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Protective Effect of Grapes of Beer Seeds and Hops Leaves as Powder in Treatment of Kidney Functions on Nephrotoxic Rats

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Abstract:

This study was conducted to investigate the protective effect of different concentrations (2.5% and 5%) of grapes of beer (*Arctostaphylos uva-ursi*) seeds and hops (*Humuls lupulus*) leaves and their mixture as powder on nephrotoxic rats. Forty eight white male albino rats, weighing 150±10g were used in this study. The rats were divided into 8 groups, (n=6 rats).

One was kept as a control negative group while the other groups were injected by gentamicin (10 mg/kg body weight) once day for 10 days. Glucose level, serum liver functions (ALT, AST and ALP), kidney function markers (urea, uric acid and creatinine), total cholesterol, triglycerides, and lipid profile (HDL-c, LDL-c and VIDL-c) were determined. The obtained results revealed that grapes of beers seeds and hops leaves powder and their mixture improved liver functions, kidney functions, serum glucose levels, and lipid profile in rats. The best results recorded for 5% mixture and recommended for used as a beverage drink to improve kidney functions. Also hops diet alone, seems to be of better action compered to grapes of bear diet alone.

Key words: Rats, Herbs, Kidney disorder, Biochemical analysis.

Introduction

The kidneys are a pair of kidney bean–shaped organs located just above the waist, between the peritoneum and the back of the abdomen. The two kidneys lie behind the liver and the intestines in the small of the back. They are partially protected by the 11^{th} and 12^{th} pair of ribs **(Chopra *et al*., 2013)**.

Chronic kidney disease (CKD) is a worldwide public health problem, with adverse outcomes of kidney failure, cardiovascular disease (CVD), and premature death. A simple definition and classification of kidney disease is necessary for international development and implementation of clinical practice guidelines **(Eknoyan *et al*., 2004)**.

The kidney plays a vital role in the maintenance of normal blood volume/pressure and the regulation of acid -base balance. Approximately one - fourth of the cardiac out is filtered through the kidney. The kidneys also play a great role in urine excretion as they are the path way for removal of the waste products of absorption and metabolism. Which include ammonia, urea, creatinine, phospgorus, water, sodium and potassium, the kidney produces erythropoietin hormone, deficiency of this hormone results in profound anemia. A decrease in kidney functions greatly affects metabolism and nutritional status **(Miller and Klahr, 2005).**

Grapes of beers are a well-known source of polyphenols. More than two-thirds of dietary polyphenols are in the form of flavonoids and more than two-thirds of grape flavonoids (catechin, epicatechin, and their oligomers procyanidins) are located in grape seeds. Dietary elements rich in flavonoids, including extra virgin olive oil and grape seed extracts, have anti-inflammatory and anti-oxidant properties, and are thought to be protective against CVD by improving serum lipid profiles, reducing inflammatory cytokines, and preventing low-density lipoprotein (LDL) oxidation .Grape seed extracts have demonstrated positive effects on inflammation, insulin resistance ,oxidative stress, blood pressure, and platelet function, all of which are important determinants of vascular endothelial function, in various patient populations **(Covas *et al*., 2006)**.

Grape of beers seed is a complex polyphenolics mixture containing flavonoïds, non flavonoïds, proanthocyanidins exhibiting multi-organ

protection in various experimental settings .For instance, GSE protects the heart, the liver ,the brain and the kidney against high fat diet (HFD)-induced obesity and lipotoxicity in rat. Furthermore high dosage GSE was even shown to improve renal injury in type 2 diabetic rats through its anti-oxidant and anti-inflammatory properties and also to protect against arsenic, cisplatin, amikacin and cyclosporine a-induced nephrotoxicity **(Zhang *et al.*, 2014)**.

Grapes of bear seeds are contains water, carbohydrates, proteins, lipids, compounds with important biological properties such as fiber, vitamin c and phenolic compounds (tannins, phenolic acids, anthocyanins and resveratrol) organic acids: Tartaric, malic, citric, succinic; vitamins: A, B1, B2, B3, B5, B6, C, K, minerals: Calcium, potassium, phosphorus, magnesium, sodium, iron, manganese, phosphorus, sulfur and zinc **(Ahmad *et al*., 2011)**.

Arctostaphylos uva-ursi (L.) is a drug used for treatment of pain, diuretic, contact dermatitis, kidney stone removal and urinary tract infections **(Adesunloye, 2003)**.

A hop cone, the female flower of the dioecious hop plant (*Humulus lupulus*), is an important raw material used for brewing beer. The cone of hop plant contains bitter acids, terpenoids, and polyphenols, and is therefore closely associated with the flavor of beer. Only the cone is used as the raw material why only the female plant is used for hop production. Unpollinated cones are good quality raw materials, whereas using male plants, which are not needed for cone production, result in poor quality product and, hence, are not cultivated intentionally **(Matsunaga *et al*., 2000)**.

