Evaluation of Therapeutic Effect of Cantaloupe, Grape and Pumpkin Seeds on Cisplatin-Induced Nephrotoxicity in Rats

[1]Ereny Wilson Nagib, and [2]Nareman S. Eshak
[1]Home Economics Department, Faculty of Specific Education, Ain Shams University, Egypt.
[2]Home Economics Department, Faculty of Specific Education, Assiut University, Egypt.
Correspondence: e-mail: nariman_saeed@aun.edu.eg, Fax: 002 0882143536

مجلة البحوث في مجالات التربية النوعية

معرف البحث الرقمي DOI: 10.21608/jedu.2022.123367.1608

المجلد الثامن العدد 43 . نوفمبر 2022

الترقيم الدولي

P-ISSN: 1687-3424 E- ISSN: 2735-3346

موقع المجلة عبر بنك المعرفة المصري https://jedu.journals.ekb.eg/

موقع المجلة http://jrfse.minia.edu.eg/Hom

العنوان: كلية التربية النوعية . جامعة المنيا . جمهورية مصر العربية

Evaluation of Therapeutic Effect of Cantaloupe, Grape and Pumpkin Seeds on Cisplatin-Induced Nephrotoxicity in Rats

[1]Ereny Wilson Nagib, and [2]Nareman S. Eshak

[1]Home Economics Department, Faculty of Specific Education, Ain Shams University, Egypt.

[2]Home Economics Department, Faculty of Specific Education, Assiut University, Egypt.

Abstract

Cisplatin is a chemotherapeutic drug used to treat cancer patients. The main secondary effect results from Cisplatin treatment is nephrotoxicity. The objective of this study was to evaluate the possible therapeutic effect of cantaloupe, grape, and pumpkin seeds on Cisplatin induced nephrotoxicity in rats. **Materials and Methods**: forty two rats were randomly assigned (7/group). **G1**, (-ve) control, **G2**, (+ve) control rats were injected with Cisplatin (6 mg/kg body weight) for one time, **G3,4,5,6** rats injected and were received 7.5% of (cantaloupe, grape, and pumpkin seeds) or a mixture of all, respectively. Blood samples were collected, and the renal tissues of the rats were removed. Biological analyses were calculated. **Results**: injected Cisplatin in rats increased levels of plasma cholesterol (TC), triglycerides (TG), Very low-density lipoprotein cholesterol (VLDL), (LDL), and decrease high-density lipoprotein (HDL), and caused abnormal renal functions. For the treated groups, body weight gain (BWG), food intake (FI), and feed efficiency ratio (FER) and also histological changes improved for seeds diets groups. Serum creatinine, urea, uric acid, and nitric oxide concentrations were significantly increased at ($P<0.5$) in (+ve) group compared to the (-ve) group, while albumin was significantly lower at ($P<0.5$), in contrast to the treated groups with seeds.

Key Words: fruit seeds, renal dysfunction, lipid profile, body weight gain.

Introduction:

The kidney is a vital organ in the body. The kidneys are located on the right and left sides behind the abdominal cavity in the shape of a bean. The kidneys perform many functions of the body such as excretion, filtration, homeostasis, maintaining electrolyte balance, detoxification, and release of harmful metabolites and drugs. Several clinical conditions lead to kidney damage **(World Kidney Day, 2015).** The Kidney involves different cell types sifted through into the nephron, which is the basic utilitarian unit of the kidney. Any elevation that results in the loss of these cells can cause kidney damage and lead to renal failure **(Barnett & Cummings, 2018).** The severe damage to the kidneys subsequently leads to the death of individuals. About 10% of the world's population is affected by chronic kidney disease (CKD), and millions die each year because they cannot get affordable treatment **(World Kidney Day, 2015).** Based on the prevalence of kidney disease in Egypt of 366 per million according to **El Arbagy et al. (2016)** considering that the population of Egypt is 90,000,000. According to **Abbas et al. (2020)** the prevalence of kidney disease among Egyptians was estimated at 21, 65%.

Xenobiotics, for example, cisplatin, are currently known to exert harmful impacts by means of free radical-mediated mechanisms. Cisplatin is a chemotherapy medication used to treat patients with several cancers such as bladder, ovarian, head, neck, lung, testicular, cervical, and esophageal **(Michel and Menze, 2019).** The administration of cisplatin is largely controlled in patients with cancer due to its association with various side effects. Acute kidney injury (AKI) is the foremost severe side effect of cisplatin-induced toxicity because high doses of cisplatin are linked to nephrotoxicity **(Singh et al., 2018).**

In recent years, seeds and nuts have received growing attention due to the high nutraceutical and therapeutic value of their bioactive components **(Rezig et al., 2019).** The ability of some of these indigenous vegetables and fruits to provide and maintain good health for us at relatively cheaper costs and availability spurs and generates interest. Medicinal plants have been used as traditional and indigenous drugs for ages **(Ratnam et al., 2017).** World Health Organization (WHO) has moreover endorsed the beginning of studies to recognize and portray new herbal preparations from locally known plants and the headway of new dynamic therapeutic agents **(Yadav et al., 2017).** Universally, 80% of the total populace is assessed to only depend on plants and plant products for example cantaloupe, grape, and pumpkin) seeds as sources of medication **(Ogbera et al., 2010).**

Cantaloupe (*Cucumis melo var. cantalupensis*) seeds contain various vitamins, minerals, and unsaturated fats. It contains vitamin C, fiber, carbohydrate, potassium, sodium, calcium, phosphorus, iron, niacin, protein, polyunsaturated fat, and absolutely a lot of water. It also has high beta-carotene; it can fight free radicals and completely prevent cancer and tumors. This is recommended mainly in the case of anemia, atherosclerosis, gout, rheumatism, cardiovascular, kidney, and liver diseases **(Ivanova, 2012).** Therapeutic effects are present in cantaloupe seeds including analgesic, anti-inflammatory, and anti-oxidant effects **(Chen et al., 2014).**

Grape (*Vitis vinifera* Linn.) seeds are treated as waste if the extracts are not manufactured and it is determined that nearly 10–12 kg of grape seeds in 100 kg of wet residues **(Matthaus, 2008).** Grape seed is a complex mixture of polyphenols containing flavonoids, and proanthocyanidins that display multi-organ protection **(Turki et al., 2016).** Grape seeds are a relatively cheap source of antioxidant compounds; its proportion is 38–52% on a dry matter basis **(Cadiz-Gurrea et al., 2017)**. Procyanidins are the most common flavonoids present in grapes. Grape seed proanthocyanidin extract (GSPE) is rich in polyphenols which play an important role as a metabolic regulator and reactive oxidative species (ROS) scavenger **(Gil-Cardoso et al., 2017).** GSPE significantly protects against oxidative stress damage more effectively than vitamins C, E, and beta-carotene **(Hassan et al, 2013).** In recent years, grape seed has become increasingly popular on the market as a nutritional supplement **(Yamakoshi et**

al., 2002). High dosage was even shown to improve renal injury in rats through its anti-oxidant and anti-inflammatory properties **(Bao et al., 2015).**

Pumpkin (*Cucurbita maxima*) seeds are largely considered agro-industrial waste **(Amin et al., 2019),** they serve as energy sources for nutrients with interesting nutritional properties (**Abou-Zeid et al., 2018).** The seeds are green consumable seeds that are rich in nutty flavor. Pumpkin seeds are a nutritional treasure as they are a robust source of good quality fat, carbohydrates, minerals, protein, fibers, various antioxidants, and other phytochemical compounds **(Yu et al, 2021)**. Past investigations revealed that the seed has been used in customary medicine for the treatment of infections, including, diabetes, hypertension, kidney, and urinary issue **(Ratnam et al., 2017; Yadav et al., 2017).**

Therefore, the present study aimed to evaluate the possible therapeutic effects of cantaloupe, grape, and pumpkin seeds on Cisplatin-induced nephrotoxicity in adult male rats.

