Study the Potential Therapeutic Effect of Garden Cress (*Lepidiumsativum*) on Nephropathy Diabetic Rats: Biological and Biochemical Studies

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ABSTRACT

Garden cress powder (GCP) considered as an important medicinal plant and widely grown in several countries including Egypt. whereas it has a high content of phenolic compounds and antioxidant activity. The objective of this study were assessed the potential therapeutic effects of Garden cress on nephropathy induced by gentamicin in diabetic rats. Thirty adult male albino rats were divided into two main groups. Group I: negative control (6 rats) and group II(24 rats): nephropathy diabetic rats group were given a single dose via intraperitoneal injection of 65 mg / kg body weight of streptozotocin (STZ). Then, nephropathy was induced in diabetic rats via intraperitoneally injection daily of gentamicin (GM) 85 mg /kg body weight for 8 days. Nephropathy diabetic rats group were divided into four subgroups (6 rats each) as follow: First (control positive group), second, third and fourth group received basal diet with 5, 7.5 and 10 % of GCP, respectively. Results showed that GCP contained high amount of potassium(2950.36 g/100g), Phosphorus (944.33 g/100g), and phenolics compounds as gallic (3010.75 µg/100g), ellagic (1466.92 µg/100g) , protocatechuic (588.23 µg/100g), chlorogenic (556.75 µg/100g) , coumarin(519.52 µg/100g) and iso-ferulic(545.34 µg/100g). Feeding nephropathy diabetic rats on a daily diet containing powder of garden cress with 5, 7.5 and 10% of standard diet produced a marked reduction in the serum levels of glucose, liver and kidney functions and malondialdehyde (MDA) levels as well as elevation in the activity of glutathione transferase(GST), superoxide dismutase (SOD), total antioxidant capacity (TAC), glutathione pyroxidase (GPX) and catalase (CAT) and serum insulin levels compared to positive control group. While, supplemented diet rats with 10% of GCP was more effective in improving the previous parameters.

In conclusion, The study concluded that garden cress powder has hypoglycemic potent effects and improve renal damage induced by gentamicin in diabetic rats. So it is advice to add GCP to daily diet for kidney patients.

Keywords:Garden cress, nephropathy, streptozotocin, gentamicin, glucose, kidney function , Antioxidants, insulin, urea.

INTRODUCTION

Diabetes mellitus (DM) is a one of chronic metabolic disease characterized by chronic hyperglycemia with turmoil in the metabolism of carbohydrates, protein and fat induced insufficiency of insulin secretion or decreased sensitivity of the target tissues to insulin (Omolaoye *et al*., 2018). Chronic hyperglycemia linked with high morbidity and mortality due to cumulative damage and severe health complications in most tissues and organs, involve kidneys, heart, blood vessels, eyes, nerves and skin (Kahn *et al*., 2014). Moreover, the progression and aggravation of oxidative stress produced by the impaired metabolism which appears through several mechanisms, such as glucose autoxidation, protein glucation resulting in the development of diabetic complications as nephropathy causing renal failure, retinopathy leading to blindess, neuropathy, macro and microvascular damage and sexual dysfunction (WHO, 2016).

Diabetes produces excess reactive oxygen species which damage the capillaries in the kidney's glomeruli leading to diabetic nephropathy (Kittell, 2012). Also, the kidney is influenced by some drugs like gentamicin, which is known for its nephrotoxicity (Nale *et al*., 2012) and accumulation of gentamicin in renal tubular cells causes apoptosis, necrosis and demolition of cells (Dontabhaktuni *et al*., 2016).

Diabetic nephropathy is one of the most serious complications of diabetes and the most common cause of end-stage renal failure. At present, diabetic kidney disease affects about 15%–25% of type I diabetes patients (Hovind *et al*., 2003). Reactive oxygen species (ROS) play an important role in high glucose-induced renal injury (Ha and Lee, 2000) .

Medical plants have been used as therapeutic agents in traditional system. Before the advent of insulin and oral hypoglycemic drugs, the major form of treatment involved the use of parts of plants (Chauhan *et al.*, 2012).

Current therapeutic strategies for diabetic nephropathy are aimed at management and alleviation of the underlying pathological processes and include lifestyle modifications such as healthy diet, weight control and regular physical activity coupled with medication/drug interventions (Tran *et al*., 2015).

