

Full Length Research Paper

## Aqueous extract of *Panax notoginseng* affecting blood TC, TG and ET-1 levels in postoperative rabbits

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**This study was designed to test the postoperative protective effects of *Panax notoginseng* extract in rabbits. Carotic artery injury was induced by surgery in rabbits and then fed with *P. notoginseng* extract for 8 weeks. The serum TC, TG and ET-1 levels were examined. Results showed that administration of aqueous extracts of *P. notoginseng* significantly lowered the serum levels of TC, TG and ET-1. These results suggested that the *P. notoginseng* extract might be beneficial to postoperative recovery of rabbits with artery injury.**

**Key words:** Carotic artery injury, postoperative recovery, rabbit, TC.

### INTRODUCTION

Raw *Panax notoginseng* (Burk.) F. H. Chen (Araliaceae), a well-known medicinal herb in Asia, has a long history of use in Chinese medicine. It has been traditionally used for its hemostatic and cardiovascular effects (to arrest internal and external bleeding, reduce swelling and pain, as well as to disperse blood clots, eliminate blood stasis and promote blood circulation) (The State Pharmacopoeia Commission of PR China, 2000). Modern pharmacological studies have demonstrated that *P. notoginseng* and its ingredients possess anticarcinogenic and hepatoprotective properties, as well as protective effects on cardiovascular and cerebrovascular systems (Konoshima et al., 1999; Liu and Zhou, 2000; Liu et al., 1994; Cicero et al., 2003; Zhang et al., 1994).

Drammarane triterpene saponins are considered as the major bioactive constituents in *P. notoginseng* (Wei and Du, 1996; Cicero et al., 2003; Zhang, Wojta and Binder, 1994; Ng, 2006; Wang et al., 2006). Chronic inflammation plays a crucial role in atherogenesis (Ross, 1999). This

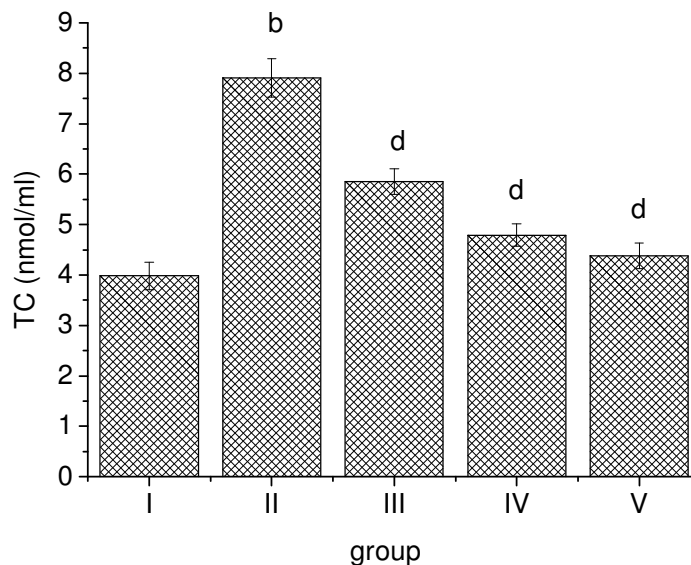
suggests that an anti-inflammatory strategy be effective in treating atherosclerosis. In this study, effect of *P. notoginseng* extract on blood TC, TG and endothelin levels were examined in rabbits with arterial injury so as to evaluate its protective effect on postoperative animals.

### MATERIALS AND METHODS

#### Plant material and preparation of the aqueous extract of panax notoginseng

*P. notoginseng* was collected in herb shop (Chongqing city, China) in March 2009. The plant material was stored at room temperature in a dry place prior to use. The preparation of *P. notoginseng* aqueous extract was realized as previously described (Zhao et al., 2009). *P. notoginseng* (100 g) was grind into fine powder, mixed with 600 ml of distilled water and then extracted in boiling water at 100°C for 1 h. The extract was filtered (Whatmann No. 1) with a Buchner filter and concentrated under vacuum. The process was repeated twice. The combined extract was put in centrifuge tubes. Tubes were centrifuged (3000 g, 15 min) and the clear supernatant fluid was collected. After centrifugation, the combined clear supernatant fluid was evaporated in a rotary evaporator and freeze-dried. The crude yield of the lyophilized *P. notoginseng* extract was approximately 28% (w/w).

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**Figure 1.** Effect of *P. notoginseng* extracts blood TC level. <sup>b</sup> $P < 0.01$ , compared with group I; <sup>d</sup> $P < 0.01$ , compared with group II.