Materials and Methods

Materials

Chemicals:

Cis–diammine dichloride platinum and kits for biochemical analysis were purchased from Sigma- Aldrich Chemical Company, Cairo Governorate, Egypt.

Samples of seeds:

Cantaloupe, grape, and pumpkin seeds were purchased from the Agriculture Research Centre, Cairo, Egypt.

Methods

Preparation of cantaloupe, grape, and pumpkin seeds powder:

Cantaloupe, grape, and pumpkin seeds were cleaned to remove all impurities, washed, and dried in a drying oven at temperature 50°C for 3 days. The seeds were milled into a fine powder using a laboratory mill (LM 120 Perten Instruments, USA) **(Nahed et al.,**

2020). The ground powder sieves on a 355 mesh sieve. The powder was packed in polyethylene bags and stored at ambient temperature until use **(Anju et al., 2018).**

Experimental diet

The basal diet was purchased from Al-Gomhorya Company (Cairo, Egypt). It consists of casein 14%, corn seed oil 10%, salt mixture 3.5%, vitamin mixture 1%, corn starch 56.7%, sucrose 10%, fiber 5%, and choline chloride 0.25% according to **Reeves et al., (1993)**

Experimental animals

Forty-two adult male Sprague- Dawley albino rats weighing (190±10)g were obtained from National Research Center in Giza-Cairo. The rats were acclimated for a week prior to enrollment in the study. They were placed in a controlled room at 23 ± 2^{o}C, with a humidity of 60±5%, and a 12-hour light-dark cycle without any stressful stimuli. All rats were housed individually in metallic cages under healthy environmental conditions and had free access to water and a standard diet. The experimental protocols were approved by the Animal-Humane ethics committee of the National Institute of Nutrition in Cairo.

Chemical analysis

Proximate analysis was carried out to assess moisture, protein, fat, ash, and fiber content of cantaloupe, grape, and pumpkin seeds were performed using the standard methods of the Association of Official Analytical Chemists **(AOAC, 2005).** The proximate analysis was performed in triplicate to obtain a mean value of all nutrients.

Carbohydrate content was calculated by the by difference:

Carbohydrate content (%) = 100 − (Moisture% + Fat% + Protein% + Ash% + Fiber %)

Phytochemicals analysis

- **Determination of total phenolic content**

The total phenolic content (TPC) of cantaloupe, grape, and pumpkin seeds was determined using the Folin-Ciocalteu's method in **Bhalodia et al., (2011)**. The unknown sample concentration was determined in terms of mg GAE/g.

- **Determination of DPPH activity**

The antioxidant activity of extracts was calculated in terms of DPPH (2,2-diphenyl-1-picryl-hydrazin-hydrate) activity using the method of **Saavedra et al., (2015).**

Induction of renal dysfunction:

Cis-Diammine Dichloride Platinum (CDDP) has been used to induce renal dysfunction. Thirty-five rats were injected intraperitoneally with a single dose of Cis-Diammine Dichloride Platinum (6 mg/kg body weight for one time) was dissolved in physiological saline solution (1mg/ml) within 1hour before injection according to **(Iseri et al., 2007 and Liu et al., 2017).**

Experimental protocol

The rats were assigned randomly into 6 equal groups (7 rats per group). **Group 1**, untreated rats (the negative control group) rats were fed on a basal diet for 6 weeks, **Group 2**, (the positive control group) rats were injected with Cis-Diammine Dichloride Platinum (6 mg/kg body weight) for one time according to **Liu et al., (2017),** and were fed on a basal diet for 6 weeks, **Group 3,** Rats were injected with Cisplatine (6 mg/kg body weight) and received 7.5% cantaloupe seeds (**Mohammed et al., 2015)** for 6 weeks, **Group 4,** Rats were injected with Cisplatine (6 mg/kg body weight) and received 7.5% grape seeds for 6 weeks, **Group 5,** Rats were injected with Cisplatine (6 mg/kg body weight) and received pumpkin seeds for 6 weeks, **Group 6** Rats were injected with Cisplatine (6 mg/kg body weight) and received 7.5% a mixed dose of cantaloupe, grape, and pumpkin seeds for 6 weeks. 7.5% of cantaloupe, grape, and pumpkin seeds were added instead of corn starch. The rats were weighed on the first day of the experiment and at the end of the experiment. They were housed individually in cylindrical wire cages.

Body weight gain (B.W.G %)

The body weight of each rat was measured by a weighing scale of electronic digital balance with an accuracy of 0.1 gram (Pushton, Henan, China), and recorded at the beginning, twice weekly in the first four weeks, and then once weekly in the following two weeks. The total diet consumed per group during the period of the experiment was calculated by subtracting the diet remaining for each at the end of the interval of weighing from that allocated to the rats at the start of the interval of all groups feed wastage was subtracted from that allocated to the rats.

Organs weight

The organs (liver–kidney) were excised, rinsed in chilled saline solution, then blotted on filter paper, and weighed separately to calculate the absolute and relative organs weight **(Li et al., 2021)**.

Collection of blood samples:

At the end of the treatment period of 6 weeks, animals were fasted for 12-16 hours and were sacrificed under light diethyl ether anesthesia. Blood samples were collected in heparinized tubes from the hepatic portal vein by cardiac puncture. Blood was centrifuged at 3500 r.p.m. for 15 min. (was used for serum preparation and the prepared serum was stored at -20°C) for various biochemical analyses **(Moke et al., 2015).**

Biological studies:

Food intake, body weight gain% (BWG %), feed efficiency ratio (FER) according to **Chapman et al. (1959)** Using the following equation.

$$BWG\ \% = \frac{\text{Final weight- Initial weight}}{\text{Initial weight}} \times 100$$

$$FER = \frac{\text{The gain in body weight (g/day)}}{\text{Food Intake (g/day)}} \times 100$$

$$\text{The relative weight of organs as a \%} = \frac{\text{Organs weight}}{\text{Animal body weight}} \times 100$$

Biochemical analysis:

Serum was used to estimate total cholesterol (TC) and high-density lipoprotein (HDL) were determined according to the colorimetric method described by **MacLachlan et al., (2000).** Total lipid was evaluated by method **Knight et al., (1972).** Determination of triglycerides (TG) in serum was done by using a Cayman colorimetric assay kit **(Cole et al., 1997).** Serum low-density lipoprotein (LDL) was calculated from the values of (TC), HDL, and triglycerides using Friedewald equation: LDL (mg/dl) = TC – (HDL-c + TG/5) **(Ahmadi et al., 2008).** Very low-density lipoprotein cholesterol (VLDL) was determined by method **Friedewald et al., (1972).** Serum nitric oxide (NO) was evaluated by nitrite reeducates method using Total Nitric Oxide Kit (Beyotime, Haimen, China, S0023) **(Cortas and Wakid, 1990).** Uric acid was determined by method **Fossati et al., (1980).** Serum urea was measured according to the modified Berthelot - Searcy method **Henry, (1991).** Serum creatinine activity was determined using the application of the Jafe reaction **(Wilson and Walker, 2000).** Albumin was evaluated by method **Doumas et al., (1971).**

Histological analysis:

After taking the blood samples, an abdominal incision was made and the kidneys were separated from the adipose tissue surrounding them. The kidney specimens were immersed rapidly in neutral buffered formalin for 36 hours. The fixed specimens were trimmed and dehydrated in ascending grades of ethyl alcohol, cleared in xylene, finally embedded in paraffin wax. Sections were cut using a microtome (4-6) microns (um) thickness and stained with Hematoxylin and Eosin (H&E) for examining microscopically **(Akomolafe et al., 2020).** The following scoring system was used for the histopathological assessment of tissues under light microscopy: 0 = normal kidney, 1 = minor injury (0–5%), 2 = moderate injury (5–25%), 3 = moderate injury (25–75%), and 4 = severe injury (75–100%) **(Colbay et al., 2010)**.