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Garden cress (GC) *Lepidium sativum* is rich in proteins, vitamins, minerals, especially calcium and iron and contain 24% fat in which 34.5 % of total fatty acids α-linolenic acid.The seeds are wealthy phenolic compounds and have high antioxidant activity compared to other cress varieties. It contains many phytochemicals with potential nutraceutical activity like glucosinolates, flavonoids, coumarins, sulphur glycosides, triterpenes, sterols and various imidazole alkaloids (Maier *et al*., 1998 and Bryan *et al.,* 2009).

Flavonoids are abundant plant phenolic compounds. More than 6000 have been identified, and some have shown to possess hypoglycemic and antidiabetic activities (Sharma *et al*., 2008).

In Unani system of medicine, seed powders and leaves of (GC) have been reported to possess diuretics, aperients and aphrodisiac properties and are recommended in inflammation, bronchitis, rheumatism and muscular pain. It is also reported to be useful in the treatment of asthma, cough and bleeding piles (Eddouks *et al.,* 2005).

The plant is also reported to possess antihemoglutinating, hypoglycemic, antihypertensive, diuretic, fracture healing properties and significant bronchodilatory activities (Chauhan *et al.,* 2012).

GC seeds shows many medicinal properties such as antidiabetic, hypocholesterolemic, antihypertensive, antidiarrheal, antispasmodic and laxative activities, it also has fracture healing hepato protective, diuretic, ant inflammatory, nephron protective enephrocurative, galactogogue ,antipyretic and analgesic potential (Gokavi *et al.,* 2004).

Diabetic and hyper lipidemic rats administered with GC seed showed a significant decrease in fasting blood glucose levels, glycosylated haemoglobin, lipid profile, total cholesterol, triglycerides and lipoprotein fractions (Chauhan *et al.,* 2012).

Therefore, the objective of this study were assessed the potential therapeutic effects of garden cress (GC) *L.sativum* on nephropathy induced by gentamicin in diabetic rats.

MATERIALS AND METHODS

Materials:

Garden cress

(GC) seed was obtained from the local market of Shibin-El kom City -Menoufia governorate Egypt.

Chemicals

Gentamicin (GM) sulfate was obtained from Memphis Company, For Pharm. & Chem. Ind. -Cairo. Streptozotocin (STZ) was obtained from Sigma-Aldrich Inc. Kits for estimating biochemical analysis were purchased from Alkan Medical Company, El-Doky, Giza, Egypt. Malondialdehyde (MDA), catalase (CAT), glutathione peroxidase (GSH.Px) and superoxide dismutase (SOD) activity Kits were obtained from Biodiagnostic Company, El-Doky, Giza, Egypt.

Animals

Thirty adult male albino rats, Sprague Drawley strain, weighing (180 ± 5g) were obtained from Medical Insects Research Institute, El-Doky, Giza, Egypt. Rats were housed individually in well aerated cages under hygienic laboratory condition in Laboratory, Faculty of Home Economics, , ShibinEl-kom, Menoufia, Egypt and fed standard diet according to AIN-93 guidelines (Reeves *et al*., 1993), for 7 days as an adaptation period.

Methods:

Experimental design:

Rats were randomly divided into two main groups. The first group, normal control (n=6). The second group: nephropathy diabetic rats (n=24) were given a single dose via intraperitoneal injection of 65 mg / kg body weight of streptozotocin (STZ) dissolved in a freshly prepared 0.01 M citrate buffer (PH 4.5) according to Yanardag *et al*., (2003). Diabetes was identified by polydipsia, poly-urea (visual observations) and measuring fasting blood glucose level after 72 h of injection of STZ. Rats with a fasting blood glucose level above 200 mg/dl were considered diabetic and were used in this study. Then, Nephropathy was induced in diabetic rats via intraperitoneally injection daily of gentamicin (GM) 85 mg / kg body weight for 8 days as described by Jeyanthi and Subramanian (2009). Nephropathy diabetic rats group were divided into four subgroups (6 rats each) as follow: First (positive control group), second, third and fourth group received standard diet plus 5, 7. 5 and 10% of GCP respectively for 30 days. At the end of the experimental period (30 day), rats were anesthetized with diethyl ether after fasting for 12h and blood samples were collected from the hepatic portal vein and centrifuged to obtain serum .

