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RESEARCH ARTICLE

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THE EFFECTS OF GINGER (*ZINGIBER OFFICINALE*) ON HISTOLOGY AND IMMUNOHISTOCHEMISTRY OF LIVER AND KIDNEY AND CERTAIN HAEMATOLOGICAL PARAMETERS IN ALLOXAN-INDUCED DIABETIC RATS

ABSTRACT:

In the present study, the hypoglycaemic potentials of ginger (*Zingiber officinale*) were studied in rats (four groups: control, ginger, diabetics and diabetics treated with ginger). Ginger extract was daily orally administered (400 mg/kg,) for 4 weeks to alloxan-induced diabetic rats (150 mg/kg). Fasting blood serum was analysed for blood glucose, insulin, creatinine, blood urea nitrogen, aspartate aminotransferase, alanine aminotransferase, haemoglobin concentration, and erythrocytes, leucocytes, and platelets counts, and histological and immunohistochemical studies of the liver and kidney tissues. The alloxan-injected rats exhibited hyperglycaemia accompanied with increases in creatinine, uric acid, blood urea nitrogen, AST and ALT. On the other hand, there were decrease in insulin, haemoglobin concentration, erythrocytes, leucocytes and platelets counts occurred. Ginger was significantly effective in lowering serum glucose, and returned the other previously mentioned blood assays levels in the ginger-treated diabetic rats to almost normal value. A significant reduction in pyknotic nuclei, vacuolation, inflammatory infiltration cells in liver sections in the alloxan-injected rats treated with ginger. Also, reduction of the diffuse changes bring about loading of the Bowman's capsule space and adhesion of capillaries to the wall, hyalinized changes in kidney sections of the alloxan-injected rats treated with ginger. In addition, the ginger-treated diabetic sections were immunostained with Bax antibody which was more positive than diabetic group in both liver and kidney sections. The present study clearly indicates that the ginger can be effective in inhibiting hyperglycemia, and decreases the damage in liver and kidneys by enhancing insulin level. Consequently, the ginger can be used as improvement material for treatment of Diabetes mellitus and its toxicity.

KEY WORDS:

Diabetes Mellitus, Ginger, Liver, Kidney, Immunohistochemistry, Histopathology

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INTRODUCTION:

Diabetes mellitus is a major human illness implicated with numerous clinical manifestations. It is a clinical syndrome characterized by hyperglycemia due to absolute or relative deficiency of insulin. According to World Health Organization, the diabetes population is likely to increase to 300 million or more by the year 2025. Currently available therapies for diabetes include insulin and various oral antidiabetic agents such as sulfonylureas, biguanides, α-glucosidase inhibitors, and glinides, which are used as monotherapy or in combination to achieve better glycemic regulation. Many of these oral antidiabetic agents have a number of serious adverse effects. Thus, the management of diabetes without any side effects is still a challenge (Hamden *et al*., 2009).

Diabetes mellitus is a common health problem and a serious metabolic disorder associated with many functional and structural complications (Meyer *et al*., 2000). Clinical definitions of disease often obscure different mechanistic subtypes. This is particularly relevant for complex diseases such as diabetes, where combinations of multiple genes and environmental factors eventually lead to loss of functional β-cell mass and hyperglycemia. The mechanisms leading to β-cell loss may be quite diverse in the various subtypes of the disease. The two main forms of diabetes are type 1 and type 2 diabetes. Both types are characterized by progressive

β-cell failure. In type 1 diabetes, this is typically caused by an autoimmune assault against the β-cells, inducing progressive β-cell death. The pathogenesis of type 2 diabetes is more variable, comprising different degrees of β-cell failure relative to varying degrees of insulin resistance (Mordes *et al.*, 2004).

Alloxan's diabetogenic activity is primarily due to induction of oxygen free-radicals and subsequent damage to the pancreas (Halliwell and Gutteridge, 1985). Increased oxygen free-radical activity can initiate peroxidation of lipids, which in turn stimulates glycosylation of proteins, inactivation of enzymes and alterations in the structure and function of collagen, basement and other membranes. It also plays a role in the long term complications of diabetes (Boynes, 1991). Increased oxidant status in diabetes coexists with a reduction in antioxidant status (Collier *et al*., 1990) which can increase the deleterious effects of free radicals. Supplementation with non-toxic antioxidants may therefore have a chemoprotective role in diabetes (Logani and Davis, 1979). Many indigenous Indian medicinal plants have been used to manage diabetes (Anjali and Manoj, 1995) and some of them have been tested and the active principles isolated.

Before the discovery of insulin in the 1920s and the development of oral hypoglycaemic agents, diabetes mellitus was treated mainly by a combination of fasting, diet control and plant therapeutics (Bailey and Flatt, 1990). The efficacy of plants in diabetes required confirmation and, therefore, the World Health Organization, recommended assessment of traditional plant treatments for diabetes mellitus (WHO, 1980). Currently, several hundred plants have been reported to have beneficial effects in the treatment of diabetes (Srinvasan, 2005).