Statistical analysis

The obtained data of biological evaluations were statistically analyzed and were expressed as mean ± standard deviation, and comparison was done using one-way analysis of variance and Duncan's multiple range tests. Significant differences between different groups were accepted at $p \leq .05$ (**Snedecor and Cochran, (1967).**

Results and Discussion

Table (1): Gross chemical composition of cantaloupe, grape, and pumpkin seeds (% on DWT)*

Types of Seeds	Moisture %	Protein %	Fat %	Ash %	Fiber %	Carbohydrate %
Cantaloupe seeds	5.95 ^{b}± 0.27	20.31 ^{a}± 1.36	29.21 ^{a}± 1.47	3.14 ^{b}± 0.17	28.10 ^{a}± 0.88	13.29 ^{b}±0.77
Grapes seeds	9.91 ^{b}± 0.29	11.41 ^{b}± 1.37	16.71 ^{b}± 1.49	2.93 ^{bc}± 0.19	33.38 ^{a}± 0.50	25.66 ^{a}± 0.89
Pumpkin seeds	6.97 ^{b}± 0.28	28.40 ^{a}± 1.38	29.33 ^{a}± 1.48	4.40 ^{b}± 0.18	18.26 ^{a}± 0.89	13.36 ^{b}± 0.79

* dwt basis= dry weight basis   Each value is expressed as the mean± SD (n=3)
Means in the same column with different letters are significantly different at P≤ 0.05

The mean values for the chemical composition of cantaloupe, grape, and pumpkin seeds are tabulated in **Table (1)**. Moisture content was found in the range of 5.95-9.91% for seeds. Hence the low moisture content of seeds indicates their stability against microbial attack and potential longer shelf life **(Nishant and Neeraj, 2018)**. The protein content was low in grape seeds, followed by, cantaloupe and pumpkin seeds. The fat content in seeds ranged from 16.71 to 35.33%. The high-fat content of seeds makes them valuable for their use as a vibrant commercial source of edible oil **(Arunima and Vivek, 2021)**. Ash content of a food product is an index to the nutritive value (mineral content, safety, and quality) **(Agoreyo et al., 2011)**. The ash content of seeds varied from 2.93-4.40. Dietary fiber plays several roles including increasing the shelf life of food products **(Kurek and Wyrwisz, 2015)**. According to **(Schneeman, 2002)** crude fiber contributes to a healthy digestive and metabolic system in human. Carbohydrate values were 13.29, 22.66, and 22.54 in cantaloupe, grape, and pumpkin seeds respectively. The high carbohydrate content that the samples indicate is a good source of energy for the body.

Hence, nutritionists can recommend the application of dried foods into energy foods **(Sultana et al., 2015).** The results in the present study are consistent with the previous observations of **(Ren et al., 2013)** for cantaloupe seeds, **Hanaa et al., (2015)** for grape seeds, and **Arunima and Vivek (2021) and Krimer, (2020)** for pumpkin seeds.

Table (2): Total phenolic compounds and antioxidant activity of cantaloupe, grape, and pumpkin seeds (% on DWT)*

Types of Seeds	Total phenolic (mg GAE/g)	Antioxidant activity (DPPH)
Cantaloupe seeds	51 ^{a}± 0.67	14 ^{a}± 0.47
Grapes seeds	59 ^{a}± 0.34	21 ^{a}± 0.44
Pumpkin seeds	50 ^{a}± 0.39	13 ^{a}± 0.41

* dwt basis= dry weight basis Each value is expressed as the mean± SD (n=3)
Means in the same column with different letters are significantly different at P≤ 0.05

In the present study, the total phenolic and antioxidant activity of cantaloupe, grape, and pumpkin seeds were shown in **Table (2).** This study has demonstrated that the total phenolic compounds in seeds ranged from 50- 95(mg GAE/g)**.** The value of total phenolic compounds is closed to those reported by **Rababah et al., (2008)** who found that the total phenols of different grape seed cultivars extract ranged from 4.66 to 5.12g/100g. Grape seeds are richer in phenols than skins or pulp **(Canals et al., 2008)**. It was well known that phenolic acids act as antioxidants not only because they are able to donate hydrogen or electrons but also, stable radical intermediates, which prevent oxidation of various food components, especially fatty acids and oils **(Hanaa et al., 2015).** Seeds showed a slight difference in antioxidant activity with the maximum value for the grape seeds (21) and the minimum value for the pumpkin seeds (13). Antioxidants and total phenolic compounds act as non-enzymatic antioxidants that essentially help in eradicating. Reactive oxygen species (ROS) benefit plants as well as human health **(Kiani et al., 2021).** These results are in agreement with the results of **Akomolafe et al. (2020)** who reported TPC 32.90 mg GAE/g in the pumpkin seeds.

Table (3): Effect of feeding cantaloupe, grape, and pumpkin seeds on body weight gain (B.W.G%), feed intake (FI), and feed efficiency ratio (FER) of Cisplatin injected rats

Groups	Initial body weight (g)	Final body weight (g)	Body weight gain (g)	B.W.G %	Feed intake(g) (FI)	Feed efficiency ratio (FER)
Group1 Control (-ve)	194[a] ±1.32	262[a] ±2.71	68[a] ±11.13	35.05 [a]± 0.18	714[a] ±31.84	0.095[a]± 0.002
Group2 Control (+ve)	193 [a] ±1.75	237[c] ±2.04	44[c] ±4.45	22.79 [b]± 0.838	588[c] ±55.82	0.075[c]± 0.001
Group 3	191 [a] ±3.82	241[bc] ±1.05	50[bc] ±6.09	26.18[b]± 1.019	627[b] ±21.78	0.079[c]± 0.001
Group 4	191 [a] ±4.03	244[bc] ±7.24	53[bc] ±3.52	27.75[b]± 0.793	630[b] ±61.36	0.084 [bc]± 0.001
Group 5	192 [a] ±3.9	250[b] ±7.18	58[b] ±4.51	30.21[a] ± 0.862	672[b] ±42.45	0.086[b]± 0.002
Group 6	193 [a] ±6.62	252[b] ±5.96	59[b] ±1.34	30.57[a] ± 1.039	673[b] ±43.75	0.088[b]± 0.003

Means in the same column with different letters are significantly different at P≤ 0.05

Data presented in **Table 3** showed that there was a significant ($p \leq .05$) reduction in the B.W.G of cisplatin-induced nephrotoxic untreated group (+ve) when compared with normal control (-ve) or treated groups with different seeds (3, 4, 5, and 6). It could be noticed that there is no significant difference between the values of B.W.G on groups 3, 4. Also, there is no significant difference between groups 5 and 6. Group 6 recorded the best result of all treatments as compared to the (+ve) group. This is in simultaneousness by **Nematbakhsh et al., (2013)** who found that Cisplatin-incited nephrotoxic untreated rodents exhibited tremendous decreases in body weight and augmentations in kidney/body weight proportion when appeared differently in relation to the control group. The decrease in body weight observed in cisplatin-induced nephrotoxic untreated rats may be due to a decrease in urine concentrating ability secondary to a decrease in the papillary hypertonicity as reported by some researchers. Grape, cantaloupe, pumpkin seeds, and a mixture of all seeds administration had apparent therapeutic effects on body weight and kidney/body weight proportion in comparison with cisplatin-induced nephrotoxic untreated rats. Data presented in the same **Table 3** illustrate that control (+ve) had FI (588 ±55.82g). There was a difference significantly ($P<0.05$) between control (+ve) and normal rats control (-ve). Also, the mean values of groups 3, 4, 5, and 6 were significantly higher than control (+ve) which were 627±21.78, 630±61.36, 672 ±42.45, and 673±43.75 respectively. There is no significant difference between the 3, 4, 5, and 6 groups in FI. It is clear from **Table 3** that group 6 had a significantly higher mean value ±SD of FER than control **(+ve)** and all treatment groups (3, 4, 5, and 6). The obtained results are in the same trend as **Bakr, (2009), Shehata, (2012), Riad, (2014), and Elbanna, (2014)** for hepatic rats. Also, **Abd El-Meged and Al-Shehri (2020), and Mohammed et al., (2015)** found in hepatic rats a gradual increase in relative BWG, FI, and FER when feeding on cantaloupe, and pumpkin seeds.