Biological evaluation:

During the experimental period (30 day), the consumed feeding was recorded every day, body weight gain (BWG%) and feed efficiency ratio (FER) were calculated according to Chapman *et al*., (1959) using the following equations:

$$\text{Body weight gain (BWG\%)} = \frac{\text{(Final weight-Initial weight)}}{\text{Initial weight}} \text{ X } 100$$

$$\text{Feed efficiency ratio (FER)} = \frac{\text{Gain in body weight(g)}}{\text{Feed intake(g)/30}}$$

Chemical Analysis:

Moisture, protein, fat, fiber and ash contents of GC were determined according to methods described by the AOAC (2010). Carbohydrates contents were estimated by difference.

Determination of minerals contents were determined according to the method of AOAC (2005). Determination of Phenolic compounds of GC extract were determined according to (Goupy*et al.* 1999).

Biochemical analysis:

The serum levels of glucose was determined according to Trinder (1969). Insulin was estimated according to(Cordero-Herrera*et al*., 2015). Urea, creatinine and uric acid levels were estimated according to Trinder, (1969); Tietz, (1986) and Fossati *et al*., (1980), respectively. BUN was estimated according to (Philip, 1994).

Aspartate aminotransaminase(AST) and alanine aminotransferase (ALT) were measured by according to method described by Henry, (1974) and Yound, (1975), respectively. Also alkaline phosphatase (ALP), was estimated according the method of IFCC, (1983). Glutathione peroxidase (GPX), superoxide dismutase (SOD), catalase (CAT), glutathione s-transferases (GSTs), total antioxidant capacity (TAC) and malondialdehyde (MDA) were measured by method of Zhao *et al*., (2001); Sun *et al*., (1988); Diego,(2011); Hegsted *et al*., (1941); Koracevic *et al*., (2001); Satoh, (1978) and Ohkawa *et al*., (1979), respectively.

Statistical analysis

Results were expressed as the mean ± SD. Data for multiple variable comparisons were analyzed by one-way analysis of variance (ANOVA). For the comparison of significance between groups, Duncan's test was used as a post hoc test according to the statistical package program (Artimage and Berry, 1987).

RESULTS AND DISCUSSION

Chemical composition of GC was presented in table (1) data showed that protein (21.61) g/100g, carbohydrate (27.80) g/100g, fat (32.28) g/100g and fiber (6.75) g/100g were high in GC while moisture (6.73) g/100g and ash (4.83) g/100g were low. These results show that the macronutrients are considerably high for human nutrition. in addition, the above findings are almost in accordance with the outcomes reported by Doke and Guha (2017) who reported that the garden cress seeds contain 25% of protein, 14-24% of lipids, 33-54% of carbohydrates and 8% of crude fiber. Zia-Ul-Haq *et al.* (2012) observed that the proximate chemical composition of GC was 2.9%,, 23.2%, 24.2% 30.7%, 11.9% and 7.1% for moisture, crude fat, protein,carbohydrate, fiber and ash, respectively.

Table 1. Chemical composition of GCP g/100g dry weight

Constituent of GCP	g/100g
Moisture	6.73
Crude protein	21.61
Fat	32.28
Crude fiber	6.75
Ash	4.83
Total carbohydrate	27.80

Content of minerals of GCP is presented in table 2 data showed that GCP has high content of potassium 2950.36 mg/100g and Phosphorus 944.33 mg/100g,While contained a medium quantity of calcium 210.23 mg/100g, sodium 230.35 mg/100g and Magnesium325.00 mg/100g. finally, zinc 2.96 mg/100g was low. Shail *et al*. (2016) and Doke and Ghua (2017) reported that GC seeds are a good source of minerals such as, phosphorus magnesium and potassium.

