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The Hypolipidemic Effects of *Artemisia sieberi* (*A. herba-alba*) in Alloxan Induced Diabetic Rats

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Abstract: The present study was designed to evaluate the antidiabetic and hypolipidemic effects of aqueous extract of *Artemisia sieberi* aerial part in normal and alloxan diabetic rats. Forty male Wister rats with body weight of 180-200 g divided into four groups two control and two experimental groups: Group 1-injected with physiological saline, group 2-received orally water extract of *Artemisia sieberi* (39 g kg^{-1} b.wt.) and served as control. Groups 3 and 4 including diabetic rats, group 3 received 10 mL kg^{-1} tap water and served as control and group 5 given orally water extract of *Artemisia sieberi* (0.39 g kg^{-1} b.wt.). At the end of the experimental period (14 days), animals in all four groups were fasted for 12 h and blood samples were taken for the determination of serum glucose total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol and total cholesterol/HDL cholesterol (TC/HDL-C). The treatment was given for 2 weeks. After the treatment a significant reduction was observed in fasting serum glucose levels in the treated diabetic's rats. *Artemisia sieberi* treatment showed considerable lowering of serum total cholesterol, triglycerides, LDL cholesterol, TC/HDL-C and an increase in HDL cholesterol in the treated diabetic group. These results suggest that the oral administration of *Artemisia sieberi* aqueous extract of the aerial part possesses antidiabetic and hypolipidemic effects in alloxan-induced diabetic rats.

Key words: *Artemisia sieberi*, cholesterol, triglycerides, HDL cholesterol, LDL cholesterol

INTRODUCTION

Diabetes is a disorder of carbohydrate, fat and protein attributed to a diminished production of insulin or mounting resistance to its action. Chronic hyperglycaemia during diabetes causes glycation of body proteins that in turn leads to secondary complications affecting eyes, kidneys, nerves and arteries (Kameswara Rao *et al*., 1999). Along with hyperglycaemia and abnormalities in serum lipids (Virella-Lopes and Virella, 2003; NCEP, 2002) diabetes is associated with microvascular and macravascular complications which are the majors causes of morbidity and death in diabetic subjects (Nagappa *et al*., 2003). It can be managed by exercise, diet and pharmaceutical drugs, which are either too expensive or have undesirable sides effects or contraindications (Serrano, 1990). The search for more effective and safer hypoglycemic agents therefore has continued to be an area of research of interest (Krishna *et al*., 2004; Pepato *et al*., 2003). The World Health Organization has recommended and encouraged the use of alternative therapy especially in countries where access to the conventional treatment of diabetes is not adequate (WHO, 1980). The management of diabetic patients relies on four fundamental columns: education, diet, exercise and drugs (Boriky *et al*., 1996). After insulin became available, evidence emerged suggesting that human diabetes mellitus has a multifactorial etiology. Insulin has been used in diabetes mellitus treatment. In order to discover other hypoglycemic agents, many investigations (Marrif *et al*., 1995; Saravanan and Pari, 2003; Subramoniam *et al*., 1996) have been performed in traditional medicine testing eventual hypoglycemic plants. In traditional practice medicinal plants are used in many countries to control diabetes (Saravanan and Pari, 2003; Subramoniam *et al*., 1996). Plant drugs are frequently considered to be less toxic and induce fewer side effects than synthetic ones (Pari and Umamaheswari, 2000). The oral hypoglycemic agents currently used in clinical practice have characteristic profiles of serious side effects (Williams and Pickup, 1991).

Artemisia sieberi is a well-known medicinal plant that has been used in the Middle East traditional medicine for treating various diseases including diabetes mellitus. It is

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used as an anthelminthic by the local population. The plant is also used as antimicrobial, poison antidote and emmenagogue (Nagappa *et al*., 2003).

Suleiman *et al*. (1988), Gharaibeh *et al*. (1988), Tanira *et al*. (1996) and Konuklugil *et al*. (1997) are reported to possess antidiabetic effects and have been used in many countries of Middle East and Turkey as an herbal medicine for treatment of diabetes, high blood pressure and gastrointestinal ailments.

We therefore studied the effects of *Artemisia sieberi* study on blood glucose and on lipid profile of alloxan-induced diabetic rats.