Table (4): Effect of feeding cantaloupe, grape, and pumpkin seeds on liver and kidney weight of rats

Groups	Liver weight (g)	Kidney weight (g)
Group1 Control (-ve)	3.26[b] ±0.47	0.98 [b] ±0.07
Group2 Control (+ve)	4.04[a] ±0.06	1.57 [a] ±0.21
Group 3	3.87[a] ±0.66	1.31 [a] ±0.25
Group 4	3.98[a] ±0.37	1.17 [a] ±0.25
Group 5	3.77[a] ±0.22	1.1 [a] ±0.05
Group 6	3.56[b] ±0.48	0.99 [b] ±0.33

Means in the same column with different letters are significantly different at $P \leq 0.05$

It could be noticed in **Table (4)** that, in the cisplatin-induced nephrotoxic untreated group, there was a significant (P≤.05) increase in the liver and kidney weight in comparison with the control (-ve) group. However, the feeding on cantaloupe, grape, and pumpkin seeds inclusive diet prevented this effect of cisplatin by significantly (P≤.05) decreased kidney weights in comparison with the cisplatin-induced nephrotoxic untreated group, though the decrease was not up to the control level. Nevertheless, there was no statistical difference between the rats in groups (+ve, 3, 4, 5). Also, there was no statistical difference between the rats in group 6 compared to the control (-ve) group. The rise in kidney weight proportion showed that the kidneys of cisplatin-induced nephrotoxic untreated rats were harmed **(Lin et al., 2018)**. It has been reported that toxic kidneys gain weight as the damage increases **(Haghighi et al., 2012).** These results are in agreement with those reported by **Riad (2014), and Elbanna (2014)** who found in hepatic rats that an increase in all organs weight increased, while treatment with tested plants reversed such a change.

Date presented in **Table (5)** showed that injection of Cisplatin led to a significant ($P<0.05$) increase in (TC), (VLDL), (LDL), (TG), and (TL) and a significant ($P<0.05$) decrease in (HDL) in rats. Feeding by cantaloupe, grape, pumpkin seeds and a mixture of all seeds significantly decreased the (TC), (VLDL), (LDL), (TG), and (TL) but significantly increased (HDL) when compared to (+ve) control rats. These results are in agreement with those reported by **Zamani et al., (2007)** who found in hyperlipidemic New Zealand rabbits that the pulp and the seeds of *Citrullus colocynthis* were assessed for their effects on the lipid profile. In the treated groups (3, 4, 5, 6), lipid profiles were significantly decreased when compared to the control group ($P<0.05$). These results are in agreement with those reported by **Talabani and Tofiq (2012)**, who found a significant drop in serum total cholesterol and triglyceride observed at 120 h after the first administration of colocynth seeds oil. The present results are also in agreement with **Nicolle et al., (2003)** concluded that pumpkin seeds consumption modifies cholesterol absorption and these effects could be interesting for cardiovascular protection. Also, he showed that feeding the pumpkin seeds diet resulted in a decrease of cholesterol and triglycerides in plasma in animals fed on cholesterol-supplemented diets.

Table (5): Effect of feeding cantaloupe, grape, and pumpkin seeds on total cholesterol (TC), very Low-Density Lipoprotein Cholesterol (VLDL-c), Low-Density Lipoprotein Cholesterol (LDL-c), High-Density Lipoprotein Cholesterol (HDL-c), triglycerides (TG), and Total lipids (TL) of Cisplatin injected rats

Groups	TC (mg/dl)	vLDL (mg/dl)	LDL(mg/dl)	HDL(mg/dl)	TG (mg/dl)	TL (mg/dl)
Group 1 Control (-ve)	88.99[c] ±5.09	14.92[bc]±0.56	22.40[bc]±4.79	53.93[a]±1.12	72.93[c]±2.11	309.91[c] ±2.60
Group 2 Control (+ve)	139.78[a]±2.85	27.98[a] ±0.85	58.69[a] ±3.82	51.69[b]±1.17	146.07[a]±4.91	444.49 [a] ±3.12
Group 3	95.09 [b] ±3.87	17.40[b] ±0.68	24.60[b] ±2.13	53.44[a]±1.60	86.01 [b] ±5.03	316.80[b]±31.07
Group 4	93.44 [b] ±2.51	16.23[b] ±0.52	23.97[b] ±4.42	53.96[a]±1.01	85.7.0[b]±3.00	313.53[b]±34.36
Group 5	94.99 [b] ±4.8	17.59[b] ±1.13	24.57[b] ±4.04	53.67[a]±0.94	86.99 [b] ±3.95	317.00 [b] ±3.51
Group 6	91.16 [b] ±2.4	15.06[b] ±1.07	22.10[bc]±4.98	53.61[a]±0.97	78.07[bc]±2.51	312.19[bc]±4.31

Means in the same column with different letters are significantly different at $P \leq 0.05$

Data were presented in **Table 6** showed that intraperitoneal administration of cisplatin prompted renal harm in the untreated group as appeared by significant (P<0.05) ascent in serum creatinine, urea, uric acid, and nitric oxide levels just as significant (P<0.05) decline in serum albumin levels in contrast with the control (+ve) group. Feeding by cantaloupe, grape, pumpkin seeds, and a mixture of all seeds significantly reduced these concentrations in (3, 4, 5, 6) groups compared with the control (+ve) nephrotoxic group. Creatinine, synthesized in the liver, passes into the circulation where it is taken up almost entirely by the skeletal muscles. Its retention in the blood is evidence of kidney impairment. Therefore, the reduced levels of creatinine in serum may imply that the seed mixture had interfered with creatinine metabolism and its eventual excretion from the blood. Urea is the main product of protein catabolism. The increase in serum urea level in the cisplatin group indicates impairment in the normal kidney function of the animal, as the mechanism of removing it from the blood might have been affected. It may also be an indication of dysfunction at the glomerular and tubular levels of the kidney **(Barakat, 2011).**

Table (6): Effect of feeding cantaloupe, grape, and pumpkin seeds on renal function tests in serum

Groups	Albumin (mg/dl)	Creatinine (mg/dl)	Urea (mg/dl)	Uric acid (mg/dl)	Nitric oxide (mg/dl)
Group 1 Control (-ve)	3.12^{a} ±0.98	0.52^{b}±0.88	18.99^{c}±1.94	1.55^{b}±0.18	11.97^{bc}±0.89
Group 2 Control (+ve)	2.38^{b}±0.41	1.95^{a}±0.27	29.17^{a}±1.16	2.93^{a}±0.18	27.50^{a} ±1.84
Group 3	3.06^{a} ±0.58	0.73^{b}±0.22	21.07^{b}±0.51	1.62^{b}±0.41	13.26^{b} ±1.00
Group 4	3.09^{a} ±0.32	0.69^{b}±0.09	20.36^{b}±0.42	1.61^{b}±0.33	13.10^{b} ±0.84
Group 5	3.05^{a} ±0.27	0.74^{b}±0.09	21.21^{b}±0.30	1.63^{b}±0.16	13.81^{b} ±1.43
Group 6	3.10^{a} ±0.46	0.68^{b}±0.91	19.19^{bc}±0.33	1.58^{b}±0.14	13.04^{b} ±3.32

