Effect of pulp and rind water melon *(Citrullus lanatus)* powder on gentamicin-induced nephrotoxicity in rats

Fathya G. El-Nahas[1] and Amira Hamdy Darweesh[2]
[1]Home Economic Dep., Faculty of Specific Education, Menoufia University, Egypt.
[2]Nutrition and Food Science Dep. , Faculty of Home Economic, Menoufia University, Egypt.

Abstract

This study was conducted to evaluate the chemical composition of watermelon (*Citrullus lanatus*) pulp and rind powders, as well as to investigate their potential therapeutic effects on gentamicin-induced nephrotoxicityin rats. Forty adult female albino rats (Sprague-Dawley strain) were divided into eight groups. The first group was normal rats as a negative control group, while the other seven groups were fed a basal diet and injected with gentamicin to induce nephrotoxicity. One of them was the positive group, while the remaining six groups were fed a basal diet supplemented with 2.5%, 5%, and 7.5% of either watermelon pulp or rind powder, respectively, for 28 days. The results revealed that the content of moisture, dietary fiber, carbohydrates, total calories, total phenols, total flavonoids, and 2,2-diphenyl-1-picrylhydrazyl (DPPH%) of watermelon pulp powder was significantly higher than its content in the rind powder. In contrast, the rind powder contained considerably higher concentrations of tested minerals, except for iron and potassium, which were more abundant in the pulp. In addition, levels of AST, ALT, ALP, GGT, urea, uric acid, creatinine, MDA, and blood glucose were dramatically decreased in the nephritic watermelon pulp-treated groups. In contrast, levels of TP, Alb, GPX, SOD, CAT, GSTs, and TAC were greatly increased. Regarding levels of K and P, they decreased while levels of Na and Ca increased in nephritic-treated groups with pulp and rind powder, especially at 7.5%. So, this study proved that pulp and rind powder are effective in treating kidney diseases and protecting against associated complications. It also contains many vital compounds that play an important and effective role in metabolic processes and performance during the life cycle.

Key words: kidney functions- blood glucose – malondialdehyde - antioxidant enzymes-liver enzymes.

Introduction

The kidney serves as the primary organ indispensable for the human body to accomplish and execute various critical functions. These include but are not limited to preserving bone density, regulating hormonal balance, producing erythrocytes, and maintaining fluid homeostasis and blood pressure. They also play a part in the metabolism of carbohydrates, proteins, lipids, and other nutrients, as well as filtering and eliminating nitrogenous and xenobiotic toxicants, including potentially dangerous chemical substances in the environment, because of their special biochemical, anatomical,and physiological characteristics. The kidney's multitude of metabolizing enzymes and transporters, incredibly high renal blood flow, and capacity to collect various solutes during the formation of urine are all characteristics that contribute to the kidney's great sensitivity to xenobiotics **(Molaei *et al*., 2021).**Kidney diseases can be classified based on the temporal onset into acute kidney injury (AKI) and chronic kidney disease (CKD). CKD is defined as a progressive decline in renal function persisting for more than three months. Both AKI and CKD are closely associated with the overproduction of reactive oxygen species (ROS) and reactive nitrogen species (RNS), which contribute to oxidative stress and subsequent tissue damage. AKI patients are more likely to progress to CKD, and whether tubular cells recover sufficiently is a major factor in whether this happens (Nephrotoxicity). Nephrotoxicity is characterized as the swift decline in renal function resulting from the deleterious impact of chemicals and pharmaceuticals. Nephrotoxicity is a term used to describe the hazardous impact of some substances on the kidney, including both toxins and medications **(Perazella and Rosner, 2022).** Nephrotoxins are substances displaying nephrotoxicity. Moulds and fungi, chemotherapy drugs like cisplatin, antibiotics like gentmicin, nonsteroidal anti-inflammatory drugs (NSAIDs), and metals like lead, arsenic, and mercury are some of the different substances that can cause nephrotoxicity. Drug-induced nephrotoxicity represents approximately 19–26% of all hospital cases. Numerous mechanisms contribute to drug-induced nephrotoxicity, including altered glomerular hemodynamics ,altered glomerular hemodynamics renal tubular cytotoxicity,crystal nephropathy, inflammation ,rhabdomyolysis, and thrombotic microangiopathy **(Yu *et al.,* 2021).** These consequences can be mostly attributed to increased ROS production by the renal mitochondria, which harms cellular macromolecules like proteins, lipids, and DNA and eventually causes the death of kidney cells **(Ali *et al.*,2021).**Gentamicin (GM), a key member of the aminoglycoside (AG) class of bactericidal antibiotics, is frequently prescribed to treat serious Gram-negative bacterial infections, including endocarditis, sepsis, pneumonia, pelvic inflammatory disease, meningitis, urinary tract infections, and bone infections (**Balakumar *et al*., 2010).** Nephrotoxicity and ototoxicity, including vestibular and/or cochlear damage, are among the major side effects of GM. GM's primary dose-limiting adverse effect is nephrotoxicity. The recent mechanisms of GM-induced renal complications are oxidative stress, apoptosis, fibrosis, inflammation, crystal nephropathy, rhabdomyolysis, and thrombotic microangiopathy. These consequences can be mostly attributed to increased ROS production by the renal mitochondria, which harm cellular macromolecules like proteins, lipids, and DNA and eventually cause the death of kidney cells (**Huang *et al.*, 2020, and Althunibat *et al*., 2022)**.Watermelon (*Citrulluslanatus*) is a Cucurbitacea family tropical plant. It is most prevalent in South East Asia and Africa. The melon (*Cucumis melo* L.) is a member of the family Cucurbitaceae.It contains antioxidants such as vitamin C, beta-carotene, citrulline, and others that are found naturally. Additionally, red flesh watermelon is a rich source of lycopene. The seventeen compounds present in watermelon are classified into the following five groups: acids, alcohol, ketone, epoxy compounds, and hydrocarbons. In addition, watermelon is an excellent source of numerous antioxidant molecules, including L-citrulline, which serves as a precursor for L-arginine in the kidney, in addition to both essential and non-essential amino acids **(Rahman *et al*., 2013).** L-arginine serves as the substrate for nitric oxide synthase during the synthesis of nitric oxide. Nitric oxide functions as a novel hydroxyl radical scavenger and is an essential signaling molecule involved in the regulation of a wide variety of physiological and cellular processes (**Naknaen *et al.*, 2016).** As a laxative fruit, melons aid in the elimination of waste products and urine sediments, and they are also highly effective in the treatment of constipation. Antiulcerogenic, antidiabetic, anti-plasmodial, analgesic, antimicrobial, laxative, anti-inflammatory, antioxidant, and hepatoprotective properties are all attributed to watermelon **(Oyenihi *et al.*, 2016 and Renner *et al.*, 2017).** The pink flesh of the watermelon is consumed uncooked or incorporated into juices and salads, while the rind is disposed of as an unnecessary by product.It is frequently consumed as a pickle in the southern region of the United States and has been proposed as a possible dietary fiber substitute for wheat flour in the preparation of cookies and cakes

(Naknaen *et al.,* 2016 and Oyenihi *et al.,* 2016).Therefore, the aim of this study aimed to evaluate the effects of varying concentrations of watermelon pulp and rind powder on biochemical and oxidative stress markers in a gentamicin-induced nephrotoxicity in rats.

Materials and Methods

Materials

Plant material

Watermelon (*Citrullus lanatus*) was procured from the nearby market in Shebin-El kom City, Menoufia Governorate, Egypt, in accordance with the specifications provided by the Menoufia University Agriculture Crops Department.

Rats

Rats weighing (135±5g) were obtained from the ophthalmology institute medical analysis department in Giza.;Animals care and Use Committee (IACUC) of Menoufia University provided ethical consideration for this study (Reg.No.,MUFHE/F/NFS/39/24)

Chemicals

Chemical kits and GM (aminoglycoside antibiotics) were obtained from El- Gomhoria Company for Trading Drugs, Chemicals and Medical Instruments, Cairo, Egypt.

Methods

Preparation of watermelon pulp and rind powders

The watermelon rind, which had been isolated from the freshly washed watermelon fruits, was sliced into small segments using a sharp knife in order to extract water before being distributed in air dryer trays. The pulp and rind were dried at 50.5°C for a duration of 48 hours, or until their moisture content reached 11%. Following this, the dehydrated components were reduced to powder using a laboratory disc mill (Braun AG Frankfurt Type: KM 32, Germany) and subsequently stored at 4°C for subsequent analysis **(Russo, 2001)**.

