Accessing the Hypoglycemic effects of Seed Extract from Celery (*Apium Graveolens*) in Alloxan-Induced Diabetic Rats

ABSTRACT

The present study is aimed to evaluate the potential mechanism of antidiabetic action of seed extract celery (Apium graveolens) and its effects on some hematological and biochemical parameters in alloxan-induced diabetic rats. This study was conducted on fifty experimental animals. Adult albino rats (Sprague-Dawely strain) weighing about 220 g each were used throughout the study. Fifty rats were randomly assigned to five experimental groups of 10 rats each: Group 1 - received normal saline (0.5ml/kg), and serves as control. Group II - gavaged daily for thirty days with 1ml of the extract at doses of 425 mg/kg body wt and served as control. Group III - Untreated diabetic rats that received two doses of alloxan 150mg/kg. Group IV - Treated diabetic rats for thirty consecutive days with 1ml of the extract at a dose of 425 mg/kg body wt. Group V: Treated diabetic rats for thirty consecutive days with 14.2 mg/kg of metformin. Several hematological and biochemical parameters were assessed. It was found that the administration of ethanol extract of *A. graveolens* produced significant reduction in blood glucose level in diabetic rats after thirty days of treatment. However, there was a significant (P=.05) increase of insulin secretion. Also, the RBC and WBC count, PCV and neutrophil percentage decreased significantly (P=.05). This study indicated that the ethanol extract increased the RBC and WBC counts, PCV, ESR, and neutrophil percentage in diabetic rats. However, the WBC count of the extract - treated diabetic group was still lower than those of control values. Administration of the extract resulted in a significant reduction in the mean values of serum cholesterol, triglyceride, LDL-C, ESR, urea, uric acid, creatinine accompanied by an increase in the mean values of total protein, albumin, insulin, HDL-C, neutrophile count and PCV in diabetic rats. No significant changes in these parameters were found in the control group. Effects produced by this extract were closely similar to a standard antidiabetic drug, metformin. ($p<0.05$) hypoglycemic effects in alloxan-induced diabetic rats, protection against body weight loss of diabetic animals and might alleviate diabetes-induced disturbances of some biochemical and hematological parameters. This study was dedicated to monitoring changes in the lipid profile.

Keywords: Alloxan, metformin, seed extract,

1. INTRODUCTION

Diabetes mellitus is the major endocrine disorder (Burke JP, et al., 2003) responsible for renal failure, blindness or diabetic cataract (Therefore B, 1990), poor metabolic control (Donnelly R, et al., 2003) and increased risk of

cardiovascular disease including atherosclerosis and AGE (advanced glycation end) products (Yokozawa T, Nakagawa T. 2004). The influence of other endocrine and non-endocrine organs other than the pancreas on diabetes mellitus is documented (Virella-Lopes et al., 2003). Occasionally other endocrine disorders such as abnormal thyroid hormones levels are found in diabetes mellitus (Risérus U, Willet W. 2009). Hyperglycemia has been recently implicated in the induction of oxidative stress which, in turn, leads to the initiation and development of diabetic complications. Diabetic complications are many and include physical disability, kidney failure, visual impairment, cardiovascular disease and sexual dysfunction (Selvin E et al., 2010. Cavanagh, P, 2004). Several synthetic compounds have been used as therapeutic drugs for control of DM, including metformin (Abbasi F et al., 2004, Cheng C et al., 2006, Irshaid F et al., 2009). This drug is widely used in Jordan to regulate blood glucose level. However, most synthetic drugs only regulate blood glucose level and does not completely cure DM but prevent or delay the onset of its complications (Engelgau M et al., 2003. Behnam-Rassouli M et al., 2010). Therefore, the insufficient protection by these drugs necessitates the need for new treatment to prevent or delay these complications. The use of natural products such as plant extracts is a common practice in Jordan for relieving and treating several diseases including DM (Irshaid F et al., 2009, Wang B et al., 2011). It was shown that *A. graveolens* extracts have different beneficial biological activities as reported by Jiao et al. (2003) concerning its antibiotic activity. The isolated compounds from the seeds exhibited antioxidant and inhibitory effects of cyclooxygenase and topoisomerase enzymes (type I and II). (Momin and Nair, 2002).