Means in the same column with different letters are significantly different at $P \leq 0.05$

These results in **Table 6** agree with that reported by **Abd Elwahab, (2021)** who reported that there was a trend in lower levels of rising in serum creatinine and urea after treatment with grape, guava seeds extract, and a mixture of both. Increased levels of serum urea, creatinine which usually occurs in certain forms of infection and in chemical toxicity sufficient result in the glomerular filtration are significantly indicated by compromising renal function **(Yadav et al., 2016).** The increase in the level of urea and creatinine in serum as observed in cisplatin-induced untreated rats in this study suggests compromised functional integrity of the kidney. Hypoalbuminemia is a strong predictor of death in patients with renal failure as it is the most abundant protein in renal urine. Patients with lower serum albumin levels have consistently higher morbidity rates **(Viswanathan et al., 2004).** The significant decrease in serum albumin in untreated rats induced by cisplatin also indicated renal impairment. However, pretreatment with the dietary inclusion of pumpkin seeds inhibits the nephrotoxic effect of cisplatin. This was demonstrated by a significant decrease in urea and creatinine levels in the dietary pumpkin seeds intake groups compared to the untreated group with cisplatin-induced nephrotoxicity. It also increased low albumin levels indicating the seeds' protective ability against kidney damage as shown in a report by **Lin et al. (2018), and Yadav and Upasani, (2018).** On the contrary, these results disagree with that reported by **Al-Ghaithi et al., (2004)** who found that Citrullus colocynthis (Handal) plant extract did not have any effect on blood urea. The obtained results in Table 6 showed a significant ($P<0.05$) decrease in Albumin level in the control (+ve) group compared to the control (-ve) and treated groups. Meanwhile, the groups treated with cantaloupe, grape, pumpkin seeds, and a mixture of all seeds exhibited no significant difference in albumin, creatinine, urea, uric acid, and nitric oxide as compared with the control (-ve) group.

Histological examination of kidney sections stained with H&E from the normal control (-ve) rats (Group1) revealed a normal appearance of glomeruli and proximal and renal tubules. Previous studies confirmed that cisplatin may cause glomerular wounds, tubular necrosis, and damage **(Khan, Khan, & Sahreen, 2012).** This is in line with the outcomes of the current study which indicated various histological alterations including congestion of inter-tubular blood capillaries and renal blood vessels **(Figure 1b)** with perivascular cellular infiltrations in the renal cortex with vacuolar degeneration in the wall of renal blood vessels **(Figure 1b)**.

Fig. 1: Histological examination of (H&E×400) stained sections of kidney tissue taken from treated and untreated rats

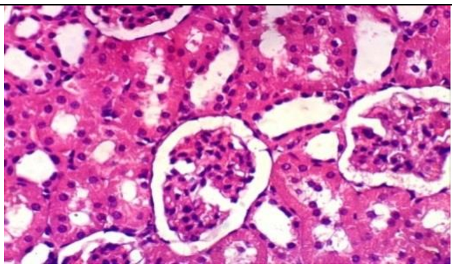

Photo (a): Kidney of rat from group 1(control negative) showing a normal histological structure of renal parenchyma **(H & E X 400)**

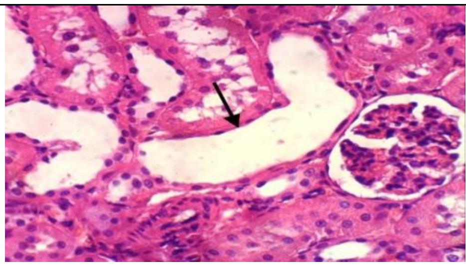

Photo (b): Kidney of rat from group 2 (control positive) showing Cystic dilatation of some renal tubules **(H & E X 400)**.

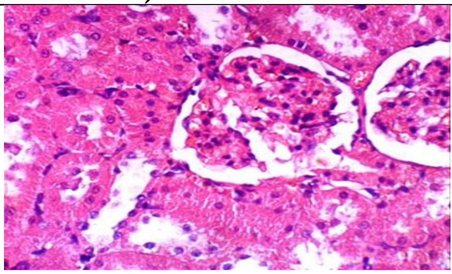

Photo (c): Kidney of rat from group 3 (cantaloupe seeds 7.5%) showing no histopathological changes **(H & E X 400)**.

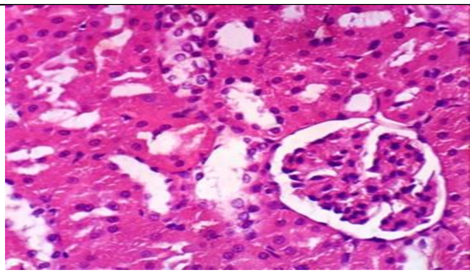

Photo (d): Kidney of rat from group 4 (grape seeds 7.5%) showing no histopathological changes **(H & E X 400)**.

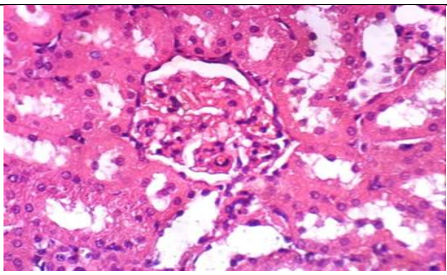

Photo (e): Kidney of rat from group 5 (pumpkin seeds 7.5%) showing no histopathological changes **(H & E X 400)**.

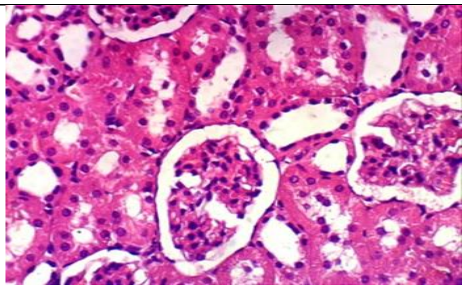

Photo (f): Kidney of rat from group 6 (mixture of all seeds) showing no histopathological changes **(H & E X 400).**

Tubular damage was estimated as moderate to severe based on the Klausner classification (black arrow). Our findings were in line with **Prerna et al., (2021),** and **Al-Rashidy et al., (2018)** who showed that using cisplatin causes the architectural loss of renal tubules with peritubular dilatation along with severe vascular congestion. Cisplatin-induced renal nephrotoxicity occurs due to either cisplatin being poorly soluble at acidic pH so it precipitates in renal tubules and induces tubular injury or its metabolites or due to its inhibitory effect on dihydrofolate reeducates enzyme **(Rizk et al, 2018).**

Also, histological examination of the kidney tissues obtained from the treated groups with cantaloupe, grape, and pumpkin seeds and a mixture of all seeds, revealed that no histopathological changes in dilatation/atrophy were seen in the proximal and distal tubules as illustrated in **Fig. 1.** Similar findings were reported previously by **Barakat et al. (2020).** Tubular epithelium appeared normal, **Figure 1(c, d, e, f).** Similar data were recorded by **Yun et al., (2020)** and **Gulsum et al., (2012)** in grape seeds who recorded that administration of grape seed decreased the cisplatin-induced nephrotoxicity by increasing antioxidant enzymes in rats. The powerful antioxidant activity of grape seed extract could protect the kidney against induced nephropathy **(Ozkan et al., 2012).** Also, these results agree with **Amin et al., (2014)** for pumpkin seeds who demonstrated that pumpkin seeds have significantly announced improvement of renal structures with as well as attenuated histopathological alterations in cisplatin-injected rats. Due to decrease to decreased renal acidity. So, renal histological changes improved.