Ginger *(Zingiber officinale)* has been used in traditional oriental medicines for long time. Its extract and major pungent principles have been shown to exhibit a variety of biological activities (Wei *et al.,* 2005). It has been used to treat a number of medical conditions, including headache, cold and arthritis (Grant and Lutz, 2000). Ginger reduces symptoms in patients with nausea associated with pregnancy, motion sickness (kinetosis disease) and postoperative nausea and vomiting (Philips *et al.,* 1993). Ginger extract possesses anti-oxidative characteristics, since it can scavenge superoxide anions and hydroxyl radicals (Cao *et al.,* 1993). Gingerol from ginger inhibited, at high concentrations, ascorbate/ferrous complex induced lipid peroxidation in rat liver microsomes (Reddy and Lokesh 1992). Gingerol isolated from Zingiber was shown to inhibit platelet function due to inhibition of thromboxane formation (Guh *et al*., 1995), and ginger was also suggested to interfere with inflammation processes (Ozaki *et al*., 1991). Furthermore, ginger acts as a hypolipidemic agent in cholesterol-fed rabbits (Bhandari *et al*., 1998). Feeding rats ginger significantly elevated the activity of hepatic cholesterol-7α-hydroxylase, the rate-limiting enzyme in bile acids biosynthesis, thereby stimulating cholesterol conversion to bile acids, resulting in elimination of cholesterol from the body (Srinivasan and Sambaiah, 1991). In addition, a pure constituent from ginger [E-8 beta, 17 epoxylabd-12-ene-15, 16-dial (ZT)], was shown to inhibit cholesterol biosynthesis in homogenated rat liver (Tanabe *et al*., 1993).

The present study aimed to investigate the effects of standardized ginger extract on the alleviating certain biological parameters of diabetes mellitus induced by alloxan in rats.

MATERIAL AND METHODS:

Experimental animals

The Animal Care Ethics Committee of Fayoum University, Faculty of Science, Egypt, approved the study. Male Wistar rats (100-120 g) were obtained from the animal facility of the University. The rats were housed at 25^0C, with a 12-h dark/light cycle, and were fed standard rat chow and given free access to water. Eight animals were included in each group. Four groups were used: untreated control rats, ginger treated rats, diabetic rats, and ginger-treated diabetic rats.

Experimental design

Diabetes was induced by a single intraperitoneal injection of 150 mg/kg monohydrated alloxan (Sigma, St. Louis, MO, USA) dissolved in sterile 0.9% saline (Behr *et al*., 2008). Rats were made to fast prior to alloxan administration. The control rats were injected with the vehicle alone. Two days later, the development of diabetes was confirmed by measuring glucose levels in blood samples taken from the tail vein. Rats with blood glucose levels of 250 mg/dl or more were considered diabetic. The plasma glucose levels in the controls remained below this level along the duration of the study. Three days before the induction of diabetes, at 9.00 a.m., the diabetic *Z. officinale*-treated group was given the aqueous extract of *Z. officinale* at 400 mg/kg by oral gastric tube every day for 4 weeks after diabetes mellitus was confirmed (Olayaki *et al*., 2007).

Blood collection

At the end of the experimental period (4 weeks), the animals in all the four groups were fasted for 12 h. The rats were sacrificed by cervical dislocation, jugular vein was exposed and cut with a sterile scalpel, and the rats were bled into EDTA-

coated specimen bottles. Plasma was obtained from a portion of the blood sample by centrifugation at 3000 rpm for 5 min. All plasma samples were stored in the refrigerator at 4^0C before analysis for liver functions, kidney functions, uric acid and insulin (Evelson *et al*., 2005; Thompson, 2008). Blood glucose concentration was measured immediately by the glucose oxidase method (Yenson, 1986).

Hematologic analyses

All hematologic parameters were determined by an automated hematologic analyzer using whole blood sample.

Histopathological examinations

All tissue specimens were obtained from the same region of the right lobe of the liver and right kidney which were fixed in 10% buffered formalin, processed for embedding in paraffin wax by routine protocols and 5µm-thick sections were then cut by microtome. The sections were stained with haematoxylin/eosin using a routine protocol and examined using an Olympus BX50 photomicroscope. The pathological findings of examination using light microscopy were recorded.

