

# Effect of Ginseng Extract Supplementation on Renal Functions in Diabetic Rats

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## Abstract

As incidence of diabetes is increasing worldwide, besides it is associated with complications, the present study aimed to investigate the effect of a traditional botanical, ginseng on diabetes induced alterations in kidney functions. Thirty male rats were used in the study by randomly allocating them into three groups, each of ten rats, namely the control group, diabetes group (D), and diabetes+ ginseng group (DG). The latter two groups were rendered diabetic by I/P injection of streptozotocin (50 mg/kg). Daily ginseng extract was administered orally (100 mg/kg BW), one week post streptozotocin (STZ) injection. Ninety days post STZ injection; rats were sacrificed, where serum and kidneys were obtained for determination of metabolic profile, serum electrolytes, kidney function tests, renal tissue enzymes, and renal antioxidant status, together with histopathology. The obtained results revealed a modest improvement in metabolic profile due to ginseng extract administration. However, the kidney functions were greatly improved as evidenced by amelioration of urea nitrogen, creatinine, total protein concentrations and serum electrolytes. Also an increase was noted in renal tissue enzymes and antioxidants with a decrease in malondialdehyde and renal pathology. In conclusion, ginseng extract may be of supportive treatment to combat diabetes complications.

**Keywords:** Antioxidants, Diabetes, Electrolytes, Ginseng extract, Kidney, Metabolic profile

## 1. Introduction

Diabetes is a chronic disorder that arises from either, defects in peripheral insulin action and/or insulin secretion resulting in hyperglycemia (Ferrannini, 1998). Abnormally elevated blood glucose level causes oxidative stress and the formation of advanced glycation end products which result in diabetic complications (Baynes, 1991; and Ahmed, 2005). Among the complications, nephropathy seems to be prevalent (Selby et al., 1990 and; Held et al., 1991). Clinical trials suggest that there is no effective treatment for diabetic nephropathy, thus efforts are focusing on traditional herbal medicine to find a novel therapeutic agents for treatment of diabetic nephropathy (Kang et al., 2006).

Ginseng has a long history of medicinal use in the oriental regions as a tonic to promote health (Han et al., 2006). Extensive reports point to ginseng as having many physiological and/or pharmacological effects on immune, cardiovascular, central nervous systems and endocrine glands (Nah et al., 1995; and Attele et al., 1999). Besides, ginseng also possesses anti aging, anti stress and anti tumor properties (Kaneko and Nakanishi, 2004). In addition, several researches give evidences that ginseng possesses anti diabetic properties through lowering blood glucose effect (Sotaniemi et al., 1995; and Ohnishi et al., 1996) and stimulating sugar metabolism (Xie et al., 2005).

Thus the present study aimed to evaluate the possible beneficial effect of ginseng on diabetic nephropathy, and to clarify whether this beneficial effect is related to metabolic pool adjustment or renal antioxidant status in diabetic rats.

## 2. Materials and Methods

Thirty male Sprague-Dawley rats, weighing 150-200 g were used in this study. Rats were obtained from the National Research Center, Giza, Egypt, and housed in plastic cages with saw dust bedding, where food and water were provided *ad-libitum*. Rats were maintained on 12:12 hour light-dark cycle. After one week of adaptation, rats were allocated into three equal groups of 10 rats each. First group served as normal control and was injected intraperitoneally with 0.2 ml of 0.05 M citrate buffer, pH 4.5, while the second and third groups were rendered

diabetic by intraperitoneal injection of streptozotocin (STZ) 50 mg/kg dissolved in 0.05 M citrate buffer, pH 4.5 (Stephen Morris et al., 1996). One week post STZ injection, blood samples were collected by orbital sinus technique for determination of blood glucose concentrations, thus confirming induction of diabetes. Diabetic rats were then divided into diabetic control group (DC) and diabetic group supplemented with standardized Korean panax ginseng extract C.A. Mayer (GGE)\*. Ginseng extract was supplied at a rate of 100mg/Kg body weight, dissolved in 100 ml of distilled water and administered by stomach tube (Kang et al., 2006). Ginseng supplementation started one week post STZ injection and lasted for 90 days.

### 2.1 Sampling

**Blood:** Ninety days post STZ injection rats were anaesthetized by deep ether inhalation, sacrificed by decapitation, where trunk blood were obtained and sera were separated and kept at -20 C<sup>0</sup> till assays were carried out.

#### 2.1.1 Serum biochemical analysis

##### 2.1.1.1 Metabolic profile

The parameters were analyzed by spectrophotometry including serum glucose (Trinder, 1969), triglycerides (Wahlefeld, 1974), total cholesterol (Allian, 1974) and high density lipoprotein (Finley et al., 1978). The kits used for determination of the metabolic profile were obtained from Stanbio laboratory U.S.A. INC. Low density lipoproteins (LDL) was calculated according to Friedewald et al. (1972).

##### 2.1.1.2 Kidney function tests

The parameters determined were blood urea nitrogen (Fawcett and Scott, 1960), uric acid (Rebar et al., 1978), creatinine (Houot, 1985), and total protein (Henry, 1964). The kits used were obtained from QuimicaClinicaApplicada, Spain, bioMerieux laboratory, France, and Bio-Analytics, Palm City, USA.

