2008. We studied the antihyperlipidemic activities of the 10 extracts of aboveground and underground parts of *P. lactiflora*, determined total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL) and high-density lipoprotein (HDL) activities in blood serum rats.

Animals and diets. In this study, we used 110 adult males of Wistar rats weighing about 180-200 g, obtained from Beijing. All rats were divided into 13 groups, namely control group (CG), hypercholesterolemia diet group (HD), treatment group (SIM), treatment group (PL1 – PL5) (underground part), and treatment group (PL6 – PL10) (aboveground part). Every group was consisted of 8 rats. They were housed in standardized environmental conditions (22–24° and 12-hour light/dark cycle from 8.00 AM to 8.00 PM) with food and water freely available. The period of feeding (14 days) was carried out with different dietary formulations.

Thus, 10 rats received a control group (CG), while another group (n=8) was fed a hypercholesterolemia diet (HD) enriched in pig oil (1% by weight) and cholesterol (0.3% by weight). The rats in control group (CG) were given normal food and water of free doses, and

Table 1. Name of the rat groups and their diet characteristics.

| Number of groups | Character | Extracts and diet |
|------------------|-----------|---|
| I | CG | Normal diet + water |
| II | HD | Fat saturated diet (FF) + water |
| III | SVTT | HD + Simvastatin+ water |
| IV | PL1 | HD + EtOH extract of the underground part + water |
| V | PL2 | HD + EtOAc extract of the underground part + water |
| VI | PL3 | HD + DCM extract of the underground part |
| VII | PL4 | HD + n-BuOH extract of the underground part + water |
| VIII | PL5 | HD + water extract of the underground part + water |
| IX | PL6 | HD + EtOH extract of the aboveground part + water |
| X | PL7 | HD + EtOAc extract of the aboveground part + water |
| XI | PL8 | HD + DCM extract of the aboveground part + water |
| XII | PL9 | HD + n-BuOH extract of the aboveground part + water |
| XIII | PL10 | HD + water extract of the aboveground part + water |

CG – control group, HD – hypercholesterolemic diet, SVTT – simvastatin, PL1-PL10 – extract of *P. lactiflora*, EtOH – ethanol, EtOAc – ethyl acetate, DCM – dichloromethane, n-BuOH – n-butanol.

for all groups were fed with hypercholesterolemia diet for two weeks. Rats of treatment group (SVTT) treated with 10 mg/kg oral dose of simvastatine, the treatment group HD fed with hypercholesterolemia diet received 20 mg/kg doses. The treatment groups (PL1–PL10) received 60 mg/kg doses of aboveground part.

Experimental procedure. At the end of the experimental period, the rats were fasted after 15 days and then collected blood from artery. Serum was separated from blood samples and total cholesterol (TC), high-density lipoproteins (HDL), low-density lipoproteins (LDL) and triglyceride (TG) were measured by using appropriate kits supplied by BIOSINO BIO-TECHNOLOGY and SCIENCE INC (Beijing China).

Statistical analysis. The results are expressed as the mean \pm SEM and they were statistically evaluated by the Student's T-test or by one-way analysis of variance (ANOVA) test as appropriate. Differences were considered statistically significant if the *P*-value was < 0.05 .

Results

Hyperlipidemia was evidenced by elevated levels of serum TG, TC, LDL-C, and VLDL-C hyperlipidemic rat models also exhibited hyperlipidemia. The oral administration of 10 extracts (60mg/kg, p.o., once daily) of aboveground and underground parts of *P. lactiflora* reduced TC, TG, LDL levels in the blood serum of hyperlipidemic rats.

Effect on serum total cholesterol level. Rats fed with HD for 14 days had serum TC level of 6.70 mmol/ml ± 0.2 when measured on 15th day. This was significantly higher ($P < 0.001$) when compared to serum TC levels in normal control group rats (1.84 ± 0.131 mmol/ml). HD rats treated with simvastatin (10mg/kg, p.o, once daily) had serum level of 3.25 ± 0 when measured on 15th day. This was significantly lower ($P < 0.05$) when compared to serum TC levels in normal control

group rats (1.84 ± 0.131 mmol/ml). HD rats treated with n-BuOH extract of the underground part (120mg/kg, p.o, once daily) had serum TC level of 4.02 ± 0.72 mmol/ml, when measured on 15th day. This was significantly lower ($P < 0.05$) when compared to serum TC levels in normal control group rats (1.84 ± 0.131 mmol/ml).

Effect on serum triglyceride level. Rats fed with HD for 14 days had serum TG level of 1.97mmol/ml ± 0.10 when measured on 15th day. This was significantly higher ($P < 0.1$) when compared to serum TG levels in normal control group rats (1.66 ± 0.40 mmol/ml). HD rats treated with simvastatin (10 mg/kg, p.o, once daily) had serum level of 1.29 ± 0.19 when measured on 15th day. This was significantly lower ($P < 0.5$) when compared to serum TG levels in normal control group rats (1.66 ± 0.4 mmol/ml). HD rats treated with n-BuOH extract of the underground part (120 mg/kg, p.o, once daily) had serum TC level of 4.02 ± 0.72 mmol/ml when measured on 15th day. This was significantly lower ($P < 0.05$) when compared to serum TC levels in normal control group rats (1.84 ± 0.131 mmol/ml).