Chemical composition of watermelon pulp and rind powder

The moisture, protein, fat, ash, and dietary fiber contents of watermelon pulp and rind powder (triplicate sample) were identified in accordance with **A.O.A.C. (2012)** through the determination of their chemical composition. The difference in these components was utilized to calculate the total carbohydrates.

Determination of mineral content

The mineral concentrations in both the pulp and rind powders were analyzed using atomic absorption spectrophotometry (Perkin–Elmer Instrument Model 2380, Germany), in accordance with the guidelines set forth by the **A.O.A.C. (2012).**

Determination of some vitamins

The concentrations of thiamine (B1), ascorbic acid (vitamin C), Riboflavin(B2) , niacin (B3), and pyridoxine (B6) were ascertained using the spectrophotometric techniques documented by **Onwuka (2005)**.The determination of β-carotene and lycopene was carried out according to the method outlined by **Okwu and Josiah (2006)**.

Determination of total flavonoid

A colorimetric method for aluminum chloride was developed by **Park *et al.* (1997)**.

Determination of total phenols

The identification of phenolic compounds in dried plant powders (DDP) was accomplished by employing the **Singleton and Rossi (1965)** method and the Folin- Ciocalteu reagent.

Determination of 2,2-diphenyl-1-picrylhydrazyl (DPPH)

The DPPH free radical scavenging capabilities of DDP were assessed using the method proposed by **Xu and Chang (2007)**.

Nephrotoxicity induction

Normal healthy male albino rats were injected with 10 mg of GM (aminoglycosides antibiotics) /kg once daily for 10 days **(Farombi and Ekor, 2006).**

Experimental design

Forty adult female healthy albino rats (Sprague-Dawley strain) weighing (135±5 g) were maintained in wire cages in the laboratory under hygienic conditions with adequate ventilation. During the adaptation period of seven consecutive days, these rats were fed a basal diet consisting of the following components: cornstarch (69.5%), casein (10%), corn oil (10%), salt mixture (4%), vitamin mixture (1%), bran (5%), methionine (0.3%), and choline chloride (0.2%) **(Reeves *et al.*,1993)**. Rats were introduced to new diets using specialized non-scattering feeding cups in order to prevent feed contamination and loss. Daily inspections were conducted to ensure that water tubes protruding through the wire cage from inverted bottles supporting the side of the cage were supplying water to the rats.

Five rats comprised each of the eight groups; the weights of the rats in each group were nearly identical. The initial group (G1) served as the negative control and was provided with a basal diet. As a positive control, the second group consisted of nephrotoxicity rats that were administered a basal diet and injected with GM. Nephrotoxicity rats comprised Groups (3, 4, 5), and (6, 7, 8); for the duration of the experiment (28 days), they were provided with basal diets supplemented with 2.5%, 5%, and 7.5% watermelon pulp or rind powder, respectively.

Collection of blood

The experiment concluded with the rats fasting overnight and for two hours for water. Subsequently, the rats were anesthetized, sacrificed, and blood samples were extracted from the aorta. Following a 10-minute centrifugation at 3000 rounds per minute (r.p.m.), the blood samples were filtered to separate the serum. The collected serum was then transferred to a dry, sterile Eppendorf and stored at -20°C until further use **(Schemer, 1967).**

Assay of serum biochemical parameters

The following methods were utilized to determine kidney function parameters: urea, uric acid, and creatinine: **Patton & Crouch (1977); Fossati *et al*. (1980); and Bonsens & Taussky (1984),** in that order.Liver functions included alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), total protein (TP), serum gamma-glutamyltransferase (GGT), albumin (Alb), globulin (Glb), and albumin/globulin ratio (Alb/Glb ratio), which were determined by the methods of **Henry (1974), Young (1975), IFCC (1983), Gowenlock *et al*. (1988)**, **Spencer & Price (1977),** and **Srivastava *et al*. (2002)**, respectively.Potassium (K), sodium (Na), phosphorus (P), and calcium (Ca) were described by **Nicoli (2003).** Catalase (CAT), glutathione peroxidase (GPX), glutathione S-transferases (GSTs), superoxide dismutase (SOD), malondialdehyde (MDA), and total antioxidant capacity (TAC) were measured by the methods of **Zhao (2001), Sun et al. (1988), Aebi (1983),**

Schumann and Klauke (2003), Koracevic (2001), and Ohkawa *et al.* (1979), respectively.

Statistical analysis

The statistical package for social sciences SPSS (Statistic Program Sigmastat, Statistical Soft-Ware, SAS Institute, Cary, NC) was utilized to conduct analysis of variance on the data. A one-way analysis of variance (ANOVA) test was employed to examine the impacts of various treatments. Duncan's multiple range test was utilized to determine significance between groups, and a p-value of less than 0.05 was utilized to denote this **(Snedecor and Cochran, 1967)**.

Results and discussion

Table 1 reveals the chemical constituents of dried watermelon pulp and its rind . The table presents the results indicating that the moisture, dietary fiber, carbohydrate, and total calorie contents of dried watermelon pulp were significantly greater than those found in the watermelon rind. Conversely, the protein, fat, and ash contents of the rind were significantly higher in comparison to those of the pulp powder. In the same table , the content of all tested minerals in the watermelon rind (WR) was significantly higher than that of the pulp, except for the content of iron and potassium. The dry weight percentages of ash, fat, and protein in WR were determined by **Al-Sayed and Ahmed (2013)** to be 11.17%, 2.44 %, and 13.09%, respectively. The fiber content of watermelon rind, as determined by dry weight, surpasses that of sample pulp. Consequently, the health benefits associated with fiber food consumption have been the subject of the most extensive research **(Malkki, 2001).** According to **Abu-Hiamed (2017)**, watermelon rinds contained 10.61% moisture, 13.09% ash, 2.44% fat, 11.17% protein, and 56.00% total carbohydrates. These percentages indicate that watermelon rinds have the potential to be utilized as dietary materials to treat various diseases. The K content within the flesh and rind of watermelon fruits is significantly elevated in comparison to that of other minerals. The concentration of the minerals under investigation in this study was found to be greater in the rind than in the sample pulp**(Huang *et al.* 2016).** In the study conducted by **Gladvin *et al*. (2017)**, the chemical parameters of WR minerals have been, in order, 254.25 mg of calcium, 268.28 mg of phosphorous, 345.48 mg of magnesium, and 12.76 mg of iron.

Table (1): Chemical composition of 100 g dried watermelon pulp and its rind

Constitutes	Pulp powder	Rind powder
Moisture	13.02±2.56 [a]	10.17±1.93 [b]
Protein	1.05±0.06 [b]	11.97±0.58 [a]
Fat	0.81±0.02 [b]	2.02±0.02 [a]
Dietary fiber	33.01±2.65 [a]	43.12±3.11 [b]
Ash	2.45±0.05 [b]	10.79±0.79 [a]
Carbohydrates	49.66±5.22 [a]	21.93±6.83 [b]
Calories	210.13±7.88 [a]	153.78±8.34 [b]
Calcium	181.66±7.88 [b]	243.56±6.21 [a]
Phosphorous	234.64±9.03 [b]	276.93±4.22 [a]
Sodium	137.54±2.86 [b]	512.84±8.11 [a]
Magnesium	18.76±0.65 [b]	301.77±5.38 [a]
Iron	15.32±1.03 [a]	13.08±1.21 [b]
Potassium	315.76±5.33 [a]	289.92±4.66 [b]
Zinc	1.12±0.05 [b]	2.87±2.64 [a]
Selenium	2.43±0.33 [b]	23.33±0.93 [a]

Values are expressed as mean ± SD; n = 3, Values in the same row having different superscripts letters are significantly (*P≤0.05*).

The concentrations of the vitamins (C, B1, lycopene, B2, β-carotene, niacin, and pyridoxine) in the pulp and rind powder of watermelon are shown in Table 2. Vitamin C and lycopene concentrations in the pulp of watermelon are remarkably high compared to the rind content, while the other vitamins (B2, B1, carotene, B3, and pyridoxine) in the WR are higher than their contents in the pulp. The concentration of provitamin A (β-carotene) in the interior pulp is significantly greater than that in the rind. The β-carotene values in this study are significantly greater than the values of carotenoids reported by **Johnson *et al.* (2013)** for watermelon pulp and rind (15 and 76.9 mg/100 g, respectively). The watermelon fruit possesses antioxidant properties, as indicated by the concentrations of lycopene, vitamin C, and β-carotene. These compounds function to counteract the harmful effects of oxidative stress and the associated ailments they cause. **(ESHA, 2017).** Adults are advised to consume 60 mg of vitamin C per day, whereas children are prescribed 20 mg **(Asghar *et al.*, 2013)**. Vitamin C is necessary for the production of blood, collagen, and hormones. In addition, it prevents scurvy, promotes bone and tooth development, and functions as an antioxidant against free radicals.

