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ANTIHYPERLIPIDEMIC EFFECTS OF HYDROALCOHOLIC LEAF EXTRACT OF *TEUCRIUM POLIUM* IN HYPERCHOLESTEROLEMIC RATS

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Abstract:
Hyperlipidemia is one of the most important factors contributing to the cardiovascular diseases. There are various chemical drugs for regulating the lipid profile level. According to the side effects proved for the chemical drugs, we, in the current research paper, investigate the effect of wall germander (Teucrium polium) hydroalcoholic extract effect on the lipid profile in the hypercholesterolemic rats. Wistar male rats, ranging in weight from 150 g to 180 g, were assigned to four groups (n=5): control group (ordinary diet), sham group (high, 2%, cholesterol dietary regime), experimental group one (high, 2%, cholesterol dietary regime plus 0.85mg/ml Teucrium polium hydroalcoholic extract) and experimental group two (high, 2%, cholesterol dietary regime plus 1.7mg/ml Teucrium polium hydroalcoholic extract). The treatment was run in an eight-week period with the termination of which blood samples were collected from the animals. To determine the lipid profile, commercial diagnostic kits were applied. The results were analyzed by the use of SPSS software, ver. 16. From the week six on, the weights of the rats from the experimental group two (high, 2%, cholesterol diet plus 1.7 mg/ml Teucrium polium hydroalcoholic extract) showed a significant decrease ($P<0.05$) even in comparison to the control group (ordinary diet). The serum level of triglycerides, cholesterol and LDL-c was found significantly decreased in the experimental group two ($P<0.001$) as compared to Sham group but it did not any significant change in contrast to the control group. In experimental group one (high, 2%, cholesterol dietary regime plus 0.85 mg/ml Teucrium polium hydroalcoholic extract), only the cholesterol and TG serum levels were found significantly decreased in respect to the sham group ($P<0.05$ and $P<0.001$, respectively). Regarding the lipoprotein amount, a significant increase was documented in the experimental group two, featuring high density cholesterol (HDL-c), in contrast to the sham group ($P<0.001$). The present study's findings indicated that an appropriate dosage of T. Polium can cause the regulation of lipid profile as well as the weights of the hypercholesterolemic rats. According to the side effects of the chemical drugs similar in their functions to the effect of T. polium, it can be suggested as an antihyperlipidemic drug.

Keywords: *Hyperlipidemic, Teucrium polium, Lipid profile, Medical plants, Rat.*

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INTRODUCTION:

Cardiovascular diseases are the major cause of mortalities in the majority of the countries [1-5] and the number of these patients is increasing as the senescence prevails [6]. Treating the blood lipidic profile disorders causes a considerable decrease in the microvascular and coronary heart diseases [7]. The low blood levels of high-density lipoprotein (HDL), cholesterol and high LDL, obesity, hypertension, diabetes, smoking, sedentary lifestyles that constitute the majority of the risk factors are all controllable [8-10]. When the cholesterol levels goes up, the production of superoxide free radicals in the veins doubles and the synthesis and secretion of endothelium derived vasodilators is reduced [11]. Nowadays, the use of natural antioxidants extant in the medicinal herbs and diets has undergone an increase due to their high capacity of expelling the free radicals and reduction of oxidative damages associated with various diseases [12, 13]. These natural antioxidants not only protect us from the fatty acids existent in the foodstuff but they also are accompanied by healthcare benefits as well in such a manner that they are known to have prevented the damages resulting from biological declines [14]. Medicinal herbs are among the sources rich in various antioxidants and effectively capable of moderating the oxidative stress stemming from cardiovascular or renal injuries (15, 16]. Although various ingredients of these herbs can have antioxidant effects, phenolic compounds are the most important ingredients of such plants [17]. Flavonoids are groups of phenolic compounds that are considered as strong antioxidants controlling the lipidic peroxidation [18, 19]. Teucrium Polium L., belonging to the family Lamiaceae, is a medicinal plant featuring a high antioxidant potential [20]. T. Polium is abundantly found in Iran. The plant is usually consumed as herbal tea and in traditional medicine. T. Polium is especially used as an appetizer for children and also as a condiment for the various foods. The tea prepared by brewing the leaves and the flowers of this plant is consumed as a drink having a lot of fans [21]. There are many biological activities reported for T. Polium and it has been proved to have anti-inflammatory, pain-relieving, antibacterial, anti-hypertension, antivirus and hypoglycemic effects [22-29]. The present study investigates the effect of T. Polium hydroalcoholic extract on the lipid profile in hyperlipidemic rats.