The methanol extract of celery showed a significant hepatoprotective activity compared to the paracetamol and thioacetamide in treated rats (Bahar et al., 2002). Celery was also found to have anticarcinogenic and antiproliferation activities (Sultan et al. 2005). *A. graveolens* was reported to exhibit anti-inflammatory activity in experimental animals (ALHindawi et al., 1989; Atta and Alkofahi 1998). Celery seeds have gastroprotective effect probably mediated through non-prostaglandin E2 production (Whitehouse et al., 2001). Extracts of root and leaves of *A. graveolens* show a potential activity as a scavenger of free OH and DPPH radicals as well as inhibiting of the liposomal peroxidation. Therefore, they can act as antioxidants (Popovic et al., 2006).

The part of celery extract responsible for the hypocholesterolaemic action is the sugar or amino acid side chains, which mainly lowered the total cholesterol level by increasing the bile acid excretion (Tsi et al., 1995: Tsi and Tsi 2000). Ko et al., (1991) reported that the apigenin isolated from *A. graveolens* relaxes rat thoracic aorta mainly by suppressing the Ca 2+ influx through both voltage- and receptor-operated calcium channels (Mansi et al., 2009). A significant hepatoprotective activity of the methanol extract of the celery seeds was reported. Choochote et al. (2004) who used the hexane fraction of *A. graveolens* seeds reported that it has a strong repellent activity against a wide range of mosquito species belonging to various genera. Therefore, it has been concluded that it can act as an effective personal protection measure against mosquito bites and the diseases caused by mosquito-borne pathogens (Tuetun et al., 2004). The antihyperlipidemic properties of aqueous celery extract were studied in rats and at the end of the experiment, a significant reduction in the serum total

cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglyceride (TG) concentrations in the celery-treated rats were observed. However, the concentration of hepatic TG was significantly higher in the celery-treated group than in the control group (Tsi and Tan, 1995, 2000). A previous study was reported that the animals that were given a daily dose of a compound extracted from celery seed experienced a 12% reduction in their blood pressure over a four-week period, also it may reduce artery-clogging cholesterol (Blumenthal, 1998). This study was dedicated to monitoring changes in the blood glucose and some hematological parameters in alloxan-induced diabetic rats under the hypoglycemic effects of celery seed extract.

2. MATERIAL AND METHODS

2.1 Plant processing

Brown carmocarp seeds of *A. graveolens* were purchased from the local market (Amman). The seeds were planted in the greenhouse of the Department of Biological Sciences, Faculty of Science, University of Jordan. The plant was taxonomically identified by direct comparison with authenticate sample and with the help of Prof. Dawoud Al-Eisawi, Department of Biological Sciences, University of Jordan. A voucher specimen (Number APO-05) was deposited at the Department of Pharmaceutical Sciences, Faculty of Pharmacy, University of Jordan. *A. graveolens* seeds (3 kg) were finely powdered and infused using hot water overnight. Plant materials were then extracted by Soxhlet apparatus using 96% ethanol for 2 h. The solvent was then distilled off under reduced pressure below 50°C using Rotavapor. The dark brown residual extract which equals to 188 g was kept in refrigerator at 4°C until use. The yield of the ethanol extract was 6.26%.

2.2 Animal Model

This study was conducted the fifty experimental animals. All animals were housed, fed and treated in accordance with the in house guidelines for animal protection to minimize pain and discomfort. Adult albino rats (Sprague-Dawely strain) weighing about 220 g each were used throughout the study. The animals were left for a week to adapt to the room conditions (temperature, humidity, light and dark period, aeration, and caging). Food and water were provided ad libitum. Animals were described as fasted were deprived of food for at least 12 h but were allowed free access to drinking water.

2.3 Alloxan-induce hyperglycemia

Rats were made diabetic by injecting alloxan monohydrate "B.O.H chemical LTD England" intraperitoneally at a dose of 150ml/kg (dissolved in fresh normal saline) to 18h fasted rat. Every week after injection, blood was collected from the hearts of all surviving rats and blood glucose levels were determined. Rats with blood sugar levels of 200 to 450mg/100 ml were considered as diabetic and were used in the study.