Vitamin C inhibits, reduces, and terminates the formation of free radicals through the donation of an electron and hydrogen, thereby converting vitamin C to dehydro vitamin C and thereby altering its chemical structure. Vitamin A functions as an antioxidant in the human body and is critical for physiological processes such as reproduction, bone development, and eyesight **(Generalić *et al.*, 2019)**.

Table (2): Vitamins content of dried watermelon pulp and its rind

Vitamins	Pulp powder	Rind powder
Vit.C(mg)	32.97±8.54 [a]	12.93±0.36 [b]
Thiamine mg	0.06±10.43 [b]	1.03±0.25 [a]
Lycopene (provitamin A) mcg	4467.54±9.76 [a]	27.54±2.44 [b]
Riboflavin mg	0.12±0.03 [b]	2.13±0.86 [a]
β-carotene (provitamin A) mg	18.65±1.34 [b]	80.78±7.92 [a]
Niacin mg	0.11±0.01 [b]	1.95±0.12 [a]
Pyridoxine mg	0.13±0.02 [b]	3.43±0.04 [a]

Values are expressed as mean ± SD; n = 3, Values in the same row having different superscripts letters are significantly (*P≤0.05*).

The percentages of total phenols, total flavonoids, and 2, 2-diphenyl-1-picrylhydrazyl (DPPH%) found in the pulp and rind of watermelons were determined for this study, as shown in Table 3. The three parameters were significantly higher in the pulp than the rind ,total phenols were higher in the pulp and rind than the total flavonoids. The DPPH assay was utilized to evaluate the antioxidant property due to its extensive application in screening antioxidant activity and its capability to detect active compounds even at low concentrations **(Sreedhar *et al.*, 2010)**. The assay results indicated that both the rind and the peel exhibited scavenging activity surpassing 50%, a level comparable to that of vitamin C, a widely recognized antioxidant. The pulp exhibited significant scavenging activity. This finding is consistent with a previous study **(Asghar *et al.*, 2013)** that demonstrated that peel extracts of watermelon fruit exhibited substantial free radical scavenging activity. The correlation between the antioxidant activity and the total phenolic compound was observed in the present study. The pulp contained the highest concentration of phenolic compounds, while the rind contained the lowest. This suggests that the antioxidant effects observed may be attributed to the presence of these phenolic compounds. Phenolics and flavonoids function as antioxidants through the elimination of free radicals, chelation of metals, and inhibition of lipid peroxidation. Position C3 of the flavonoid composition contains the hydroxyl group(–OH),which participates in chelating and scavenging processes **(Generalić *et al.*, 2019)**.

Table (3): Total phenols, total flavonoids and DPPH of dried watermelon pulp and its rind

Compounds	Pulp powder	Rind powder
Total phenols ppm	1050.76±4.87 [a]	375.87±2.07 [b]
Total flavonoid ppm	431.05±6.83 [a]	287.96±6.94 [b]
DPPH (%)	59.65± 5.32 [a]	51.75±5.04 [b]

Values are expressed as mean±SD; n = 3, Values in the same row having different superscripts letters are significantly (*P≤0.05*).

The mean levels of creatinine, urea, and uric acid in rats with GM - induced nephrotoxicity, as influenced by the concentrations of watermelon pulp and rind powder, are presented in Table 4. It was shown that these levels of nephritic in the positive control group were significantly greater than those in the negative control group (*P≤0.05*). The kidney function of all nephritic rats that were fed diets containing pulp and rind powder at concentrations of 2.5%, 5%, and 7.5% was significantly impaired when compared to the nephritic positive control group. 7.5% was the best level in both tested materials on kidney functions while this level in pulp groups was more effective than the rind group . Groups fed on 5% rind powder and 2.5% pulp powder showed nonsignificant changes between each other and also, the same result was detected between the levels of 7.5% rind powder and 5% pulp powder. Consistent with previous studies indicating that WR is an abundant source of bioactive and antioxidant molecules (e.g., beta-carotene, lycopene, alkaloids, vitamin C, saponin, flavonoids, cardiac glycosides, moisture, phenol, protein, lipids, carbohydrates, and fiber), the results of this study demonstrate that WR enhances antioxidant defense. Similarly, an increase in serum nitric oxide was observed in response to watermelon rind. This finding is consistent with a study that documented the abundance of citrulline, a well-established nitric oxide stimulant, in WR **(Mandel *et al*., 2005)**. Nitric oxide enhances resistance to oxidative stress through its mechanism of action as a hydroxyl radical scavenger, according to subsequent studies **(Akashi *et al.*, 2004)**. Therefore, the current study's findings regarding the reduction in oxidative stress in rats treated with WR may be attributed to a mechanism dependent on nitric oxide. Watermelon pulp is an excellent source of lycopene and provitamin A carotenoids. It is significant to mention that the carotenoid confers health benefits to the body due to its antioxidant properties. Melon pulp is an excellent source of fat, vitamin C, and flavonoids. Furthermore, it is regarded as a significant reservoir of ß-carotene, as well as a vital supply of vitamins B1 and B6, as well as minerals including calcium and magnesium. Due to the diuretic properties and high water content of watermelon and honeydew melon, a number of these fruits may aid in reducing creatinine levels and preventing renal damage. Adequate hydration is critical for healthy kidney operation and efficient elimination of waste (**Garcia *et al.*, 2012 and Siddiqui *et al*., 2018).**

Table (3): Creatinine, urea, and uric acid of gentamicin-induced nephrotoxicity rats as affecting by watermelon pulp and rind powder levels (mg/dl)

Groups	Creatinine	Urea	Uric acid
Negative control ($G_{1)}$	0.76±0.011 [f]	15.99±1.82 [e]	1.88±0.34 [e]
Positive control (G2)	1.43±0.04 [a]	35.01±1.32 [a]	4.21±0.04 [a]
Rats fed on 2.5% watermelon rind (G3)	1.40±0.03 [a]	34.50±1.12 [a]	4.07±0.02 [a]
Rats fed on 5% watermelon rind (G4)	1.36±0.012 [c]	30.86±0.82 [b]	3.73±0.07 [b]
Rats fed on 7.5% watermelon rind (G5)	1.30±0.032 [d]	25.55±0.43 [d]	3.21±0.11 [c]
Rats fed on 2.5% watermelon pulp (G6)	1.35±0.01 [c]	32.64±1.72 [b]	3.86±0.19 [b]
Rats fed on 5% watermelon pulp (G7)	1.23±0.07 [d]	25.67±1.09 [d]	3.31±0.06 [c]
Rats fed on 7.5% watermelon pulp (G8)	1.11±0.02 [e]	18.83±1.32 [e]	2.91±0.16 [d]
LSD	0.03	2.08	0.16

Values are expressed as mean ± SD; n = 3, Values in the same row having different superscripts letters are significantly (*P≤0.05*).