MATERIALS AND METHODS:

After T. Polium plants were collected from Rumeshgan region in Lorestan Province, it was subjected to scientific verification by the plant biology department of Lorestan's Basic Sciences University. Sufficient amount of plant leaves were dried and milled. The obtained powder was soaked for three days in a hydroalcoholic solution (20 water: 80 ethanol) and then filtered by the use of Whatman's filtering paper so as to purify the extract. The solution was condensed in a rotary evaporator device, then placed in a 30°C-40°C oven and finally a dry extract was obtained. A total number of 20 Wistar male rats, ranging in an approximate weight from 150g to 180 g were procured from Tehran Pastor Institute and kept in standard light and temperature conditions for a week before the onset of the experiments. The rats were randomly assigned to four groups (n=5): Control group received an ordinary dietary regime plus 2cc drug solution; sham group was fed on a high cholesterol (2%) plus 2cc of the drug solution; experimental group one was given a high cholesterol (2%) dietary regime plus 0.85mg/ml T. polium hydroalcoholic extract; and, experimental group two that received a high cholesterol (2%) dietary regime plus 1.7 mg/ml T. polium hydroalcoholic extract. The blood samples were taken from all the rats once on the first day of experiment initiation and then in the last day of the week eight of the experiment. To determine the serum concentration of HDL-c, TG and total cholesterol, there was made use of diagnostic kits manufactured by Pars Azmoun Iran Company which were measured by means of Autoanalyzer device (made by American Abbott Company). Fried Wald formula was applied to determine LDL-c values [30]. LDL-Cholesterol = Total Cholesterol – HDL-Cholesterol (Triglycerides ÷ 5). The results were analyzed in SPSS 16 by taking advantage of one-way variance analysis (ANOVA). For every group, the entire data have been extracted based on the results in the format of five rats' Means ± SD calculations. In all of the analyses, the significant was set in $P<0.05$.

RESULTS:

The rats' weights were measured weekly. In the week four, the experimental group two that had been treated by a high-cholesterol dietary regime plus 1.7 mg/ml T. polium hydroalcoholic extract indicated a significant weight loss ($P<0.01$) in contrast to sham group (fed on a high cholesterol diet). In the week six, the weights of the rats from control group ($P<0.001$), experimental group one ($P<0.01$) and experimental group two ($P<0.001$) demonstrated a significant reduction as compared to the sham group. In the end of the research, to wit on the last day of the week eight, as well, the mean weight of the entire groups showed a significant decrease in comparison to the sham group ($P<0.001$)(Table 1). According to the results, the mean serum levels of triglycerides, cholesterol and LDL-c of the sham group, treated by

a high cholesterol (2%) dietary regime as well as the experimental group one that had been fed on a high cholesterol (2%) regime plus 0.85 mg/ml of T. polium hydroalcoholic extract indicated a significant increase in comparison to the control group (P<0.001) but the serum levels of the three factors mentioned above were not suggestive of a significant change in the experimental group two that had been treated by a high-cholesterol dietary regime plus 1.7 mg/ml T. polium hydroalcoholic extract as compared to the control group (Diagram 1-3). The serum levels measured for the two groups, i.e. sham and experimental group one, demonstrated an inverse trend in terms of the previous biochemical factors in such a manner that the serum level of HDL-c was found significantly decreased (P<0.001) in respect to control group. The serum value of this factor did not undergo a significant change in the experimental group two in contrast to the control group (Diagram 4).

Table 1: The means weight in different groups in during the eight weeks of experiment.

Weeks / Groups	Mean ± SD				
	1st week	**2st week**	**4st week**	**6st week**	**8st week**
Control	155.20±4.86	167.20±5.26	193.20±7.66	215.00±6.44 [b]	235.80±8.55 [b]
Sham	156.20±5.54	169.00±5.70	207.60±10.69	237.80±8.40	268.80±11.18
Experimental group 1	160.60±5.54	166.80±5.01	195.60±9.39	216.60±6.54 [a]	240.00±10.55 [b]
Experimental group 2	159.00±4.30	168.60±5.72	185.20±7.98 [a]	199.20±7.32 [b]	215.60±12.75 [b]
Control	155.20±4.86	167.20±5.26	193.20±7.66	215.00±6.44 [b]	235.80±8.55 [b]

