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Original Article

Antioxidant effect of aqueous extract of sumac *(Rhus coriaria* L.*)* in the alloxan-induced diabetic rats

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Abstract

In this experimental study, 30 adult male Wistar rats divided into 5 groups (n=6). Experimental rats were treated with one intraperitoneal injection of 120 mg/kgbw Alloxan monohydrate alone or in combination with 28 days of oral administration with aqueous extract of *Rhus coriaria* (50, 100 and 250 mg/kgbw) while the control rats received normal saline. At the end of the study, blood glucose, malondialdehyde concentration and catalase activities of kidney and liver tissues were determined. Treatment with *Rhus coriaria* extract resulted in a significant reduction in blood glucose, and the liver and kidney tissue contents of malondialdehyde in comparison to diabetic group ($P<0.05$). Furthermore, diabetic group treated with extract showed a significant increase in catalase activities of the liver and kidney ($P<0.05$). The present study showed that *Rhus coriaria* could be effective in decreasing diabetic complication and this effect is attributed to the antioxidant activity of the plant.

Introduction

Diabetes mellitus as a metabolic disorder leads to chronic hyperglycaemia with disturbances metabolism of carbohydrate, fat and protein (1). The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs in the body, especially the eyes, liver, kidneys, nerves, heart, pancreas itself, and blood vessels (2).

During progression of diabetes mellitus, altered metabolism of lipids, carbohydrates and proteins

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increases lipid peroxides and / or oxidative stress leads to increase production of reactive oxygen species (ROS) (3, 4). Also antioxidant capacity decreases in diabetes mellitus (5).

Antioxidant defense mechanisms including antioxidant enzyme-systems are important for the protection of the cells and tissues against oxidative damage (2).

Malondialdehyde (MDA) is a highly toxic product formed in part by lipid oxidation derived free radicals. Many studies have shown that its concentration is considerably in diabetes mellitus, correlating with poor glycaemic control. Many herbal such as: Barberry, Estragon, *Rhus coriaria*, *Cinnamomum zelanicum*, *Hypericum perforatum* and onion known anti diabetic effects and use to patient treatment (3). Sumac (*Rhus coriaria* L.), belonging to the *Anacardiaceae* family, is a small tree or shrub. It grows in Mediterranean countries, North Africa, South Europe, Afghanistan and Iran (6, 7). Many studies show the antioxdant effect of sumac and its derivatives, such as the extract (8-10). Mavlyanov *et al*. (1997) reported that fruits of *Rhus coriaria* contain flavonols, phenolic acid, hydrolysable tannin, anthocyans and organic acid (7).

Due to antioxidant and free radical scavenging activities of *Rhus coriaria*, we planned to study effect of aqueous extract of *Rhus coriaria* on Malondialdehyde (MDA) levels and catalase (CAT) activity in liver and kidney of diabetic rats.

Methods

Animals

Thirty healthy, male, Wistar rats weighing 180-230 g, were used in this study. They were housed under standard laboratory conditions of light, temperature and humidity. All animals were treated in accordance to the Principles of Laboratory Animal Care. The experimental protocol was approved by the Animal Ethical Committee in accordance with the guide for the care and use of laboratory animals prepared by Urmia University. All Rats were fed a standard diet and water. The rats randomly divided into 5 experimental groups (n=6). Control rats were injected with physiological serum the same volume of injection material. Group II rats (Diabetic), were diabetic by injecting 120 mg/kgbw dose in intraperitoneal Alloxan monohydrate (11). Control rats were injected with the necessary volume of physiological serum. Group II contracted diabetes by being intraperitoneally injecting 120 mg/kgbw Alloxan. The rats of third (D+S1), fourth (D+S2), and fifth group (D+S3), in addition to the same treatment, were fed 50, 100 and 250 mg/kgbw of aqueous extract of Rhus coriaria L, respectively for 4 weeks.

Blood glucose determination

Blood samples were collected from the tail vein. Basal glucose levels were determined, using an automated blood glucose analyzer (Glucometer ACCUE CHECH). Sample collections were then made 72 h after alloxan injection and blood glucose concentrations were determined. Rats with blood glucose concentrations above 200 mg/dl were declared diabetic and were used in the experimental group. Furthermore, after 28 days of treatment, the levels of blood glucose were determined. In the 28th day, (at the end of the treatment period), the rats were killed with diethyl ether. The liver and kidney tissues of each animal were removed, cleaned, dried and processed for biochemical measurements.