Effect on serum HDL level. Rats fed with HD for 14 days had serum HDL level of (0.29 mmol/ml ± 0.08) when measured on day of 15. This was significantly higher ($P < 0.01$) when compared to serum HDL levels in normal control group rats (0.78 mmol/ml ± 0.40). HD rats treated with simvastatin (10 mg/kg, p.o, once daily) had serum level of 0.76 mmol/ml ± 0.16 , when measured on day of 15. This was not significantly lower ($P < 0.5$) when compared to serum HDL levels in normal control group rats (0.78 mmol/ml ± 0.4). The HD rats treated with water extract of the aboveground part (120 mg/kg, p.o, once daily) had serum HDL level of 0.91 mmol/ml ± 0.13 , when measured on day of 15. This was not significantly higher ($P < 0.5$), when compared to serum HDL levels in normal control group rats (0.78 mmol/ml ± 0.4).

Effect on serum LDL level. Rats fed with HD for 14 days had serum LDL level of 4.84 mmol/

Table 2. Effect of extracts of the aboveground and underground parts of *P. lactiflora* on serum lipid concentrations of diet-induced hyperlipidemic rats

| Name of groups | CG | HD | SVTT | PL1 | PL2 | PL3 | PL4 | PL5 | PL6 | PL7 | PL8 | PL9 | PL10 |
|----------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| TC | 1.84 | 6.70 | 3.25 | 5.78 | 5.24 | 4.98 | 4.02 | 4.40 | 5.49 | 5.43 | 4.58 | 5.91 | 5.23 |
| TG | 1.66 | 1.97 | 1.29 | 1.46 | 1.29 | 1.27 | 1.26 | 1.28 | 1.51 | 1.62 | 1.21 | 1.33 | 1.33 |
| HDL | 0.78 | 0.29 | 0.76 | 0.31 | 0.29 | 0.71 | 0.47 | 0.61 | 0.43 | 0.89 | 0.64 | 0.51 | 0.51 |
| LDL | 0.65 | 4.84 | 2.14 | 3.73 | 3.78 | 3.36 | 3.08 | 3.09 | 3.83 | 3.90 | 3.64 | 3.81 | 3.95 |

ml±0.32 when measured on day of 15. This was not significantly higher ($P < 0.1$) when compared to serum LDL levels in normal control group rats (0.65 mmol/ml±0.075). HD rats treated with simvastatin (10 mg/kg, p.o, once daily) had serum level of 2.13 mmol/ml±0.93 when measured on day of 15. This was not significantly lower ($P < 0.5$) when compared to serum LDL levels in normal control group rats (0.65 mmol/ml±0.075). HD rats treated n-BuOH extract of the underground part (120 mg/kg, p.o, once daily) had serum LDL level of 0.91mmol/ml±0.13 when measured on day of 15. This was not significantly lower ($P < 0.5$) when compared to serum LDL levels in normal control group rats (0.65 mmol/ml±0.075).

Discussion

In our study we chose atherogenic diet, which contains the common ingredients in our daily food. Cholesterol feeding has been used to elevate serum or tissue cholesterol levels to assess the hypercholesteremia related metabolic disturbances in animals (Holmgren & Broun, 1995). Cholesterol feeding alone, however does not affect the serum TG level. It is assumed that a high level of saturated fat in addition to the cholesterol is required to significantly elevate serum TG level in rat model (Watts *et al.*, 1994).

Diet containing saturated fatty acids increases the activity of HMG CoA – reductase, the rate-determining enzyme in cholesterol biosynthesis; this may be due to higher availability of acetyl CoA, which stimulated the cholesterol genesis rate (Bradley–Hillgarther *et al.*, 1995). Moreover, this could be associated with a down regulation in LDL receptors by the cholesterol and saturated fatty acids in the diet, which could also explain the elevation of serum LDL-C levels either by changing hepatic LDLR (LDL-receptor) activity, the LDL-C production rate or both (Dietschy, 1998).

The activity of cholesterol ester transfer protein (CETP), a key enzyme in reverse cholesterol transport or mediates the transfer of cholesterol esters from HDL-C to triglyceride-rich particles in exchange for triglycerides. This leads to increased plasma concentration of TG decreased concentration of HDL-C (van Aalst-Cohen *et al.*, 2004). Therefore, it seems that *P. lactiflora* influenced lipid metabolism under our experimental conditions.

Acknowledgements

This study was supported by the Institute of Macromolecular Chemistry and Mongolian Medicine, Inner Mongolia, Huhhot, China. The plant material was identified by Dr. Kh. Otgonbileg.

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