a: P<0.01; b: P<0.001

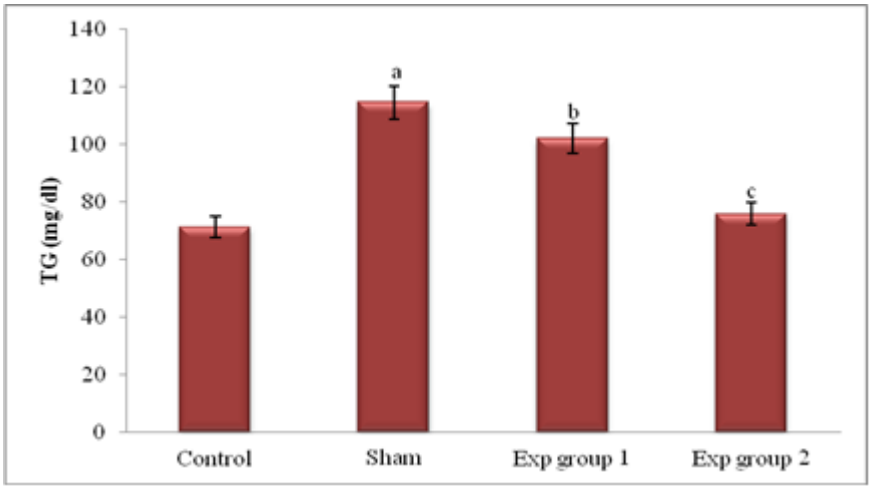

Fig 1: Teucrium Polium hydroalcoholic extract effect on TG amount during the eight weeks of experiment.
The P values for the following comparisons are as follows: end level serum of Sham vs. Control group (a=0.000); end level serum of Exp group1 vs. Control group (b=0.000); end level serum of Exp group2 vs. Control group (c=0.773). The mean difference is significant at the 0.05 level.

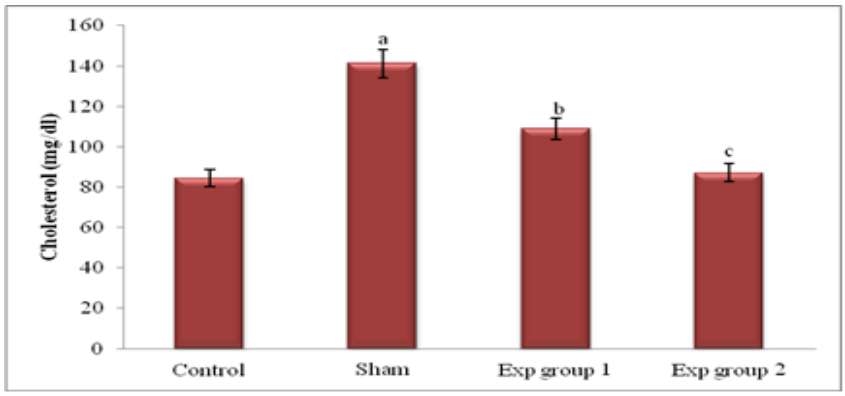

Fig 2: Teucrium Polium hydroalcoholic extract effect on Cholesterol amount during the eight weeks of experiment.

The P values for the following comparisons are as follows: end level serum of Sham vs. Control group (a=0.000); end level serum of Exp group1 vs. Control group (b=0.000); end level serum of Exp group2 vs. Control group (c=0.982). The mean difference is significant at the 0.05 level.

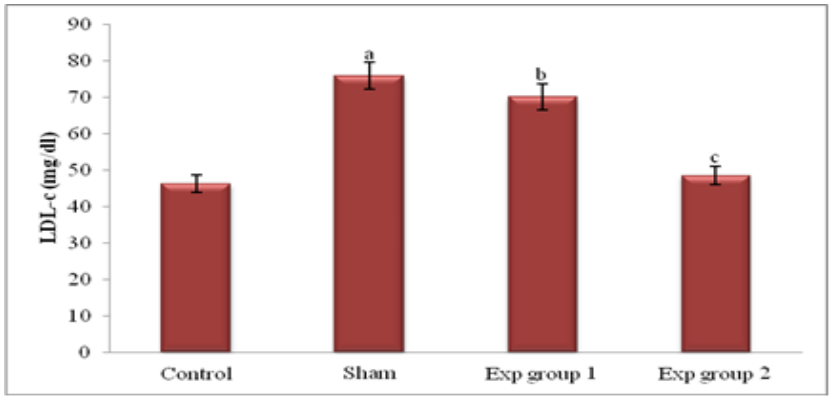

Fig 3. Teucrium Polium hydroalcoholic extract effect on LDL-c amount during the eight weeks of experiment.

The P values for the following comparisons are as follows: end level serum of Sham vs. Control group (a=0.000); end level serum of Exp group1 vs. Control group (b=0.000); end level serum of Exp group2 vs. Control group (c=0.967). The mean difference is significant at the 0.05 level.