Hop plant was long recognized only for its sedative (for insomnia) and antimicrobial (beer-stabilizing) properties. More concise studies revealed that hop plant or constituting substances possess several other biological properties such as strong antioxidative action, estrogenic activity, anti-inflammatory action, and several anticarcinogenic features like apoptosis-inducing, antimetastatic, antiproliferative, anti-invasive, or antiangiogenic properties**. (Nozawa *et al*., 2005)**

The chemical composition of fresh dried hop cones, such as resins (15-30), essential oils (0.5-3%), proteins (15%), polyphenols (4%), lipids, waxes trace -25%, cellulose (43%), ash (8), moisture (10%) and amino acids (0.1%). The hop essential oils are also important to the

brewer as they provide flavour and aroma characteristics to the beer **(Roberts *et al.*, 2006)**.

This study was conducted to investigate the effect of different levels (2.5% and 5%) of grape of beers seeds, hops and their mixture as powder on nephrotoxic rats.

Material and Methods

Materials

The plant used:

Grapes of beer seeds (*Arctostaphlos uva-uris*) and hops leaves (*humulus lupulus.*) were purchased from a local market, Shebin El-Kom City, Menoufia Governorate, Egypt.

Gentamycin:

Impaired kidney can be induced in normal healthy male albino rats by intra-peritoneal injection of gentamicin (aminoglycosides antibiotics) obtained from Memphis Co. form Pharm. Chem. Ind., Cairo., A.R.E.at 10 mg/kg/day for 10 days in which the nephrotoxicity, one of the adverse reaction of gentamicin takes place.

- **Experimental animals**

A total of 48 adult normal male albino rats Sprague Dawley strain weighing 150g were obtained from Vaccine and Immunity Organization, Ministry of Health, Helwan Farm, Cairo, Egypt.

The chemical kits

Chemical kits used for determination the (TC, TG, HDL-c, ALT, AST, ALP, bilirubin, urea, creatinine and uric acid) were obtained from Al-Gomhoria for Drug, Chemicals, Medicals, Instruments Company, Cairo, Egypt.

Methods

Preparations of plants

To prepare the dried grapes seeds and hops leaves was obtained from local market, seeds and leaves were washed thoroughly under running tap water, shade dried, and ground to a fine powder using an air mill (Molunix, Al-Araby, company, Egypt).

Experimental design

Forty eight male white albino rats, Sprague Dawley Strain, 10 weeks age, weighing (150) ± 10g, were used in this experiment. All rats were fed on basal diet (casein diet) prepared according to **American**

Institute of Nutrition, AIN, (1993) for 7 consecutive days. After this adaptation period, rats are divided into 8 groups, (n=6) rats as follows:

- **Group (1):** Rats fed on basal diet as a control negative (-ve).
- **Group (2):** Rats injected intraperitoneally with (aminoglycosides antibiotics) garamycin (10 mg/kg) every 24 hr. for 10 days to induce nephrotoxicity, one of the adverse reactions takes place as a positive control group.
- **Group (3):** A group injected by gentamycin fed on basal diet and 2.5% grapes of beer seeds as powder of diet.
- **Group (4):** A group injected by gentamycin fed on basal diet and 5% grapes of beer seeds as powder of diet.
- **Group (5):** A group injected by gentamycin fed on basal diet and 2.5% hops leaves as powder of diet.
- **Group (6):** A group injected by gentamicin fed on basal diet and 5% hops leaves as powder of diet.
- **Group (7):** A group injected by gentamycin fed on basal diet and 2.5% mixture as powder of diet.
- **Group (8):** A group injected by gentamicin fed on basal diet and 5% mixture as powder of diet.

During the experimental period, the body weight and food intake were estimated weekly and the general behavior of rats was observed.

The experiment will take 28 days, at the end of the experimental period each rat weight separately then, rats are slaughtered and collect blood samples. Blood samples were centrifuged at (4000 rpm) for ten minute to separate blood serum, then kept in deep freezer till using extracting the liver, spleen and kidney.

Blood sampling

Blood samples were collected after 12 hour fasting at the end of the experiment. Using the retro-orbital method by means of a micro capillary glass tubes, blood was collected into a dry clean centrifugal tube and left to clot in a water bath (37°C) at room temperature for half an hour. The blood was centrifuged for 10 minutes at 4000 rpm to separate the serum in clean glass well stoppered and stored at and kept (-20°C) until analysis **(Schermer, 1967).**

Biochemical analysis

Lipids profile

Determination of total cholesterol

Colorimetric method for cholesterol was determined according to **Richmond, (1973)**.