Immunohistochemistry

The liver and kidneys tissues were immunohistochemical reactions according to the ABC technique described by Hsu *et al*. (1981). The procedure involved the following steps: (1) staining of formalin-fixed tissues requires boiling tissue sections in 1mM EDTA, pH 8. For 20 minutes; (2) after cooling, the sections were washed in distilled water for 10 min; (3) non-specific binding of antibodies was blocked by incubation with normal goat serum (DAKO) with 10% dilution; (4) All sections were subsequently incubated with the primary Bax antibody (apoptotic marker) with dilution 1: 100 (Lab Vision Corporation, USA) at room temperature for 30 min (5) the sections were washed in phosphate buffer saline (PBS); (6) These sections were then incubated for a further 30 min at room temperature with biotin-conjugated goat anti-rabbit IgG (1:100; Vector, Burlingame, CA, USA). (7) the sections were washed in PBS; (8) the sections were incubated with ABC complex (DAKO); (9) the sections were washed in PBS (10) The sites of Bax expression were visualized as cytoplasmic browncolor products with diaminobenzidine (DAB) reaction.; (11) the sections were washed in tap water for 10 min and then dehydrated; (12) the nuclei were stained with hematoxylin as counterstain. All dilutions and thorough washes between steps were performed using phosphate buffered saline unless otherwise specified. All steps were carried out at room temperature unless otherwise specified. As a negative control, primary antibody was replaced with PBS. The categories of the positive Bax stain as the following: +++ for strong (>50%), ++ for moderate (50%-25%) and + for weak (<25%).

Statistical analysis

The data were expressed as mean ± standard deviation (SD) and analyzed using (ANOVA) by SPSS 11 for window®.

RESULTS:

The blood glucose was increased significantly in treated alloxan-induced diabetic rats (group 3) as compared to normal rats ($p<0.05$). But in alloxan-induced diabetic rats which treated with *Z. officinal* extract, the significant decreased blood glucose levels ($p<0.0001$) was recorded. While no changes in blood glucose levels was observed in normal group.

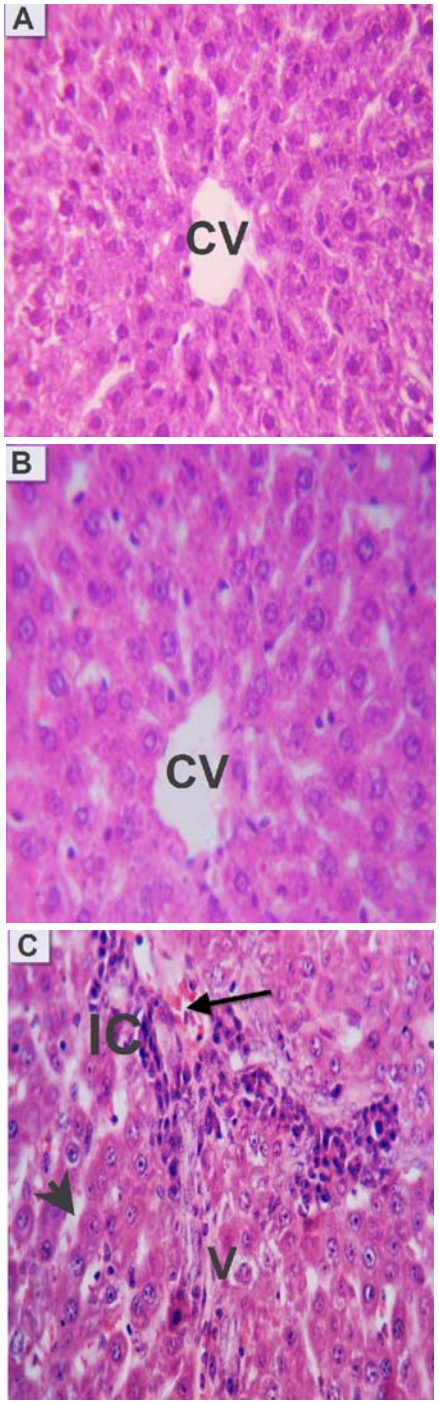
Table 1 indicates that treatment of diabetic rats with a single dose of alloxan (150 ml kg^{-1} body wt.) led to the development of severe hepatic injuries as compared to rats treated with ginger (400 mg/kg BW). As shown, marked increase in the concentrations of creatinine, BUN, uric acid AST and ALT (*P* value <0.05 for all) and decrease in insulin concentration, RBCs, WBCs, haemoglobin and platelets were evident in alloxan injected rats alone when compared with those treated with ginger and the control. Also, significant improvements were recorded in glucose, insulin, AST, ALT, BUN, HB, WBCs and platelets levels (*P* value $<10^{-6}$, 10^{-6}, 0.001, 10^{-6}, 0.001, 0.042, 10^{-6} and 0.002, respectively).

