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Hypolipidemic Effects of Ethanolic and Aqueous Extracts of Urtica Dioica in Rats

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Abstract: Lipid profile changes can be seen in metabolic syndrome and especially diabetes mellitus. The aim of this investigation is to assess the effect of ethanolic and aqueous leave extracts of this plant on serum lipid level in diabetic animal model. This study was carried out on 45 Wistar rats randomly distributed in 3 groups rats. Treatment groups received 150 mg/kg of alloxan intraperitoneally. Then rats were fed ethanolic and aqueous extracts of *Urtica dioica* leave in 50 mg/kg/day doses, for two weeks. After treatment, the serum lipids level were measured. Our studies showed significantly lower levels of triglyceride, cholesterol, LDL-C in both of groups of rats that were treated with ethanolic or aqueous extracts of leave *Urtica dioica* as compared with the control group of rat,($p<0.05$). The results of this study suggest that *Urtica dioica* leave extracts improve lipid tolerance in alloxan induced diabetic rat.

Key words: Aqueous extracts · Ethanolic extracts · Lipid · Rat · *Urtica dioica*

INTRODUCTION

Cardiac morbidity and mortality are directly related to hyperlipidemia. In addition, hypercholesterolemia is an important coronary risk factor [1]. Also, lipid profile changes can be seen in metabolic syndrome and especially diabetes mellitus (DM). Metabolic syndrome (MS) is highly significant as a major cause of DM and cardiovascular diseases and has become one of the major public health challenges worldwide [2, 3]. Lipid peroxidation is one of the early processes of atherosclerosis. It is generally assumed that some antioxidants can prevent atherosclerosis by protecting LDL from oxidation and are also associated with an anti hypercholesterolemic effect [4].

Research in herbal medicine has increased in the world as a way to rescue ancient traditions as well as an alternative solution to health problems in cities. The author and his colleagues investigated on the *in vivo* and *in vitro* effects of aqueous and alcoholic extracts of some herbal plants in DM. Our latest studies indicated that the aqueous and alcoholic extract of *Teucrium polium L*. flower and *Urtica dioica* leaves can decrease glucose level and increase insulin secretion, Acetyl coenzyme A carboxylase (ACC), Nucleoside diphosphate kinase (NDPK) activities in the alloxan diabetic animals [5, 6].

As there is growing literature on medicinal plants, it has shown that *Urtica dioica* (*U. dioica)* decreased the lipid peroxidation and liver enzymes activity [7]. The administration of *U. dioica* can effectively adjust the activities of liver enzymes [8]. Earlier studies have suggested that *U. dioica* decrease the lipid peroxidation [9]. Preliminary studies revealed that *U. dioica* is shown as a diuretic and with hypotensive effect [10]. As reported by some investigators indicating the benefits of using extract of the leaves plant for the use in allergic rhinitis and diabetes [11, 12] as well as other disorders like prostatic hyperplasia [13, 14], inflammation, hypotensive and hypoglycemic [6, 15]. Some researchers reported the benefits of using some herbal plants for the use in treatment of hyperlipidemia [16, 17].

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In our ongoing research project on medicinal plants used for the treatment of disease, we undertook the present study in order to evaluate the potential value of *U. dioica* for the management of hyperlipidemic conditions in animal models. The purpose of this research was to investigate the effect of *U. dioica* extract on serum lipids profile.

MATERIALS AND METHODS

Plant Material: *U. dioica* leaves were collected in May from the vicinity of Gatab village, Babol, North of Iran. It was certified by the Center for Agricultural Research and Natural Resources of Mazandaran Province, Iran. The leaves were dried at room temperature while keeping away from direct sunlight and then powdered (6).

Extractions: In order to prepare the aqueous concentrate, 100 g of dry *U. dioica* leaves were dissolved in two litres of distilled water and were boiled in 20 minutes. The non soluble part was then separated using mesh and the solution passed two times through Whatman paper No. 2. The macerate was filtered and aqueous was evaporated on a rotator evaporator at 60°C to reduce the solution volume to 1/6 of initial value. For the preparation of ethanolic solution, 100 g of dry powder was dissolved in one litre of 70 degree 5% ethanol and mixed by a shaker for 24 hours in room temperature. Again the non soluble part was separated using mesh and the solution was passed two times through Whatman paper No. 2. The macerate was filtered and ethanol was evaporated on a rotator evaporator at 60°C under the vacuum to reduce the solution volume to 1/6 of initial value. Both aqueous and ethanol solutions were kept for 4 days under hood to let the solvents evaporate. Finally, the extract was stored at-20 °C.

Animals: We used forty five 8-to 12-week-old rats weighing approximately 200-240 g. The rats of closed colony were prepared from the animal center of Babol University, Babol, Iran. Age-matched rats were used as control animals. The rats were housed in suspended bracket cages in a climate-controlled room at 22±5 °C with 12L:12D lighting cycle. Food and water were provided *ad libitum*. All procedures were in accordance with animal experimental guidelines of Babol University. Also, the protocols involving animals were approved by Babol University Animal Care and Use Committee. The approval of the Ethics Committee of Babol University was also obtained (No: 1825). Animals were not fed for at least 12 h. Hyperglycemia was induced by intraperitoneal injection (150 mg/kg, i.p) of freshly prepared solution of alloxan monohydrate dissolved in distilled water.