##### 2.1.1.3 Electrolytes concentrations

Serum sodium and potassium concentrations were assayed using flame photometer according to the method of Varely (1976). Serum total calcium and magnesium were determined spectrophotometrically according to the methods of (Ratliff and Hall, 1973) and (Gindler and Heth, 1971) respectively.

**Kidney:** Immediately, post decapitation and trunk blood collection, kidneys were removed, washed with ice cold saline and their wet weight were obtained using analytical balance (Sartorius 1702) for determination of their relative weights. One kidney was fixed in 10% formol-saline for histopathological examination according to the method of George (1981), while the other kidney was kept in liquid nitrogen (-196 C<sup>0</sup>) for determination of activities of renal tissue enzymes and antioxidant status.

#### 2.1.2 Renal tissue tests

2.1.2.1 Renal tissue protein concentration was determined according to the procedure adopted by Lowery et al. (1951).

##### 2.1.2.2 Renal tissue enzymes

Activities of renal alkaline phosphatase (ALP) and  $\gamma$  glutamyltransferase ( $\gamma$  GT) were determined in renal homogenate (Loeby and Quimby, 1989) according to the method of Teitz (1970) and Szasz (1969) respectively.

##### 2.1.2.3 Renal antioxidant status

This was accomplished by measuring malondialdehyde, as one of the main end products of lipid peroxidation (Yoshioka et al., 1979), superoxide dismutase (Jewett and Rocklin, 1993) and glutathione S-transferase (Habig et al., 1974) activities.

### 2.2 Statistical analysis

Data are presented as means  $\pm$ S.E., and analyzed by one way ANOVA according to the method of Snedecor and Cochran (1980). Groups were compared by the least significant difference test (LSD) at the 5% level of probability.

## 3. Results

### 3.1 Serum biochemical analysis

#### 3.1.1 Metabolic profile

Data presented in table (1) clarifies that serum glucose concentration of the DC group was elevated significantly compared to both, the diabetic group supplemented with ginseng (DG) and the control group. Moreover, the

control group had the lowest values compared to either the DC or DG groups. Similarly, the same table shows that the total cholesterol concentration was raised in the DC compared to the DG, and the control group. Concentration of the above mentioned parameter in the control group was significantly lower when compared to the DG. Additionally, the DG showed a significantly higher concentration of triglycerides when compared to the control group, and a significantly lower concentration compared to the DC. Concerning the HDL and LDL concentrations, data shown in the same table demonstrated a decrease in HDL and an increase in LDL concentrations in DC compared to the control and DG groups. However, these parameters showed on the contrary an increase in HDL and a decrease in LDL in DG group compared to DC group, but the values remained significantly different than those of the control group.

### 3.1.2 Kidney function tests

It is obvious from the results shown in table (2) that blood urea nitrogen, creatinine, and uric acid concentrations were elevated in the DC compared to the recorded control values, while the recorded concentrations were lower in the DG compared to DC. As for total protein, diabetes resulted in significant decrease in concentration compared to both DG and control groups.

### 3.1.3 Serum electrolytes concentrations

It is clear from the data presented in table (3) that apart from potassium (K), the concentrations of all measured electrolytes were significantly low in the DC compared to either the control or DG groups. On the other hand, concentrations of the electrolytes in DG and control groups did not differ significantly.

Data shown in table (4) showed that, highest kidney relative weights were recorded in the DC, while DG showed significantly lower relative weights compared to the DC.

## 3.2 Renal tissue tests

### 3.2.1 Renal tissue enzymes

Results illustrated in table (5) revealed that enzyme activities of ALP and  $\gamma$  glutamyl transaminase ( $\gamma$  GT) were lowered in DC group, while there were no significant differences between activities of the former enzymes between the control and DG groups.

### 3.2.2 Renal antioxidant status

The presented results shown in table (6) showed that enzymes activities of superoxide dismutase (SOD) and glutathione S-transferase (GST) were reduced, while malondialdehyde (MDA) concentration were increased in the DC compared to either the DG or the control groups. Values of the above mentioned parameters did not differ significantly between the control and DG groups.

### 3.2.3 Histopathological findings

Kidneys of the DC group suffered from severe pathological changes represented by diffuse thickening of most of the Bowman's capsule with fibrous connective tissues (Fig1), moreover, many glomeruli of the DC showed either diffuse glomerular sclerosis (Fig2) or glomerular atrophy and accumulation of proteinous material in Bowman's space (Fig3). Similarly hyaline cast was present in the lumen of proximal convoluted tubules, additionally, some epithelial cells showed coagulative necrosis in which the cytoplasm appeared deeply eosinophilic with complete disappearance of nucleus or appearance of nucleus as a ghost (Fig4). Kidneys of the DG showed normal glomerular tufts with slight hypercellularity (Fig5).