MATERIALS AND METHODS

This study conducted during April and May, 2007 and all analysis conducted in the reference medical laboratories.

Animals: Three month old male Wister rats with body weight of 150-200 g were obtained from the animal house in the Jordanian University of Technology. The animals were fed on standard pellet diet and water *ad libitum*.

Test drugs: Plant material was prepared according to the traditional method: The above-ground parts of *Artemisia sieberi* were powdered and dissolved in distilled water for 16 h with occasionally shaking each 2 h. The extract was filtered. The filtrate was adjusted to concentration of 8.5 mg mL^{-1} of *Artemisia sieberi.*

Experimental induction of diabetes in rats: The rats were injected intraperitoneally with alloxan monohydrate (BDH Chemicals Ltd., England) dissolved in sterile normal saline at a dose of 150 mg kg^{-1} b.wt. (Prince and Menon, 2000). Blood samples were drawn at weekly intervals till the end of study. Fasting blood glucose estimation, body weight, food and water intake measurement were done on day 0, 7 and 14 of the study.

Experimental design: A total of 40 diabetic rats were used in the experiment. Twenty of rats used as control, Normal rats were divided randomly into 2 groups of 10 rats each and treated as follows:

A: Groups 1 and 2 including normal rats were treated as follows:

Group 1 injected with physiological saline and Group 2 received orally water extract of *Artemisia sieberi* (0.39 g kg^{-1} b.wt.) and served as control.

B: Groups 3 and 4 including diabetic rats were treated as follows:

Group 3 received 10 mL kg^{-1} tap water and served as control and group 5 given orally water extract of *Artemisia sieberi* (39 g kg^{-1} b.wt.). The animals were carefully monitored every day and weighed every week (2 weeks). No sign of toxicity was noticed on the behavior and general health of the animals when exposed to extract. Animals described as fasted were deprived of food for at least 12 h but allowed free access to drinking water.

Blood collecting: Blood samples were drawn from rats in plain tubes and allowed to clot, the centrifuged to obtain serum using a bench top centrifuge (Cenformix).

Determination of serum glucose and lipid profile: Serum glucose and lipid profile was determined after 12-14 h of fasting, including: Total Cholesterol (TC); triglycerides (TG); High-Density Lipoprotein Cholesterol (HDL-C) Low-Density Lipoprotein Cholesterol (LDL-C) by using commercial analytical kits from Sigma (St. Louis, Mo, USA).

Statistical analysis: The data were analyzed with one way ANOVA in SPSS 10. Duncan's test was used in all data where appropriate.

RESULTS

Significant ($p<0.001$) weight loss was observed in untreated diabetic rats (group 3) than untreated normal rats (group 1) (Table 1). Treatment with aqueous extract of *Artemisia sieberi* (group 4) improved the weight gain compared to untreated diabetic rats. The blood glucose was increased significantly in untreated alloxan-diabetic rats (group 3) as compared to untreated normal rats ($p<0.001$). Administration of *Artemisia sieberi* lids to significant decrease in blood glucose levels in diabetics treated groups ($p<0.001$), while no decrease in blood glucose levels was observed in normal treated group (Table 2).

The food and water intake (Table 3, 4) ($p<0.001$) increased significantly in untreated diabetic rats compared to untreated normal rats. Significant reduction ($p<0.001$) of food intake and water intake were noticed after the treatment with *Artemisia sieberi*. No effect of the extract was noticed in normal rats. Serum total cholesterol, triglycerides, LDL cholesterol and (TC/HDL) were significantly elevated in untreated diabetic rats as compared to untreated normal rats ($p<0.001$). All lipids parameters tested were improved after the treatment with aqueous extract of *Artemisia sieberi.* No effect was observed in treated normal rats (Table 5).

