Hydroalcoholic Extract of Valerian, Blood Factors, and Atherosclerotic Plaque Formation in Male Hypercholesterolemic Rabbits

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ABSTRACT

Cardiovascular diseases and atherosclerosis that develops through gradual fatty deposits in the lower part of vascular endothelium are the main causes of death in the world. This research intended to study the effects of hydroalcoholic extract of valerian on the quantity of lipoproteins and on the development of atherosclerosis in the aortas of male hypercholesterolemic rabbits. This empirical research was carried out on 30 male New Zealand rabbits that were divided into 5 groups each with 6 members. The control group received no medicine. Sham group one were given 10 ml of corn oil (a cholesterol solvent) every day, sham group two 10 ml of cholesterol every day, and the experimental groups one and two 50 and 200 ml of hydroalcoholic extract of valerian, respectively. At the completion of the research, the data was analyzed using ANOVA and Duncan's test, and Excel was employed to draw the figures. Concentrations of HDL, LDL, and triglycerides in the cholesterol sham group increased significantly compared to the control group, but significantly decreased in the experimental groups compared to the cholesterol sham group. Valerian improves HDL, LDL, and triglyceride levels in male hypercholesterolemic rabbits.

Key words: Valerian, hypercholesterolemic, atherosclerosis, rabbit.

INTRODUCTION

Atherosclerosis, commonly called hardening of the arteries, is a vascular disease; and it is very important to know and control factors that cause and aggravate it¹. This disease has always been the most important cause of death in developed countries and accounts for about 50% of deaths² ³. In the United States, coronary heart disease is the main cause of death in men over the age of 40 and women over the age of 65⁴. Atherosclerosis results from lipid deposits in large and medium-sized arteries⁵ ⁶ and causes hardening of artery walls, which is followed by decreased elasticity and narrowing of blood vessels that eventually results in reduced blood supply to important body organs including the heart and the brain⁷.

Although increased plasma lipids is a known risk factor for vascular diseases, in about half of patients the levels of these lipids do not change and, hence, the increased risk for coronary heart disease cannot be explained. Therefore, this disease can be better diagnosed in these patients by measuring the apolipoprotein level⁸.

At present, this disease can be effectively prevented in people susceptible to it by monitoring various blood biochemical factors. Hyperlipidemia, diabetes mellitus, age, gender, hypertension, and smoking are important risk factors for cardiovascular diseases and cause total and serum cholesterol and LDL-C to rise and HDL-C to fall abnormally⁹ ¹⁰. High cholesterol concentration in blood plasma, which is often detected as low-density lipoprotein (LDL), is considered the most important cause of
atherosclerosis. Research has shown oxidation of this compound (LDL oxidation) signifies the first stage in the development of atherosclerosis in cardiovascular diseases\textsuperscript{11, 12}. LDL oxidation plays an important part in the development of atherosclerosis. Utilization of oxidants in food materials leads to LDL oxidation that causes the development, and progress, of atherosclerosis\textsuperscript{13}. When LDL is oxidized, the affinity it has for its receptor decreases. Accumulation of oxidized LDL in macrophages leads to the formation of foam cells and the development of atherosclerosis\textsuperscript{14}.

Since atherosclerosis is considered an inflammatory disease, inflammation and factors influencing it are potential risk factors\textsuperscript{15, 16}, and research has indicated acute-phase proteins are useful in predicting the risk for cardiovascular diseases\textsuperscript{17}.

Controlling these risk factors is important in preventing atherosclerosis, and nowadays use of medicinal plants for controlling the risk factors has attracted interest\textsuperscript{18}.

In traditional Iranian and Islamic medical sources, utilization of plants including valerian for treating digestive disorders and indigestion together with flatulence and/or constipation attracted interest\textsuperscript{19}. Valerian is an herbaceous plant with a strong stem and height of 0.5-2 m growing wildly in sparsely-treed forests\textsuperscript{20}. Its roots and rhizomes contain amidon, tannin, glucose, formic acid, acetic acid, and a large quantity of manganese\textsuperscript{21}. Valerian roots have strong antispasmodic effects. They were used in traditional medicine to also cure problems of nervous origin, hysteria, as a reducer of urine volume in diabetics, for curing insomnia and expelling stomach gas, and as an antispasmodic and a tranquilizer\textsuperscript{22}. Moreover, valerian roots are used to treat nervous disorders, especially dizziness, nerve pain, headache, migraine, anxiety, disorders associated with menopause, continuous hiccups, and stomach pain\textsuperscript{23}. In recent research on valerian, its hypnotic, antispasmodic, analgesic, and blood pressure reducer effects have been mentioned\textsuperscript{26}. Phytochemical studies have indicated valerian is rich in flavonoids that are mainly in the form of flavanols and have antioxidant properties\textsuperscript{21}.