The levels of K and phosphorous increased in the nephrotic-positive control group, while ca and Na decreased. Significant differences were observed in (Na), (Ca), (K), and (P) values between the nephritic positive control group and the negative control group **(Fig. 1)**. Nephritic rats that were provided with diets supplemented with watermelon pulp powder at concentrations of 2.5%, 5%, and 7.5% exhibited significantly increased levels of N and Ca , while these same levels decreased significantly (*P≤0.05*) in K and P. The effects of WR powder were consistent with the aforementioned results. Low antioxidant activity and chronic inflammation are both associated with CKD. The antioxidant status impairment associated with watermelon pulp may be more pronounced in populations with multiple comorbidities and chronic kidney disease. Watermelon pulp and rind powder contain lycopene, vitamin C, author phenols, and beta-carotene, all of which have been shown to be effective against diabetes, arthritis, asthma, cancer, inflammatory bowel syndrome, Parkinson's disease, and Alzheimer's disease. Magnesium, calcium, and P, among others, were among the macro-elements in greater abundance. These are the most vital minerals. Powdered WR is distinguished by its abundance of the most examined minerals (both macro-elements and micro-elements) and its diuretic properties. Research has demonstrated that the excretion of Na+ and K+ ions was reduced, resulting in elevated concentrations in the blood (hypernatremia, hyperkalemia), reduced levels in the urine (hyperuricemia), and elevated concentrations in the serum (urea, hyperuricemia, urinary creatinine) **(Guo & Wang, 2013; Aderiye *et al*., 2020; Nkoana *et al*., 2022)**. K is an essential component of bodily fluids and the cells responsible for monitoring blood pressure and heart rate. Strokes and coronary heart disease are both prevented by potassium. Both Ca and K are essential for osmotic progression in the body to maintain electrolytic balance and the degree to which body fluids contribute to an alkaline body pH **(Lee *et al*., 2018).**

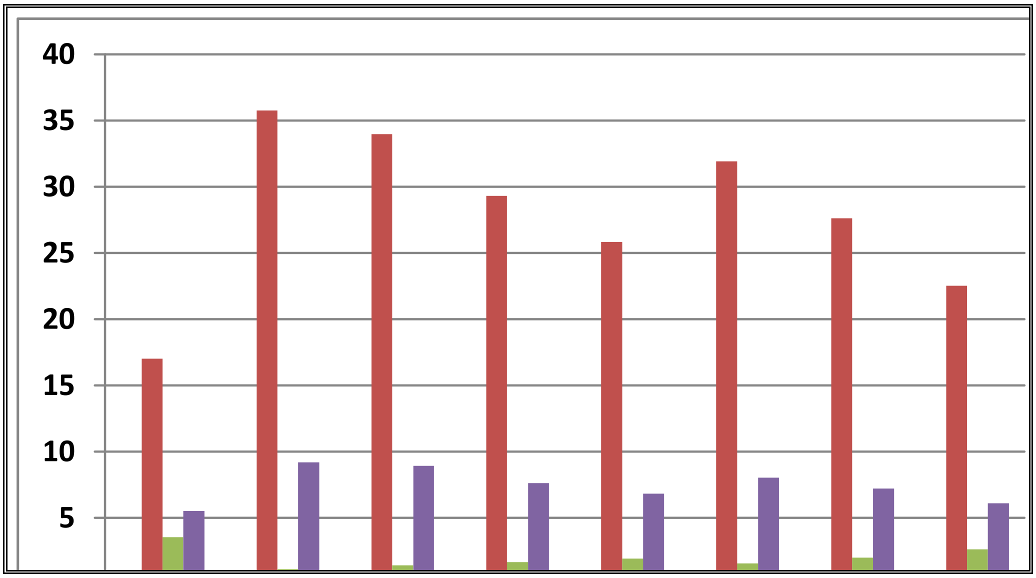

Fig.(1): Sodium (Na), potassium (K), calcium (Ca) and phosphorus (P) of gentamicin-induced nephrotoxicity rats as affecting by watermelon pulp and rind powder levels

The liver enzymes of all nephrotoxicity-treated rats on a basal diet supplemented with varying percentages (2.5, 5 %, and 7.5 %) of watermelon pulp and rind powder were found to be significantly reduced (*P≤0.05*) in comparison to the positive control group (**Table 4)**. The highest effect was measured at 7.5%, and watermelon pulp contained more beneficial compounds than its rind. The group that was provided with 7.5% pulp powder did not differ significantly from the negative control group. Similarly, there were no significant alterations observed between the positive control group and the group that was fed 2.5% rind powder. Powdered watermelon pulp aids the liver in the digestion of ammonia (a byproduct of protein synthesis), thereby relieving renal burden and facilitating fluid elimination. Potassium-rich watermelon is an excellent natural electrolyte that aids in the regulation of nerve and muscle function. In addition to aiding in the fight against inflammation, the vitamin C's high content serves as an antioxidant that is vital for optimal metabolic processes. contain polyphenols, which are antioxidants that may aid in protecting the liver from damage. Lycopene is abundant in watermelon juice, which contains approximately 40% more than raw tomatoes.The antioxidant properties of water melon juice have been ascribed to its significant lycopene content, which activates the antioxidant response element transcription system and stimulates enzymes of the cellular antioxidant defense systems, according to studies(**Erhirhie and Ekene, 2013 & Chaturvedi *et al.,* 2014)**. WR enhances hepatic function by inhibiting the activity of enzymes that lead to liver damage. The capacity for this could be attributed to its highly potent phytochemical components, which have demonstrated antioxidant characteristics. Carotenoids, citrulline, pectin, and citrulline comprise WR. These compounds are abundant in functional groups, including carboxylic (hydroxyl) and hydroxyl (cellulose) groups(watermelon rind). In addition to aiding in the fight against inflammation, the vitamin C's high content serves as an antioxidant that is vital for optimal metabolic processes. K is an essential element that supports proper nerve and muscle function. Lycopene significantly reduces the levels of serum ALT, AST, glutathione, and superoxide dismutase, according to **Jiang *et al.* (2016).**

Table (4): Liver enzymes of gentamicin induced nephrotoxicity rats as affecting by watermelon pulp and rind powder levels.

Groups	AST	ALT	ALP	GGT
Negative control ($G_{1)}$	36.21±2.82 [d]	34.44±2.87 [d]	75.44±0.74 [f]	3.22±0.09 [d]
Positive control (G2)	57.31±1.32 [a]	53.61± 1.65 [a]	96.33±2.47 [a]	5.22±0.12 [a]
Rats fed on 2.5% watermelon rind (G3)	55.65±2.41 [a]	50.31±0.99 [a]	94.22±1.45 [a]	5.08±0.17 [a]
Rats fed on 5% watermelon rind (G4)	51.55±1.05 [b]	46.63±0.91 [b]	88.54±1.26 [c]	4.36±0.32 [b]
Rats fed on 7.5% watermelon rind (G5)	47.22±3.10 [c]	41.32±2.19 [c]	83.76±0.87 [d]	3.75±0.61 [c]
Rats fed on 2.5% watermelon pulp (G6)	50.61±2.22 [b]	48.96±1.88 [b]	92.97±1.39 [b]	4.65±0.52 [b]
Rats fed on 5% watermelon pulp (G7)	44.55±1.89 [c]	42.63±3.05 [c]	86.54±2.44 [d]	4.06±0.65 [c]
Rats fed on 7.5% watermelon pulp (G8)	39.08±3.11 [d]	36.32±2.04 [d]	79.99±0.75 [e]	3.31±0.03 [d]
LSD	3.22	3.89	3.20	0.32

Values are expressed as mean ± SD; n = 3, Values in the same column having different superscripts letters are significantly (*P≤0.05*).

Glb ,Alb, Serum TP and the Alb /Glb ratio of treated and non-treated GM -induced nephrotoxicity rats are revealed in **Table 5** .There are no significant differences in the levels of Alb , Glb ,TP and Alb/Glb in groups with 5% rind and 2.5% pulp powder and also, among 7.5% rind and 5% watermelon pulp powder . All treated groups in levels of rind and pulp caused significant decreases in TP, Alb, Glb and Alb/Glb when compared to the positive control group. The serum protein fractions exhibited optimal performance in the 7.5% pulp powder group. The most prevalent protein present in the bloodstream is Alb. Maintaining osmotic pressure, the mechanism that prevents fluids from escaping blood vessels and into surrounding tissues, is its primary function. Glbs are a class of blood proteins that are present in various configurations. Beta and alpha Glbs inhibit certain enzymes and function as transporters.Immunoglobulins,orgamma globulins , function as antibodies. They serve a crucial function in the immune system by binding to pathogens such as viruses. While the liver is the primary producer of both Alb and Glb, certain types of Glb are also synthesized by white blood cells. A normal albumin-to-globulin ratio is typically observed to be between 1.1 and 2.5; however, this range may differ among laboratories conducting the analysis. Due to the fact that Alb is typically slightly more abundant in the blood than Glb, a normal ratio is marginally greater than 1. As an illustration, the typical range for total Alb in the blood is 34 to 54 g/L, while the recommended range for total Glb is 20 to 39 g/L **(Janice, 1990).** The data that was acquired corresponds to the results reported by **Adebayo *et al.,* (2018),** who reported that watermelon contains the essential amino acid L-arginine, which promotes wound healing and functions in the reproductive, respiratory, renal, gastrointestinal, hepatic, and immune systems. The results obtained were consistent with the assertions made by **Omotoso (2018)** that *Citrullus lanatus* lycopene possesses potential as a nutraceutical and, as an antioxidant, offers defense against oxidative damage and free radicals. **Bazabang *et al*. (2018)** found that the consumption of watermelon pulp significantly decreased plasma concentrations of AST, ALT, ALP, and total protein (*P≤0.05*).

