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THE EFFECTS OF *TEUCRIUM POLIUM L.* ON ATHEROSCLEROTIC PLAQUES IN HYPERCHOLESTEROLEMIC IN RATS

Mansour Amraei[1, 2†], Ehsan Shirzadpour[3†], Seyedeh Fatemeh Mousavi[4], Safoura Mohamadpour[4], Azim Hasanbeigi[5*]

[1]Biotechnology and Medicinal Plants Research Center, Ilam University of Medical Sciences, Ilam, Iran.
[2]Department of Physiology, Faculty of Medicine, Ilam University of Medical Sciences, Ilam, Iran.
[3]Department of Clinical Biochemistry, Faculty of Medicine, Ilam University of Medical Sciences, Ilam, Iran.
[4]Prevention of Psychosocial Injuries Research Center, Ilam University of Medical Sciences, Ilam, Iran.
[5]Department of Public Health, Faculty of Health, Ilam University of Medical Sciences, Ilam, Iran.

Abstract:
Cardiovascular diseases are amongst the most important mortality causes worldwide. Therefore, it is necessary to offer a drug that meanwhile lacking the side effects of the similar chemical medications is capable of reducing the risk factors of such diseases. In the present study, the effect of hydroalcoholic extract taken from the plant Teucrium Polium on the atherosclerotic plaques has been studied herein. In the current research paper, 20 male Wistar rats with mean weights ranging from 150 g to 180 g were randomly divided to four groups: a control group and a sham group that, respectively, received ordinary dietary regimen and high cholesterol (2%) nutrition. Experimental groups 1 and 2 that received ordinary dietary regimens plus Teucrium Polium extracts, with dosages equal to 0.85 mg/ml and 1.7 mg/ml, respectively, on a daily basis. After eight weeks of treatment, the rats' aortas were dissected and kept in 10% formalin solution to undergo histological evaluations. The weight results were analyzed in SPSS software by the use of one-way variance analysis (ANOVA). There was not observed any atherogenic lesion in the control group that had received a normal nutrition. In sham group that had received high cholesterol dietary regimen, atheroma plaques were visible. Experimental groups 1&2 that had been treated with extract dosages of 0.85 mg/ml and 1.7 mg/ml, no sign of any atherogenic lesion and plaque formation was observed even with their being fed on a high cholesterol dietary regime. Also, the sham group members' mean weights showed a significant increase in respect to the control group. Experimental group two demonstrated a significant reduction of weight in contrast to the control group. The hydroalcoholic extract of Teucrium Polium was interestingly successful in preventing the atherosclerotic plaques. According to the side effects of the anti-atherosclerotic chemical medications, it seems that the use of traditional medicine and the medicinal herbs can be an appropriate solution to the reduction of cardiovascular diseases.

Keywords: *Atherosclerotic plaques, Teucrium polium, cardiovascular disease, Medical plants.*

†These authors contributed equally to this work.

Correspondence author:
Azim Hasanbeigi,
Department of Public Health,
Faculty of Health,
Ilam University of Medical Sciences,
Ilam, Iran. Email: azim1836 @yahoo.com,
Tel: +988432227147; Fax: +988432235723

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INTRODUCTION:

Atherosclerosis is caused as a result of hyperlipidemia and fat oxidation which account for a substantial rate of the mortalities [1] and are regarded as the major causes of cardiovascular diseases, including the coronary artery sclerosis and vascular ailments [2]. Hyperlipidemia increases the production of superoxide that leads to the inactivation of the nitric oxide thereby a substantial damage to the endothelial in the entire stage of atherosclerosis development [3]. In platelets, hypercholesterolemia leads to the increase in the secretion of serotonin as well as collagen, adenosine diphosphate (ADP), thromboxane and plaque buildup. Therefore, the thrombosis in vascular lesions is associated with the ischemic events and atherosclerosis progress [4]. Inflammation, as well, plays an important role in the entire stages of atherosclerosis from the beginning to the growth and it is followed by such events like plaque rupturing and subsequently acute vascular disorders [5]. Inflammations occur with the increase in oxidative pressures and they are usually accompanied by an increase in CRP level [6]. CRP (C-reactive protein) is a non-specific inflammatory protein that develops with the increase in the cholesterol level and it is considered as an important factor in predicting the cardiovascular diseases [7]. Compounds like dissolved fibers, Vitamin E, flavonoids and sterols posses anti-atherosclerotic properties and also they have been found exhibiting antioxidant and anti-inflammatory effects plus endothelial activity preservation [8]. The results of the studies indicate that there is an inverse relationship between the consumption of vegetables and fruits and inflammatory genes' expression and the significant reduction in CRP level [9, 10]. Fruits and vegetables are inter alia the most important food sources which are rich in fiber and they contain flavonoids and cartenoids featuring anti-inflammatory attributes, although their anti-inflammation mechanism is not well clarified [11, 12]. Medicinal plants, as sources of various antioxidants, can be very effective in adjusting the oxidative stress resulting from cardiovascular or renal damages [13, 14]. Although various compounds residing in plant parts can possess antioxidant effects, but a substantial part of such effects are attributed to phenolic ingredients. One medicinal plant that has drawn the attentions of even Hippocrates and Galen in traditional medicine is the Teucrium Polium. Teucrium Polium or Poleigamander is an herbaceous plant that belongs to the race Labiatae [15-17]. The extracts derived of the plant contain diterpenoids, glycoside, methoxy Jen Guanin and volatile essences. The most frequently found of these essences are Germacrene, beta caryophyllene, Humulin and caryophyllene oxide [17]. The results of some studies are also implying the lack of side effects for the plant extracts [18, 19]. According to the daily increasing consumption of the medicinal plants as well as due to the side effects reported for the chemical drugs, the present study investigates the effect of hydroalcoholic extracts of Teucrium Polium on the atherosclerotic plaques.