Measurement of liver and kidney tissue contents of MDA

MDA concentration was determined by using the method described by Draper based on TBA (2-thiobarbituric acid) reactivity. Briefly, 2.5 mL of 10% trichloracetic acid and 0.5 mL of sample were added into tubes and mixed. After incubating for 15 min at 90°C and cooling with cold water the mixture was centrifuged at 3000 rpm for 10 min. Two milliliters of supernatant were taken and 1 ml of 0.675% TBA was added. The tubes were sealed and incubated at 90°C for 15 min and then cooled to room temperature. The optical density was measured at 532 nm by a spectrophotometer (12).

Measurement of liver and kidney CAT activity

The activity of CAT was determined by using the

method described by Aebi. 1 ml H_2O_2 and 2 ml of sample were added into tubes and mixed. Then optical density was measured at 240 nm by a spectrophotometer (13).

Statistical analysis

Oneway analysis of variance (ANOVA) and Tukey statistical test were used to compare these parameters in the study group. The results were expressed as mean±S.E.M (standard error of means). P-values less than 0.05 were considered significant.

Results

The blood glucose levels of rats included in this study are presented in Figure 1. Alloxan induced a significant increase of blood glucose in comparison with control group (P<0.05) (Fig. 1). Furthermore, compared diabetic group, in the extract-treated group (50, 100 and 250 mg/kgbw), there was a significant

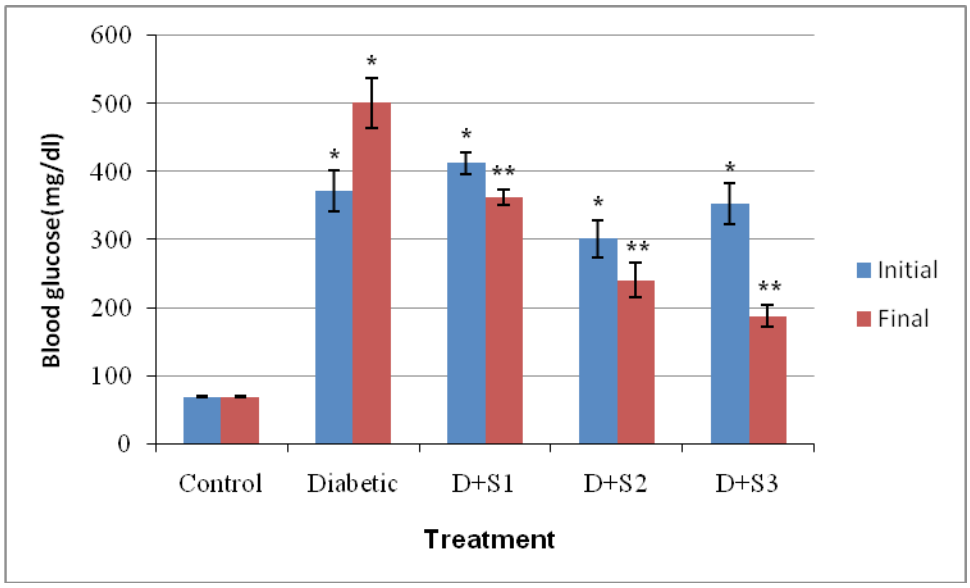

Fig. 1 : Blood glucose levels (mg/dl) in experimental groups.
*: significant difference in comparison with control group (P<0.05).
**: significant difference in comparison with diabetic group (P<0.05).