## 4. Discussion

Diabetes mellitus is a disorder characterized by hyperglycemia which causes considerable long term complications of diabetes. The present investigation showed that ginseng extract (GE) resulted in reduction of the elevated blood glucose concentration in diabetic rats, an effect that was attributed in former studies to ginseng enhancement of glucose uptake through stimulating translocation of glucose transporter GLUT4, inhibition of intracellular inflammatory molecules as Jun N-terminal kinase (JNK) which causes serine phosphorylation to insulin receptor substrate and consequently leads to interruption of signal transduction from insulin receptor to downstream molecules and insulin resistance (Ye, 2007; and Zhang et al., 2008), and activation of peroxisome proliferator activated receptor  $\gamma$  which improves insulin resistance, promotes adipocyte differentiation and induces apoptosis in large adipocytes (Han et al., 2006). Additionally, other investigators recorded a definite insulinogenic properties of ginseng (Davydov et al., 1990) or direct and indirect stimulatory on  $\beta$  cell secretion of insulin (Waki et al., 1982; and Lee et al., 2006). The results obtained in the present investigation concerning blood glucose concentration are in agreement with those of Sotaniemi (1995),

Sievenpiper et al. (2006) Vuksan et al. (2008), who reported that ginseng reduced fasting blood glucose concentrations, HbA1C, glucose induced insulin release and improved insulin sensitivity in diabetic patients.

Concerning lipid profile, the present investigation showed that ginseng lowered total cholesterol, triglycerides and LDL. This effect seems to be favorable since diabetes resulted in elevated lipid profile and decrease in HDL cholesterol resulting in rapid progression of macroangiopathy leading to increased incidence of hypertension and cardiovascular disease (Steiner, 2000). The decrement induced by GE is a function of multiple integrated mechanisms including binding to PPAR $\alpha$  which increases  $\beta$  oxidation of fatty acids and consequently reduces lipid accumulation (Michalik et al., 2006), inhibition of pancreatic lipase activity there by reducing lipid digestion (Karu et al., 2007), inhibition of neuropeptide Y expression in hypothalamus (Kim et al., 2005) which is involved in stimulation of food intake, and inhibition of activity of some key enzymes involved in cholesterol and triglyceride synthesis as  $\beta$  methyl glutryl-CoA reductase and cholesterol 7  $\alpha$  hydroxylase (Qureshi et al., 1983). The obtained results coincide with those of Yamamoto et al. (1983), Kim and Park (2003), and Cho et al. (2006) who showed that ginseng reduced total cholesterol, triglycerides, LDL, but increased HDL, however the study contradicts those of Yoon et al. (2003) who showed that ginseng elevated lipid profile through inhibition of PPAR $\alpha$  functions and Banz et al. (2007) who showed that ginseng extract did not affect triglycerides concentration in diabetic rats.

The current investigation revealed that induction of diabetes resulted in elevation of serum urea, uric acid and creatinine concentrations. These parameters are considered a significant markers of renal dysfunction (Almdal and Vilstrup, 1988; Prakasam et al., 2004; and Fekete et al., 2008). Ginseng extract administration resulted in decrement of these parameters, a finding that was in agreement with that of Badr El-Din (1997) and Kang et al. (2008) who reported ameliorated renal dysfunction of diabetic rats by the ginseng extract or 20(S)-ginsenoside Rg3 administrations. Associated with progress of diabetes, a state of decreased total protein concentration is evidenced, which may have resulted from either hyperfiltration induced diabetic nephropathy and/or increased protein catabolism (Mauer, 1981; and Prakasam et al., 2004). Similarly, GE ameliorated this decrease in serum protein concentration, an effect that was previously reported in many studies due to administration of different herbal products in diabetic rats (Mansour and Newairy, 2000; and Prakasam et al., 2004). The protein depletion ameliorating activity of ginseng extract is less likely to be associated with a correction in metabolic parameters, since GE effect appears to be only modest concerning correction of metabolic deficit induced by diabetes (glucose, total cholesterol, and triglycerides concentrations). Hence, it is more likely that GE ameliorated the diabetic nephropathy, thus limited urinary protein excretion. This result goes hand in hand with those of Kang et al. (2006) and Kim et al. (2007) who reported that ginseng decreased urinary protein levels in diabetic rats.

In the present investigation, diabetes was associated with electrolyte imbalance, where a decrease in serum Na, Ca, and Mg, with increased serum K were recorded. This may be attributed to the state of hyperglycemia that produces an osmotic diuresis that causes marked urinary losses of water and electrolytes, a condition that may be aggravated by urinary excretion of ketones which obligates additional electrolyte loss (Oh et al., 2007). Concerning sodium, additionally, there is translocation of Na<sup>+</sup>,K<sup>+</sup>-ATPase pumps from the basolateral membrane of proximal convoluted tubules to the cytosol which leads to a decrease in sodium pumping from renal tubules to the blood (Fekete et al., 2008). Also, expression of sodium channel proteins in the collecting ducts and distal convoluted tubules was altered leading to increased fractional excretion of sodium in urine (Oh et al., 2007). Similarly, serum magnesium was shown to be decreased in previous studies (Nasri, 2006; and Sharma et al., 2007). This decrement was attributed to glycosuria-related hypermagnesuria, nutritional factors or hyperinsulinaemia (Maltezos et al., 2004). As for serum calcium previous researches showed lower concentration in diabetes which was associated with a decrease in boneminer content and increased urinary excretion of calcium and phosphate (Fogh-Andersen et al., 1982; and McBain et al., 1988). The decrease was a result of several factors and in particular to glycosuria, but a whole range of metabolic changes including chronic acidosis, insulin deficiency, impaired parathormone action, and changed vitamin D metabolism could be implicated (Hough and Avioli, 1984). On the contrary, the rise in serum potassium, is evidenced because of the extracellular migration in response to acidosis, however, potassium is also lost in large quantities in urine (Sjöquist et al., 1998). Ginseng extract, in the present investigation, resulted in correction of such electrolyte imbalance. This correction may have resulted from either a decrease in urine volume induced by ginseng administration which resulted in improvement of the metabolic abnormalities (Kang et al., 2006). However, since the reported amelioration in the metabolic deficits appears to be only modest, one would expect a rather direct effect of ginseng on renal tissues.