Table (5): Protein status of gentamicin induced nephrotoxicity rats as affecting by watermelon pulp and rind powder levels

Groups	Total protein (g/L)	Albumin (g/L)	Globulin (g/dl)	Alb/Glb ratio
Negative control (G1)	67.24±2.20 [d]	37.18±4.18 [d]	29.06±2.49 [d]	1.28±0.53 [d]
Positive control (G2)	86.14±2.41 [a]	55.33±3.90 [a]	30.81±3.33 [a]	1.80±0.78 [a]
Rats fed on 2.5% watermelon rind (G3)	84.15±2.22 [a]	53.64±1.52 [a]	30.51±2.57 [a]	1.76±0.02 [a]
Rats fed on 5% watermelon rind (G4)	78.81±5.75 [b]	48.72±1.51 [b]	30.09±1.20 [b]	1.62±0.07 [b]
Rats fed on 7.5% watermelon rind (G5)	74.84±5.50 [c]	45.06±1.27 [c]	29.78±1.71 [c]	1.51±0.01 [c]
Rats fed on 2.5% watermelon pulp (G6)	78.82±2.22 [b]	48.54±1.52 [b]	30.28±2.57 [b]	1.60±0.02 [b]
Rats fed on 5% watermelon pulp (G7)	72.92±5.75 [c]	43.32±1.51 [c]	29.60±1.20 [c]	1.46±0.07 [c]
Rats fed on 7.5% watermelon pulp (G8)	67.99±5.50 [d]	38.76±1.27 [d]	29.23±1.71 [d]	1.33±0.0 1 [d]
LSD	3.34	2.16	0.30	0.09

Values are expressed as mean ± SD; n = 3, Values in the same row having different superscripts letters are significantly (*P≤0.05*).

Comparing the positive nephritic control group to the group consuming watermelon pulp and rind powder, the levels of these substances significantly increased GPX, SOD, and CAT **(Table 6)**. Respiratory enzyme repair was observed to be the most effective effect of the 7.5% pulp treatment in nephritic rats. Arginine's bioavailability is enhanced by the rapid absorption of 80% of the ingested aggregate of citrulline from watermelon. In addition to its antioxidant and vasodilatory properties, citrulline regulates nitric oxide in humans. Citracil significantly impacts a wide range of human health domains, including skeletal and muscular strength, diabetes, immunology, and neurology **(Perkins *et al*., 2012)**. Lycopene is the carotenoid that gives watermelons their characteristic red hue. As widely recognized antioxidants, lycopene and vitamins C offer numerous health advantages to humans. Numerous chronic diseases, including oncogenesis and diabetes, may be inhibited by lycopene. Central to the protective antioxidant mechanism is the capacity to scavenge singlet oxygen. Attributable to the generation of free radicals and their interactions with macromolecules, the oxidation of proteins, lipids, and DNA induces a multitude of metabolic system disorders. Regarding pathogenic infections, lycopene plays a crucial defensive role **(Sase *et al.,* 2013)**. Lycopene protects the DNA of white blood cells as one of its antioxidant functions. Furthermore, it is worth noting that watermelon juice, which weighs around eight ounces, contains a multitude of vitamins and nutrients, including lycopene, potassium, anthraquinones, and vitamin C and A **(Lee *et al.,* 2018)**. Watermelon fruit extracts, which contain anthraquinones and have moderate concentrations of phenolic compounds, have historically been utilized to treat constipation and stomachache.

Table (6): GPX, SOD and CAT of gentamicin-induced nephrotoxicity rats as affecting by watermelon pulp and rind powder levels

Groups	GPX (ng/dl)	SOD (U/L)	CAT(mmoL/L)
Negative control ($G_{1)}$	82.13±3.07 [a]	53.05±0.99 [a]	70.04±0.97 [a]
Positive control (G2)	52.14±1.95 [f]	28.24±2.1 1 [f]	37.61±2.06 [f]
Rats fed on 2.5% watermelon rind (G3)	57.32±1.33 [e]	31.13±1.01 [e]	42.86±1.64 [e]
Rats fed on 5% watermelon rind (G4)	62.33±2.22 [d]	35.76±1.88 [d]	46.93±2.04 [d]
Rats fed on 7.5% watermelon rind (G5)	67.08±3.07 [c]	39.67±2.75 [c]	51.95±1.24 [c]
Rats fed on 2.5% watermelon pulp (G6)	60.99±0.85 [d]	34.56±2.17 [d]	44.09±0.34 [d]
Rats fed on 5% watermelon pulp (G7)	67.22±0.94 [c]	39.33±2.39 [c]	50.06±0.94 [c]
Rats fed on 7.5% watermelon pulp (G8)	72.55±2.13 [b]	44.03±1.03 [b]	56.45±1.08 [b]
LSD	3.11	2.89	3.46

Values are expressed as mean ± SD; n = 3, Values in the same row having different superscripts letters are significantly (*P≤0.05*).Glutathione pyroxidasesuperoxide ،GPX: :dismutaseSOD, Catalase:CAT.

In comparison to the positive control group, administration of watermelon pulp and rind powder at a concentration of 7.5% resulted in a significant increase in the mean values of GST and TA. Conversely, administration of the same level of MDA decreased the mean values significantly, owing to its impact on antioxidant enzyme enhancement (Table 7). The data presented in the same table validated that the nephritic control group exhibited significant reductions in GST and TAC, whereas MDA demonstrated significant increases in comparison to the negative control group. These changes were significantly reversed by treatment with watermelon juice, which also significantly decreased MDA levels in both organs, indicating that watermelon juice has protective effects against ethanolic-induced oxidative damage. Prior to ethanol administration, the glutathione levels in the liver and brain of rats treated with water melon juice increased significantly ($P \leq 0.05$). This increase could be attributed to either the direct scavenging of reactive oxygen species (ROS) by water melon juice or an upregulation of GSH synthesis **(Lee *et al.*, 2018)**.Oxidative stress etiology serves as the fundamental precursor to a multitude of metabolic dysfunctions. ROS production can be significantly increased through uncontrolled oxidation. The accumulation of free radicals may contribute to the destruction of endothelium-dependent vasodilation and atherosclerosis via nitric oxide inactivation. Robust ROS are continuously produced in conventional metabolic pathways. Diet, smoking, environmental factors, and exercise may all contribute to an increase in ROS accumulation. Lycopene plays a role in metabolism-based therapy by preventing the oxidative destruction of lymphocytes and in the short-term development of LDL oxidation (**Erdman *et al*., 2009).**The generation of ROS disrupts the oxidative equilibrium, initiates lipid oxidation, and continuously generates double allylic hydrogen atoms. The generation of hypochlorous acid serves as the foundation for cellular destruction facilitated by neutrophil-catalyzed oxidative damage. The human body produces antioxidant enzymes such as SOD and GPX in response to this circumstance. It is a crucial role in the initial line of defense by converting singlet oxygen into hydrogen peroxide via superoxide dismutase. The process by which hydrogen peroxide is converted to water is CAT and GSH-Px enzymes. Disruption may ensue subsequent to necrosis or apoptosis if an excessive amount of ROS is generated; otherwise, these enzymes operate synchronously. Lycopene in the diet may serve to inhibit disproportionate ROS production **(Pinto *et al*., 2014).**Oxidative stress is widely recognized as being highly pronounced in chronic diseases. A wide range of diseases, including but not limited to cancer, osteoporosis, cardiovascular complications, cataract formation, and diabetes pathogenesis, are frequently linked to free radicals. Lycopene decreased MDA and lipid peroxide levels in hypertensive patients in a manner comparable to that of the SOD, GSH-Px, and reduced glutathione. Lycopene was discovered to effectively increase GSH levels and decrease MDA levels in coronary artery disease. An investigation was conducted on the effects of lycopene on cisplatin-induced lipid peroxidation and nephrotoxicity in male Wistar rats. The lycopene-fed rats exhibited a significant decrease in renal Bax protein, an indicator of low oxidative stress. Additionally, the impact of lycopene supplementation on markers of oxidative stress was assessed. For a duration of two months, human subjects were administered lycopene in order to assess its impact on subsequent LDL and MDA assessments. In order to identify any potential adverse effects, lymphocytes were also examined. A significant decrease of 17% in LDL oxidation and 21% in TBARS value was observed in the control group of subjects that were provided with lycopene(**Cai *et al.*,2016).**