2.4 Experimental Design

The fifty rats were randomly assigned to 5 experimental groups of 10 rats each:
Group 1 - Received normal saline (0.5ml/kg), and served as control.
Group II - gavaged daily for thirty days with 1ml of the extract at doses of 425 mg/kg body wt and served as control.
Group III - Untreated diabetic rats that received two doses of alloxan 150mg/kg.
Group IV - Treated diabetic rats for thirty consecutive days with 1ml of the extract at a dose of 425 mg/kg body wt.
Group V: Treated diabetic rats for thirty consecutive days with 14.2 mg/kg of metformin
Metformin was purchased from Bristol-Myers Squibb Company, UK. The seed extract and metformin were daily given, using an intragastric tube for 6 weeks. All rats were maintained in these treatment regimens for six weeks with free access to food and water. At the end of the experimental period, blood samples were taken from these experimental rats by cardiac puncture protocol. Rats were sacrificed by cervical dislocation under light ether anesthesia. These experiments complied with the guidelines of our animal ethics committee, which was established in accordance with the internationally accepted principles for laboratory animal use and care.

2.5 Blood Sample Collection

By the end of each experiment, the rats were reweighed, starved for 24 hours and sacrificed under chloroform anesthesia. 5ml of blood was collected from each animal by cardiac puncture using sterile needle and syringe. Part of the blood sample was put into test tubes and allowed to clot for 30 minutes before centrifuging using a bench top centrifuge (Cenformix). The remaining blood sample was put in an EDTA bottle for hematological determinations.

2.6 Hematological analysis

The CBC was performed on an automated hematology analyzer using well mixed whole blood to which EDTA was added to prevent clotting. (ESR) determined by Westergren method, differential WBC count was performed on Giemsa stained blood smears. Total protein, albumin, urea, uric acid, and creatinine analyses Total protein, albumin, blood urea, uric acid and creatinine levels were also determined by using Bio-Merieux Kit (Bio- Meraux Lab reagent and product, France). Insulin determination Serum Insulin was measured by radioimmunoassay methods (CEA-JRE-SORIN Firm, France).

2.7 Statistical analysis

The results were expressed as mean ± standard deviation. Differences between control and experimental groups were estimated using student›s t-test analysis. Within-group comparisons were performed by analysis of variance using ANOVA test. Differences were considered significant if p= 05

3. RESULTS

Chromatograms were examined before and after spraying under UV and daylight to detect the presence of flavonoids, coumarins, alkaloids, and terpenes **(Table 1).** Upon gavaging the animals in control and vehicle groups with one ml of the solutions, the number of survived animals were recorded after 24 h of treatment. Animals were gavaged with one ml of the prepared doses; 30, 40, 50, 60, 70, 80, 85, 90, 95, 100 mg/20 g. After 24 h of injection the dead and survived animals were recorded **(Table 2).** Changes in body weight in all groups are shown in **(Table 3)**. Significant ($P \leq 0.05$) weight loss was observed in treated diabetic rats than untreated normal rats. Treatment with 1ml of the extract at a dose of 425 mg/kg body wt and 14.2 mg/kg of metformin respectively improved the weight gain compared to untreated diabetic rats. The blood glucose was increased significantly in untreated alloxan-induced diabetic rats **(Table 4)** as compared to untreated normal rats ($P \leq 0.05$). Administration of 425 mg/kg body wt and 14.2 mg/kg of metformin respectively leads

to significant (P≤0.05) decrease of the blood glucose levels in diabetics treated groups (P≤0.05). The administration of alloxan-induced diabetes significantly increased the glucose levels of the rats. The extract produced a significant decrease (p<0.05) in blood glucose level in diabetic rats after 30 days of treatment by significantly increasing (p<0.05) the secretion of insulin. The hypoglycemic effects of *A. graveolens* seed extract on the diabetic rats were observed within 2 h, continued for about 8 h, and lasted to the end of the experiment (30 days).

The administration of extract at a dose of 425 mg/kg body wt indicates significant decrease (p<0.05) of blood glucose concentration and the increase of serum insulin was found to be anti-diabetic. None of the animals treated with extract showed any visible serious symptoms of toxicity; however, there were mild signs of respiratory distress, diarrhea, and convulsions. This indicates that *A. graveolens* seed extract may not cause any toxic effect on the body It was also found that the RBC and WBC count, PCV and neutrophil percentage significantly decreased (p<0.05) and the heart rate significantly increased (p<0.05) in diabetic rats throughout the experiment. The oral administration of water extracts of *A. graveolens* seed (425 mg/kg) significantly increased ((p<0.05) RBC, PCV, ESR, and neutrophil percentage in diabetic rats. However, the WBC count of the *A. graveolens* seed extract - treated diabetic group was still lower than those of control values **(Table 5).**

In this study, it has also been observed in **table 6** that there is a significant decrease in the concentration of total cholesterol, triglycerides, LDL cholesterol and a significant increase in HDL cholesterol in the treated groups. As can be seen in table 7, the mean values of urea, uric acid, and creatinine were significantly higher in the untreated diabetic rats as compared to the control rats ($p < 0.05$). Treatment of the diabetic rats with seed extract (425 mg/kg) and metformin for thirty days caused a significant decrease in urea, uric acid, and creatinine as compared to the untreated diabetic group ($p < 0.05$). In addition, the average values of total protein and albumin levels in the untreated diabetic rats were significantly lower ($p < 0.05$) than that of the control rats.