As for renal tissue enzymes, the present investigation assayed the activities of renal ALP and  $\gamma$ GT in renal tissues instead of assaying them in urine, despite the fact that many studies have demonstrated that excreted

urinary enzymes are useful biomarkers for evaluation and diagnosis of tubular dysfunction or injury and that tubular damage most likely precedes glomerular damage in diabetic nephropathy so urinary enzyme excretion can be used as an early predictor of tubular dysfunction (Jung et al., 1988; D'Amico and Bazzi, 2003; and Uslu et al., 2005). This modification was done to overcome some difficulties in assaying urinary enzymes activities, as urinary enzyme inhibitors (Horpacsy, 1988) and altered pH due to diabetic ketoacidosis (Turecky and Uhlikova, 2003). ALP, and  $\gamma$ GT are located in the brush-border membrane of the nephron (Turecky and Uhlikova, 2003). When the tubular cells are damaged, they release these enzymes into ultrafiltrate and thus the enzyme activities in urine increase (Yaqoob et al., 1994). The current study demonstrated decreased enzymatic activities of ALP and  $\gamma$ GT in renal tissues of the diabetic group reflecting tubular dysfunction, a finding that was further documented by histopathology, where hyaline cast was present in the lumen of tubules together with coagulative necrosis of the cells. The reported tubular pathological finding corroborates those of Magil (1995) and Morrison et al. (2005) who recorded a similar pathological finding in tubular damage induced by obesity in rats. Ginseng extract group exhibited near to normal histological picture, a result which was confirmed by higher renal tissue ALP and GT activities. This finding, correlated with the finding of increased serum electrolytes concentration in particular sodium and calcium ions in the DG group.

Concerning the renal antioxidant status, the current study revealed increased oxidative stress due to diabetes which was evidenced by increased tissue concentration of malondaldehyde and depletion of antioxidant enzymes concentration. This was accompanied by significant glomerular pathology, namely glomerular sclerosis or glomerular atrophy and accumulation of proteinous material in Bowman's space together with thickening of Bowman's capsule membrane. The reported oxidative stress resulted from hyperglycemia-induced increases in glucose autooxidation, protein glycation and the subsequent oxidative degradation of glycated protein leading to enhanced production of reactive oxygen species (Kakkar et al., 1997).

Oxidative stress may be both, the cause and the result of tissue damage, a primary and a secondary source of diabetic pathology (Baynes and Thorpe, 1996). The recorded rise in tissue concentration of malondaldehyde, an index of endogenous lipid peroxidation, has been also reported by Turk et al. (2002) in diabetic patients and Kim et al. (2008) in diabetic rats reflecting increased state of oxidative stress. Both oxidative stress and advanced glycation end products result in Nuclear factor-kappa (NF- $\kappa$ ) activation which is normally present in the cytoplasm of eukaryotic cells as an inactive complex with the inhibitor binding protein  $\kappa$ B (Kang et al., 2006). When cells are exposed to various external stimuli, such as reactive oxygen species or advanced glycation end products, inhibitor binding protein  $\kappa$ B undergoes rapid phosphorylation with subsequent ubiquitination, leading to the proteasome mediated degradation of this inhibitor (Ahmed, 2005). Nuclear factor-kappa translocates to the nucleus, where it binds to enhancer regions of target genes, specially cyclooxygenase-2 (COX-2), inducible nitric oxide synthase (iNOS) genes, thereby altering their expression (Surh et al., 2001). Cyclooxygenase-2 and inducible nitric oxide synthase expression was found to be increased in kidney of STZ-induced diabetic rats where they were involved in pathogenesis of nephropathy (Diabetes control and complications trial research Group, 1993). Cyclooxygenase-2 increased the conversion of arachidonate to prostaglandin E<sub>2</sub>, prostaglandin F<sub>2 $\alpha$</sub> , prostaglandin D<sub>2</sub>, and thromboxane B<sub>2</sub> in glomeruli of diabetic rats thereby implicated in the alterations in renal hemodynamics in diabetes (Komers et al., 2001). Although nitric oxide is a simple inorganic radical exhibiting diverse physiological functions, including the regulation of neurotransmission and vascular tone yet it could react with superoxide yielding peroxynitrite which is a potent nitrating and oxidizing agent that can nitrate and oxidize various biomolecules, such as thiols, lipids, carbohydrates, and nucleic acids (Jarašūnienė and Šimaitis, 2003; Kasina et al., 2005; and Marcondes, 2006).