Table 1. The biochemical and haematological analyses of different rats groups

group parameter	Control group	Ginger group	Diabetic group	Diabetic and ginger group
Creatinin mg/dl	0.820± 0.0852	0.775± 0.0733	1.3450± 0.268*	0.9410± 0.075
BUN mg	15.893± 0.818	16.420± 1.086	25.67± 1.542*	17.72± 0.696*
Uric acid mg/dl	3.263± 0.249	3.340± 0.217	3.820± 0.052*	3.152± 0.345
Glucose mg/dl	104±11	110±12	310±23*	139±22*
Insulin pg/ml	32±1.62*	34±0.86*	12±0.98*	28±1.32*
AST Ul^{-1}	49±8.2	51±5.6	107±23.4*	72±10.3*
ALT Ul^{-1}	46±9.2	43±8.4	125±20.8*	79±11.3*
RBCs (10^6mm^{-3})	5.4±0.46	5.8±0.38	4.2±0.45*	5.13±0.71
HB%	13.9±0.6	14.30±0.6	12.7±0.4*	13.44±0.51*
WBCs (10^3mm^{-3})	6.8±0.64	7.1±0.89	4.1±0.49*	5.4±0.70*
Platele.(10^3mm^{-3})	289±65	274±46	185±19*	226±21*

The histopatholgical observations

The histopathology of the liver and kidney sections of control (intact) and control animals given ginger were showed the same (Figs. 1A & 1B). Excessive vacuolization and pyknotic nuclei in hepatocytes were observed in diabetic rats compared to the control groups. In addition, liver sections of this group revealed sinusoidal dilations and hyperemia (blood congestion) in sinusoids and central veins (Fig. 1C). In diabetic group receiving ginger an ordinary histological appearance was accompanied by minor vacuolization in some cells (Fig. 1D).



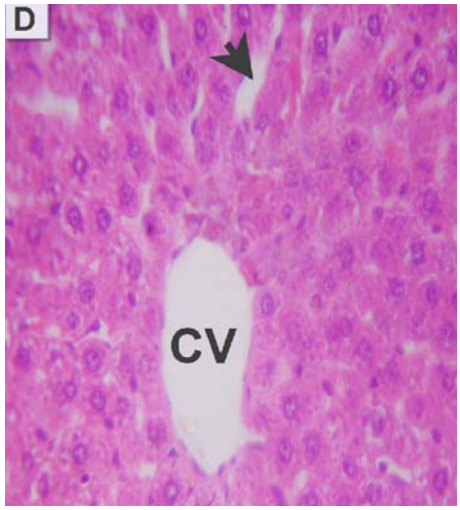
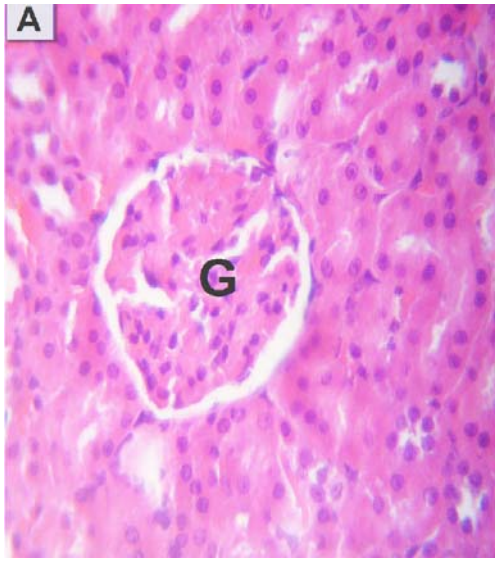


Fig. 1. Photomicrograph of liver sections stained with H & E (magnification × 250). A: Group I (vehicle) control rats. B: ginger-treated rats C: diabetic rats with shrunken nuclei, inflammatory cells (IC), congested central vein (Arrow), dilated blood sinusoid (arrowhead) and vacuolation (V). D: Group-IV (diabetic rats treated with *ginger extract)* with less changes and near the normal architecture.

Figure 2 shows the changes in kidney histology of the different groups. Figure 2A represents kidney section from healthy rats. As shown in figure 2B, mesengial matrix augmentation and glomerular proliferation had occurred in all cases of ginger-treated rats. In alloxan-induced diabetic's rats, the diffuse changes bring about loading of the Bowman's capsule space and adhesion of capillaries to the wall were recorded where the some glomeruli were seen to be associated with hyalinization. Tubules diffusely showed cellular inflammation whereas vascular degeneration changes were seen mostly in distal areas (Fig. 2C). The alloxan-induced diabetic rats treated with ginger had mesengial matrix augmentation, glomerular proliferation and hyalinization were markedly attenuated in all cases (Fig. 2D).