Determination of serum triglycerides

Serum triglyceride was determined by enzymatic colorimetric method used to determine triglycerides according to **Young and Pestaner, (1975)**.

Determination of high density lipoprotein (HDL-c):

HDL-c was determined according to the method described by **Friedewaid (1972) and Grodon and Amer (1977)**.

Calculation of very low density lipoprotein cholesterol (VLDL-c)

VLDL-c was calculated in mg/dl according to **Lee and Nieman (1996)** using the following equation:

VLDL-c (mg/dl) = Triglycerides / 5

Calculation of low density lipoprotein cholesterol (LDL-c)

LDL-c was calculated in mg/dl according to **Lee and Nieman (1996)** as follows:

LDL-c (mg/dl) = Total cholesterol – HDL-c – VLDL-c.

Liver functions

Determination of serum alanine amino transferase (ALT), serum aspartate amino transferase (AST), according to the method of **Chawla (2003) and Srivastava *et al.*, (2002).**

Kidney functions*:*

Determination of serum urea:

Urea was determination by enzymatic method according to **Patton and Crouch (1977).**

Determination of serum creatinine:

Serum creatinine was determined according to the method described by **Henry (1974).**

Determination of serum uric acid:

Serum uric acid was determined calorimetrically according to the method of **Henry (1974).**

Determination of blood glucose:

Enzymatic determination of plasma glucose was carried out calorimetrically according to the method of **Tinder (1969).**

Statistical analysis:

Data were analyzed using a completely randomized design **(SPSS, 2010)** when a significant main effect was detected, the means were separated with the student-Newman-Keuls test. Differences between treatments of ($P \leq 0.05$) were considered significant **Wolfinger and Chang, (1995)**.

Results and Discussion

Effect of grapes of beer seeds, hops leaves and their mixtures as powder on serum total cholesterol and triglycerides of nephrotoxic rats

Data tabulated in Table (1) showed that the mean value of serum triglycerides and total cholesterol of nephrotoxic rats fed on various diets. It could be observed that the TG value of control (+) group was significantly higher than control (-) group, being 105 and 70 mg/dl, respectively.

All nephrotoxic rats fed on different diets revealed significant decrease in TG mean values as compared to control (+) group .The values were 84.5, 79, 81, 76, 74.5 and 72.5 mg/dl for 3,4,5,6,7, and 8, respectively. Numerically, the best serum Triglycerides was observed for group 8 (5% mixture powder, 72.5 mg/dl) when compared to (control positive group, 105 mg/dl).

On the other hand, the mean value of serum total cholesterol of nephrotoxic rats fed on various diets. It could be observed that the mean value of control (+) group was higher than control (-) group, being 120 and 83 mg/dl, respectively, showing significant difference as compared to control (+) group.

All nephrotoxic rats fed on different diets revealed significant decrease in mean values as compared to control (+) group. The values were 102, 94, 97, 92, 89 and 86 mg/dl for 3, 4, 5, 6, 7, and 8, respectively. Numerically, the best serum total cholesterol was observed for group 8 (5% mixture powder, 86 mg/dl) when compared to (control positive group, 246.65 mg/dl). These result are in agreement with the study by **Song *et al*., (2014)** they reported that 28 days of administration of grape seed powder was found to be capable of reducing the levels of

serum lipids (TC, TG and LDL-c) and preventing occurrences of fatty liver among rats.

Chedraui *et al.*, (2008)they reported that the hops 500 mg/kg showed significant reductions in total cholesterol , along with tendencies for reduction in the levels of TG and LDL-C. These results are similar to those observed in dyslipidemia due to estrogen reduction being alleviated by estrogen replacement therapy. Furthermore, hops flowers have been observed to have efficacy related to lipid metabolism. A clinical study reported that TC and LDL-C levels decreased during the 3-month intake of hops flower and that HDL-C levels increased after 1 year of administration .Many studies have also reported about a link between menopausal conditions and elevated blood lipid levels.

Effect of grape of beer seeds, hops leaves and their mixtures as powder on serum lipid profiles of nephrotoxic rats

Data presented in Table (2) showed that the mean value of serum high density lipoprotein of nephrotoxic rats fed on various diets. It could be concluded that the mean value of control (+) group was lower than control (-) group, being 28.5 and 45mg/dl, respectively, showing a significant difference as compared to control (+) group.