The large quantities of valerian used in traditional medicine, and its useful and influential effects and very low toxicity, prompted us to study its effects on the progress of atherosclerosis in male hypercholesterolemic rabbits.

**MATERIALS AND METHODS**

**Preparation of the extract**

Valerian plants were dried for 10 days at room temperature and powdered using an electric grinder. One hundred grams of the powder were then soaked in 96% ethanol for 72 hours, filtered, and concentrated using a vacuum distillation apparatus. The concentrated solution was decanted in three stages (once with 100 and twice with 50 ml of chloroform). The solution obtained from the last stage was poured in a container, dried at 50ºC under sterile conditions, and kept in a dark glass bottle at 4ºC\textsuperscript{27}.

**Grouping and treating rabbits**

Thirty male New Zealand rabbits each weighing 2000-2500 grams were bought from the Razi Research Institute and kept for two weeks in the animal den at the Islamic Azad University of Jahrom to get acclimated. They were fed the base diet of Super Fosskon Standard Rabbit Chow (which included protein, fiber, and fats at 14, 150, and 30 g/kg, respectively) during these two weeks\textsuperscript{28}. The rabbits were then divided into 5 groups each with 6 members and fed the following diets by gavage for 45 days\textsuperscript{29}:

- **Group 1** (control group) received the ordinary diet
- **Group 2** (sham group one) were given corn oil as a cholesterol solvent
- **Group 3** (Sham group two) were fed a high cholesterol (5% cholesterol) diet\textsuperscript{28}
- **Group 4** (Experimental group one) received a high cholesterol diet together with the minimum dose of valerian extract (200 mg/kg)
- **Group 5** (Experimental group two) were given a high cholesterol diet together with the
maximum dose of valerian extract (800 mg/kg). During this period, the rabbits had free access to food and water. To prepare a high cholesterol diet, the cholesterol bought from the German Merck Company constituted one percent of the daily diet.

**Measuring biochemical factors**

Before administering the diets, and at the completion of the research, the rabbits were weighed. Blood samples were taken from the heart of each rabbit and the sera were used to determine total cholesterol, triglycerides, LDL, and HDL concentrations using biological kits and a Hitachi Model 902 Automatic Analyzer.

**Statistical Analysis**

Results were analyzed in the form of Mean±SD. ANOVA and Duncan’s test were employed for studying the biochemical results and to compare the means of the experimental groups using SPSS 17, and Excel was employed for drawing the figures.

**RESULTS**

Figure 1 shows weights of rabbits in experimental group two significantly decreased compared to those in the control and the sham groups (p<0.05), but the weights of rabbits in the corn oil and cholesterol sham groups significantly increased compared to those in the control group.

Figure 2 indicates HDL levels in the groups receiving cholesterol significantly increased (p<0.05), and HDL levels in experimental group two increased compared to experimental group.

Figure 3 shows weights of rabbits in the sham group receiving cholesterol significantly increased compared to the control group, but HDL levels in experimental group two (that were given a high cholesterol diet with the maximum dose of valerian extract) decreased significantly (p<0.05).
Figure 4, which presents changes in cholesterol levels in the various groups, shows total cholesterol significantly increased in the group treated with cholesterol (p<0.05), but cholesterol levels significantly decreased in groups that were given valerian extract together with high cholesterol diets (p<0.05).

Figure 5, which shows changes in triglycerides levels, indicates triglycerides levels significantly increased in the group receiving cholesterol (p<0.05) but significantly decreased in experimental groups one and two compared to the sham group receiving cholesterol (p<0.05).

**DISCUSSION**

In this research, high cholesterol diets increased total cholesterol, triglycerides, and LDL levels, and use of these diets also significantly reduced HDL concentrations. Similar changes were reported in previous studies30.