Conclusion

In conclusion, Cisplatin consumption causes severe histopathological changes in kidney tissues in rats. Feeding the cantaloupe, grape, and pumpkin seeds have a therapeutic effect on renal damage induced by chronic Cisplatin administration. Future studies may be suggested to evaluate the effectiveness and advantages of using other seeds that have a therapeutic effect on injected Cisplatin rats.

References

Abbas M., Rady D., Radwan I., et al. (2020): The occurrence of periodontal diseases and its correlation with different risk factors among a convenient sample of adult Egyptian population: a cross sectional study. F1000research. 8: 1740.

Abd El-Meged L., and Al-Shehri K. (2020): The Therapeutic Effects of Pumpkin Seeds on Rats Injected with Carbon Tetrachloride (CCl4). Ann Med Health Sci Res; 10: 895-902.

Abd Elwahab S., Mohamed M., Abdel-maksoud A., and Sadek E. (2021): Nephro-Protective Effects of Grape and Guava Seeds Extracts on Gentamicin Induced Nephrotoxicity in Rats. Journal of Environmental Sciences (JES); 50 (9); 4; 333- 357.

Abou-Zeid S., AbuBakr H., and Mohamed M., El-Bahrawy A. (2018): Ameliorative effect of pumpkin seed oil against emamectin induced toxicity in mice, Biomed. Pharmacother. 98; 242–251.

Agoreyo B., Akpiroroh O., Orukpe O., Osaweren and Owabor C. (2011): The effects of various drying methods on the nutritional composition of Musa paradisiaca, Dioscorea rotundata and Colocasia esculenta. Asian Journal of Biochemistry. 6(6):458-464.

Ahmadi S., Boroumand M., Gohari-Moghaddam, K., and Tajik P. (2008): The impact of low serum triglyceride on LDL-cholesterol estimation. Arch Iran Med.,11: 318-21.

Akomolafe S., Olasehinde T., Oyeleye S., Aluko B., Adewale O., and Ijomon O. (2020): Curcumin administration mitigates cyclophosphamide- induced oxidative damage and restores alteration of enzymes associated with cognitive function in rats' brain. Neurotoxicity Research, 38, 199–210.

Al-Ghaithi F., El-Ridi M., Adeghate E., and Amiri M. (2004): Biochemical effects of *Citrullus colocynthis* in normal and diabetic rats. Molecular & Cellular Biochemistry, 261(1-2):143-9.

Al-Rashidy A., Salem R., Alhosary A., Wahdan M., Elnemr G. and Hassan K. (2018): Role of erythropoietin in methotrexate-induced nephrotoxicity in adult male albino rats. J. Nephropharmacol. 7(2), 156-163.

Amin M., Islam T., Uddin M., Uddin M., Rahman M., Satter M. (2019): Comparative study on nutrient contents in the different parts of indigenous and hybrid varieties of pumpkin (Cucurbita maxima Linn.), Heliyon 5 (9) e02462.

Amin K., Sana'a R., Wala'a G. and Shima'a M. (2014): Effects of orlistat and herbal mixture extract on renal function and oxidative stress biomarkers in a rat model of high fat diet. Int. J. Biochem. Res. & Review 4(2), 173-178.

Anju K., Kumari B., Surekha A. and Preethi R. (2018): Preparation of pumpkin powder and pumpkin seed kernel powder for supplementation in weaning mix and cookies. International Journal of Chemical Studies; 6(5): 167-175.

AOAC (2005): Official method of Analysis. 18th Edition, Association of Officiating Analytical Chemists, Washington DC, Method 935.14 and 992.24.

Arunima S., and Vivek K. (2021): Nutritional, phytochemical, and antimicrobial attributes of seeds and kernels of different pumpkin cultivars. Food Frontiers; 1–12.

Bakr S. (2009): Therapeutic and Immunological Impacts of Some Plant Materials on Feeding to Albino Rats Inflicted with Liver Physiological Disorder. Ph. D. Thesis, Faculty of Home Economics, Minufia University.

Bao L., Zhang Z., Dai X., Ding Y., Jiang Y., Li Y. and Li Y. (2015): Effects of grape seed proanthocyanidin extract on renal injury in type 2 diabetic rats. Molecular medicine reports.11:645-652.

Barnett L., and Cummings B. (2018): Nephrotoxicity and Renal Pathophysiology: A Contemporary Perspective. Toxicological Sciences, 164(2), 379–390.

Barakat L. and Mahmoud R. (2011): The antiatherogenic, renal protective and immunomodulatory effects of purslane, pumpkin and flax seeds on hypercholesterolemic rats. N. Am. J. Med. Sci. **3**(9), 411-417.

Barakat L., Barakat N., Zakaria M., and Khirallah S. (2020): Protective role of zinc oxide nanoparticles in kidney injury induced by cisplatin in rats. Life Sci. 262,1- 9.

Bhalodia N., Nariya P., Acharya R., and Shukla V. (2011): Evaluation of in vitro antioxidant activity of flowers of Cassia fistula Linn. International Journal of Pharmtech Research, 3, 589–599.

Cadiz-Gurrea, M.; Borrás-Linares, I.; Lozano-Sánchez, J.; Joven, J.; Fernández-Arroyo, S. (2017): Segura-Carretero, A. Cocoa and grape seed byproducts as a source of antioxidant and anti-inflammatory proanthocyanidins. Int. J. Mol. Sci.18, 376.

Canals R., Del Carmen-Llaudy M., Canals J. and Zamora F. (2008): Influence of the elimination of seeds on the colour, phenolic composition and astringency of red wine. European Food and Research Technology, 226(5): 1183-119.

Chapman D., Castilla R., and Campbell J. (1959): Evaluation of Protein in Food. I. A method for the deterinination of protein efficiency ratio. Can J Biochem Phosiol; 37:679-686.

Chen L., Kang Y. and Suh J. (2014): Roasting processed oriental melon (Cucumis melo L. var. makuwa Makino) seed influenced the triglyceride profile and the inhibitory potential against key enzymes relevant for hyperglycemia. Food Res. Int., 56: 236-242.

Colbay M., Yuksel S., Uslan I., Acarturk G., Karaman O., Bas O., Mollaoglu H., Yagmurca M., Ozen O. (2010): Novel approach for the prevention of contrast nephropathy. Exp Toxicol Pathol; 62: 81–89.

Cole T., Klotzsch S., and McNamara J. (1997): Measurement of Triglyceride Concentration in Handbook of Lipoprotein Testing. Pbl Washington DC: Ed. AACC Press.

Cortas N. and Wakid N. (1990): Determination of inorganic nitrate in serum and urine by a kinetic cadmium-reduction method. Clin Chem., 36:1440–1443.

Doumas B., Watson W. and Biggs H. (1971): Albumin standards and the measurement of serum albumin with bromocresol green. Clinica Chimica Acta, 31, 87-93.

El-Arbagy A., Yassin Y., Boshra B. (2016): Study of prevalence of end stage renal disease in Assiut governorate, upper Egypt. Menoufia Med J. 29:222–7.

Elbanna S. (2014): Phytochemicals in Artichoke *(Cyncirci scolymus, L.)* and their effects on liver disorder initiation by carbon tetra chloride. M.Sc Thesis, Faculty of Home Economics, Minufia University.

Fossati P., Prencipe L., and Berti G. (1980): Use of 3, 5-Dichloro-2-Hydroxybenzenesulfonic Acid/4-Aminophenazone Chromogenic System in Direct Enzymic Assay of Uric Acid in Serum and Urine. Clinical Chemistry, 26, 227-231.