The present investigation demonstrated efficacy of ginseng extract in reversing deleterious effect of diabetic oxidative stress, which was documented by amelioration recorded in kidney function tests electrolyte concentrations and histopathology. This ameliorative effect of ginseng may be attributed to either its ability to bind to glucocorticoid receptor triggering transcriptional activation of glucocorticoid response elements promoting cell proliferation and enhances the survival rate of new-born cells (Lee et al., 1997; Shen and Zhang, 2003), and/or its free radical scavenging, metal ion and hydroxyl radicals chelating abilities (Lim et al., 1997; Fu and Ji, 2003). Moreover, ginsenoside fractions have been shown to induce the cytosolic antioxidant enzyme superoxide dismutase via enhanced nuclear protein binding to its gene regulatory sequences (Chang et al., 1999). The reported results concerning the decrease in superoxide dismutase during diabetes agreed with those of Godin et al. (1988) who showed a decrease in Cu-Zn SOD activity in renal tissues during diabetes, however they contradicted those of Kakkar et al. (1995) and Limaye et al. (2003) who demonstrated either a no change or an increase in SOD activity in renal tissues of diabetic rats. Similarly, the present study demonstrated a diabetes induced decrease in glutathione S-transferase (GSTs) enzyme activities. Glutathione S-transferase belong to a

superfamily of multifunctional isoenzymes playing a crucial role in the detoxifying mechanisms of drugs and xenobiotics by preventing the binding of reactive metabolites to cellular proteins, and modulating the by-products of oxidative stress by catalyzing the conjugation of electrophilic moieties to glutathione (Hayes et al., 2005). Ginseng extract administration seemed to restore activities of these group of enzymes to the activities recorded for the control group, a result that agreed with that of Guma et al. (2007) who showed that wild ginseng pretreatment returned GST activity to control levels after being decreased by benzo  $\alpha$  pyrene toxicity and Shah et al. (2005) who showed that ginseng administration restored to near normal level of GSTs in the groups subjected to oxidative stress in brain tissues induced by hypoperfusion/reperfusion.

In conclusion, ginseng extract appears to be of benefit for delaying diabetes induced nephropathy, an effect that seems to be independent on correction of the metabolic deficits but rather dependent on antioxidant property of ginseng.

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## Notes

- 1- \*G.G.E. is a standardized ginseng extract obtained from Dansk Droge A/S Copenhagen Denmark.
- 2- The author is grateful to Dr. EmanBakr Professor of Pathology for interpretation of histopathology results and Dr. WafaaFelfel Ph.D. Biochemistry for assessment of renal antioxidant status.

Table 1. Effect of ginseng extract administration on serum metabolic profile of diabetic rats

Group Parameter	Control group	Diabetic group	Diabetes+ ginseng extract (100 mg) group	L.S.D
Glucose (mg/dl)	81.12 <sup>a</sup> ±1.96	412.70 <sup>b</sup> ±11.83	304.29 <sup>c</sup> ±5.51	22.12
Total cholesterol (mg/dl)	72.33 <sup>a</sup> ±4.31	186.71 <sup>b</sup> ±5.43	137.82 <sup>c</sup> ±4.60	13.94
Triglycerides (mg/dl)	34.66 <sup>a</sup> ±2.00	87.00 <sup>b</sup> ±2.15	63.66 <sup>c</sup> ±2.06	6.01
High density cholesterol (mg/dl)	27.50 <sup>a</sup> ±1.69	14.90 <sup>b</sup> ±0.48	21.10 <sup>c</sup> ±0.95	3.34
Low density cholesterol (mg/dl)	37.91 <sup>a</sup> ±2.50	154.38 <sup>b</sup> ±5.45	104.71 <sup>c</sup> ±5.06	13.15

Data presented as mean ± SE, n=10, P<0.05.

Means having different superscripts are significantly different.

Table 2. Effect of ginseng extract administration on kidney function tests of diabetic rats

Group Parameter	Control group	Diabetic group	Diabetes+ ginseng extract (100 mg) group	L.S.D
Blood urea nitrogen (mg/dl)	9.90 <sup>a</sup> ±0.33	29.55 <sup>b</sup> ±0.86	14.10 <sup>c</sup> ±0.34	2.64
Creatinine (mg/dl)	0.86 <sup>a</sup> ±0.085	3.51 <sup>b</sup> ±0.231	2.04 <sup>c</sup> ±0.072	0.43
uric acid (mg/dl)	1.87 <sup>a</sup> ±0.11	7.80 <sup>b</sup> ±0.24	5.31 <sup>c</sup> ±0.29	0.813
Total protein (g/dl)	6.70 <sup>a</sup> ±0.11	4.99 <sup>b</sup> ±0.06	5.99 <sup>c</sup> ±0.07	0.24

Data presented as mean ± SE, n=10, P<0.05.

Means having different superscripts are significantly different.