All nephrotoxic rats fed on different diets revealed a significant increase in mean values as compared to control (+) group. The values were 38.5, 40.5, 38.6, 41.5, 42.5 and 43 mg/dl for 3, 4, 5, 6, 7, and 8, respectively. Rats fed on groups 3, 4, 5 and 6 showed no significant differences ($p \leq 0.005$). Rats fed on group 7, 8 showed no significant difference ($p \leq 0.005$). Finally, the best serum high density lipoprotein was observed for group 8 (5% mixture powder, 43 mg/dl) when compared to (control positive group, 28.5 mg/dl**.**

On the other hand, the mean value of serum low density lipoprotein of nephrotoxic rats fed on various diets. It could be indicated that the mean value of control (+) group was higher than control (-) group, being 46.6 and 24 mg/dl, respectively, showing significant difference as compared to control (+) group.

All nephrotoxic rats fed on different diets revealed significant decrease in mean values as compared to control (+) group. The values were 38.6 , 40.7, 42.2, 35.3, 31.7 and 28.5 mg/dl for 3, 4, 5, 6, 7, and 8, respectively.

Rats fed on group 8 (5 % mixture powder, 28.5 mg/dl) recorded the best serum low density lipoprotein was observed for group 8 (5% mixture powder, 28.5 mg/dl) (LDL-c) when compared to (control negative group, 46.6 mg/dl).

In case of VLDL-c, the mean value of serum very low density lipoprotein of nephrotoxic rats fed on various diets. It could be observed that the mean value of control (+) group was higher than control (-) group, being 21.8 and 14 mg/dl, respectively, showing significant difference as compared to control (+) group.

All nephrotoxic rats fed on different diets revealed significant decrease in mean values as compared to control (+) group. The values were 16.9, 15.8, 16.2, 15.2, 14.8 and 14.5 mg/dl for 3, 4, 5, 6, 7, and 8, respectively.

Numerically, the better serum very low density lipoprotein (VLDL-c) was observed for group 8 (5% mixture powder, 14.5 mg/dl) when compared to (control positive group, 21.8 mg/dl). These results agreement with **(Myers *et al.*, 2009)** graps sseeds affects cholesterol by several mechanisms whereby polyphenols participate in hepatic cholesterol and lipoprotein metabolism. This mechanism works by reducing cholesterol absorption and decreasing the delivery of cholesterol to the liver, which in turn reduces plasma cholesterol. Additionally, polyphenols affect apolipoproteins (apo) A and B, which are emerging as risk factors for CVD, modify Very Low Density Lipoproteins (VLDL) particles and reduce plasma triglyceride (TG) levels due to possible increased lipoprotein lipase (LPL) activity, which leads to decreased LDL in the circulation.

Castilla *et al.*, (2008) that grape juice can have an effect on blood lipids. Studies using 100 mL/day of concentrated Bobal grape juice for 14 days shown a decrease in total cholesterol (TC), LDL-C and apo B-100 ($p < 0.001$) in 38 and 32 healthy and hemodialysis patients, whereas the HPL-C and apo A-1 values increased ($p < 0.001$) and ($p < 0.01$).

Chen and Blumbrg (2009) Polyphenols 0f hops flowers, through their antioxidant potential, improve lipid profiles, and prevent the oxidation of LDL induced by metal ions (copper and iron) or by tert-butyl hydroperoxide. However, polyphenolic substances are able to enhance the concentration of HDL cholesterol in plasma.

Effect of grapes of beer seeds, hops leaves and its mixtures on liver functions of nephrotoxic rats

Data in Table (3) revealed that the mean value of serum ALT of nephrotoxic rats fed on various diets. It could be noticed that the mean value of control (+) group was higher than control (-) group, being 55 and 28.5 U/L, respectively, showing significant difference as compared to control (+) group. All nephrotoxic rats fed on different diets revealed significant decrease in mean values as compared to control (+) group .The values were 50.5, 42, 40.5, 36, 33 and 30.7 mg/dl for 3, 4, 5, 6, 7 and 8, respectively. Rats feed on group n 4, 5 showed no significant differences ($p< 0.005$). Rats fed on group n 2, 3, 6, 7 and 8 showed very high significant differences ($p \leq 0.005$). Numerically, the best serum ALT was observed for group 8 (5% mixture powder, 30.7 U/L) when compared to (control positive group, 55 U/L).

Data in Table (3) revealed that the mean value of serum AST of nephrotoxic rats fed on various diets. It could be noticed that the mean value of control (+) group was higher than control (-) group, being 65 and 23.15 U/L, respectively, showing significant difference as compared to control (+) group. All nephrotoxic rats fed on different diets revealed significant decrease in mean values as compared to control (+) group. The values were 56.5, 52.85, 60.5, 48.5, 38.35 and 33.75 U/L for 3, 4, 5, 6, 7, and 8, respectively. Rats fed on groups 2, 3, 4, 5, 6, 7 and 8 showed very high significant differences ($p \leq 0.005$). Numerically, the best serum AST was observed for group 8 (5% mixture powder, 33.75 /L) when compared to (control positive group, 65 U/L).