MATERIALS AND METHODS:

Teucrium Polium was collected from Roomeshgan region in Lorestan Province and it was verified in a herbariumic identification by the plant biology department of the Lorestan University's faculty of Basic Sciences. After being dried and milled, the plant powder was placed in a hydroalcoholic solvent (composed of water and ethanol for a ratio of 20:80, respectively). Whatman filter papers were utilized to refine the extract. After being condensed in a rotary device, the solution was placed in a 30-40 degree centigrade oven and its dried extract was finally acquired. Twenty male adult Wistar rats, with mean weights ranging from 150gr to 180gr, were purchased from Tehran Pastor Institute to undergo the study process. The animals were kept in the ambient temperature 22±3c°, humidity 55±2 and a 12-h light/dark period. The rats were randomly assigned to four five-member groups. The control and sham groups that received daily ordinary nutrition and high-cholesterol dietary regime (2%), respectively, were gavage-fed 2cc of the drug solution so as to have identical conditions the same as what the experimental groups 1&2 were exposed to. Besides the high-cholesterol dietary regime (2%), the experimental groups 1&2 received hydroalcoholic extract of Teucrium Polium with dosages equal to 0.85 mg/ml and 1.7 mg/ml, respectively. The rats underwent an eight-week treatment period. The weights of the entire animals were measured and recorded during this eight week period. In the end of the week eight, the rats were put to anesthesia by the use of ether with careful adherence to the ethical codes and the biopsy was carried out in a systematic manner. The hearts and the aortas were dissected by the use of a sterile incision and they were kept in a 10% buffer solution for 24 hours in order to be stained by hematoxylin and eosin (H&E). Slides were prepared after staining of the tissues. Finally, the histological investigations by the use of a photomicroscope were carried out. The weight results were analyzed by the use of SPSS software, ver.16, and one-way variance analysis (ANOVA). The significance level chosen herein was $P<0.05$.

Ethics Code: the present study has been granted an ethic code (ir.medilam.1394.58) by the ethics committee of Ilam University of Medical Sciences.

RESULTS:

The results were indicative of a significant increase in the mean weights of the hypercholesterolemic sham group, as compared to the control group that had received ordinary nutrition. Experimental group two, that had been treated with a 1.7 mg/ml dosage of Teucrium Polium extract and had received high-cholesterol nutrition demonstrated a significant reduction of weight in contrast to the control group (Figure 1). As it is observed, the results of the present study indicated that the sham group hypercholesterolemic rats have developed atheroma plaques. Control group that had undergone a normal trend in terms of nutrition did not show any sign of atherogenic lesion development and atheroma plaque formation. According to the images, no sign and symptom of plaque creation can be figured out in experimental groups 1&2, whereas these two groups had also received high-cholesterol dietary regimen like the sham group (Figure 2).

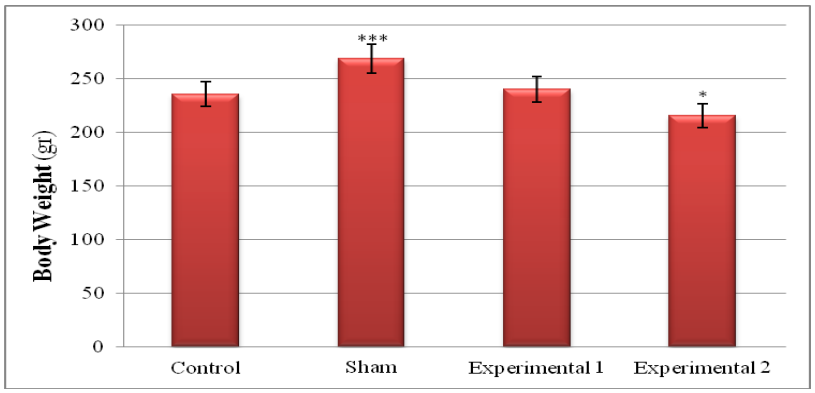


Fig 1: Comparing the weights of the various groups the 8th week study (*: P<0.001; *: P<0.05).**