Table 3. Effect of ginseng extract administration on serum electrolyte concentrations of diabetic rats

Group Parameter	Control group	Diabetic group	Diabetes+ ginseng extract (100 mg) group	L.S.D
Sodium (meq/L)	160.20 <sup>a</sup> ±0.51	154.10 <sup>b</sup> ±0.66	159.80 <sup>a</sup> ±0.61	1.73
Potassium (meq/L)	6.29 <sup>a</sup> ±0.22	7.73 <sup>b</sup> ±0.087	6.43 <sup>a</sup> ±0.21	0.54
Calcium (meq/L)	11.00 <sup>a</sup> ±0.11	7.88 <sup>b</sup> ±0.13	10.72 <sup>a</sup> ±0.16	0.39
Magnesium (meq/L)	4.74 <sup>a</sup> ±0.11	1.78 <sup>b</sup> ±0.047	3.90 <sup>a</sup> ±0.14	1.01

Data presented as mean ± SE, n=10, P<0.05.

Means having different superscripts are significantly different.

Table 4. Effect of ginseng extract administration on relative kidney weight (%) of diabetic rats

<b>Group</b> <b>Parameter</b>	<b>Control group</b>	<b>Diabetic group</b>	<b>Diabetes+ ginseng extract (100 mg) group</b>	<b>L.S.D</b>
Kidney weight%	0.54 <sup>a</sup> ±0.016	0.92 <sup>b</sup> ±0.063	0.58 <sup>a</sup> ±0.023	0.116

Data presented as mean ± SE, n=10, P<0.05.

Means having different superscripts are significantly different.

Table 5. Effect of ginseng extract administration on renal tissue enzyme activities of diabetic rats

<b>Group</b> <b>Parameter</b>	<b>Control group</b>	<b>Diabetic group</b>	<b>Diabetes+ ginseng extract (100 mg) group</b>	<b>L.S.D</b>
Alkaline phosphatase (U/mg tissue)	889.83 <sup>a</sup> ±17.87	576.04 <sup>b</sup> ±27.11	900.85 <sup>a</sup> ±20.02	63.90
γ glutamyltransferase (U/mg tissue)	119.03 <sup>a</sup> ±4.12	58.50 <sup>b</sup> ±3.79	110.50 <sup>a</sup> ±4.42	11.94

Data presented as mean ± SE, n=10, P<0.05.

Means having different superscripts are significantly different.

Table 6. Effect of ginseng extract administration on renal antioxidant status of diabetic rats

<b>Group</b> <b>Parameter</b>	<b>Control group</b>	<b>Diabetic group</b>	<b>Diabetes+ ginseng extract (100 mg) group</b>	<b>L.S.D</b>
Malondialdehyde (µmol/mg tissue)	1.45 <sup>a</sup> ±0.051	4.69 <sup>b</sup> ±0.39	1.36 <sup>a</sup> ±0.06	0.66
Superoxide dismutase (EU/mg protein)	51.32 <sup>a</sup> ±0.66	27.29 <sup>b</sup> ±0.55	50.63 <sup>a</sup> ±0.91	2.09
Glutathione S-transferase (EU/mg protein)	0.25 <sup>a</sup> ±0.013	0.063 <sup>b</sup> 0.007	0.23 <sup>a</sup> 0.011	0.032

Data presented as mean ± SE, n=10, P<0.05.

Means having different superscripts are significantly different.

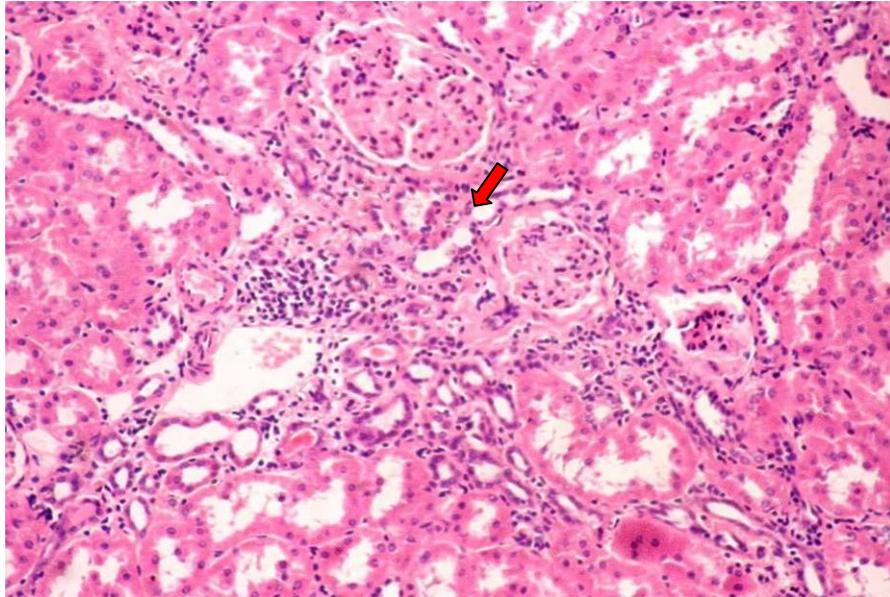


Figure 1. The kidneys of diabetic rats showed severe pathological lesions represented by thickening of the wall of most glomerular Bowman's capsule by fibrous connective tissue