Data given in Table (3) showed that the mean value of serum ALP of nephrotoxic rats fed on various diets. It could be noticed that the mean value of control (+) group was higher than control (-) group, being 62 and 28.5 mg/dl, respectively, showing significant difference as compared to control (+) group.

All nephrotoxic rats fed on different diets revealed significant decrease in mean values as compared to control (+) group. The values were 48.5 ,45 ,46 .5 , 39, 36 and 34.7 mg/dl, for 3,4,5,6,7, and 8, ,respectively .Rats fed on groupn2,3,4,5,6,7 and 8 showed very high significant differences ($p \leq 0.005$) . Numerically, the best serum ALP was observed for group 8 (5% mixture powder,34.7 mg/dl,) when compared to (control positive group,62 mg/dl,).

Also in agreement with **Dulundu *et al* (2009)** who indicated that the antioxidant effect has been described for grap seed extract (GSE) proanthocyanidins in diabetic rats and has been shown to lead to a decrease in the oxidant generation and lipid peroxidation. Also, a protective effect of GSE has been reported on reperfusion-induced injury in rats. GSE could reverse ALT, AST and histological alterations induced by the injury. The therapeutic effect of GSE was established against bile duct ligation-induced hepatic fibrosis, where oxidative stress takes place; while a 28-day administration of 50 mg/day of GSE successfully decreased ALT and AST after the damage.

Also in agree **Lieber *et al* (2003)** ment with Pre-treatment with low (0.1 mg/kg b.w.) or high (0.4 mg/kg b.w.) doses of XN significantly decreased the level of lipid peroxidation. A low XN dose decreased lipid peroxidation level by 33.5% in liver, 31.9% in kidney, 4.2% in lung, 4.9% in heart and 7.4% in brain compared with the controls, which lacked XN pre-treatment. Pre-treatment with a high dose of XN decreased the level of peroxidation, by 72.6% in liver and 50.05% in kidney, but this decrease was only 14.4% lung, 0.7% in heart and 7.2% in brain. These results suggest that pre-treatment with XN strongly reduces lipid peroxidation in tissues more affected by ROS, because the effect was not significant in tissues (lung, heart and brain) where the oxidative changes were small. The effect of binge ethanol treatment on the generation of hydrogen peroxide was studied to confirm this point.

Effect of grapes of beer seeds, hops leaves and their mixtures as powder on kidney functions of nephrotoxic rats

The mean value of serum creatinine of nephrotoxic rats fed on various diets as shown in Table (4). It could be observed that the mean value of creatinine of control (+) group was higher than control (-) group, being 64 and 26.2 mg/dl, respectively, showing significant difference as compared to control (+) group.

All nephrotoxic rats fed on different diets revealed significant decrease in mean values as compared to control (+) group. The values were 56, 54.35, 40.5, 38.10, 36.5 and 30.10 mg/dl for 3, 4, 5, 6, 7, and 8, respectively.

Rats fed on groups 3, 4 and 5, 6 showed no significant difference.rats fed on groups 2, 7, 8 significant difference . The best treatment of serum creatinine was recorded for group 8 (5% mixture

powder, 30.10 mg/dl) when compared to (control positive group, 64 mg/dl).

On the other hand, the mean value of serum uric acid of nephrotoxic rats fed on various diets. It could be noticed that the mean value of control (+) group was higher than control (-) group, being 4.30 and 2.20 mg/dl, respectively, showing significant difference as compared to control (+) group.

All nephrotoxic rats fed on different diets revealed significant decrease in mean values as compared to control (+) group. The values were 3.05, 2.54, 3, 2.70, 2.65 and 2.40 mg/dl for 3, 4, 5, 6, 7, and 8, respectively.

Rats fed on groups 3, 4, 5, 6, 7 and 8 showed very high no significant differences ($p \leq 0.05$). While, the highest uric acid level of treated group 3 recorded for group fed on 2.5% grapes of beer seeds but, the lowest value recorded for group fed on 5% plant mixture with no significant difference ($P \leq 0.05$). The mean values were 3.05 and 2.40 mg/dl, respectively.

In case of serum urea, data revealed that the mean value of serum urea of nephrotoxic rats fed on various diets. It could be noticed that the mean value of control (+) group was higher than control (-) group, being 67.05 and 30 mg/dl, respectively, showing significant difference as compared to control (+) group.