On the other hand, in the diabetic groups treated with seed extract (425 mg/kg) or metformin, the average values of total protein and albumin levels significantly ($p < 0.05$) increased, as compared with those of the untreated diabetic group.

4. DISCUSSION

Alloxan-induces diabetes by damaging the insulin-secreting cells of the pancreas leads to hyperglycaemia (Szudelski, 2001). 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, dialuric acid; establish a redox cycle with the formation of superoxide 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 the ethanol extracts of *A. graveolens* 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 ethanol extract of *A. graveolens* and metformin 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 (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 ethanol extract of *A. graveolens* or metformin 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 ethanol extract of *A. graveolens* or metformin.

The present study indicated that ethanol extract of *A. graveolens* or metformin treatment might ameliorate some disturbed hematological parameters of diabetic rats. It has been suggested that anemia occurrence in DM is due to the increased non-enzymatic glycosylation of RBC membrane proteins, which correlates with hyperglycemia (Hamed, S et al., 2010). Oxidation of these glycosylated membrane proteins and hyperglycemia in DM caused an increase in the production of lipid peroxides causing the hemolysis of RBC. In this study, the RBC membrane lipid peroxide levels in diabetic rats were not measured. However, (Jaouhari, J et al., 2000) demonstrated that serum lipid peroxide level increased in diabetic rabbits. Thus, increased RBC count of ethanol extract of *A. graveolens* or metformin treatment rats could be due to the lowered lipid peroxide level in RBC membrane leading to decreased susceptibility of RBC to hemolysis. Since non-enzymatic glycosylations of membrane proteins correlate with hyperglycemia (Krishna, B et al., 2004), it might be suggested that ethanol extract of *A. graveolens* or metformin produced its effect by decreasing the elevated glucose. However, more studies by measuring the RBC fragility, and serum folic acid, iron, cobalt, vitamin B12, and calcium levels are needed to demonstrate the exact mechanism of action of ethanol extract of *A. graveolens* or metformin on increased RBC count of diabetic rats. Neutrophils ingest and kill bacteria and have been called the body's first line of defense against bacterial infections (Cavalher-Machado SC et al., 2004). It has been postulated that the body's defense mechanism against infections was disturbed due to the disturbed neutrophil function in diabetes (Moriguchi P et al., 2005). In this study, we demonstrated that ethanol extract of *A. graveolens* or metformin treatment increased the lowered neutrophil percentage of WBC to the level of control. This result indicated that ethanol extract of *A. graveolens* or metformin treatment might also increase the defense mechanism of the body against infections. In diabetic rats, Alloxan-induced diabetes increased the heart rate while ethanol extract of *A. graveolens* or metformin treatment decreased it to control level. The increased heart rate in diabetic rats was probably due to the increased sympathetic output produced by diabetes-induced anemia. In the present study, it was found that the heart rate decreased and also RBC count increased to control level in ethanol extract of *A. graveolens* or metformin treated rats. Therefore, decreased heart rate could also be due to a normalized RBC count in these rats.

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 mobilization of **fatty acid**s from the peripheral depots since insulin inhibits the hormone-sensitive lipase. On the other hand, glucagon, catecholamine, 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 addition to marked hyperglycemia, our result revealed that the alloxan-induced diabetic rats developed notable hyperlipidaemia. Diabetes-induced hyperlipidaemia was observed in diabetic experimental animal models, and it is associated with an increase of mobilization of fat from fat cells and lipid metabolism due to the inability to utilize glucose properly (Mithieux G et al., 2002; Sachdewa A and Khemani LD , 2003). This is very important since elevated concentrations of cholesterol, triglyceride, and LDL-C are important risk factors in the development of arterioscleroses in diabetes mellitus. 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). Administration of ethanol extract of *A. graveolens* or metformin normalized serum lipids, secondary to the diabetic state. Diabetes-induced hyperlipidemia is attributable to the excess mobilization of fat from the adipose due to the underutilization of glucose (Krishna et al., 2004).