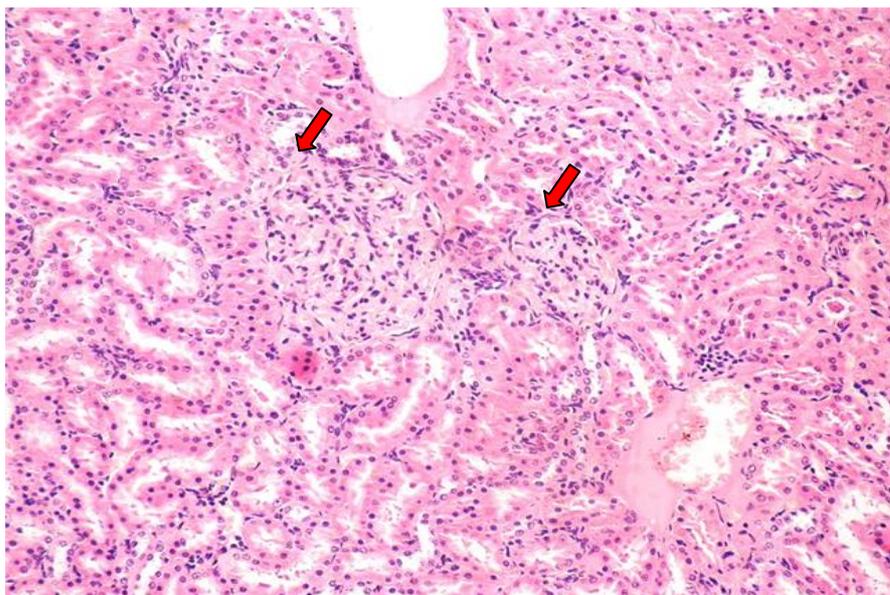


Figure 2. The kidneys of diabetic rats showing glomerulosclerosis

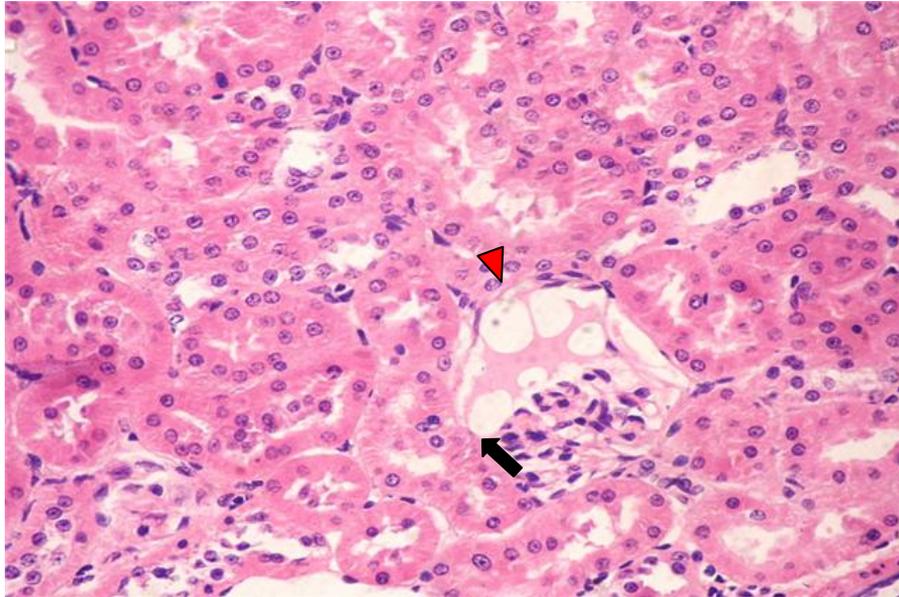


Figure 3. The kidneys of diabetic rats showing glomerular atrophy (arrow) and proteinaceous material in Bowman's space (arrow head)