Table 2. Minerals content of GCP mg/100g

Minerals of GC	g/100g
Potassium (K)	2950.36
Calcium (Ca)	210.23
Phosphorus(P)	944.33
Magnesium (Mg)	325
Sodium (Na)	230.35
Zinc (Zn)	2.96

Data in table (3) show that a phenolic compounds in GC It is clear to notice that the highest phenolics compounds of GC extract recorded for gallic, ellagic, protocatechuic, chlorogenic, coumarin and Iso- ferulic. The values were 3010.75, 1466.92, 588.23, 556.75, 519.52 and 545.34 mg/100g, respectively. All of these play an important role in improving the human health by participating in the antioxidant defense system against free radical generation. These results are in agreement with Zia-Ul-Haq *et al*. (2012) and Ait Yahia *et al*. (2018).

And also Sethiya *et al.*, 2014 who reported Gallic acid and Protocatechuic acid are phytochemicals that are considered to be a potential source of functional food ingredients for their high antioxidant capacity.

Flavonoids are abundant plant phenolic compounds more than 6000 have been identified, and some have shown to possess hypoglycemic and antidiabetic activities (Sharma *et al*., 2008).

Data presented in Table (4) illustrate the effect of GCP on BWG, FI and FER of nephropathy diabetic rats. It could be observed that the mean value of BWG, FI and FER of positive control group significantly ($P \leq 0.05$) decreased in nephropathy diabetic rats compared to normal control rats these results are in agreement with (Wang *et al.*, 2011) who reported that diabetes was associated with reduced body weight when compared with the control rats. More over nephropathy diabetic rats supplemented with 5, 7.5 and 10% of GCP resulted in increase ($P \leq 0.05$) in BWG, FI and FER compared with positive control rats.

Table 3. phenolic compounds in GC extract

phenolic compounds	(µg/100g)
Gallic	3010.75
Pyrogallol	6.99
4-Aminobenzoic	128.88
Protocatechuic	588.23
Catechein	108.61
Chlorogenic	556.75
Catechol	177.74
Caffiene	215.55
P.oH. benzoic	28.85
Caffeic	248.30
Vanillic	425.79
p-Coumaric	115.86
Ferulic	79.40
Iso- ferulic	545.34
Ellagic	1466.92
Benzoic	276.76
α- Coumaric	37.77
3,4,5.Methoxy Cinnamic	83.04
Coumarin	519.52
Salicylic	73.50
Cinnamic	114.965

Table 4. Effect of GCP on body weight gain (BWG%), feed intake (FI) and feed efficiency ratio (FER) of nephropathy diabetic rats

Groups / Parameter	Normal Control	Nephropathy Diabetic Rats			
		Positive Control	GCP		
			5%	7.5%	10%
BWG %	$63.50^{a}\pm2.150$	$19.75^{e}\pm0.830$	$32.25^{d}\pm1.320$	$47.88^{c}\pm1.340$	$59.38^{b}\pm2.200$
FI	$365.2^{a}\pm2.645$	$225.2^{e}\pm1.841$	$250.2^{d}\pm1.335$	$295^{c}\pm1.749$	$359.4^{b}\pm2.371$
FER	$0.285^{a}\pm0.011$	$0.143^{c}\pm0.005$	$0.210^{b}\pm0.009$	$0.265^{a}\pm0.012$	$0.266^{a}\pm0.013$

Values were expressed as mean±SD. Values within the same row having different superscript letters are significantly different at $P \leq 0.05$. BWG: body weight gain, FI: feed intake, FER: feed efficiency ratio ,GCP: Garden cress powder.

The best results were recorded for the group which was fed on 10% of GCP compared with control (+) group. These results confirmed the results of Windisch *et al.,* (2007) who found that the increased feed intake with increasing level of GC may indicate its positive influence on appetite of the study animals and nutrient digestion. Also, This result is in consistence with that Beejmohun *et al.,* (2014) who found that the total body weight (g) in negative group showed a significant decrease as a result of induction of diabetes, whereas it increased with treating with cinnamon and cress seed methanol extract.