Table 1: Effect of treatment with aqueous extract of *Artemisia sieberi* for 2 weeks on body weight g in normal and diabetic rats

Groups	Day 0	Day 7	Day 14	Significance
1	192.3±7.14	204.3±6.91	218.8±9.87	p = 0.000<0.001
2	187.0±6.02	199.4±5.39	211.5±7.32	p = 0.000<0.001
3	169.6±4.35	185.7±6.03	196.6±7.13	p = 0.000<0.001
4	218.9±7.04	205.0±7.98	197.5±8.60	p = 0.000<0.001

Table 2: Effect of treatment with aqueous extract of *Artemisia sieberi* for 2 weeks on serum glucose concentration (mg dL^{-1}) in normal and diabetic rats

Groups	Day 0	Day 7	Day 14	Significance
1	86.7±5.03	85.8±7.25	87.8±11.24	p = 0.000<0.001
2	83.7±5.32	84.2±7.24	82.7±7.24	p = 0.000<0.001
3	75.9±4.37	340.7±26.12	312.5±26.76	p = 0.000<0.001
4	128.5±15.42	218.9±28.95	315.3±26.72	p = 0.000<0.001

Table 3: Effect of treatment with aqueous extract of *Artemisia sieberi* for 2 weeks on food intake (g day^{-1}) in normal and diabetic rats

Groups	Day 0	Day 7	Day 14	Significance
1	18.6±1.19	17.5±1.50	15.4±1.64	p = 0.000<0.001
2	13.6±1.05	13.9±1.18	12.6±1.25	p = 0.000<0.001
3	34.5±3.23	29.9±3.06	26.2±4.07	p = 0.000<0.001
4	26.7±4.19	32.5±4.19	28.3±4.29	p = 0.000<0.001

Table 4: Effect of treatment with aqueous extract of *Artemisia sieberi* for 2 weeks on water intake (mL day^{-1}) in normal and diabetic rats

Groups	Day 0	Day 7	Day 14	Significance
1	18.9±2.68	20.5±2.91	17.6±2.77	p = 0.000<0.001
2	18.1±1.70	17.3±1.42	17.8±1.45	p = 0.000<0.001
3	73.8±5.87	86.2±4.62	75.9±4.37	p = 0.000<0.001
4	88.0±4.37	83.0±7.99	57.0±7.12	p = 0.000<0.001

Table 5: Effect of treatment with aqueous extract of *Artemisia sieberi* for 2 weeks on serum lipid profile concentration in normal and diabetic rats

Parameters	Group 1	Group 2	Group 3	Group 4	Significant
Cholesterol	85.2±9.76	79.9±10.14	130.8±7.92	101.5±9.12	p = 0.000<0.001
Triglycerides	95.5±11.50	95.6±13.12	150.3±9.23	94.9±5.64	p = 0.000<0.001
HDL-C	30.8±3.89	29.1±1.83	32.5±3.10	22.2±3.27	p = 0.000<0.001
LDL-C	21.5±3.38	19.7±2.51	75.4±6.2102	54.8±4.59	p = 0.000<0.001

DISCUSSION

Alloxan induces diabetes by damaging the insulin secreting cells of the pancreas leading to hyperglycaemia (Szudelski, 2001). An observation in this study correlates with the previous research finding, in that the blood glucose levels significantly increased in alloxan untreated diabetic rats. Alloxan induces damage and death of pancreatic islet-cells in several experimental animal models, thus causing diabetes mellitus and decreasing the secretion of insulin. The cytotoxic action of this diabetogenic agent is mediated by reactive oxygen species, Alloxan and the product of its reduction, dial uric acid; establish a redox cycle with the formation of super oxide radicals. These radicals undergo dismutation to hydrogen peroxide. Thereafter highly reactive hydroxyl radicals are formed by the Fenton reaction. The action of reactive oxygen species with a simultaneous massive increase in cytosolic calcium concentration causes rapid destruction of β-cells. The blood glucose data obtained clearly indicate that aqueous extract from *Artemisia sieberi* produced significant hypoglycemic effects in alloxan-induced diabetic rats. The obtained results were similar to those obtained by Marrif *et al.* (1995) and Twaij and Al-Badr (1988) and it is possible that the plant may reverse the catabolic features of insulin deficiency, decrease the release of glucagon or increase that of insulin, stimulate directly glycolysis in peripheral tissues, increase glucose removal from blood or reduce glucose absorption from the gastrointestinal tract (Marrif *et al.*, 1995). Hypoglycemic effects of *Artemisia sieberi* could, possibly, be due to increased peripheral glucose utilization. Inhibition of the proximal tubular reabsorption mechanism for glucose in the kidneys, if any, can also contribute towards blood lowering effect (Sharma *et al.*, 1983). Body weight in all diabetic rats was increased. This is the normal effect of diabetes mellitus. After the treatment of the diabetic rats, their body weight increased again. Similar effects were also observed by other researchers (Boriky *et al.*, 1996; Twaij and Al-Badr, 1988; Sharma *et al.*, 1983). The synthetic oral hypoglycemic agents can produce a series of side effects. As can be seen from the study, rats treated with *Artemisia sieberi* showed only mild visible undesirable clinical symptoms. We have noticed a significant reduction in food and water intake in alloxan diabetic rats. This could be the result of improved glycaemic control produced by aqueous extract of *Artemisia sieberi.*