Table (7): Antioxidant enzymatic glutathione transferase (GST), total antioxidant capacity (TAC) and oxidant enzymatic malondialdehyde (MDA) of gentamicin-induced nephrotoxicity rats as affecting by watermelon pulp and rind powder levels

Groups	GST(mmoL/L)	TAC(nmoL/L)	MDA(nmoL/L)
Negative control ($G_{1)}$	35.11±2.08 [a]	1.87±0.01 [a]	16.03±2.11 [f]
Positive control (G2)	16.22±0.97 [f]	0.87±0.11 [f]	33.89[a]±0.89
Rats fed on 2.5% watermelon rind (G3)	19.45±0.08 [e]	0.90±0.15 [e]	30.11±0.67 [b]
Rats fed on 5% watermelon rind (G4)	23.52±1.36 [d]	0.94±0.12 [d]	27.62±1.46 [c]
Rats fed on 7.5% watermelon rind (G5)	27.28±2.04 [c]	0.99±0.07 [c]	24.71±0.75 [d]
Rats fed on 2.5% watermelon pulp (G6)	21.11±1.33 [d]	0.92±0.07 [d]	26.65±1.23 [c]
Rats fed on 5% watermelon pulp (G7)	26.09±2.01 [c]	0.97±0.11 [c]	22.99±0.89 [d]
Rats fed on 7.5% watermelon pulp (G8)	31.04±1.32 [b]	1.04±0.14 [b]	18.71±0.75 [e]
LSD	2.86	0.04	3.01

Values are expressed as mean ± SD; n = 3, Values in the same row having different superscripts letters are significantly (*P≤0.05*).

The findings illustrated in Figure 2 the progressive hypoglycemic impact of watermelon pulp and rind powder on the fasting blood glucose levels of rats with nephritis. Results in the same table described that level glucose in nephritic control group was much higher than the negative control group. All nephritic rats fed on a diet containing 7.5% followed by 5% watermelon pulp and rind powder showed a significant decrease in glucose compared to the positive nephritic control group. The potential hypoglycemic and antioxidant properties of plant secondary metabolites, such as flavonoids and polyphenols, found in watermelon rind, contribute to its anti-diabetic effects. In addition, watermelon is among the limited number of foods that possess citrulline, an effective precursor for the synthesis of arginine, by nature. Arginine has been documented to possess a multitude of biological activities **(Abdel Gawad *et al.*, 2016)**. In diabetic rats, dietary arginine supplementation reduces the concentration of glucose in the serum. Watermelon consumption was reported to increase plasma arginine concentration in humans, which is an intriguing finding. The watermelon rind possesses the capacity to stimulate the proliferation of quiescent cells and replenish depleted cells. While the precise mechanism remains unknown, it has been demonstrated that the regeneration of pancreatic β cells is induced by the active constituents (flavonoids and polyphenols, among others), which may act singly or synergistically. Lycopene provides human beings with protection against a wide range of pathogenic assaults, including those that give rise to numerous metabolic syndromes. The protective properties are attributed to the ability to scavenge singlet oxygen. In addition, numerous authors have documented that lycopene possesses protective properties against oxidative damage and free radicals, in addition to its potential as a nutraceutical. Lycopene is involved in the regulation of cellular division and differentiation.The presence of mitotic figures between islet cells in this group of animals may be explained in this way. **(Perkins *et al*.,2012 and Pinto *et al*., 2014)**. **Ahn *et al.* (2011)** reached the conclusion that lycopene possesses the capacity to enhance glucose metabolism and insulin sensitivity. Additionally, **Kolawole *et al*. (2016)** stated that watermelon rind extract is regarded as a hypoglycemic and hyperinsulinemic concentrated source of nutrients.

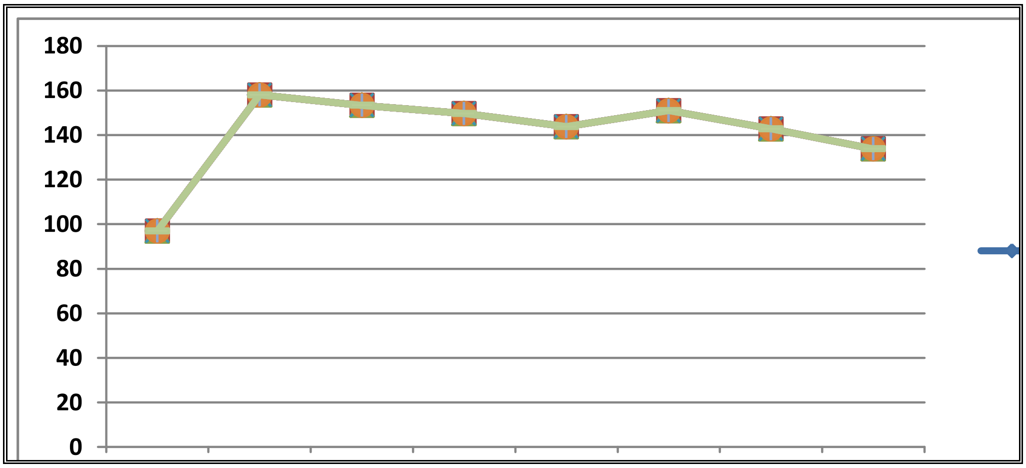

Fig. (2): Blood glucose of gentamicin-induced nephrotoxicity rats as affecting by watermelon pulp and rind powder levels

Conculsion :

The present study demonstrated that both watermelon (*Citrullus lanatus*) pulp and rind powders possess notable nutritional value and exhibit effective protection against gentamicin-induced nephrotoxicity in rats. Biochemical analysis showed that each powder contains bioactive compounds that counteract oxidative stress and inflammation, thereby safeguarding renal function. These findings suggest that watermelon by-products, especially the pulp, could serve as natural, effective agents for protecting and treating kidney diseases and related metabolic complications.

References

Abdel Gawad, S.; Fikry, H.; Amin, M.M.; Elmahdi, A.R. and Abd Elaziz, D. (2016): Effect of Apitherapy on The Pancreas and Liver Of Strep to zotacin Induced Diabetic rats. A Biochemical and Histological Study. European Journal of Pharmace.,3(7):555-565.

Abu-Hiamed, H.A. (2017): Chemical Composition Flavonoids and -sitosterol Contents of Pulp and Rind of Watermelon (*Citrullus lanatu*s) Fruit. Pakistan Journal of Nutrition, 16: 502-507.

Adebayo, A.O.; Innocent Alozie. and Chuke-Okeke ,O.S.(2018): Evaluating the influence of Citrulluslanatus seed extracts on electrolytes, urea and creatinine in Streptozotocin induced diabetic albino rats. Abasyn Journal of Life Sciences, 1 (2): 87-94.

Aderiye, B.I.; David, O.M.; Fagbohun, E.D.; Faleye. J. and Olajide, O.M.(2020): Immunomodulatory and phytomedicinal properties of watermelon juice and pulp (*Citrullus lanatus* L): A review. GSC Biol. Pharm. Sci., 11: 153-165.

Aebi, H. E. (1983): In: Methods in Enzymatic Analysis, New York, Academic press; 273-302.

Ahn, J.; Choi, W.; Kim, S. (2011): Antidiabetic effect of watermelon (*Citrullus vulgaris Schrad*) on Streptozotocin-induced diabetic mice. Food Sci. Biotechnol., 20(1): 251-154.

Akashi, K. ; Nishimura, N. ; Ishida, Y. and Yokota, A.(2004): Potent hydroxylradical-scavenging activity of drought-induced type-2 metallothionein inwild watermelon .Biochem. Biophys. Res. Commun., 323 (1) : 72-78.

Ali, F.E.M.; Sayed, A.M.; El-Bahrawy, A.H.; Omar, Z.M.M. and Hassanein, E.H.M.(2021): Targeting KEAP1/Nrf2, AKT, and PPAR-γ signals as a potential protective mechanism of diosmin against gentamicin-induced nephrotoxicity. Life Sci.,275:119349.

Al-Sayed, H.M.A. and Ahmed, A.R. (2013): Utilization of watermelon rinds and sharlyn melon peels as a natural source of dietary fiber and antioxidants in cake. Ann. Agric. Sci., 58: 83-95.