The data in Table (5) reflects the effect of GCP on kidney function of nephropathy diabetic rats level of urea, uric acid, creatinine and BUN in serum .These were used as biochemical marks to evaluate the renal injury. in diabetes, high glucose level for long time caused kidney damages and impairment in renal function resulting in elevation in the levels of urea, uric acid and creatinine which are considered as markers of renal dysfunction. From the table it can be observed that serum urea, creatinine, BUN and uric acid levels were significantly higher ($P \leq 0.05$) in positive control rats than that in normal control rats, This elevation in serum markers of kidney function found to be an indicator of decrease in glomerular filtration rate and tissue injury. These results are compatible with the findings of Jain and Somani, (2015). As well as, hyperglycemia caused a significant elevation in markers of renal dysfunction (Elizabeth and Harris, 2005). Data in the same table showed supplementation nephropathy diabetic rats with 10% of *L.Sativum* powder led to a significant ($P \leq 0.05$) reduction in levels of urea, uric acid creatinine and BUN levels compared to nephropathy diabetic rats supplemented with 5 and 7.5% of *L.Sativum* powder. These results are in agreement with Qusti, (2016) who showed that treating the diabetic rats with GC and cinnamon by different concentration of methanol extract,, caused a significant decrease in serum urea, creatinine, uric acid, and urine albumin. Also this result agrees with Kumar *et al.,* (2014) who explicated this amelioration in renal function is due to the presence of flavonoids and steroidal compounds. These results confirmed the results of Xu *et al*., (2016) who found that flavonoids and phenolic compounds protected against diabetic nephropathy in STZ-induced diabetic rat improving blood urea nitrogen, creatinine and urine as well as kidney tissue damage, with a reduction in mitochondrial damage.

The data in Table (6) showed the effect of GCP on antioxidant enzymes as glutathione pyroxidase (GPX), superoxide dismutase (SOD), catalase (CAT), glutathione transferase (GST), total antioxidant capacity (TAC) and oxidant enzymatic as malondialdehyde (MDA) in serum of nephropathy diabetic rats. In biological system, there is a balance between the production and neutralization of (ROS). This balance is maintained by the presence of natural antioxidants and antioxidant enzymes such as catalase and glutathione peroxidase. The enhancement of lipid peroxidation or the decrease of antioxidant protection present in metabolic diseases or bad lifestyle can induce endothelial dysfunction (Lubrano and Balzan, 2015). There were significantly ($p \leq 0.05$) increase of (MDA) level and decrease of (CAT), (GPX), (GST), (GSH.Px) and (SOD) activities in positive control rats comparing to normal control rats. These results are in agreement with Rajashkar *et al*., (2012) who mentioned that gentamicin increases the generation of ROS which led to reduce the activities of antioxidant enzymes and by depleting intracellular concentrations of GSH during the process of combating oxidative stress, which enhances lipid peroxidation. Also, Saddala *et al*., (2013) who reported that diabetes mellitus associated with a free radical induced lipid peroxidation and reduction in antioxidant enzymes activity.

On the other hand whereas feeding nephropathy diabetic rats with 10% of GCP led to improve the activity of CAT, SOD, GPX, GST and TAC as well as the level of MDA showed significant decrease ($p \leq 0.05$) as compared with positive control rats. this positive effect of *L.Sativum* may be attributed to its antioxidant and free radical scavenging abilities.

Table 5. Effect of GCP on urea (mg/dl), uric acid (mg/dl) creatinine (mg/dl) and BUN of nephropathy diabetic rats

Groups / Parameter	Normal Control	Nephropathy Diabetic Rats			
		Positive Control	GCP 5%	GCP 7.5%	GCP 10%
Urea (mg/dl)	$19.22^{d}\pm0.712$	$34.75^{a}\pm1.351$	$30.60^{b}\pm1.172$	$26.32^{c}\pm1.012$	$19.85^{d}\pm0.943$
Uric acid (mg/dl)	$1.41^{d}\pm0.057$	$3.62^{a}\pm0.176$	$2.51^{b}\pm0.121$	$1.99^{c}\pm0.098$	$1.52^{d}\pm0.071$
Creatinine (mg/dl)	$0.53^{d}\pm0.011$	$1.57^{a}\pm0.074$	$1.36^{b}\pm0.063$	$0.96^{c}\pm0.047$	$0.50^{d}\pm0.024$
BUN	$11.41^{d}\pm 0.82$	$24.57^{a}\pm 3.32$	$23.95^{a}\pm 0.85$	$20^{b}\pm 0.82$	$15.37^{c}\pm 0.65$

Values were expressed as mean±SD. Values within the same row having different superscript letters are significantly different at $P \leq 0.05$. BUN: Blood Urea Nitrogen ,GCP: Garden cress powder.