#### Animal protocol

Thirty male white rabbits (3.1 kg) were used in this study. After this conditioning period, 26 animals were subjected to balloon injury of the thoracic aorta. Briefly, animals were anesthetized with an intramuscular injection of 25 mg/kg ketamine and 5 mg/kg xylazine and the right carotid artery isolated through a mid-line neck incision using a combination of blunt and sharp dissection. The distal carotid was ligated with a 3-0 silk suture and a 4 French arterial sheath inserted through an arteriotomy in right carotid artery. Using a 0.014" steerable guidewire the sheath was advanced into the descending aorta under fluoroscopic guidance. A 2 French Fogarty balloon catheter was then advanced through the sheath into the descending aorta. The balloon was then inflated with a 1 ml syringe such that moderate resistance was encountered on catheter withdrawal. This process was repeated for a total of three balloon passes, then the sheath withdrawn, the proximal carotid artery ligated, the incision closed, and animals permitted to recover for a further 8 weeks. During this time the animals were randomly assigned to the model control and three levels (300, 600 and 900 mg/kg b.w.) of fed *P. notoginseng* extracts. Model control animals were fed with basic diet and received same volume of vehicle. Another 10 animals were fed with basic diet and received same volume of vehicle. At the end of the study the animals were euthanized with an intravenous sodium phenobarbital (120 mg/kg) injection, plasma collected.

Triacylglycerol (TG) contents in plasma were determined with enzymatic method kit (BioSystems kit, Spain) using glycerol as a standard. Total cholesterol (TC) in plasma was measured with enzymatic method (DiaSystem kit, Germany) using cholesterol as a standard. Plasma endothelin level was measured according to method.

#### Statistical analysis

Statistical analysis of data was performed using SPSS software. Group comparisons were determined by two-way ANOVA. Unless noted, values are expressed as mean  $\pm$  SEM and *n* represents the

number of animals. In the figures values at each time point represent the mean  $\pm$  SEM of each 6 animals. A *p*-value less than 0.05 were considered statistically significant.

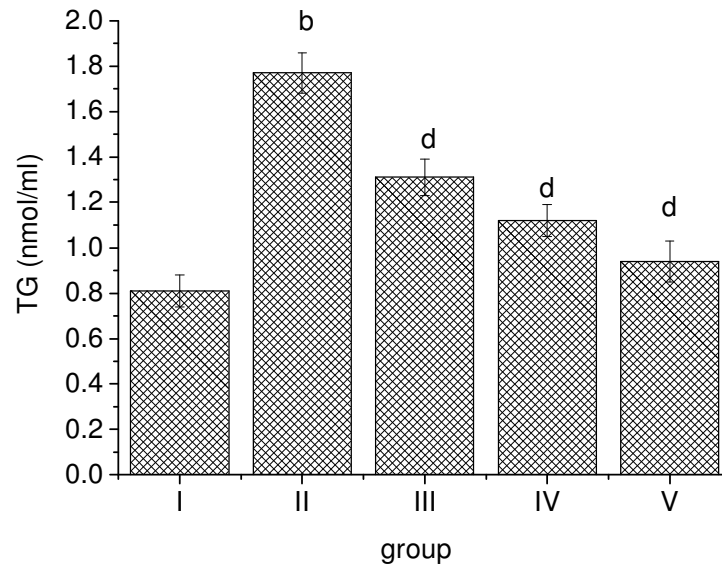
#### RESULTS

One-way ANOVA showed an overall significant effect of *P. notoginseng* extracts treatment on blood TC, TG, and endothelin levels ( $P < 0.01$ ). As shown in Figures 1, 2 and 3, TC, TG and endothelin levels of animals in model control group was significantly ( $P < 0.01$ ) increased compared to normal control animals. Treatment of animals with *P. notoginseng* extracts (300, 600 and 900 mg/kg) markedly reduced blood TC, TG, and endothelin levels in a dose-dependent manner ( $P < 0.01$ ) compared to model control animals.

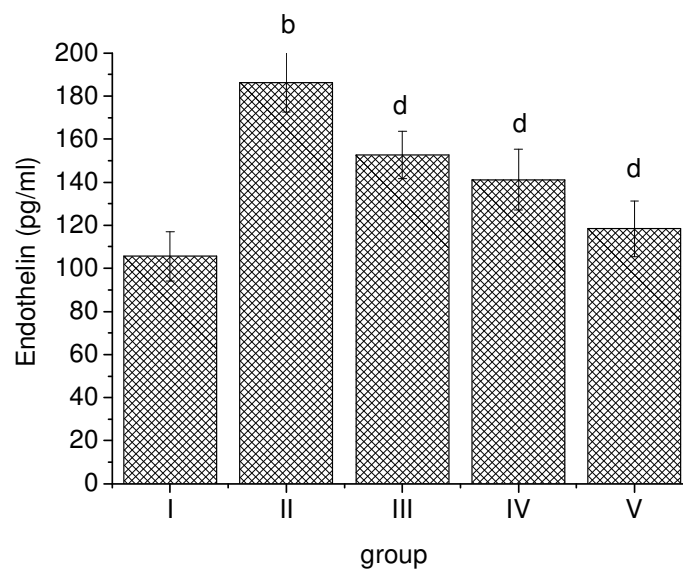
#### DISCUSSION

Coronary heart disease (CHD), also called coronary artery disease, affects about 14 million men and women in the United States. Disease develops when a combination of fatty material, calcium, and scar tissue (plaque) builds up in the arteries that supply the heart with blood. Through these arteries, called the coronary arteries, the heart muscle (myocardium) gets the oxygen and other nutrients it needs to pump blood (Wang et al., 2003).