We have noticed elevated serum lipids in alloxan-diabetic rats. Lipids play an important role in the pathogenesis of diabetes mellitus. The level of serum lipids is usually raised in diabetes and such an elevation represents a risk factor for coronary heart disease (Mironova *et al*., 2000). Lowering of serum lipids levels through dietary or drugs therapy seems to be associated with a decrease in the risk of vascular disease (Scott and Grundy, 1999). The abnormal high concentration of serum lipids in diabetes is mainly due to the increase in the mobilisation of fatty acids from the peripheral depots, since insulin inhibits the hormone sensitive lipase. On the other hand, glucagon, catecholamines and other hormones enhance lipolysis. The marked hyperlipidemia that characterizes the diabetic state may therefore be regarded as a consequence of the uninhibited actions of lipolytic hormones on the fat depots (AL-shamaony *et al*., 1994).

In our study, we have also observed an increase in the concentration of total cholesterol, triglycerides, LDL cholesterol and TC/HDL-C in alloxan untreated diabetic rats. Hyperlipidemia is a recognized consequence of diabetes mellitus (Pushparaj *et al*., 2000; Pepato *et al*., 2003; Sharma *et al*., 1983). Administration of aqueous extract of *Artemisia sieberi* normalized serum lipids, secondary to the diabetic state. Diabetes-induced hyperlipidemia is attributable to excess mobilization of fat from the adipose due to the under utilization of glucose (Krishna *et al*., 2004). The ability of aqueous extract of A*rtemisia sieberi* reduce the levels of plasma lipids in diabetic rats by the increasing the utilization of glucose, thereby depressing the mobilization of fat.

CONCLUSION

Present findings indicate that an aqueous extract of *Artemisia sieberi* can lower the blood glucose and serum lipids in allowance diabetic's rats. This is of interest, since elevated concentrations of both are risk factors in the development of arteriosclerosis in diabetes mellitus. The recommendation for the production drug from the extract of *Artemisia sieberi* as hypolipidemic and hypoglycemic agent.

REFERENCES

Al-shamaony, L., S.M. Al-khaznaji and H.A.A. Tway, 1994. Hypoglycemic effect of *Artemisia herba alba* II. Effect of valuable extract on some blood parameters, in diabetic animals. J. Ethnopharmacol., 43: 167-171.

Boriky, D., M. Berrada, M. Talbi, G. Keravis and F. Rouessac, 1996. Eudesmanolides from *Artemisia herba-alba.* Photochemistry, 43: 309-311.

Gharaibeh, M.N., H.H. Elayan and A.S. Salhab, 1988. Hypoglycemic effects of *Teucrium polium*. J. Ethnopharmacol., 24 (1): 93-99.

Kameswara Rao, B., M.M. Kesavulu, R. Giri and A. Rao, 1999. Antidiabetic and hypolipidemic effects of *Momordica cymbalaria* Hook, fruit powder in alloxan diabetic rats. J. Ethnopharmacol., 67: 103-109.

Konuklugil, B., G. Deniz, O. Yildiz, S. Senoz and S. Saygi, 1997. Hypoglycemic effect of *Teucrium polium* in rats. Fitoterapia, 68 (1): 39-41.

Krishna, B., S. Nammi, M.K. Kota and R.V. Krishna Rao, 2004. Evaluation of hypoglycemic and antihyperglycaemic effects of *Datura metel* Linn. seeds in normal and alloxan-induced diabetic rats. J. Ethnopharmacol., 9: 95-98.

Marrif, H.I., B.H. Ali and K.M. Hassan, 1995. Some pharmacological studies on *Artemisia herba-alba* (Asso) in rabbits and mice. J. Ethnopharmacol., 49: 51-55.