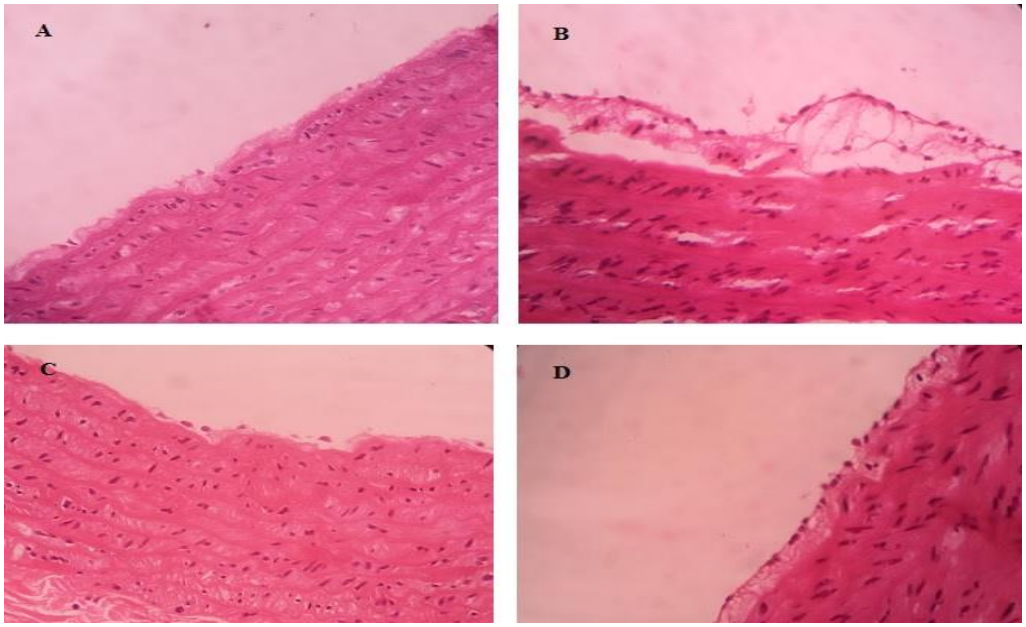


Fig 2: Histologic observations of the aorta section. Stained with hematoxylin and eosin, magnification x40. A: Control group; B: Sham group; C: Experimental group 1; D: Experimental group 2.

DISCUSSION:

The present study investigated the effect of hydroalcoholic extracts of Teucrium Polium plant on the atherosclerotic plaques. Also, the effect of the foresaid extract on the animals' weight was evaluated. In the current study, the higher dosages of the Teucrium Polium extracts was found correlating with the weight reductions in the experimental group two. This finding complies with the results obtained in the other applied researches in which the Teucrium Polium's hydroalcoholic extract effects had been studied [20, 21]. Teucrium Polium is a plant that has drawn the attentions of even Hippocrates and Galen. In recent years, the anti-diabetes, anti-spasm, pain relieving and anti-inflammatory effects of Teucrium Polium are well justified [22-25]. In a study by Skouti et al, the rats' treatment by Teucrium Polium brought about a reduction in serum cholesterol level. However, in another study that was undertaken for a period of one month on the rats, the consumption of Teucrium Polium extracts caused increases in cholesterol level and TG [21, 26]. The reason behind such contradicting results could be related to the treatment method and the type of the extract. The reports in some of the studies signify that the anti-hyperlipidemic effects of Teucrium Polium extracts pertain to flavonoids [27-29]. Flavonoid compounds are members of polyphenol family that possess protective effects against the hepatic damages caused due to the various poisons. Flavonoids oxidation by the free radicals leads to the creation of less-active and more stable radicals and the increase in the reaction of the hydroxyl group extant in the flavonoids results in the inactivation of the radicals [30]. These ingredients also control the HMG-COA reductase activity and lead to the reduction in hepatic cholesterol and prevent fatty liver development [31]. Moreover, there are numerous studies that have been carried out on the Teucrium Polium extracts' antioxidant effects all of which have confirmed such effects for Teucrium Polium [25, 32-35]. One of these studies was by Sharififar et al. The results of their study indicated that the extract of this plant exerts controlling effects on the lipid peroxidation, possesses revitalization potentials and a property of collecting the free radicals [25]. Hasani et al, as well, investigated the antioxidant activities of the Teucrium Polium extracts and concluded that the Teucrium Polium significantly elevates the antioxidant capacities in the animals [34]. Due to the same reason, it possesses liver protection characteristics that protect the liver against the lipid peroxidation [35]. Probably, Teucrium Polium influences the lipid profile and regulates the serum level of such biochemical factors thereby to inhibit the expression of risk factors giving rise to the formation of atherosclerotic plaques and consequently the vein walls are kept in a normal state.

CONCLUSION:

According to the daily increasing use of the medicinal herbs and their consumption for such purposes as preventing and treating the diseases worldwide and considering their very limited side effects in contrast to the chemical drugs, the use of Teucrium Polium as an antiatherosclerotic drug seems to be an appropriate solution. Of course, it is suggested that there is a need for performing more and further research in this regard so as to accurately determine the plant's extract precise mechanism of action.

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