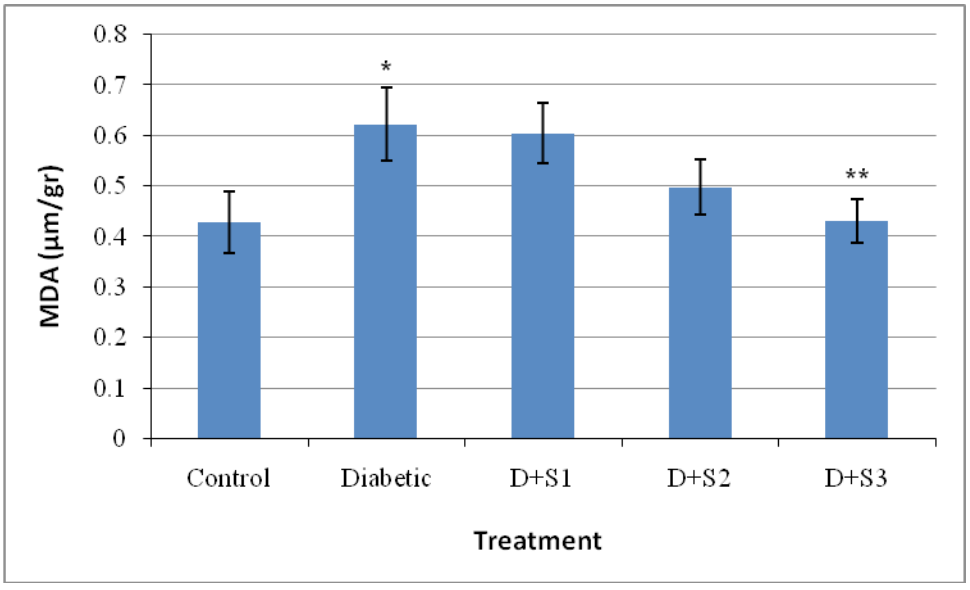

Fig. 2 : The kidney MDA (µm/gr) levels in experimental groups.
*: significant difference in comparison with control group (P<0.05).
**: significant difference in comparison with diabetic group (P<0.05).

decrease in blood contents of glucose (P<0.05) (Fig. 1).

MDA levels in diabetic rats were significantly higher than in control group (P<0.05) (Figs. 2, 3). Treatment with extracts of *Rhus coriaria* (250 mg/kgbw) resulted in a significant reeducation in MDA levels of kidney and liver tissues (P<0.05) (Figs. 2, 3). In diabetic rats there was a significant decrease in CAT activity when compared to the control rats (P<0.05) (Figs. 4, 5). Furthermore, diabetic group treated with extract (250 mg/kgbw) showed a significant increase in CAT activity in kidney and liver tissues (P<0.05) (Figs. 4, 5).

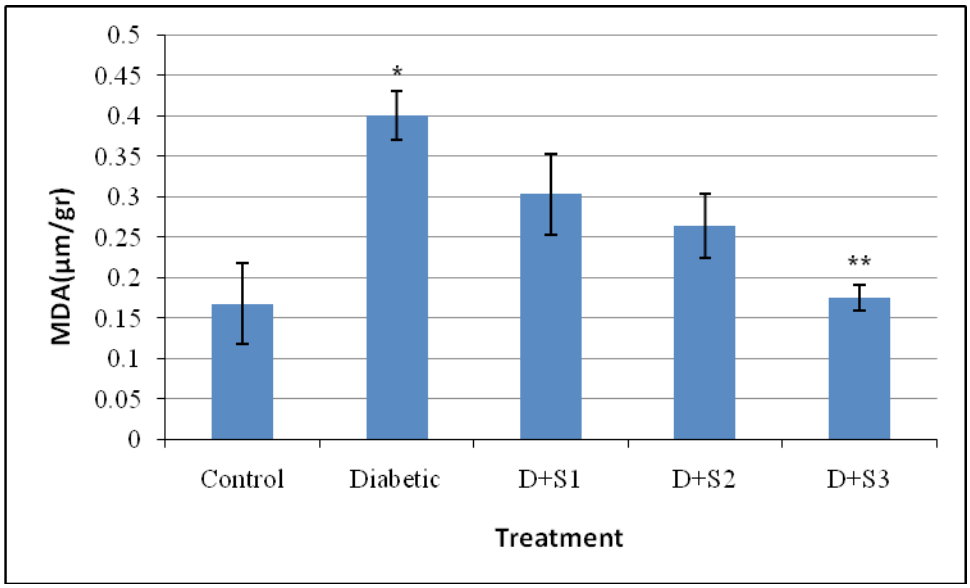

Fig. 3: The liver MDA (µm/gr) levels in experimental groups.
*: significant difference in comparison with control group (P<0.05).
**: significant difference in comparison with diabetic group (P<0.05).