Althunibat, O.Y.; Abukhalil, M.H.; Aladaileh, S.H.; Qaralleh, H.; Al-Amarat, W. and Alfwuaires, M.A.(2022): Formononetin Ameliorates Renal Dysfunction, Oxidative Stress, Inflammation, and Apoptosis and Upregulates Nrf2/HO-1 Signaling in a Rat Model of Gentamicin-Induced Nephrotoxicity. Front Pharmacol.,13:916732.

AOAC, Association of Official Analytical Chemists (2012): George, W.L. 19th Edition, ch. 4, No. 968.08,56. USA.

Asghar, M.N. ;Shahzad, M.T.; Nadeem, I. ;Ashraf,C.M. (2013): Phytochemical and in vitro total antioxidant capacity analyses of peel extracts of different cultivars of Cucumismelo and Citrullus lanatus.Pharm. Biol., 51 (2): 226-232

Balakumar, P.; Rohilla, A. and Thangathirupathi, A.(2010): Gentamicin-induced nephrotoxicity: Do we have a promising therapeutic approach to blunt it? Pharmacol. Res.,62:179- 86.

Bazabang,S.A.;Monday- N.;Adebisi,S.S and Wusa, K.. (2018): Hepatoprotective Effects of Aqueous Extract of Watermelon (Citrulluslanatus) Seeds on Ethanol-Induced Oxidative Damage in Wister Rats.Sub-Saharan African Journal of Medicine ,(5)4 : 66-92.

Bonsens, K. E., and Taussky, D. H. (1984): Determination of serum creatinine. Journal of Chemical Investigation, 27, 648–660.

Cai, B., Luo, Y. L., Wang, S. J., Wei, W. Y., Zhang, X. H., Huang, W., Li, T., Zhang, M., Wu, N., & Roodrajeetsing, G. (2016):Does citrulline have protective effects on liver injury in septic rats? BioMed Research International, 2016, Article 1469590. https://doi.org/10. 1155/ 2016/ 1469590

Chaturvedi, P., Pipedi-Tshekiso, M., andTumed, A. (2014): Supplementation with watermelon renders protection against toxicity induced by paracetamol in albino rats: The mutual and fine interaction of antioxidants prevented the cellular damage. International Journal of Food, Agriculture, and Veterinary Sciences, 4(1), 102–111.

Erdman, J. W. Jr., Ford, N. A., and Lindshield, B. L. (2009): Are the health attributes of lycopene related to its antioxidant function? Archives of Biochemistry and Biophysics, 483(2), 229–235. https://doi.org/10.1016/ j.abb.2008.10.022

ESHA.(2017): The food processor, version 10.12.0. Watermelon Nutritional Profile, ESHA Research, Salem, Oregan, USA

Farombi, E. O., and Ekor, M. (2006): Curcumin attenuates gentamicin-induced renal oxidative damage in rats. Food and Chemical Toxicology, 44(9), 1443–1448.doi: 10.1016/j.fct.2006.05.005.

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(2), 227–231.

Garcia-Mas, J.; Benjak, A.; Sanseverino, W.; Bourgeois, M.; Mir, G. and González, V.M. (2012): The genome of melon (*Cucumis melo* L.). Proc. Natl. Acad. Sci.,109:11872-7.https://doi.org/10.1073/pnas.1205415109

Generalić, M.; Skroza, D. ; Ljubenkov, I.; Katalinić, V. and Šimat, V. (2019): Antioxidant and antimicrobial potential of phenolic metabolites from traditionally used mediterranean herbs and spices Foods, 8 (11) : 579.

Gladvin1, G.; Sudhaakr, G.; Swathi1, V. and Santhisri, K. V. (2017): Mineral and Vitamin Compositions Contents in Watermelon Peel (Rind) International Journal of Current Microbiology and Applied Sciences ISSN: 2319-7706 Special Issue-5: 129-133.

Gowenlock, A. H., McMurray, J. R., and McLauchlan, D. M. (1988): Varley's Practical Clinical Biochemistry (6th ed.). CBC Publishers and Distributors.

Guo C.H. and Wang C.L. (2013): Effect of zinc supplementation on plasma copper/zinc ratios, oxidative stress and immunological status on haemodialysis patients. Int. J. Med. Sci., 10: 79-89.

Henry, R. J. (1974): Clinical Chemistry principles and Techniques 2nd Ed, Harper and Publishers, New York, Philadelphia.

Huang, H., Jin, W. W., Huang, M., Ji, H., Capen, D. E., and Xia, Y. (2020): Gentamicin-induced acute kidney injury in an animal model involves programmed necrosis of the collecting duct. Journal of the American Society of Nephrology, 31(9), 2097–2115.

Huang, Y.; Zhao, L.; Kong, Q.; Cheng F. and Niu M. (2016): Comprehensive mineral nutrition analysis of watermelon grafted onto two different rootstocks. Horticultural Plant Journal, 2(2), 105–113.

IFCC (1983): International Federation of Clinical Chemistry. Methods for the measurement of catalytic concentration of enzymes – Part 5: IFCC methods for alkaline phosphatase. Journal of Clinical Chemistry and Clinical Biochemistry, 21(11), 731–748.

Janice, T. B. (1990): Clinical methods: The history, physical, and laboratory examinations (3rd ed., Chapter 101: Serum albumin and globulin). In H. K. Walker, W. D. Hall, & J. W. Hurst (Eds.), Boston: Butterworths.

Jiang, W., Guo, M. H., and Hai, X. (2016): Hepatoprotective and antioxidant effects of lycopene on non-alcoholic fatty liver disease in rat. World Journal of Gastroenterology, 22(46), 10180–10188. https://doi.org/10.3748/wjg.v22.i46.10180

Johnson, J. T., Lennox, J. A., Ujong, V. P., Odey, M. O., Fila, W. O., Edim, P. N., and Dasofunjo, K. (2013): Comparative vitamins content of pulp, seed and rind of fresh and dried watermelon (*Citrullus lanatus*). International Journal of Science and Technology, 2, 99–103.

Kolawole, T. A., Ojeka, S. O., and Dapper, D. V. (2016): Anti-diabetic effects of the methanolic extract of the rind of Citrullus lanatus (watermelon) in alloxan-induced diabetes in male albino Wistar rats. Journal of Medicine and Medical Sciences, 7(2), 23–29.

Koracevic, D. C. (2001):Method for the measurement of antioxidant activity in human fluids. Journal of Clinical Pathology, 54, 356–361.

Lee, H. G., Jo, Y., Ameer, K., and Kwon, J. H. (2018): Optimization of green extraction methods for cinnamic acid and cinnamaldehyde from cinnamon (*Cinnamomum cassia*) by response surface methodology. Food Science and Biotechnology, 27, 1607–1617.

Malkki, Y. (2001): Physical properties of dietary fiber as keys to physiological functions. Cereal Foods World, 46: 196-199.

Mandel, H., Levy, N., Izkovitch, S., and Korman, S. H. (2005): Elevated plasma citrulline and arginine due to consumption of Citrullus vulgaris (watermelon). Journal of Inherited Metabolic Disease, 28(4), 467–472.

Molaei, E., Molaei, A., Abedi, F., Hayes, A. W., and Karimi, G. (2021): Nephroprotective activity of natural products against chemical toxicants: The role of Nrf2/ARE signaling pathway. Food Science & Nutrition, 9(6), 3362–3384.doi: 10.1002/fsn3.2320.

Naknaen, P., Itthisoponkul, T., Sondee, A., and Angsombat, N. (2016): Utilization of watermelon rind waste as a potential source of dietary fiber to improve health promoting properties and reduce glycemic index for cookie making. Food Science and Biotechnology, 25(2), 415–424.

Nicoli Diana, S. (2003): Pocket Guide to Diagnostic Tests. LANGE Clinical Science.

Nkoana, D. K., Mashilo, J., Shimelis, H., and Ngwepe, R. M. (2022): Nutritional, phytochemical compositions and natural therapeutic values of citron watermelon (Citrullus lanatus var. citroides): A review. South African Journal of Botany, 145, 65–77.

Ohkawa, H., Ohishi, N., & Yagi, K. (1979): Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Analytical Biochemistry, 95(2), 351–358.

Okwu, D. E., and Josiah, C. (2006): Evaluation of the chemical composition of two Nigerian medicinal plants. African Journal of Biotechnology, 5(4), 357–361.