All nephrotoxic rats fed on different diets indicated significant decrease in mean values as compared to control (+) group. The values were 51.75, 44.15, 53.60, 42.38, 37.90 and 34.60 mg/dl for 3, 4, 5, 6, 7, and 8, respectively. Rats fed on groups 4, 6and 3,5 showed very high no significant differences ($P \leq 0.05$).Rats fed on group 2, 7, 8 showed very high significant differences ($p \leq 0.05$). While, the highest urea level of treated group 5 recorded for group fed on 2.5% hops leaves but, the lowest value recorded for group fed on 5% plant mixture with significant difference ($P \leq 0.05$). The mean values were 53.60 and 34.60 mg/dl, respectively.

These results in agreement with **Charradi *et al*., (2012)** who reported that the effect of a 6-month-long supplementation with GSE on some renal hemodynamic parameters of patients suffering from kidney deficiency. GSE increased 1/plasma creatinine ratio by 19.42 % and decreased proteinuria by -32.67% but had no significant effect on

plasma urea and uric acid. Moreover GSE slightly improved GFR by +18.70% (36.74 ±5.74 versus 43.62±3.68)

De Zeeuw *et al*., (2004) reported that GSE improves some kidney function parameters as it enhances GFR and clearly lowers proteinuria. This result is of utmost importance as reduction in proteinuria to the lowest achievable level is an important predictor of long term renal protection as it is increasingly recognized that proteinuria may actually be pathological and etiological in CKD progress and not just symptomatic An association between hyperuricemia and CKD in middle-aged population has also been recently described. As in our present case GSE affects both plasma, urine urea and uric acid, its clinical use could be envisaged as an uric acid-lowering therapy substitute to allopurinol.

Ohno *et al*., (2011) reported that total flavonoids of hops at 200 mg/kg significantly reduced creatinine ($P<0.01$) and serum urea nitrogen ($P\leq0.01$) compared with the hyperuricemic control group. In addition, at a dose of 100 mg/kg, hops did not affect serum creatinine, but restored the elevated serum urea nitrogen ($P\leq0.01$) in potassium oxonate-treated mice.

Pak *et al.*, (2017) reported that administration of an oral dose of 100 and 200mg/kg hops to hyperuricemic mice reduced the serum uric acid levels to 197.0±12.0 µmol/L and 246.6±26.8 µmol/L, respectively. In the same treatment, the serum uric acid levels of mice decreased to 114.6±24.7 µmol/L when allopurinol was used at a dose of 10 mg/kg.

Effect of grapes of beer seeds and hops leaves and their mixture as powder on glucose level of nephrotoxic rats.

Data presented in Table (5) showed that the mean value of serum glucose of nephrotoxic rats fed on various diets. It could be observed that the mean value of control (+) group was higher than control (-) group, being 169.75 and 100.25 mg /dl, respectively, showing a significant difference as compared to control (+) group.

All nephrotoxic rats fed on different diets revealed a significant decrease in mean values as compared to control (+) group. The mean values were 154, 148, 145.75, 135.90, 134.60 and 121.50 mg/dl for 3, 4, 5, 6, 7, and 8, respectively .

Rats fed on groups 2, 3, 4, 5, 6, 7 and 8 showed very high significant differences ($p \leq 0.05$). Numerically, the best serum glucose was observed for group 8 (5% mixture powder, 121.50 mg /dl) when

compared to (control positive group, 169.75 mg/dl). These result are in agreement with **Zern *et al*., (2005)** who reported that grape supplementation for a variable time (2-24 weeks)-provided in the form of powder, juice, or seed extracts-improved several metabolic abnormalities, significantly lowered blood pressure and reduced oxidative stress markers, i.e., oxidized LDL. With regard to glucose metabolism, a recent meta-analysis. evaluating nine clinical trials performed in patients with type 2 diabetes mellitus (DM2) demonstrated the efficacy of resveratrol in reducing fasting glucose and improving insulin sensitivity with no relevant effect on glycated hemoglobin.

Kirkwood *et al*., (2013) Nutritional approaches using phytonutrients for the prevention or treatment of type 2 diabetes mellitus (T2DM) are a rapidly emerging trend. Xanthohumol (XN) has been reported to enhance the metabolism of plasma glucose. A high (XN) is The most abundant prenylated flavonoid in hops is xanthohumol dose (16.9 mg/kg) exerted beneficial effects on body weight and glucose metabolism in obese male rats. This suggests that XN holds promise as a therapeutic agent for treating obesity and dysregulation of both glucose metabolism and the metabolic syndrome. Levels of plasma glucose, plasma, and hepatic triglyceride in KK-Ay mice decreased when fed with XN. The XN-fed mice also showed decreased amounts of water intake, lowered weights of white adipose tissue, and exhibited increased levels of plasma adiponectin.