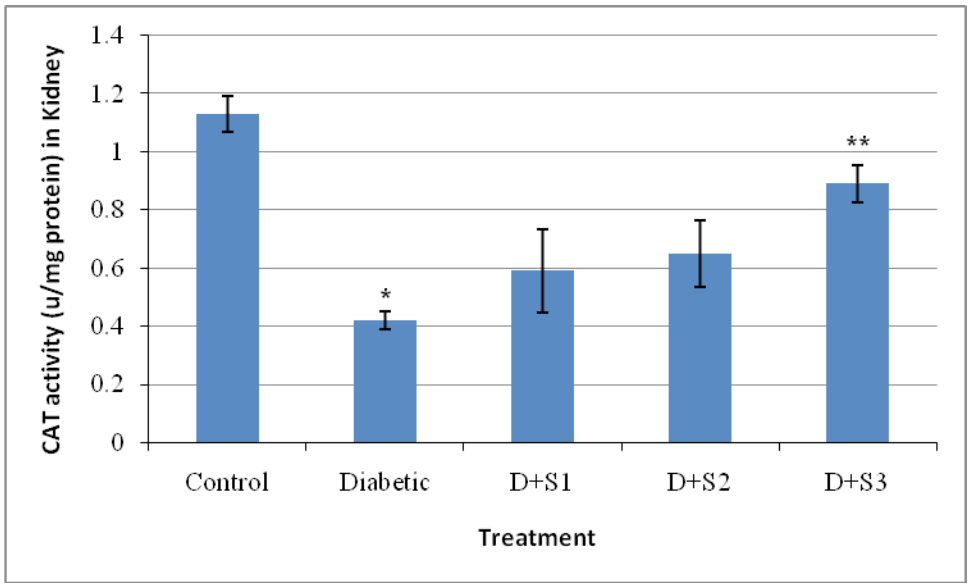

Fig. 4: CAT activity (u/mg protein) of the kidney in experimental groups.
*: significant difference in comparison with control group (P<0.05).
**: significant difference in comparison with diabetic group (P<0.05).

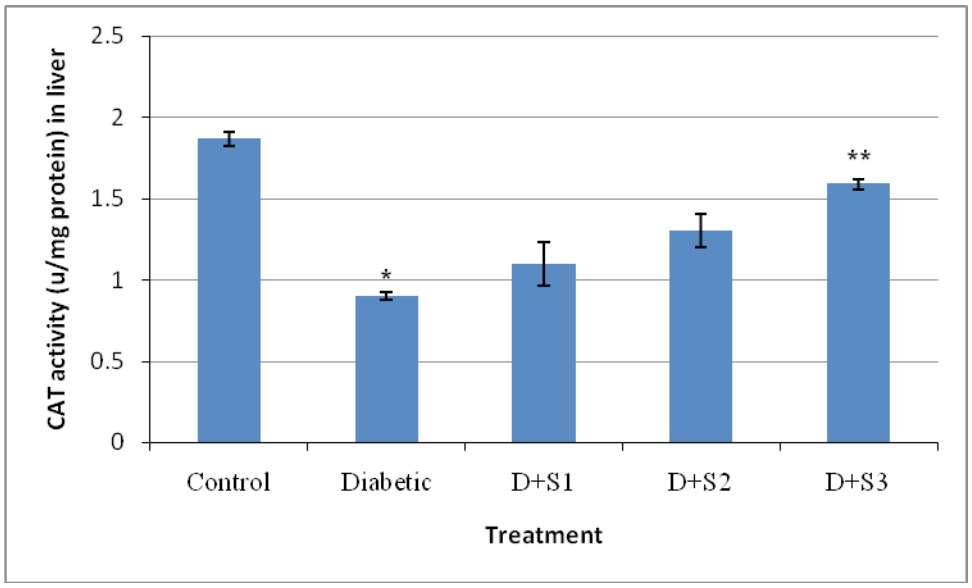

Fig. 5 : CAT activity (u/mg protein) of the liver in experimental groups.
*: significant difference in comparison with control group (P<0.05).
**: significant difference in comparison with diabetic group (P<0.05).