Mironova, M.A., R.L. Klein, G.T. Virella and M.F. Lopes-Virella, 2000. Anti-modified LDL antibodies, LDL-containing immune complexes and susceptibility of LDL to *in vitro* oxidation in patients with type 2 diabetes. Diabetes, 49: 1033-1049.

Nagappa, A.N., P.A. Thakurdesai, N. Venkat Rao and J. Singh, 2003. Antidiabetic activity of *Terminalia catappa* Linn. fruits. J. Ethnopharmacol., 88: 45-50.

NCEP (Third Report of the National Cholesterol Education Program), 2002. Expert panel on detection, evaluation and treatment of high blood cholesterol in adult (Adult Treatment Panel III) final report. Circulation, 106: 3143-3421.

Pari, L. and J. Umamaheswari, 2000. Antihyperglycaemic activity of *Musa sapientum* flowers: Effect on lipid peroxidation in alloxan diabetic rats. Phytother. Res., 14: 1-3.

Pepato, M.T., A.M. Baviera, R.C. Vendramini, M.P. Perez, I.C. Kettelhut and I.L. Brunetti, 2003. *Cissus sicyoides* (Princess wine) in the long term treatment of streptozotocin-diabetic rats. Biotechnol. Applied Biochem., 37: 15-20.

Prince, P.S.M. and V.P. Menon, 2000. Hypoglycemic and other related action of *Tinospora codifolia* roots in alloxan rats. J. Ethnopharmacol., 70: 19-25.

Pushparaj, P., C.H. Tan and B.K.H. Tan, 2000. Effects of *Averrhoa bilimbi* leaf extract on blood glucose and lipids in streptozotocin-diabetic rats. J. Ethnopharmacol., 72: 69-76.

Saravanan, G. and L. Pari, 2003. Effect of Cogent db, an herbal drug, on serum and tissue lipid metabolism in experimental hyperglycemic rats. Diabetes Obesity Metab., 5: 156-162.

Scott, M. and Grundy, 1999. Diabetes and cardiovascular disease. Circulation, 100: 1134-1146.

Serrano, J.J., 1990. Toxico pharmacological of medicinal plants in experiments Actes du 1er Colloque Europeen d'Ethnopharmacologie. Office de la Recherche Scientifique et Techniques d'Outre Mer (ORSTOM)., pp: 210-218.

Sharma, M.K., A.K. Khare and H. Feroz, 1983. Effect of neem oil on blood glucose levels of normal, hyperglycemic and diabetic animals. Indian Med. Gaz., 117: 380-383.

Subramoniam, A., P. Pushpangadan, S. Rajasekharan, D.A. Evans, P.G. Latha and R. Valsaraj, 1996. Effects of Artemisia pallens wall on blood glucose levels in normal and alloxan-induced diabetic rats. J. Ethnopharmacol., 50: 13-17.

Suleiman, M.S., A.S. Abdul-Ghani, S. Al-Khalil and R.E. Amin, 1998. Effect of Teucrium polium boiled leaf extract on intestinal motility and blood pressure. J. Ethnopharmacol., 22 (1): 111-116.

Szudelski, T., 2001. The mechanism of alloxan and streptozotocin action in β cells of the rat pancreas. Physiol. Res., 50: 536-546.

Tanira, M.O., I.A. Wasfi, M. Al Homsi and A.K. Bashir, 1996. Toxicological effects of *Teucrium stocksianum* after acute and chronic administration in rats. J. Pharm. Phanrmacol., 48 (10): 1098-1102.

Twaij, H.A.A. and A. Al-Badr, 1988. Hypoglycemic activity of *Artemisia herba-alba*. J. Ethnopharmacol., 24: 123-126.

Virella-Lopes, M.F. and G. Virella, 2003. The role of immune and inflammatory processes in the development of macrovascular disease in diabetes. Frontiers Biosc, 8: 750-768.

WHO, 1980. WHO Expert Committee on Diabetes Mellitus, Second Report, Technical Report series 646. World Health Organisation, Geneva.

Williams, G. and J. Pickup, 1991. New Drugs in the Management of Diabetes Mellitus. In: Textbook of Diabetes, Pickup, J.C. and G. Williams (Eds.). II Blackwell, Oxford, pp: 977-993.