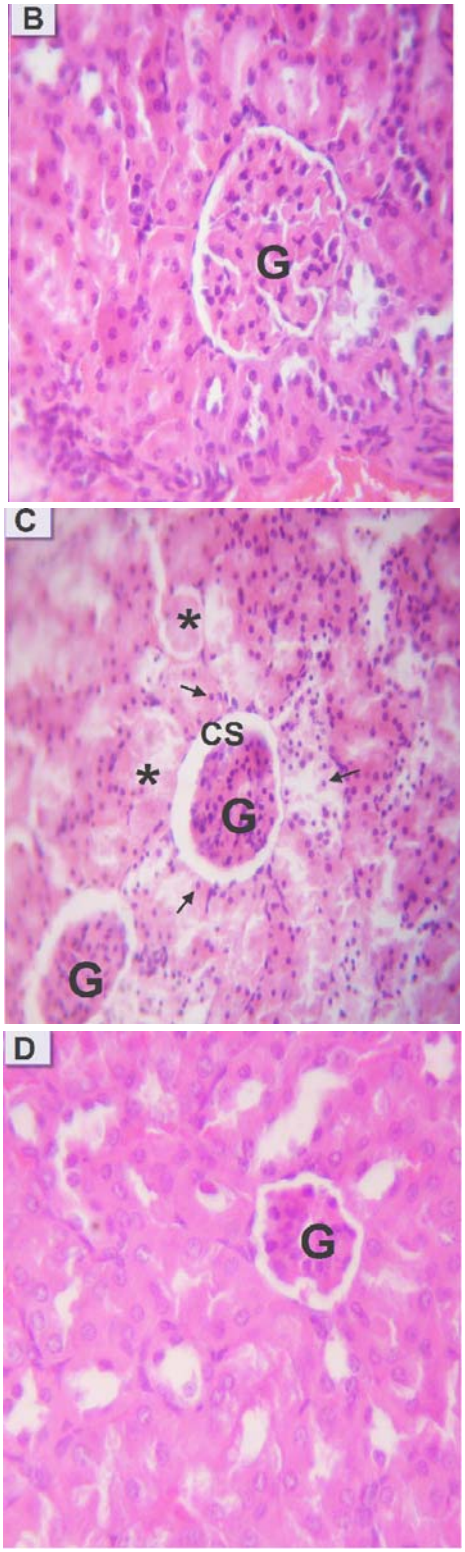
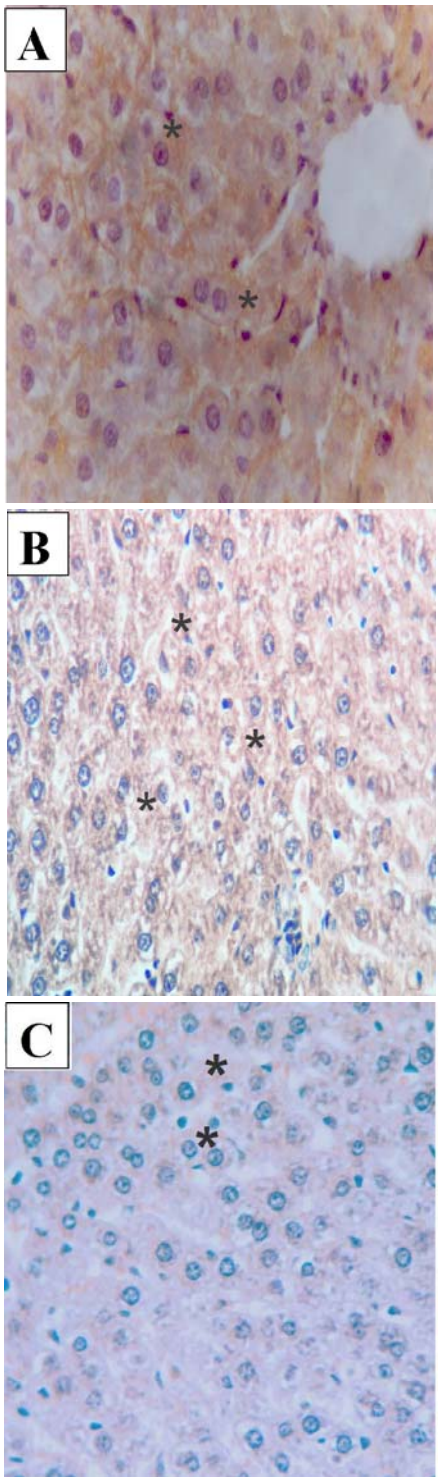


Fig. 2. Photomicrograph of liver sections stained with H & E (magnification × 250). A: Renal histology of control rats. B: Ginger treated rats showing normal glomerular (G) and tubular structures. C: Diabetic rats group demonstrating glomerular atrophy, haylization (*), pyknotic nuclei (arrows) and severe degeneration of the renal tubules. D: Diabetic treated with ginger rats showing well-preserved glomerulus and tubules.

Bax immunostaining expression

The Bax immunostaining expression was strong (over 50% stained cells) cytoplasmic stain observation in liver sections of control and ginger groups (Figs 3A & 3B) but moderate (25%-50%stained cells) stain in diabetic rats treated with ginger (Fig. 3C), but cytoplasmic Bax staining in diabetic liver sections were very weak; <25% stained cells (Fig.3D).