Alloxan-Induced Hyperglycemia: The rats were not fed 14 h before injection. The alloxan solution (alloxan monohydrate from Sigma Co, USA.) was prepared and 0.7 ml with 150 mg/kg dose was injected intraperitoneally to rats in the hyperglycemic group. In addition, 0.7 ml normal saline was injected to rats in the control groups. The rats with fasting glycemia more than 250 mg/dl were used as diabetic.

Animals Administration: The animals were randomly divided into three groups: (I), The diabetic animals that received 150 mg/kg Alloxan intraperitoneally and did not receive any extract. (II), The diabetic animals received 150 mg/kg Alloxan intraperitoneally and were treated with aqueous extract. (III), The diabetic animals received 150 mg/kg Alloxan intraperitoneally and were treated with ethanolic extract. After 72 hours, while the rats were not fed for 14 hours, their blood samples were obtained from conjunctiva. Levels of serum lipids were measured. Then, 24 hrs after obtaining blood samples, the rats were treated orally with 50 mg/kg/d *U. dioica* leave extracts or distilled water (as the control) for 14 days. Upon completion of this period, the blood samples were obtained again to measure the lipids levels. Diabetes was induced in the rats by intraperitoneal injection of 150 mg alloxan/kg in sterile distilled water.

Biochemical Analysis: The sera levels of triglycerides, total cholesterol, high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were determined using enzymatic kits (Pars Azmoon, Tehran, Iran).

Statistical Analysis: All values are presented as mean ± standard error. Statistical analysis was done using SPSS version 16, One-Way ANOVA test and probability values <0.05 were considered to be statistically significant.

RESULTS

The treatment of rats with aqueous extract of *U. dioica* induced a significant $P<0.05$ reduction of total serum cholesterol and triglyceride as compared with the untreated group; also a reduction in low-density

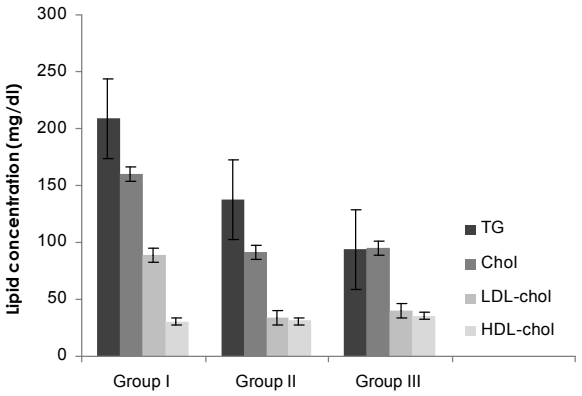

Fig. 1: Serum lipid profile after two weeks treatment with aqueous and ethanolic extracts of *Urtica dioica* in alloxan-induced diabetic rats. Group I: Control, Group II: treatment with aqueous extract, Group III: treatment with ethanolic extract.

lipoprotein cholesterol levels in treatment groups was observed ($P<0.05$). In addition, the treatment of diabetic rats with ethanolic extract of *U. dioica* induced a significant reduction of total serum cholesterol, triglyceride and LDL-cholesterol as compared with control ($P<0.05$). The increase of HDL-cholesterol levels in treatment groups compared with control group were not significant. Figure 1 shows the triglyceride, cholesterol, LDL-cholesterol and HDL-cholesterol level after treatment with aqueous and ethanolic extracts in alloxan-induced diabetic rats.

DISCUSSION

The results of present study showed that alcoholic *U. dioica* extract significantly reduced the level of serum triglyceride and cholesterol. In addition, treated with *U. dioica* leave extract in alloxan diabetic rats caused a significant decrease in LDL-cholesterol level of blood. Hyperlipidemia, particularly hypercholesterolemia play a key role in the development of coronary artery disease and atherosclerosis [18]. Cardiac morbidity and mortality are directly related to serum cholesterol levels [1, 18]. Hypolipidemic property of several extracts have been described and it has been found that treatment with different plant extracts are useful in achieving and maintaining low plasma levels of total cholesterol [16,17,19].

The results of our study showed that aqueous *U. dioica* extract significantly reduced the level of serum triglyceride and cholesterol. This observation is in good agreement with the results obtained by other investigators [7, 9]. Also, treated with aqueous *U. dioica* leave extract in alloxan-diabetic rats caused a significant decrease in serum LDL-cholesterol. The mechanism(s) of hypolipidemic activity of *U. dioica* is unknown but it may be due to direct activating effect on lipoprotein lipase, a vital enzyme in the metabolism of triglyceride or prevention of production of cholesterol in the liver by blocking HMG-CoA reductase. It could also be due to presence of phytochemicals such as organosulphur compounds similar to some other herbal plants [7-9, 20, 21].

It has been found that Urtica dioica extract can decrease the peroxidation of lipids [8, 9]. The presence of antioxidant of constituents may play a role in the observed hypolipidemic effects. This hypothesis can be considered as one of the mechanisms by which this extract can regulate the lipid homeostasis. However, this result does not exclude the other mechanisms regulating the lipid homeostasis. Further studies are needed to elucidate the other mechanisms of anti-hyperlipidemic action of *U. dioica*. We will be examining these problems in greater details as we go forward.

CONCLUSION

The observed lipid-reducing actions of the aqueous and alcoholic extracts of *U. dioica* indicated that this plant possesses some potential medicinal values and explained its in medical use. This aspect together with mechanism role of the plant extract responsible for hypolipidemic merits further studies. Our studies on hypolipidemic activity of the *U. dioica* remedies are in progress to elucidate their mode of action.

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Conflict of Interest: There are no conflicts of interest.

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