One of the herbal medicines, *P. notoginseng* Buck F.H. Chen. (Araliaceae) root is highly prized for its therapeutic abilities to stop haemorrhages, to influence blood circulation and to act as a tonic agent, and also is the



**Figure 2.** Effect of *P. notoginseng* extracts blood TG level. <sup>b</sup> $P < 0.01$ , compared with group I; <sup>d</sup> $P < 0.01$ , compared with group II.



**Figure 3.** Effect of *P. notoginseng* extracts blood ET-1 level. <sup>b</sup> $P < 0.01$ , compared with group I; <sup>d</sup> $P < 0.01$ , compared with group II.

most common drug to treat chronic liver disease in Korea. The main root of this plant, named notoginseng, is used for treatment of trauma and bleeding due to internal and external injury. The plant is also known to have many pharmacological activities such as limitation of liver injury, anti-tumor effect, and alteration of the functional balance of the immune system (Li, 1998). Recently, the plant is widely being used by patients with chronic hepatitis. The water-extract of *P. notoginseng* Buck F.H. Chen. (Araliaceae) root (PNS) prevented liver fibrosis as well

as the development of HCC in patients with cirrhosis (Zhang et al., 1998). Recent study of us has demonstrated that *P. notoginseng* saponins (PNS) could attenuate atherosclerosis in rats via their regulation of the blood lipid profile and their anti-inflammatory roles (Zhang et al., 2008). In addition to the aforementioned results, *in vitro* study is also one requisite for the complete elucidation of PNS pharmacological actions. Cholesterol is required to build and maintain membranes; it modulates membrane fluidity over the range of

physiological temperatures. The hydroxyl group on cholesterol interacts with the polar head groups of the membrane phospholipids and sphingolipids, while the bulky steroid and the hydrocarbon chain are embedded in the membrane, alongside the nonpolar fatty acid chain of the other lipids (Jouad et al., 2003). In this structural role, cholesterol reduces the permeability of the plasma membrane to protons (positive hydrogen ions) and sodium ions (Haines, 2001). In this study, 8 weeks of *P. notoginseng* extract dose-dependently reduced TC level in rabbits suffering from arterial injury.

Triglycerides are formed by combining glycerol with three molecules of fatty acid. Triglyceride is glyceride in which the glycerol is esterified with three fatty acids. It is the main constituent of vegetable oil and animal fats. The three fatty acids can be all different, all the same, or only two the same, they can be saturated or unsaturated fatty acids (Lemhadri et al., 2006). Chain lengths of the fatty acids in naturally occurring triglycerides can be of varying lengths but 16, 18 and 20 carbons are the most common. Natural fatty acids found in plants and animals are typically composed only of even numbers of carbon atoms due to the way they are bio-synthesised (Cheng and Wolfe, 1983). Our study showed that arterial injury-induced increased TG was significantly decreased after 8 weeks of *P. notoginseng* extract treatment.

Endothelin (ET-1) is a 21 amino acid peptide that is produced by the vascular endothelium from a 39 amino acid precursor, big ET-1, through the actions of an endothelin converting enzyme (ECE) found on the endothelial cell membrane (Motte et al., 2006). The distribution of endothelial and smooth muscle receptors helps to explain the phenomenon that systemic administration of ET-1 causes transient vasodilation (initial endothelial ETB activation) and hypotension, followed by prolonged vasoconstriction and hypertension (smooth muscle ETA and ETB activation). Direct effects of ET-1 on the heart are modified by baroreceptor reflexes in response to changes in arterial pressure following systemic administration of ET-1. ET-1 has a number of other actions besides vasoconstriction and cardiac stimulation that can indirectly affect cardiovascular function (Belaidi et al., 2009). ET-1 stimulates aldosterone secretion, decreases renal blood flow and glomerular filtration rate, and releases atrial natriuretic peptide (ANP). In this study, we could find that arterial injury-induced increased endothelin was significantly decreased after 8 weeks of *P. notoginseng* extract treatment.

In conclusion, *P. notoginseng* extract could reduce blood TC, TG and ET-1 levels in rabbits. This indicated that *P. notoginseng* extract was beneficial to postoperative recovery of some diseases.

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