Table 6. Effect of GCP on activities of (CAT), (SOD), (GPX), (GST), (TAC) and (MDA) enzymes of nephropathy diabetic rats

Groups / Parameter	Normal Control	Nephropathy Diabetic Rats			
		Positive Control	GCP		
			5%	7.5%	10%
CAT(mmoL/L)	$76.74^{a}\pm2.897$	$38.31^{d}\pm1.876$	$56.00^{c}\pm2.580$	$63.74^{b}\pm2.145$	$72.95^{a}\pm2.064$
SOD (U/L)	$55.75^{a}\pm1.985$	$31.04^{d}\pm1.502$	$43.33^{c}\pm1.951$	$47.47^{b}\pm2.135$	$53.53^{a}\pm1.641$
GPX (ng/dl)	$83.53^{a}\pm2.225$	$52.07^{d}\pm1.955$	$61.72^{c}\pm2.035$	$72.15^{b}\pm1.551$	$80.78^{a}\pm2.277$
GST(mmoL/L)	$1.94^{a}\pm0.461$	$0.86^{b}\pm0.042$	$1.40^{a}\pm0.095$	$1.62^{a}\pm0.081$	$1.90^{a}\pm0.069$
TAC(mmoL/L)	$36.97^{a}\pm1.798$	$19.94^{d}\pm1.947$	$23.35^{c}\pm1.118$	$28.12^{b}\pm1.356$	$35.88^{a}\pm1.744$
MDA(mmoL/L)	$17.17^{d}\pm0.808$	$36.63^{a}\pm1.780$	$31.21^{b}\pm1.511$	$26.32^{c}\pm1.266$	$19.11^{d}\pm0.905$

Values were expressed as mean±SD. Values within the same row having different superscript letters are significantly different at P≤ 0.05. CAT: catalase, SOD: superoxide dismutase, GPX: glutathione pyroxidase, GST: glutathione transferase TAC: total antioxidant capacity, MDA: malondialdehyde.

These results confirmed the results of Dugoua *et al*., (2007) who found that GC contain, among the natural dietary antioxidants and polyphenols in GC and have been shown to reduce oxidative stress via the inhibition of 5-lipoxygenase.

Also, Qusti *et al*., (2016) reported that treating the diabetic rats with *L*. *sativum and* cinnamon methanol extract significantly (P<0.001) increased the mean values of CAT, SOD, and GST compared with that of the positive control. This results indicate that the garden cress (*L*. *sativum*) contains high level of phenolic groups that cause scavenging of free radicals which is one of themajor antioxidation mechanisms to inhibit the chain reaction of lipid peroxidation.

Effect of GCP on glucose in blood and insulin in nephropathy diabetic rats are presented in Table (7). The nephropathy diabetic rats had higher (P≤0.05) blood glucose level than those in normal control during the experimental period. Wei *et al*., (2003) who found that STZ had a high affinity for binding to the glucose receptors present on the pancreatic β-cells, its ingestion relish the cytotoxic effect upon these cells and lead to dysfunction or cell death. This subsequently leads to alteration of insulin levels and blood glucose concentrations.However, the blood glucose level of nephropathy diabetic rats fed on GCP diets was significantly (P≤0.05) decreased by increasing GCP levels. The highest reduction in blood glucose level was found in nephropathy diabetic rats fed on 10% of GCP. These results confirmed the results of Qusti *et al*., (2016) who showed that treating the diabetic rats with *L*. *sativum* and cinnamon methanol extracts, significantly decreased the mean values of serum fasting blood sugar compared with the positive control. This result is consistence with Abdelwahab *et al*., (2014) who showed that using the aqueous *L*. *sativum* extract that can significantly reduce the blood glucose levels after a single or repeated administration. The strong hypoglycemic action of *L*. *sativum* extract is due to the presence of benzyl isothiocyanate (Prajapati *et al.*, 2014).