Discussion

Alloxan-induced diabetes in animals mimics the mechanism involving the disease by production of active oxygen species (14, 15). Based on ancient Persians traditional books, use of herbal medicine has positive effect on treatment of different diseases especially on diabetes mellitus (3). Numbers of plants which have this effect are: barberry, tarragon, sumac, cinnamon, some tea specious and onion. Investigation shows these plants contain antioxidant agents (3, 16).

Flavonoids are products of plant metabolism that have free radical scavenging properties are effective antioxidants. This utility capable herbal plants to protect tissues against free oxygen radicals and lipid peroxidation (17). Armitage *et al*. (1961) showed that in addition to gallotanin, *Rhus coriaria* contains substantial amount of flavonoids (quercitin and myrcetin) (18).

Quercetin is a well-known flavonoid and a strong antioxidant and long-term treatment of STZ diabetic animals and it has been shown to reduce oxidative stress (19).

The research efforts on *Rhus coriaria* extracts to date indicate a promising potential for this plant family to provide renewable bioproducts with the following reported desirable bioactivities: antifibrogenic (20), antifungal (21), anti-inflammatory (22), antimalarial (23), antimicrobial (24), antitumorigenic activities (25, 26), antioxidant (27), antithrombin (28), antiviral (29), hypoglycaemic (30), and leukopenic (31, 32). *Rhus coriaria* may also have potential for the prevention or treatment of atherosclerosis and its clinical manifestations (33).

In the present study, the aqueous extracts of *Rhus coriaria* effectively decreased the blood glucose in alloxan-induced diabetic rats.

Methanol extracts of *Rhus coriaria* fruits were recently studied for potential hypoglycemic activity. The crude extracts were further fractionated by ethyl acetate and n-hexane, and the ethyl acetate extracts exhibited significant hypoglycemic activity through α-amylase inhibition (87% inhibition at 50 µg/ml). The higher biological activity in the ethyl acetate extract was attributed to the presence of flavonoids (30).

In the present study, MDA levels of the liver in diabetic animals treated with extract were found to be lower than those in non-treated diabetic group.

Although the MDA level of the kidney in diabetic animals treated with *Rhus coriaria* were lower than those in non-treated diabetic group. These results provided evidence for the free radical-scavenging properties of *Rhus coriaria*.

The result was in collaborative with Pourahmad *et al*. (2010), who reported that the Malondialdehyde formation was also markedly increased following ROS formation and aqueous extracts of *Rhus coriaria* fruit prevented both malondialdehyde formation and cytotoxicity as well as subsequent lipid peroxidative sub-cellular organelle damage (mitochondria/ lysosomes) (34).

Previous studies have suggested that extract of *Rhus coriaria* fruits may be a source of natural antioxidants. The fractionated extract was an uncompetitive inhibitor of xanthine oxidase and scavenger of superoxide radical *in vitro* with IC_{50} values of 173 and 232 µg/ml, respectively (35).

Liver and kidney are essential tissues where important complications of diabetes mellitus occur. It was shown that the severity of diabetic complications in tissues is related to the damage in their oxidative-antioxidative systems. The concerted actions of various antioxidant enzymes that keep the concentration of free radicals relatively low are overwhelmed in states of oxidative stress, such as diabetes (36). In the present study, it was found that *Rhus coriaria* had effects on antioxidant enzyme activities in liver and kidney tissues. Treatment with extract of *Rhus coriaria* caused a significant increase in CAT activity in treated diabetic animals when compared with that in non-treated diabetic animals.

Adewole *et al*. (2007), studied on the effect of Quercetin on STZ-induced diabetes mellitus in rats, they reported the Quercetin caused significant increased CAT activity in STZ-induced diabetic rats (2).

On the other hand, studies had been done on serum surface of glutathione, catalase, superoxide dismutase, and fat per oxidation in liver, brain, kidney tissue show Quercetin as an antioxidant agent not only decreases free O2 specious and LDL oxidase in diabetic rats but also has therapeutic potential (37). Therefore suggested, increased use of herbal medicine, fruit, vegetables, tea which are full of flavonoids and Quercetin can decrease side effects of diabetes mellitus on liver and kidney tissue in diabetic rats.

In conclusion, it suggested that *Rhus coriaria* administration would be beneficial in the treatment of diabetes as an antioxidant and a free radical scavenger in controlling glucose levels and MDA levels, CAT activities of the kidney and liver.

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