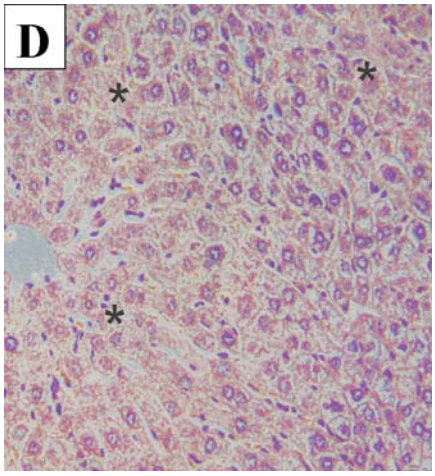
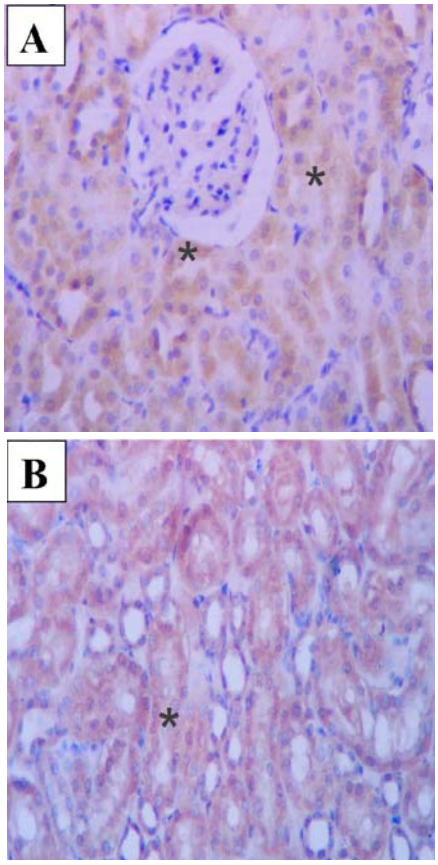


Fig. 3. Photomicrograph of liver sections from different groups show the BAX expression, cytoplasmic brown color stain (*). A: Control rats, B: Ginger treated group, C: Alloxan-induced diabetics group, D: Alloxan-induced diabetics treated with ginger. Immunoperoxidase, original magnification X 400.

The same results were shown in different renal sections in different rats groups, where in epithelial renal tubules of untreated (control) and ginger-treated groups were over-expression of Bax immunostaing (Figs 4A & 4B), but in diabetic kidney section, the Bax was weak positive stain (Fig. 4C), whereas, the diabetic-ginger treated group was moderate cytoplasmic brown stain for Bax (Fig. 4D).



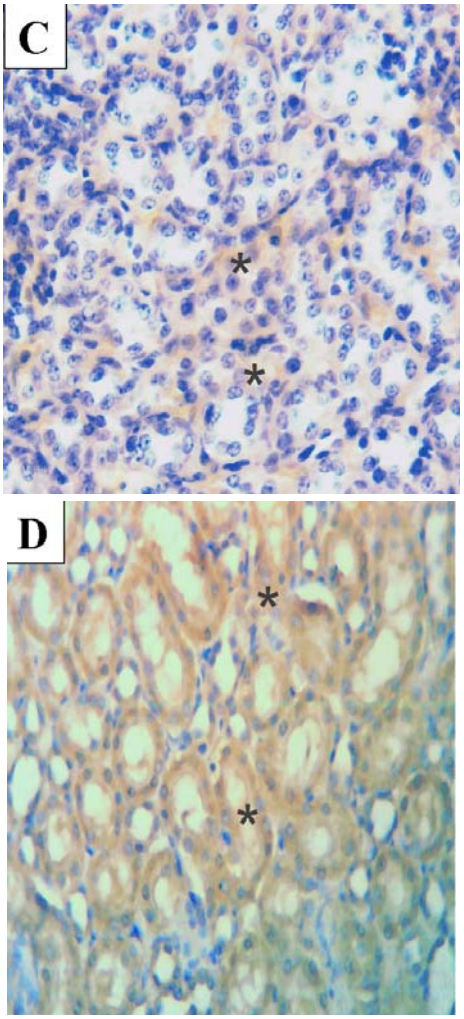


Fig. 4. Photomicrograph of Kidney sections from different groups show the BAX expression, cytoplasmic brown color stain (*). A: Control rats, B: Ginger treated group, C: Alloxan-induced diabetics group, D: Alloxan-induced diabetics treated with ginger. Immunoperoxidase, original magnification X 400.

DISCUSSION:

Diabetes mellitus is a chronic disorder caused by partial or complete insulin deficiency which produces inadequate blood glucose control and leads to acute and chronic complications (White and Baxter, 1994). Overt symptoms of diabetes mellitus include hyperglycaemia, increased water intake and polyuria (White and Baxter, 1994). Chronic complications can involve the kidneys (nephropathy), eyes, nervous system and cardiovascular system (Koda-Kimble and Carlisle, 1995). In fact, diabetes is the number one cause of chronic kidney diseases in the USA (Chua and Bakris, 2004)

The present study aimed to assess the hypoglycemic activity of some different mechanisms of action to reduce blood glucose levels with the help of plant extracts. From the present results it is assumed that the *Z.*

officinal extract could be responsible for stimulation of insulin release and the observed restoration of metabolic activities. A number of other plants have also been shown to exert hypoglycemic activity through stimulation of insulin release (Meenakshi *et al*., 2009). Diabetes was induced in experimental rats by alloxan which is known to destroy β-cells of the pancreas and inhibit insulin production (Kamanyi *et al*., 1994). It has been confirmed by observing increase levels of glucose (289-298 mg/dl) in diabetic controls rats.