On the other hand, nephropathy diabetic untreated rats (positive control) and nephropathy diabetic rats fed on GCP. diets had lower (P≤0.05) serum insulin level than the normal control rats during the experimental period. However, the serum insulin level was significantly (P≤0.05) increased by increasing the experiment period and GCP levels. The highest reduction of the serum insulin level was found in nephropathy diabetic rats fed on 10% of GCP. The results are compatible with Hamidpour *et al.*, (2015) It also possesses insulin mimetic properties because its biologically active substances enhance glucose uptake by activating insulin receptor kinase activity, autophosphorylation of theinsulin receptor, and glycogen synthase activity. Also Eddouks *et al*., (2002) confirmed that GCP has the significant antidiabetic and cytoprotective activity in type I diabetic rats through phytochemicals study in it (flavonoids and glycosides) which have able to act and stimulate pancreaticβ-cells to secrete insulin and enhance glucose metabolism.

Table 7. Effect of GCP on blood glucose and insulin of nephropathy diabetic rats

Groups / Parameter	Normal Control	Nephropathy Diabetic Rats			
		Positive Control	GCP		
			5%	7.5%	10%
Glucose(mg/dl)	$98^{e}\pm2.801$	$233^{a}\pm2.774$	$131^{b}\pm1.967$	$119^{c}\pm 2.013$	$103^{d}\pm 1.547$
Insulin(ng/mg)	$14.16^{a}\pm2.33$	$6.23^{d}\pm1.19$	$9.48^{c}\pm1.25$	$10.43^{b}\pm2.16$	$10.71^{b}\pm2.12$

Values were expressed as mean±SD. Values within the same row having different superscript letters are significantly different at P≤ 0.05.

Table 8. Effect of GCP on Liver functions ; aspartate amino transaminase (AST), alanine aminotransferase (ALT), And alkaline phosphatase (ALP) of nephropathy diabetic rats

Groups / Parameter	Normal Control	Nephropathy Diabetic Rats			
		Positive Control	GCP 5%	GCP 7.5%	GCP 10%
AST(U/L)	$101.2^{e}\pm2.530$	$181.2^{a}\pm2.851$	$152.1^{b}\pm2.532$	$135.3^{c}\pm1.785$	$112.1^{d}\pm2.160$
ALT(U/L)	$48.01^{d}\pm1.178$	$67.20^{a}\pm1.950$	$61.20^{b}\pm1.752$	$59.1^{b}\pm1.501$	$52.1^{c}\pm1.275$
ALP(U/L)	$190.1^{e}\pm2.480$	$297.1^{a}\pm3.133$	$215.2^{b}\pm2.057$	$209.1^{c}\pm1.200$	$198.3^{d}\pm1.791$

Values were expressed as mean±SD. Values within the same row having different superscript letters are significantly different at P≤ 0.05. AST: aspartate amino transaminase, ALT: alanine aminotransferase and ALP: alkaline phosphatase

Data of Table (8) indicate the effect of GCP on serum levels of Liver functions (AST, ALT and ALP enzymes) of nephropathy diabetic rats. The obtained results showed the gentamicin and STZ can cause alterations in the level of hepatic biochemical markers throw increasing the serum levels of aspartate amino transaminase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) compare with normal rats. Those data were in agreement with Ademiluyi *et al.,* (2013) who demonstrated that GM administration significantly damaged liver cells as manifested by a large increase in ALT and AST activities and total bilirubin level. Moreover, it caused a marked decrease in total protein concentration indicating a failure in liver synthetic capacity caused by GM administration. A significant decrease (P≤0.05) in the elevated level of liver enzymes was noticed in treated groups when compared with positive control rats. The best values of liver enzymes were recorded to 10% of GCP compare to (+) control rats. These data are in agreement with those of Pandit *et al*., (2012) and Zamzami *et al*., (2019) who confirmed that concurrent treatment of rabbits injured with CCl4 for 5 and 10 weeks with *L. sativum* seeds led to significantly repaired their liver enzymes such as elevation of total protein and albumin improved with decrease level of globulin.

CONCLUSION

The present study showed that the GCP *Lepidium Sativum* efficiently regulate blood glucose and improves disruption of kidney functions abnormalities associated with diabetes in STZ and gentamicin induced nephropathy diabetic rats possibly by virtue of various essential antioxidant, antidiabetic compounds. GC can thus contribute towards prevention and management of diabetes mellitus and nephropathy and it associated complications.