Table (1): Effect of grapes of beer seeds, hops leaves and their mixtures as powder on serum total cholesterol and triglycerides of nephrotoxic rats

Parameters / Groups	TG (mg/dl)	TC (mg/dl)
G_1 Control (-)	70.00e ± 0.20	83.00g ± 0.10
G_2Control (+)	105.00 ^{a} ±2.21	120.00 ^{a}±1.40
G_3(2.5 %Grapes)	84.50 ^{b}±1.30	102.00 ^{b}±0.30
G_4 (5 %Grapes)	79.00 ^{c} ±0.50	94.00 ^{d} ±0.40
G_5 (2.5 %Hops)	81.00 ^{c}± 2.15	97.00 ^{c} ±0.30
G_6 (5 %hops)	76.00 ^{d}±0.60	92.00 d±0.10
G_7(2.5 % Mixture)	74.50 ^{d}±0.10	89.00 e±0.20
G_8 (5 % Mixture)	72.50 ^{e}±0.30	86.00 f±0.30
LSD ($P \leq 0.05$)	**2.60**	**2.10**

Each value is represented as mean ± standard deviation (n =6).

Mean under the same column bearing different superscript letters are different significantly ($p \leq 0.05$).

Table (2): Effect of grapes of beer, hops and their mixtures as powder on serum lipid profiles of nephrotoxic rats

Parameters / Groups	HDL-C mg/dl	LDL- C mg/dl	VLDL- C mg/dl
G_1 Control (-)	45.00 ^{a} ±1.40	24.00 ^{g}±0.11	14.00 ^{c}±0.16
G_2 Control (+)	28.50 ^{c}± 1.20	46.60 ^{a} ± 1.35	21.80 ^{a}±1.10
G_3 (2.5 %Grapes)	38.50 ^{b}±1.15	38.60 ^{c}±1.91	16.90 ^{b}±1.52
G_4 (5 %Grapes)	40.50 ^{b}±0.30	4.70 ^{b}±0.23	15.80 ^{b}± 0.10
G_5 (2.5 %Hops)	38.60 ^{b}±0.50	42.20 ^{b}±1.30	16.20 ^{b}±1.40
G_6 (5 %hops)	39.33^{d} ±1.20	35.30 ^{d}±1.12	15.20 ^{c} ±0.50
G_7(2.5 % Mixture)	42.50 ^{a}±1.50	31.70 ^{e}±1.13	14.80 ^{c}±0.20
G_8 (5 % Mixture)	43.00b ±1.00	28.50 ^{f}±1.10	14.50 ^{c}±1.20
LSD (P≤ 0.05)	3.002	3.00	1.60

Values denote arithmetic ± standard deviation of the mean (*n* =6). HDL-C= High density lipoprotein Cholesterol. LDL =Low density lipoprotein Cholesterol. High significant differences, Mean under the same column bearing different superscript letters are different significantly ($p \leq 0.05$).

Table (3): Effect of grapes of beer seeds, hops leaves and its mixtures on liver functions of nephrotoxic rats

Parameter / Groups	(ALT) U/L	(GOT) U/L	(ALP) U/L
G1 Control (-)	28.50 ^{f} ±1.10	23.15 ^{h}± 0.80	28.50 ^{f}±1.10
G2control(+)	55.00 ^{a} ±1.35	65.00 ^{a} ± 0.40	62.00 ^{a}±1.35
G3(2.5%Grapes)	50.50 ^{b}±2.05	56.50 ^{c}± 1.20	48.50 ^{b} ±2.05
G4 (5%Grapes)	42.00 ^{c}±0.60	52.85 ^{d}± 0.90	45.00 ^{c}± 0.60
G5 (2.5% hops)	40.50 ^{c} ± 1.25	60.50 ^{b}±0.50	46.50 ^{c}±1.25
G6 (5%hops)	36.00 ^{d}±0.90	48.50 ^{e}±0.60	39.00 ^{d}±0.90
G7 (2.5% Mixture)	33.00 ^{e} ±0.90	38.35 ^{f}±0.60	36.00 ^{e}±0.90
G8 (5% Mixture)	30.70 ^{f} ±0.90	33.75 ^{g}± 0.60	34.70^{e} ±0.90
LSD ($p \leq 0.05$)	**2.25**	**2.54**	**2.01**

Each value is represented as mean ± standard deviation (*n* =6).
Mean under the same column bearing different superscript letters are different significantly ($p \leq 0.05$).