Liver cell destruction shows itself as impairment in the permeability of aspartate and alanine aminotransferase (AST & ALT, respectively), which are marker enzymes of the liver. Measurement of enzymatic activities of aminotransferase (AST and ALT) and ALP is of clinical and toxicological importance, as changes in their activities are indicative of tissue damage by toxicants or in disease conditions (Singh *et al*., 2001). In the present study, it was found that there was an increase in the serum AST and ALT activities of the diabetic group. The decrease in these enzyme levels in alloxan-diabetic rats which were administered ginger show that it ameliorates liver damage. These findings are also supported by histological findings. Also, the kidney function parameters (Creatinine, blood urea nitrogen & uric acid) were increased in diabetic group only but in control, ginger and diabetic rats treated with ginger were decreased, where the relation between group 3 (diabetic rats treated with ginger) and other control group was significant (P<0.05). Recent studies have introduced serum uric acid (UA) as a potential risk factor for developing diabetes, hypertension, stroke, and cardiovascular diseases. The value of elevated levels of UA in serum as a risk factor for diabetes development is still under scrutiny. Recent data suggest that clearance of UA is being reduced with increase in insulin resistance and UA as a marker of prediabetes period (Causevic *et al*., 2010). In the gingerol-treated cells, insulin-sensitive glucose uptake was increased. It is expected that ginger enhances the insulin-sensitivity, and improves chronic disease, such as diabetes (Sekiya *et al*., 2004). So, the production of insulin was improved in diabetic group treated with ginger.

Diabetes mellitus comprises a group of chronic metabolic disorders characterized by hyperglycemia due to abnormal insulin secretion or insulin receptor or post-receptor event affecting metabolism involving carbohydrates, proteins and fats in addition to damaging liver, kidney and β-cells of pancreas (Robertson, 2004). The functions of liver and kidney may also be affected by the changes in the levels of insulin. It is known that structural changes occur in the liver as a result of the absence of insulin in diabetes (Koyuturk *et al*., 2005). Excessive shrunken nuclei, inflammatory cells, congested central vein, dilated blood sinusoid and vacuolation are accepted as an indicator of hepatotoxic effect. So, these investigations are important findings indicating that hepatocytes are either dying or heading for necrosis. Hyperemia in sinusoids and central veins show that the liver is having difficulty in its function and is toxically damaged.

Bax is a pro-apoptotic member of the Bcl-2 family that resides in the cytosol. Together with other pro-apoptotic family members, Bax promotes apoptosis by forming homodimeric and heterodimeric complexes that result in the formation of channels or pores on the mitochondrial membrane to facilitate the release of cytochrome c and apoptosis-inducing factors (AIFs) from mitochondrial intermembrane spaces into the cytosol. The formation of these pores results in the loss of the selective ion permeability across the mitochondrial membrane. The intracisternal contents that are released into the cytosol triggers a cascade of events that culminate in the execution of apoptosis through activation of caspases (Israels and Israels, 1999). In the present study, the expression of Bax was observed in control, ginger and diabetic rats treated ginger groups in the liver and the kidney sections, where the Bax regulates the apoptosis and plays an important role in the development of multi-cellular organisms and in the regulation and maintenance of the populations in tissues under physiological and pathological conditions (Leist and Jaattela, 2001).

Apoptotic cells are characterised by a number of morphological features such as cell shrinkage, membrane blebbing, chromatin condensation and the formation of apoptotic bodies (Orrenius, 2004). Some of the morphological changes associated with apoptosis occur as a result of the activation of endogenous endonucleolytic and proteolytic (caspases) enzymes which usually determine the integrity and shape of the cytoplasm and organelles (Kasibhatla and Tseng, 2003). Furthermore, apoptosis is regulated and executed by different interplay of many genes responsive to various stimuli (Huang and Cidlowski, 2002). Endogenously produced antioxidants are the body's chief mechanism for combating the destructive nature of free radicals; nonetheless, the level of these free radical scavengers could be supplemented by the intake of foods rich with ginger. There is conclusive evidence that the ginger possess numerous ameliorating actions including induction of hypoglycemia (Al-Amin *et al*. 2006). It is highly probable that the reported corrective potentials of the ginger could also be due to their high contents of antioxidants as well as increasing antioxidants concentrations upon administration in vivo. This enhanced bioavailability of antioxidants