Friedewald W., Levy L., and Fredrickson D. (1972): Estimation of the Concentration of Low-Density Lipoprotein Cholesterol in Plasma, Without Use of the Preparative Ultracentrifuge. Clin Chem;18 (6):499-502.

Gil-Cardoso K., Gines I., Pinent M., Ardevol A., Arola L., Blay M. and Terra X. (2017): Chronic supplementation with dietary proanthocyanidins protects from diet induced intestinal alterations in obese rats. Mol. Nutr. Food Res. 61(8): 1601039.

Gulsum O., Asım O., Safak E., Mehmet A., Fulya B., and Yucesan K. (2012): Protective Effect of the Grape Seed Proanthocyanidin Extract in a Rat Model of Contrast-Induced Nephropathy. Kidney Blood Press Res; 35: 445–453.

Haghighi M., Nematbakhsh M., Talebi A., Nasri H., Ashrafi F., Roshanaei K. Safari T. (2012): The role of angiotensin II receptor 1 (AT1) blockade in cisplatin-induced nephrotoxicity in rats: Gender-related differences. Renal Failure, 34, 1046–1051.

Hanaa M., Elshafie M., Ismail H., Mahmoud M. and Ibrahim H. (2015): Chemical Studies and Phytochemical Screening of Grape Seeds (*VITIS VINIFERA L.*) Minia J. of Agric. Res. & Develop.35 (2), 313-325.

Hassan H., Isa A., El-Kholy W. and Nour S.(2013): Testicular disorders induced by plant growth regulators: cellular protection with proanthocyanidins grape seeds extract. Cytotechnology. 65(5): 851-862.

Henry J. (1991): Clinical Diagnosis and Management. 18th ed. Pbl. Philadelphia, W.B. Saunders Company; 156-159.

Iseri S., Ercan F., Gedik N., and Yuksel M. (2007): Simvastatin attenuates cisplatin-induced kidney and liver damage in rats. Toxicology 230(2-3):256-64.

Ivanova P., (2012): The melons-raw material for food processing. In: 50 years Food RDI. Food technologies and health, international scientific-practical conference, Plovdiv, Bulgaria, 8 November. Proc. Food Res. Dev. Inst.; 23-26.

Khan R., Khan M., and Sahreen S. (2012): Protective effects of rutin against potassium bromate induced nephrotoxicity in rats**.** BMC Complementary and Alternative Medicine 12(1):204.

Kiani R., Arzani A., and Maibody M. (2021): Polyphenols, flavonoids, and antioxidant activity involved in salt tolerance inwheat, Aegilops cylindrica and their amphidiploids. Frontiers in Plant Science, 12, 646221.

Krimer V. (2020): Pumpkin seeds: Phenolic acids in pumpkin seeds (Cucurbita pepo L.). In V. R. Preedy & R. R. Watson (Eds.), Nuts and seeds in health and disease prevention (533-542). Academic Press.

Knight J., Anderson S., and Rawle J. (1972): Chemical basis of the sulfo-phospho-vanillin reaction for estimating total serum lipids. Clin Chem;18 (3):199-202.

Kurek M. and Wyrwisz J. (2015): The Application of Dietary Fiber in Bread Products. J Food Process Techno. 6 (5):447.

Li L., Jun L., Hui X., Fengmei Z., Zhijun L., Hongzhi L., Jinrong Z., Zhengsheng Y. , and Yongsheng L. (2021): The Protective Effect of Anthocyanins Extracted from Aronia Melanocarpa Berry in Renal Ischemia-Reperfusion Injury in Mice. Hindawi; Mediators of Inflammation., 19 (7):1-15.

Lin M., Ko J., Liu T., Chao P., and Ou C. (2018): Protective effect of D-methionine on body weight loss, anorexia, and nephrotoxicity in cisplatin-induced chronic toxicity in rats. Integrative Cancer Therapies, 17(3), 813–824.

Liu Q., Hu S., He Y., Zhang J., Zeng X., Gong F., and Liang L., (2017): The protective effects of Zhen-Wu-Tang against cisplatin-induced acute kidney injury in rats. PLoS ONE. 12 (6), 1–12.

MacLachlan J., Wotherspoon A., Ansell R. and Brooks C. (2000): Cholesterol oxidase: sources, physical properties and analytical applications. J Steroid Biochem Mol Biol., 72: 169-95.

Matthaus B. (2008): Virgin grape seed oil: Is it really a nutritional highlight? Eur. J. Lipid Sci. Technol., 110, 645–650.

Michel H., and Menze E., (2019): Tetramethylpyrazine guards against cisplatininduced nephrotoxicity in rats through inhibiting HMGB1/TLR4/NF-jB and activating Nrf2 and PPAR-c signaling pathways. European Journal of Pharmacology. 15;857:172422.

Mohammed S., El-Dashlouty, Ehab S., EL-Din Mohammed, and Mohamed S. Mahmoud (2015): Comparative Study on Watermelon, Colocynth and Cantaloupe Seeds as Used for Treatment of Hepatointoxicated Rats. Scientific Journal of Specific Education Science; 17(1):1, 362-378.

Moke E., Erhirhie E., and Ahante E. (2015): Effects of inhaled anesthetic agents (Chloroform and Diethyl ether) on fasting blood glucose and hematological parameters in Westar rats. Sky Journal of Biochemistry Research 4(2), 013 – 015.

Nahed M., Ghada H., and Zein H. (2020): Usage of oil and powder of bottle gourd and pumpkin seeds in production of high nutritive value biscuit. Egypt. J. of Nutrition and Health; 15(1) 39-53.

Nematbakhsh M., Ashrafi F., Nasri H., Talebi A., Pezeshki Z., and Eshraghi F. (2013): A model for prediction of cisplatin induced nephrotoxicityby kidney weight in experimental rats. Journal of Research in Medical Sciences, 18, 370–373.

Nicolle C., Cardinault N., Aprikian O., Busserolles J., Grolier P., Rock E., et al. (2003): Effect of carrot intake on cholesterol metabolism and on antioxidant status in cholesterol-fed rat. European Journal of Nutrition; 42:254-261.

Nishant K. and Neeraj (2018): Study on physico-chemical and antioxidant properties of pomegranate peel. Journal of Pharmacognosy and Phytochemistry. 7(3): 2141-2147.

Ogbera A., Dada O., Adeleye F., and Jewo P. (2010): Complementary and alternative medicine use in diabetes mellitus. West African Journal of Medicine, 29(3).158–162.

Ozkan G., Sukru U., Orem A., and Ersoz S. (2012): Protective Effect of the Grape Seed Proanthocyanidin Extract in a Rat Model of Contrast-Induced Nephropathy. Kidney and Blood Pressure Research 35(6):445-453.

Prerna C., Ravi L. and Kuppulingam B. (2021): Fabrication of InGaN/Si (111) nanowire heterostructure photoanode for hydrogen generation under visible light. Applied Physics Letters 119(15):153901-1539017.

Rababah T., Ereifeja K., Al- Mahasnehb M., Ismaealc K., Hidard A. and Yange W. (2008): Total Phenolics, Antioxidant Activities, and Anthocyanins of Different Grape Seed Cultivars Grown in Jordan. International Journal of Food Properties, 11(2): 472-479.

Ratnam N., Najibullah M., and Ibrahim M. (2017): A review on Cucurbita pepo. International Journal of Pharmacognosy and Phytochemical Research, 9(9), 1190–1194.

Reeves P. et al., (1993): AIN-93 purified diets for laboratory rodents: final report of the American Institute of Nutrition ad hoc writing committee on the reformulation of the AIN-76A rodent diet. J Nutr.Nov; 123(11):1939-51.