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الملخص العربي

دراسة التأثير العلاجي المحتمل لنبات حب الرشاد على الفئران المصابة باعتلال الكلى والسكرى: دراسات بيولوجية وكيموحيوية

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يعتبر حب الرشاد نباتًا طبيًا مهمًا وينمو على نطاق واسع في العديد من البلدان بما فيها مصر ونظرا لمحتواه العالي من المركبات الفينولية ونشاطه المضاد للأكسدة. فقد افترض أنه يمكن أن يكون غذاء وظيفيًا. في هذا البحث، تم تقييم التأثيرات العلاجية المحتملة لمسحوق حب الرشاد على اعتلال الكلية المستحث بالجنتاميسين في الجرذان المصابة بداء السكري. تم استخدام ٣٠ فأر ذكور من النوع الالبينو البالغة وتم تقسيمهم إلى مجموعتين رئيسيتين. المجموعة الأولى هى المجموعة الضابطة السالبة (٦ فئران) والمجموعة الثانية (٢٤ فأر) هي مجموعة الفئران التى تم اصابتها باعتلال الكلى والسكرى والتى أعطيت جرعة واحدة من الستربتوزوتوسين عن طريق الحقن داخل البريتون مقدارها ٦٥ ملجم/ كجم من وزن الجسم، ثم بعد ذلك تمت الإصابة باعتلال الكلى للفئران المصابة بالسكر عن طريق حقنها بالجنتاميسين بجرعة يومية مقدارها٨٥ ملجم / كجم من وزن الجسم لمدة ٨ أيام متتالية. وقسمت مجموعة الفئران المصابة باعتلال الكلى والسكري إلى أربع مجموعات فرعية (٦ فئران بكل منها) على النحو التالي: المجموعة الأولى المجموعة الضابطة الموجبة والمجموعات الثانية, الثالثة والرابعة: تناولت الوجبة القياسية مضافا لها

٥ ، ٧.٥ ، ١٠٪ من مسحوق حب الرشاد لمده ٣٠ يوم. وقد أظهرت النتائج أن مسحوق حب الرشاد يحتوي على نسبة عالية من البوتاسيوم(٢٩٥٠,٣٦ جم/١٠٠جم) والفوسفور(٩٤٤,٣٣جم/١٠٠جم) ومركبات الفينول والمركبات الفينولية مثل احماض الجاللي ٣٠١٠,٧٥ ميكروجم/١٠٠جم) والاجيك (١٤٦٦,٩٢ميكروجم/١٠٠جم) وبروتوكاتيويك(٥٨٨,٢٣ ميكروجم/١٠٠جم) وكلوروجيك(٥٥٦,٧٥ ميكروجم/١٠٠جم)وكيومارين(٥١٩,٥٢ ميكروجم/١٠٠جم وأيزو فليوريك(٥٤٥,٣٢ميكروجم/١٠٠جم). وقد أدت تغذية الفئران المصابة بالاعتلال الكلوي بالسكري على نظام غذائي يومي يحتوي على مسحوق حب الرشاد بنسبة ٥ ، ٧.٥ ، ١٠٪ إلى انخفاض ملحوظ في مستويات الجلوكوز ووظائف الكبد و الكلى ومستويات المالونالدهيد في الدم بالإضافة إلى ارتفاع في نشاط مستويات الجلوتاثيون ترانسفيريز والسوبر اوكسيديز ديسميوتيز والقدرة الكلية المضادة للأكسدة والجلوتاثيون بيروكسيديز والكتاليز ومستويات الأنسولين في الدم مقارنة بالمجموعة الضابطة الموجبة. وكانت المجموعة المضاف لها مسحوق حب الرشاد بنسبة ١٠٪. أكثر فاعلية في تحسين المعايير السابقة. **في الختام** ، خلصت الدراسة إلى أن مسحوق رشاد له تأثيرات قوية على سكر الدم ويحسن التلف الكلوي الناجم عن الجنتاميسين في الفئران المصابة بداء السكري. لذلك فمن المستحسن إضافة حب الرشاد إلى النظام الغذائي اليومي لمرضى الكلى

الكلمات المفتاحية: حب الرشاد، اعتلال الكلي، الستربتوزوتوسين، الجنتاميسين، الجلوكوز، وظائف الكلى , مضادات الاكسده, الانسولين , اليوريا.