brought about by garlic and ginger could be crucial in alleviating oxidative/nitrosative injury of tissues (Anwar and Meki, 2003). Since ginger can amend pathological changes, it is highly probable that they can protect against structural changes that develop in diseased conditions. More specifically, ginger might reduce the occurrence and/or progression of structural nephropathies and, therefore, delay the onset of renal failure and ultimately the end-stage of the disease in diabetes. In the present study, the Bax expression may be eliminate cells in response to a variety of stimuli and provides protection against diabetes, inflammation as well as maintenance of homeostasis in liver and kidney tissues in control, ginger and diabetic rats treated with ginger groups. In groups 3 in both liver and kidney sections, tissue remodelling after injury is dependent on balance between cellular apoptosis and proliferation. Also, the efficient deletion by apoptosis of excessive, damaged or non-functioning hepatic and renal diabetic and infiltrating inflammatory cells is beneficial. Bax in itself does not cause cell death (apoptosis), but its elevated expression favors an entry into the apoptotic program following death signal by countering *Bcl-2* and other anti-apoptotic genes expression due to the pro-apoptotic members of *Bcl-2* such as *Bax* were activated.

CONCLUSION:

The present study demonstrates that ginger extract exerts significant protective effects against alloxan-induced diabetes mellitus by augmenting host antioxidant defense mechanisms. Thus, ginger is a promising agent for the prevention of chemicals-induced diabetes mellitus toxicity and cell damage in liver and kidneys by enhancing insulin level and sensitivity and anti-oxidant capacity.

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تأثيرات الزنجبيل الهستولوجية والهستوكيمياء مناعية على الكبد والكُلى وبعض معايير الدم فى الجرذان المستحدث بها مرض السكرى بالألوكسان

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في هذه الدراسة ، تم استخدام المستخلص المائى للزنجبيل كمنتج طبيعى لعلاج مرض السكرى وعلاج تأثيراته الضارة على الكبد والكُلى ، حيث تم تقسيم الجرذان إلى أربع مجموعات، الأولى هى المجموعة الضابطة والثانية تم تغذيتها طبيعيا وإعطائها الزنجبيل (400مجم/كجم) عن طريق الفم يوميا والمجموعة الثالثة تم حقنها فى التجويف البريتونى بالألوكسان (150مجم/كجم) محدثا مرض السكرى بعد 72 ساعة من الحقن بالألوكسان بينما المجموعة الرابعة تم حقنها كما سبق فى المجموعة الثالثة ثم تم علاجها بالزنجبيل (400مجم/كجم). تم ذبح الجرذان فى نهاية الأسبوع الرابع وأُخِذ الدم لعمل تحليل وظائف الكبد والكُلى وصورة الدم ونسبة هرمون الإنسولين. كما أُخِذ عينات من نسيج الكبد والكُلى للتشخيص النسيجى وكيمياء الأنسجة المناعية. وقد وُجِد أن المجموعة الثالثة أظهرت فرط سكر الدم والذى ترافق مع زيادة في Creatinine ، وحمض اليوريك ، اليوريا ، AST ، ALT ومن ناحية أخرى وُجِد نقص في هرمون الإنسولين ، وتركيز الهيموجلوبين ، الكريات الحمراء ، وخلايا الدم البيضاء والصفائح الدموية على عكس المجموعات الضابطة. بينما لوحظ فى المجموعة الرابعة أن الزنجبيل فعال بشكل ملحوظ في خفض السكر في الدم ، وعادت معايير الدم الأخرى السابقة لمستوياتها الطبيعية. على المستوى النسيجى، أسفر استخدام الزنجبيل عن حدوث انخفاض كبير في تكون الفجوات ، قلل من تدهور انوية الخلايا ، كما أدى إلى قلة تواجد الخلايا الإلتهابية فى نسيج الكبد. بينما فى نسيج الكُلية ،فقد أدى استخدام مستخلص الزنجبيل إلى قلة التصاق الشعيرات الدموية بجدار محفظة بومان وتقليل تدهور الأنوية بالإضافة إلى تحسن عملية التشمع التى حدثت بفعل مرض السكرى. وعلى مستوى كيمياء الأنسجة المناعية فقد وُجد ان تعبير البروتين Bax كان أكثر ايجابية فى المجموعات الأولى، الثانية، والرابعة بينما فى المجموعة المستحدث بها مرض السكرى كان تعبير البروتين ضعيف مما يدل على أن عملية موت الخلايا المبرمج (Apoptosis) كانت أقل ما يكون في تلك المجموعة بل على العكس ظهر تدهور وتحلل لأنوية الخلايا فى هذه المجموعة , كما أن نقصان هرمون الإنسولين يقلل من وجود Bax سواء كان فى نسيج الكبد أو الكُلى. تشير هذه الدراسة بوضوح إلى أن الزنجبيل يمكن أن يكون فعال في تثبيط ارتفاع السكر في الدم ،وعملية الاكسدة وتلف الخلايا والتى ممكن حدوثها في البنكرياس والكبد والكليتين من خلال تعزيز مستوى الإنسولين والحساسية والقدرة المضادة للأكسدة ، وبالتالي الحد من أضرار مرض السكري.

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