The ability of ethanol extract of *A. graveolens* or metformin reduces the levels of plasma lipids in diabetic rats by increasing the utilization of glucose, thereby depressing the mobilization of fat. Our findings are consistent with a recent study by Bavarva and Narasimhacharya (2010) which reported that leaves of Leucas cephalotes lowered both plasma and hepatic lipid profiles (total lipid, triglycerides, and cholesterol) and LDL-C while elevating the HDL-C levels (Pari L and Venkateswaran S, 2004). They suggest that these improvements in lipid profiles are most likely due to its insulin-like actions of the leaves extract. Similarly, a

previous study done by Lopes-Virella et al. (1983) reported that DM patients taking insulin injection showed not only the elevation of lipoprotein lipase activity but also lowers the plasma triglyceride concentrations (Bavarva JH and Narasimhacharya AVRL 2010). Thus, it can be concluded that the enhancement of insulin secretion or level is accompanied by the enhancement of glucose utilization as well as a reduction of lipid level in diabetic rats. It is possible to suggest that the mechanism(s) of antihyperlipidemic effect of the ethanol extract of *A. graveolens* might be similar to some of those suggested for anti-diabetic plants exhibiting antihyperlipidemic activity, such as activation of lipoprotein lipase, insulin-mediated lipolytic activity or inhibition of lipogenic enzymes or hormone-sensitive lipase (Ruzaidi A et al 2005). Similar results were observed in the effect of ethanol extract of Iris germanica L. rhizomes (Iridaceous), they indicated that ethanol extract of Iris germanica has remarkably lowered the lipid components, particularly, the cholesterol and triglycerides (Choudhury et al., 2005). Other researchers showed also that celery seed extract helped in the support of healthy blood pressure and cholesterol levels because of its beneficial effect on prostaglandin levels. Le and Elliott, (1991) at the University of Chicago Medical Center identified it as the factor in celery responsible for the blood pressure lowering effect of celery. The results suggest that the lipid-lowering action of this natural product may be mediated through inhibition of hepatic cholesterol biosynthesis, increased faucal bile acids excretion, and enhanced plasma lecithin: cholesterol acyltransferase activity, and reduction of lipid absorption in the intestine.

Our study also showed a significant decrease in serum total protein and albumin in untreated diabetic rats, whereas total protein and albumin significantly increased after the administration of this extract. The total protein and albumin levels in the blood can also be used as an indicator of liver function. Similar results were obtained when the metformin was administered orally in alloxan diabetic. These results suggest that this extract can improve some biochemical parameters that are related to liver functions. Hyperglycemia has also been recently implicated in the initiation and development of various types of diabetic complications. Nephropathy is one of these serious microvascular complications that have been observed in diabetic individuals (Engelgau MM, 2003). In addition, blood urea and creatinine concentrations were increased among uncontrolled diabetic individuals and this increase could be a result of impaired renal function due to an increased blood glucose level (Irshaid et al., 2012). Our results revealed for the first time that the mean values of these end products in that serum increased in untreated diabetic rats, while they significantly decreased after the administration of extracts. Thus, this extract might improve renal function which, in turn, leads to a reduction in these end products. It was reported that diabetic individuals had lower serum albumin concentrations as well as higher serum uric acid and urea levels than nondiabetic individuals (Ahmed I et al., 2001). Thus, the reduction in urea and creatinine levels probably can be explained by a reduction in blood glucose level. In conclusion, the present study indicates that the ethanol extract of *A. graveolens* appears to exhibit hypoglycemic and hypolipidemic
activities in alloxan-induced diabetic rats.

5. CONCLUSION

Based on the results obtained in this study, it can be concluded that oral administration of ethanol extract of *A. graveolens* treatment produced significant hypoglycemic effects in alloxan-induced diabetic rats, protection against body weight loss of diabetic animals and might alleviate the diabetes-induced disturbances of some hematological and biochemical parameters.

Ethical Approval: These experiments complied with the guidelines of our animal ethics committee, which was established in accordance with the internationally accepted principles for laboratory animal use and care.

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Tables:

Table 1: Phytochemical screening of ethanol extracts of *A. graveolens* seeds.