Results concerning the effects of various doses of the hydroalcoholic extract of valerian on lipid levels in blood serum of hypercholesterolemic rabbits are as follows. Total cholesterol, triglycerides, and LDL cholesterol levels of rabbits in the group receiving high cholesterol diets together with various doses of the extract decreased significantly, depending on the extract dose, compared to the group receiving high cholesterol diets, at the completion of the research. Moreover, HDL cholesterol concentrations in this group significantly increased (depending on the extract dose) compared to the group receiving high

![Fig. 5: Effects of valerian extract on triglycerides levels in male hypercholesterolemic rabbits](image)

Table 1: Comparison of biochemical factors and weights of rabbits in the studied group

<table>
<thead>
<tr>
<th></th>
<th>control (corn oil)</th>
<th>sham group (cholesterol)</th>
<th>experimental group 1</th>
<th>experimental group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL (mg/dl)</td>
<td>50.8±1.28a</td>
<td>61.4±1.17a</td>
<td>87.95±22.23b</td>
<td>108.25±4.39c</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>29.8±1.11a</td>
<td>32.4±1.38a</td>
<td>132.56±30.28b</td>
<td>90.73±4.59a</td>
</tr>
<tr>
<td>cholesterol (mg/dl)</td>
<td>57.83±3.147a</td>
<td>61.13±1.57a</td>
<td>759.25±80.75b</td>
<td>215.21±50.43a</td>
</tr>
<tr>
<td>triglycerides (mg/dl)</td>
<td>73.11±2.45a</td>
<td>82.25±2.89a</td>
<td>158.25±4.39b</td>
<td>201.10±49.80a</td>
</tr>
<tr>
<td>weight (gr)</td>
<td>1500.31±256.85b</td>
<td>1725.98±154.61a</td>
<td>1850.69±184.47a</td>
<td>1502.05±150.52b</td>
</tr>
</tbody>
</table>

The symbol * indicates values were presented in the form of Mean ± SEM.

The symbol * shows the statistical level employed was p<0.05.

The symbol * indicates values were presented in the form of Mean ± SEM.
cholesterol diets. The maximum extract dose was more effective in reducing cholesterol, triglycerides, and LDL levels, and in increasing HDL levels, compared to the minimum dose. These results show the effectiveness of the hydroalcoholic extract of valerian in modifying the dyslipidemia resulting from administering high cholesterol diets to the rabbits.

Previous research found one of the starting stages of atherosclerosis was the entry of low-density lipoproteins into artery walls. This caused accumulation, modification, and oxidation of low-density lipoproteins, which prevented the adhesion, migration, and differentiation of monocytes and caused inflammation. Moreover, researchers stated glycosylation and all events that increased oxidative shocks were important factors. Furthermore, previous studies showed that atherosclerosis was an inflammatory process. Inflammation, especially chronic inflammation, is one of the common complications of many diseases and weakens the immune system of the body. The inflammation process, in addition to creating infection problems, delays the healing process in the related diseases. Rhizome roots of valerian contain flavonoids, amidon, tannin, glucose, various salts, essential oil, valerinic acids, formic acid, acetic acid, and propionic acid. Studies on the total plant fractions showed the flavonoids in valerian, due to their special spatial shape, accelerate intestinal absorption, possess significant anti-inflammatory effects, increase suppression of prostaglandins, inhibit 5-lipoxygenase and, thus, normalize concentrations of biochemical factors in blood serum.

Moreover, people with hyperlipidemia require more antioxidants and their blood lipids can be reduced by adding antioxidants to their diets or through administering drugs. Phytochemical studies have shown valerian is rich in flavonoids that are mainly in the form of flavanols and possess antioxidant properties and, thus, reduce lipid peroxidation and oxidative destruction of blood vessels.

CONCLUSIONS

Results of this research indicate use of valerian extract together with high cholesterol diets reduces triglycerides, cholesterol, HDL, and LDL. This shows the strong anti-inflammatory and antioxidant properties of this extract, which reduced atherosclerotic lesions in the group receiving the extract. Considering the strong effects of this extract in reducing lesions, further research should be carried out on this plant and on its molecular mechanisms.

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REFERENCE