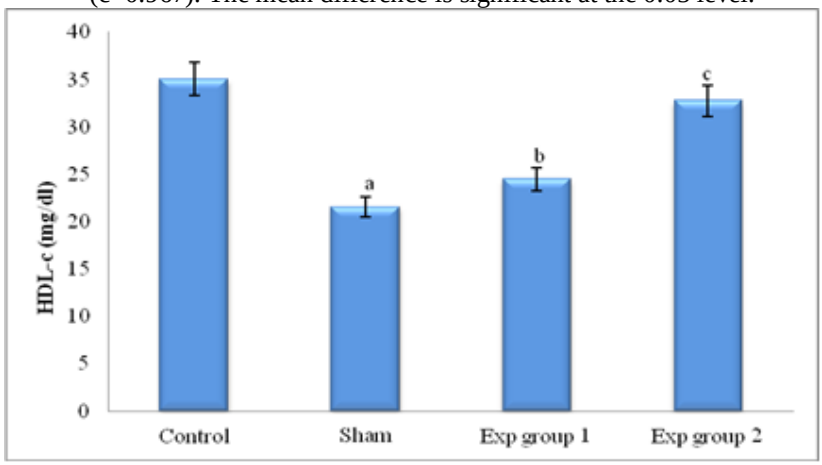

Fig 4. Teucrium Polium hydroalcoholic extract effect on HDL-c amount during the eight weeks of experiment.

The P values for the following comparisons are as follows: end level serum of Sham vs. Control group (a=0.000); end level serum of Exp group1 vs. Control group (b=0.000); end level serum of Exp group2 vs. Control group (c=0.622). The mean difference is significant at the 0.05 level.

DISCUSSION:

Our study indicated that consuming T. polium extract for eight weeks caused a significant reduction in total cholesterol, LDL-c and TG levels in contrast to the sham group and, more surprisingly, the serum level of HDL-c was found significantly increased in contrast to sham group. Such an effect is more associated with the T. polium administered in a 1.7mg/ml dosage in such a way that, even though the groups were all hypercholesterolemic, it has been able to regulate the serum concentrations of all these factors in a normal range. Another objective of the present study was figuring out the contingent effects of T. polium extract n weight control in hyperlipidemic rats. Based on the results, from the week four on, the rats' mean weight of the experimental group two that was given a high cholesterol dietary regime plus 1.7 mg/ml T. polium was found significantly lower ($P<0.05$) which is even lower than the rats from the control group (healthy rats). The results obtained in the current research paper regarding the lipidic biochemical factors are consistent with the results obtained in the other studies [31, 32]; of course, some of these studies have made use of diabetic rats. Khoshdel et al investigated the effect of T. Polium L. extract with Glibenclamide in diabetes-induced rats. After six weeks of experiment, they concluded that administering the extract to diabetes-induced rats can reduce the TG and cholesterol levels. However, the co-administering of these two drugs was not found having a significant effect on serum cholesterol level [33]. Although fat reduction mechanism exercised by T. Polium is yet to be discovered, it contains a wide spectrum of active pharmaceutical factors like alkaloids, glycosides, terpenoides, sterols, triperines and flavonoids [34, 35]. There are also conflicting findings found regarding flavonoids effects in such a way that the results obtained by some empirical and demographical studies indicate that flavonoids can decrease the plasma cholesterol level in hyperlipidemia resulting from diabetes [36]. However, there are other studies that report the little or no reduction or lack of any change in the lipoproteins and blood plasma values after increasing the flavonoids consumption [37, 38]. T. polium extract is rich in flavonoids. Some flavonoids might prevent lipid synthesis and secretion by liver [39]. Also, photochemical investigations performed on T. Polium extract are suggestive of the presence of such flavonoids as caffeic acid, ferulic acid and quercetin in this plant [40]. LDL-c and its extreme production can lead to the cardiovascular symptoms [41, 42]. Flavonoids possess antioxidant and chemical properties. Except the fat-soluble tocopherols, the most common and the most active antioxidant compounds existent naturally in the foodstuffs are flavonoids. Generally, it is believed that the flavonoids' antioxidant capabilities belong to their ability for donating hydrogen atoms thereby to destroy the free radicals produced during the lipid peroxidation [43]. In a study that was conducted for investigating the T. polium extract effect on blood cholesterol and TG level in male diabetic rats, it was made clear that the plant features blood lipid reduction effect that is exerted through reducing the blood cholesterol level. The cholesterol reduction effect is predominantly due to cholesterol intake control in the small intestines and also via preventing cholesterol from being distributed by liver. Liver plays an important role in defecating cholesterol through its secretion of bile [44]. Generally, plants rich in flavonoids can be a good source of antioxidants that contributes to the antioxidant capacity increase in an organism and protects lipid peroxidation [45].

CONCLUSION:

According to T. polium's potential antioxidant activities and its containing of ingredients rich in flavonoids, it can be added to the foodstuff in lieu of artificial antioxidants for its prevention of lipid peroxidation. In the end, to better manage the potential outcomes stemming from oxidative stress damages, it seems that further research should be carried out to acquire more precise information regarding the active ingredients as well as the flavonoids existing in this plant.

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