Compound	Ethanol Extract
Flavonoides	+++
Coumarins	++
Alkaloides	–
Terpenoids	+++

(-): Not detected, (+): Week present, (++): Moderately present, (+++): Strongly present

	30	40	5							
	7	7	7							
d	0	1	2							
	7	6	5							
	42	35	2							
	0	1	3							
	42	36	3							
x	0	3	9	14	28	56	83	88	95	100

rvived at this dose and higher doses

Table 4:

Effects of ethanol extract of A. graveolens seeds on levels of blood glucose and insulin in normal and alloxan induced diabetic rats.

Groups	Glucose level (mg/dL)	Insulin level (µU/ml)
I	88.4 ± 4.6	6.62 ± 1.8
II	89.3 ± 5.1	6.73 ± 1.0
III	245.79** ± 14.67	3.71** ± 1.4
IV	195.90** ± 6.2	5.40** ± 1.9
V	214.66* ± 5. 3	4.4 ± 1.7

Table 3

Effect of ethanol extract of *A. graveolens* seeds on body weight of rats in experimental and control groups

Groups	Initial weight (g)	Final weight (g)
I	212 ± 4.6	248 ± 22.8*
II	209 ± 3.8	253 ± 31.6*
III	219 ± 5.9	197 ± 26.5*
IV	202 ± 16.96	226± 8.28 *
V	218 ± 7.3	224 ± 14.6*

Table 5 Effect of ethanol extract from A. *graveolens* seeds on some hematological parameters of rats in experimental and control groups

Groups	RBC (x 106 µ)	WBC (x 10^3 µ)	Hb (g /dL)	PCV %	Neutrophils%	Lymphocytes%	ESR (mm h)
I	5.4±0.8	5.4 ±0.6	12.8±0.6	37±1.9	37±7.2	60±3.6	13±1.7
II	5.2±0.5	6.2 ±0.8	12.5 ± 0.9	38±2.8*	41±6.7**	66±5.2**	14±3.5
III	0.6** ± 3.9	4.2 ±0.8**	9,8±0.5**	28±3.8*	31±2.4**	54±5.8**	21±5.8
IV	4.4±0.3**	5.3 ±0.7**	11,2±0.4**	34±1.3	38±3.7**	59±8.3**	16±4.6
V	4.6±0.9**	5.1 ±0.4**	11,8±0.7**	35±1.6	39±4.9**	61±9.6**	15±1.6

Values are presented here as mean values ± standard deviation
* Statistically significant when compared to control group at $p<0.05$

Table 6: Effect of ethanol extract from *A. graveolens* seeds on total protein and albumin, urea, uric acid and creatinine levels in normal and alloxan-induced diabetic rats

Groups	Total protein (g/dL)	Albumin(g/ dL)	Urea (mg/dL)	Uric acid (mg/dL)	Creatinine (mg/dL
I	8,6 ± 1.4	3.5 ± 09	29.6 ± 4.3	1.8 ± 0.8	1.3 ± 02
II	7.5 ± 0.8	4.8 ± 0.6*	30.8 ± 2.8	1.7± 0.9	1.2 ± 0.4
III	5.4 ± 0.9 *	1.7 ± 0.4*	39.4 ± 8.5*	2.5± 0.6 *	2.4 ± 0.9*
IV	6.8 ± 0.6**	2.8 ± 0.3**	30.8 ±5.7**	1.9± 0.3**	1.6 ± 0.3**
V	7.2± 1.4 **	3.2 ± 0.4**	29.8 ±4.8**	1.9 ± 0.6**	1.5 ± 0.7**

Values are presented here as mean values ± standard deviation
* Statistically significant when compared to control group at $p<0.05$

Table 7: The hypolipidemic effect of ethanol extract from *A. graveolens* seeds in normal and alloxan induced diabetic rats

Groups	Cholesterol (mg/dl)	Triglycerides (mg/dl)	HDL-cholesterol (mg/dl)	LDL-cholesterol(mg /dl)
96.8 ± 12.6	96.8 ± 12.6	96.8 ± 12.6	37.4 ± 3.9	28.8 ± 3.6
II	78.4± 10.2	98.6 ± 13.6*	39.8 ± 3.7	22.7± 2.4

III	132± 13.8 *	145.9 ± 18.9*	29.4 ± 8.5**	20.5± 4.6 *
IV	108.9 ± 12.9**	102.6± 14.3**	42.8 ± 6.8**	36.9± 6.5**
V	98.9± 13.4 **	112.9 ± 19.6**	39.8 ± 8.3**	35.8 ± 9.4**

Values are presented here as mean values ± standard deviation

* Statistically significant when compared to control group at $p<0.05$