Ren Y., Bang H., Lee E., Gould J., Rathore K., Patil B. and Crosby K. (2013): Levels of phytoene and β-carotene in transgenic honeydew melon (Cucumis melo L. inodorus). Plant Cell, Tissue Organ Cult., 113(2): 291-301.

Rezig L., Chouaibi M., Meddeb W., Msaada K., Hamdi S., (2019): Chemical composition and bioactive compounds of Cucurbitaceae seeds: potential sources for new trends of plant oils, Process Safe. Environ. Protect. 127; 73–81.

Riad M. (2014): Utilization of Vegetable Wastes for Treatment of Hepatointoxication in CCl4 Albino Rats. M.Sc Thesis, Faculty of Home Economics, Minufia University.

Rizk F., Amira A., Lamees D., Heba H., Naglaa I., Rehab B., and Sherief A. (2018): Metformin ameliorated methotrexate-induced hepatorenal toxicity in rats in addition to its antitumor activity: two birds with one stone. Inflamm Res.; 11: 421–429.

Saavedra M., Aires A., Dias C., Almeida J., De Vasconcelos, Santos P., and Rosa E. (2015): Evaluation of the potential of squash pumpkin by-products (seeds and shell) as sources of antioxidant and bioactive compounds. Journal of Food Science and Technology, 52, 1008– 1015.

Schneeman B. (2002): Gastrointestinal physiology and functions. British Journal of Nutrition.; 88 (2): 159-163.

Shehata R. (2012): Effect of Herbs and Vegetables Seeds on Rats Inflicted with Hepatotoxicity. M.Sc Thesis, Faculty of Home Economics, Minufia University, Egypt.

Singh L. et al., (2018): Prolyl hydroxylase 2: a promising target to inhibit hypoxia-induced cellular metabolism in cancer cells. Drug Discov Today, 23(11): 1873-1882.

Snedecor G. and Cochran W. (1967): Statistical methods. 6th Edition, Ames, Lowa, the Lowa state University.

Sultana P., Dilruba E., Afzal S., Mrityunjoy B., Subed C., Golam S., Amirul I., Narayan R. and Mohammad S. (2015): Nutritional Analysis of Date Fruits (Phoenix dactylifera L.) in

Perspective of Bangladesh. American Journal of Life Sciences. 3(4): 274-278.

Talabani N., and Tofiq D. (2012): Citrullus colocynthis as a bioavailable source of beta -sitosterol, antihyperlipidemic effect of oil in rabbits. International Journal of Medicinal and Aromatic Plants, 2(3):536-539.

Turki K., Charradi K., Boukhalfa H., Belhaj M., Limam F. and Aouani E. (2016): Grape seed powder improves renal failure of chronic kidney disease patients, EXCLI journal, 27(15):424-433.

Viswanathan V., Snehalatha C., Kumutha R., Jayaraman M., and Ramachandran A. (2004): Serum albumin levels in different stages of Type 2 diabetic nephropathy patients. Indian Journal of Nephrology, 14, 89–92.

Wilson K. and Walker J. (2000): Practical Biochemistry: Principles and Techniques. 5th ed. Pbl. Cambridge, Cambridge University Press. Pp. 630-689.

World Kidney Day: Chronic Kidney Disease. (2015): http//www.worldkidneyday.org/faqs/chronic-kidney-disease.

Yadav M., Gulkari V., and Wanjari M. (2016): Bryophyllum pinnatum leaf extracts prevent formation of renal calculi in lithiatic rats. Ancient Science of Life, 36(2), 90–97.

Yadav M., Jain S., Tomar R., Prasad G., and Yadav H. (2017): Medicinal and biological potential of pumpkin: An updated review. Nutrition Research Reviews, 23, 184–190.

Yadav A., and Upasani C. (2018): Nephroprotective activity of asparagus racemosus against cisplatin-induced nephrotoxicity and renal dysfunction in experimental rats. Asian Journal of Pharmaceutical and Clinical Research, 11(12), 230–233.

Yamakoshi J., Saito M., Kataoka S., and Kikuchi M. (2002): Safety evaluation of proanthocyanidin-rich extract from grape seed. Food Chem Toxicol. 40(5):599-607.

Yu G., Zhao J., and Wei Y. (2021): Physicochemical properties and antioxidant activity of pumpkin polysaccharide (Cucurbita moschata Duchesne ex Poiret) modified by subcritical water. Foods **10**(1), 197-202.

Yun S., Chu D., He X., Zhang W. and Feng C. (2020): Protective effects of grape seed proanthocyanidins against iron overload-induced renal oxidative damage in rats. Journal of Trace Elements in Medicine and Biology. 18(57): 126407.

Zamani M., Rahimi A., Mahdavi R., Nikbakhsh M., Jabbari M., Rezazadeh H., Delazar A., Nahar L. and Sarker S. (2007): Assessment of anti-hyperlipidemic effect of *Citrullus colocynthis*. Revista Brasileira de Farmacognosia, 17(4):492-496.

تقييم التأثير العلاجي لبذور الشمام والعنب والقرع على السمية الكلوية التي يسببها السيسبلاتين في الفئران

إيريني ولسن نجيب[1] ، ناريمان سعيد اسحق[2]

1- قسم الأقتصاد المنزلي-كلية التربية النوعية- جامعة عين شمس- مصر

2- قسم الأقتصاد المنزلي-كلية التربية النوعية- جامعة أسيوط - مصر

المستخلص:

السيسبلاتين هو دواء علاجي كيميائي يستخدم لعلاج مرضى السرطانات. التأثير الثانوي الرئيسي الناتج عن علاج السيسبلاتين هو السمية الكلوية. الهدف من هذه الدراسة هو تقييم التأثير العلاجي المحتمل لبذور الشمام والعنب واليقطين علي السمية الكلوية للفئران المحقونة بالسيسبلاتين. **المواد والطرق:** تم اختيار 42 من الجرذان بشكل عشوائي (7 لكل مجموعة)، مجموعة (1): جرذان (المجموعة الضابطة السالبة) جرذان تم تغذيتها علي الوجبة الأساسية، مجموعة (2): (المجموعة الضابطة الموجبة) جرذان تم حقنها بالسيسبلاتين (6مجم/كجم من وزن الجسم) لمرة واحدة فقط ، المجموعات (3، 4، 5، 6) جرذان تم حقنها وكذلك تغذت علي 7,5% من بذور كلاً من (لبذور الشمام والعنب واليقطين) علي أو خليط منهم علي التوالي. تم إجراء التحليل الكيميائي والمواد الكيميائية النباتية لبذور الشمام والعنب واليقطين. وكذلك تم أخذ عينات الدم ، وإزالة الأنسجة الكلوية من الجرذان. تم حساب التحليلات البيولوجية. **النتائج:** أظهرت النتائج أن حقن السيسبلاتين أدى إلى ارتفاع مستويات الكوليسترول الكلي، والجليسريدات الثلاثية، والبروتين منخفض الكثافة، والبروتين عالي الكثافة وكذلك تسبب في خلل في وظائف الكلي، بالنسبة للمجموعات المعالجة التي تغذت علي البذورقد تحسن وزن الجسم ووزن الكلي والكبد والمأكول اليومي، ونسبة كفاءة التغذية ، وكذلك التغيرات النسيجية. أيضاً زاد تركيز الكرياتينين واليوريا وحمض البوليك وأكسيد النيتريك زيادة معنوية عند قيمة أقل من 5 في الفئران التي تم حقنها بالسيسبلاتين (المجموعة الموجبة) مقارنةً بالمجموعة السالبة الضابطة، بينما تركيزالألبيومين سجل إنخفاضاً معنوياً عند قيمة أقل من 5 ، على عكس المجموعات المعالجة بالبذور.

الكلمات المفتاحية: بذورالفاكهة، الفشل الكلوي ، مستوي الدهون، وزن الجسم.