Table (4): Effect of grapes of beer seeds, hops leaves and their mixtures as powder on kidney functions of nephrotoxic rats

Parameter / Groups	Creatinine	Uric acid mg/dl	Urea mg/dl
G1 Control (-)	26.20 ^{f} ± 0.40	2.20 ^{b}± 0.30	30.00 ^{f} ±1.20
G2control(+)	64.00 ^{a}± 0.60	4.30 ^{a}± 0.10	67.50 ^{a}±0.30
G3(2.5%Grapes)	56.00 b±4.04	3.5 ^{b}±0.30	51.75 ^{b}±0.50
G4 (5%Grapes)	54.35 ± 1.30	2.54 ^{b}± 0.40	44.15 ^{c}± 0.40
G5 (2.5%Hops)	40.50 ^{c}±1.30	3.00 ^{b}± 0.40	53.60 ^{b}±0.50
G6 (5%Hops)	38.10 ^{c}±1.20	2.70 ^{b}±1.50	42.38 ^{c}±0.30
G7 (2.5% Mixture)	36.50 ^{d}±1.10	2.65 ^{b}±1.40	37.90 ^{d}±0.50
G8 (5% Mixture)	30.10 ^{e}±1.30	2.40 ^{b}±1.30	34.60 ^{e}±000.8
LSD (P ≤ 0.05)	**3.13**	**1.21**	**3.00**

Each value is represented as mean ± standard deviation (n =6).
Mean under the same column bearing different superscript letters are different significantly (p ≤ 0.05).

Table (5): Effect of grapes of beer seeds, hops leaves and their mixture as powder on glucose level of nephrotoxic rats

Parameters / Groups	Glucose mg/dl
Control (-)	100.25 ^{f} ± 0.10
G2 Control (+)	169.75 ^{a} ±1.10
G3(2.5%Grapes of beer)	154.00 ^{b}±0.40
G4 (5%Grapes of beer)	148.00 ^{b}±0.30
G5 (2.5%Hops)	145.75 ^{b}±0.50
G6 (5%Hops)	135.90 ^{c}±0.10
G7 (2.5% Mixture)	134.60 ^{d} ±0.50
G8 (5% Mixture)	121.50 ^{e} ±0.20
LSD (P≤ 0.05)	**3.20**

Each value is represented as mean ± standard deviation (n =6).
Mean under the same column bearing different superscript letters are different significantly (P ≤ 0.05).

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التأثير المحتمل لبذور عنب الدب واوراق حشيشه الدينار فى علاج الخلل الحادث فى وظائف الكلى فى الفئران المصابة بالفشل الكلوي

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الملخص العربي

أجريت هذه الدراسة لمعرفه تأثير مسحوق بذور عنب الدب وأوراق حشيشة الدينار بالتركيزات المختلفة 2,5، 5% علي الفئران المصابة بالفشل الكلوى. تم استخدام 48 فأر من النوع الألبينو تتراوح أوزانهم بين 150±10جم تم تقسيمهم إلى 8 مجموعات واعتبرت واحدة منهم مجموعة ضابطة سالبة سليمة. والـ 7 مجاميع الأخرى تم حقنهم بماده جينتاميسين (10مجم/كجم من وزن الجسم) وذلك لإحداث الإصابة بالفشل الكلوى. مجموعة واحدة منهم تغذت علي الغذاء القياسي دون أي إضافات (المجموعة الضابطة الموجبة) وبقية المجاميع تغذت علي الغذاء الأساسي مضاف له التركيزات المختلفة من مسحوق بذور عنب الدب وأوراق حشيشة الدينار وخليطهما معا. وبعد انتهاء مده التجربة (28 يوم) تم تشريح الفئران وتجميع عينات الدم وتم عمل التحاليل اللازمة عن طريق تقدير مستوى السكر فى الدم وإنزيمات الكبد(انزيمات ناقله امين الالانين وانزيمات ناقله الامين الاسبارتات وانزيمات ناقله للفوسفات القلوى) وانزيمات الكلى (الكرياتنين وحمض اليورك واليوريا) ودهون الدم (الكوليستيرول الكلى والجليسريدات الثلاثيه والكوليستيرول عالى الكثافه والكوليستيرول منخفض الكثافه والكوليسترول منخفض الكثافه جدا) وأشارت النتائج المتحصل عليها إلى أن بذور عنب الدب واوراق حشيشة الدينار وخليطها معا ادوا إلى حدوث تحسن معنوياً في صورة دهون الدم ووظائف الكلى والكبد ومستوى الجلوكوز وخاصة مخلوطهما معا بتركيز 5%.

في الختام: يمكن اعتبار بذور عنب الدب وأوراق حشيشة الدينار ومزيجهم من الوسائل العلاجية القوية للتغذية في علاج الفئران المصابة بالفشل الكلوى.

الكلمات الكاشفة: الفئران، الأعشاب، الفشل الكلوى، التحاليل الكيميائية الحيوية.