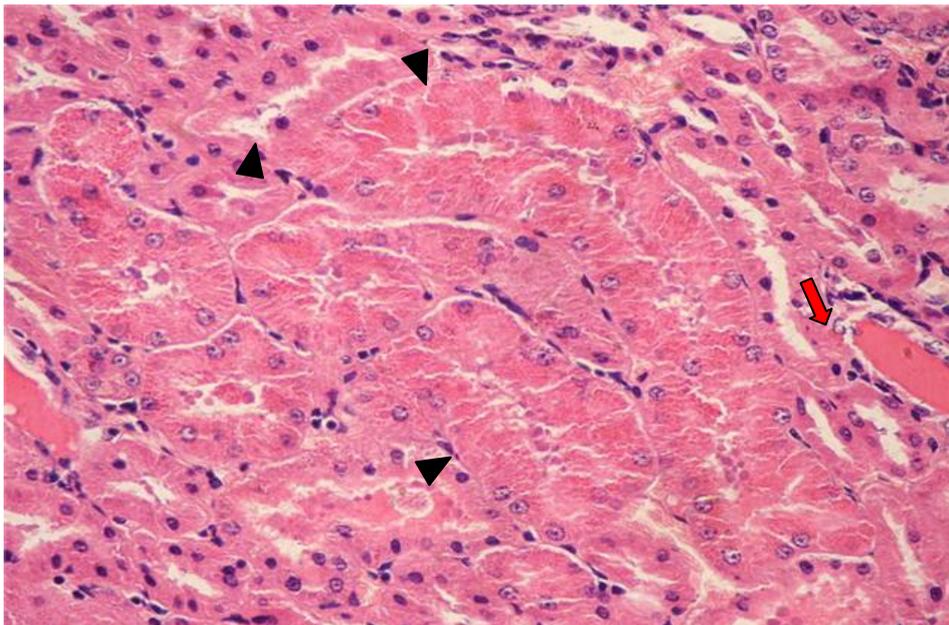


Figure 4. The kidneys of diabetic rats showing hyaline cast (arrow) and coagulative necrosis of some epithelial cells in renal tubules (arrow head) with deep eosinophilic cytoplasm and complete disappearance of nucleus or appearance of nucleus as a ghost

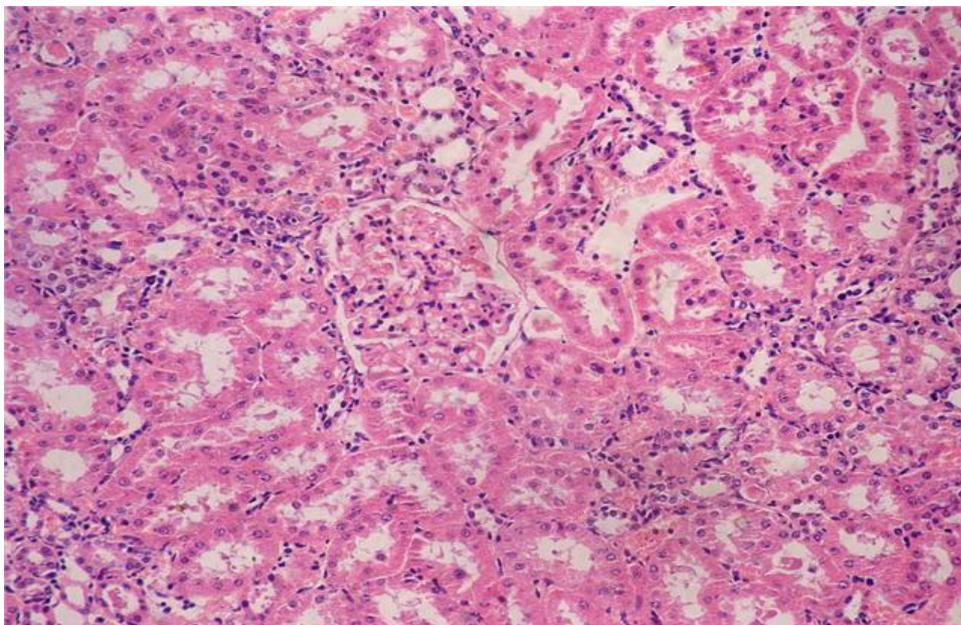


Figure 5. The kidneys of diabetic rats treated with ginseng extract showing normal glomerular tufts with slight hypercellularity

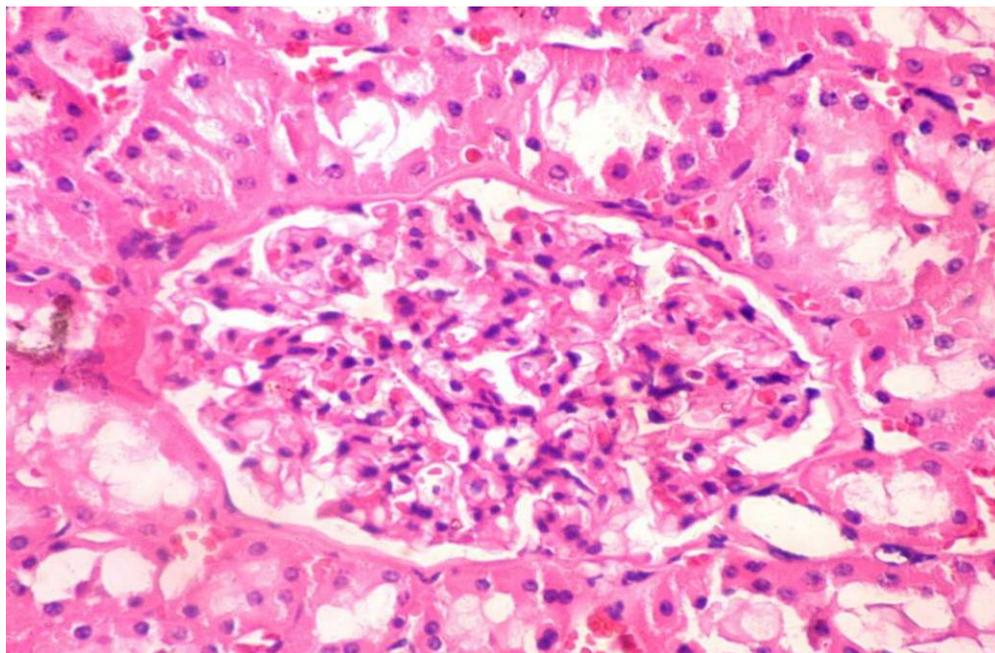


Figure 6. The kidneys of control group showing normal glomerular tufts