Omotoso, O. T. (2018): Hepatoprotective activity of aqueous and methanolic extracts of watermelon seeds on salt- and paracetamol-induced liver damage in female white rats. International Research Journal of Natural Sciences, 6(1), 1–12.

Onwuka, G.I.(2005): Food Analysis and Instrumentation: Theory and Practice. Naphthali Print, Lagos, Nigeria,95-96.

Oyenihi, O. R., Afolabi, B. A., Oyenihi, A. B., Ogunmokuna, O. J., and Oguntibeju, O. O. (2016):Hepato- and neuro-protective effects of watermelon juice on acute ethanol-induced oxidative stress in rats. Toxicology Reports, 3, 288–294.

Park, Y. K., Koo, M. H., Ikegaki, M., and Contado, J. L. (1997): Comparison of the flavonoid aglycone contents of Apis mellifera propolis from various regions of Brazil. Arquivos de Biologiae Tecnologia, 40, 97–106.

Patton, C. J., and Crouch, S. R. (1977): Enzymatic determination of urea. Journal of Analytical Chemistry, 49, 464–469.

Perazella, M. A., and Rosner, M. H. (2022):Drug-induced acute kidney injury. Clinical Journal of the American Society of Nephrology, 17, 1220–1233.

Perkins-Veazie, P., Davis, A., and Collins, J. K. (2012): Watermelon: From dessert to functional food. Israel Journal of Plant Sciences, 60(4), 395–402.

Pinto, C., Cestero, J. J., Rodríguez-Galdón, B., and Macías, P. (2014): Xanthohumol, a prenylated flavonoid from hops (*Humulus lupulus* L.): Protects rat tissues against oxidative damage after acute ethanol administration. Toxicology Reports, 1, 726–733.

Rahman, H., Priyanka, P., Lavanya, T., Srilakshmi, N., and Kumar, P. R. (2013):A review on ethnobotany, phytochemistry and pharmacology of *Citrullus lanatus* L. International Research Journal of Pharmaceutical and Applied Sciences, 3(2), 77–81.

Reeves, P. G., Nielsen, F. H., and Fahey, G. C. Jr. (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. The Journal of Nutrition, 123(11), 1939–1951. https://doi.org/10.1093/jn/123.11.1939

Renner, S.S.; Sousa, A. and Chomicki, G.(2017): Chromosome numbers, Sudanese wild forms, and classification of the watermelon genus Citrullus, with 50 names allocated to seven biological species. Taxon., 66:1393-405.

Russo, L., and Etherington, T. (2001): Non-wood news. An Information Bulletin on Non-Wood Forest Products, 8, 38–39.

Sase, A., Dahanayaka, S., Höger, H., Wu, G., and Lubec, G. (2013): Changes of hippocampal beta-alanine and citrulline levels are paralleling early and late phase of retrieval in the Morris Water Maze. Behavioural brain research, 249, 104–108. https://doi.org/10.1016/j.bbr.2013.04.033

Schermer, S. (1967): The Blood Morphology of Laboratory Animal. Longmans, Printed in Great Britain, Green and Co. Ltd., pp.350.

Schumann, G., and Klauke, R. (2003): New IFCC reference procedures for the determination of catalytic activity concentrations of five enzymes in serum: Preliminary upper reference limits obtained in hospitalized subjects. Clinica Chimica Acta, 327(1–2), 69–79.

Siddiqui, W.A.; Shahzad, M.; Shabbir, A. and Ahmad, A. (2018): Evaluation of anti-urolithiatic and diuretic activities of watermelon (*Citrullus lanatus*) using in vivo and in vitro experiments. Biomed. Pharmacother.,97:1212-21.

Singleton, V. L., and Rossi, J. A. (1965): Colorimetry of total phenolics with phosphomolybdic phosphotungstic acid reagents. American Journal of Enology and Viticulture, 16(3), 144–158.

Snedecor, G.W. and Cochran, W.G. (1967): Statistical methods 7th ed., Iowa State Univ. Press, Ames Iowa,USA.

Spencer, K., and Price, C. P. (1977): Influence of reagent quality and reaction conditions on the determination of serum albumin by the bromcresol green dye-binding method. Annals of Clinical Biochemistry, 14(2), 105–115.

Sreedhar, V., Ravindranath, L. K., Madanagopal, N., Venugopal, K., Rajasekhar, K. K., & Reddy, G. H. (2010): In-vitro antioxidant activity and free radical scavenging potential of roots of Vitex vestita. Journal of Pharmaceutical Research, 3(12), 3140–3142.

Srivastava, L. M.; Das, N. and Sinha, S. (2002): Essential of practical biochemistry CBC publishers and distributors.Biochem; Res.

Sun, V. I., Larry, W., Oberely, A., and Ving, V. (1998): A simple method for clinical assay of superoxide dismutase. Clinical Chemistry, 34(3), 497–500.

Xu, B., and Chang, S. K. (2010):Phenolic substance characterization and chemical and cell-based antioxidant activities of 11 lentils grown in the Northern United States. Journal of Agricultural and Food Chemistry, 58(3), 1509–1517.

Young, D. S. (1975): Effects of drugs on clinical laboratory tests: Determination of GOT. Clinical Chemistry, 21,

Yu, P., Duan, Z., Liu, S., Pachon, I., Ma, J., and Hemstreet, G. P. (2021): Drug-induced nephrotoxicity assessment in 3D cellular models. Micromachines, 13(1), 3. https://doi.org/10.3390/mi13010003.

تأثير مسحوق لب وقشر البطيخ (*Citrullus lanatus*)على سمية الكلى المستحثة بواسطة الجنتامايسين في الفئران

فتحية جمال النحاس[1] وأميرة حمدى درويش[2]

[1]قسم الاقتصاد المنزلي، كلية التربية النوعية جامعة المنوفية، مصر.

[2]قسم التغذية وعلوم الأغذية، كلية الاقتصاد المنزلي، جامعة المنوفية، مصر

الملخص:

تم اجراء هذه الدراسة لتحديد التركيب الكيميائي لمسحوق لب وقشره البطيخ والتأثيرات العلاجية المحتمله للفئران المصابة بالسمية الكلوية المستحثه بالجنتاميسين فى الفئران . تم تقسيم أربعين فأرا اناث من سلالة الألبينو (سبراج-داولي) إلى ثمانية مجموعات، حيث كانت المجموعة الأولى تعتبر مجموعة ضابطة سالبة بينما تم تغذية المجموعات السبع الأخرى على نظام غذائي أساسي وحقنها بالجنتامايسين لإحداث التسمم الكلوي. كانت إحدى هذه المجموعات مجموعة ضابطة موجبة ، بينما تم تغذية المجموعات السبع الأخرى على نظام غذائي أساسي يحتوي على 2.5% و 5% و7.5% من لب وقشرة البطيخ المجفف على التوالي لمدة 28 يومًا . أظهرت النتائج أن محتوى الرطوبة والألياف الغذائية والكربوهيدرات والسعرات الحرارية الكلية والفينولات الكلية والفلافونويدات الكلية و٢،٢-ديفنيل -١- بيكريلهيدرازيلDPPH) ٪ (في لب البطيخ المجفف كانت أعلى بشكل ملحوظ من محتواها في قشرة البطيخ، بينما كان محتوى المعادن المختبرة في قشرة البطيخ أعلى بشكل ملحوظ من اللب باستثناء محتوى الحديد والبوتاسيوم. بالإضافة إلى ذلك، انخفضت مستويات AST و ALT و ALPو GGT واليوريا وحمض اليوريك والكرياتينين وMDA وسكر الدم بشكل كبير في المجموعات المصابة بسمية كلوية و مضاف اليها لب البطيخ . بالإضافة إلى زيادة كبيرة في مستويات Tp, Alb, GPX, SOD. CAT,GSTs, and TAC بينما ينخفض مستوى البوتاسيوم والفوسفور فى حين يزداد مستوى الصوديوم والكالسيوم فى المجموعات المعاملة بسمحوق اللب والقشرة عند 7.5% ، أثبتت هذه الدراسة أن مسحوق اللب والقشرة لديه فعالية كبيرة في علاج أمراض الكلى وحماية الجسم من المضاعفات المرتبطة بها، كما يحتوي على العديد من المركبات الحيوية التي تلعب دورًا هامًا وفعالًا في العمليات الأيضية والأداء الحيوي خلال دورة الحياة.

الكلمات المفتاحية: وظائف الكلى، الجلوكوز في الدم، المالونديالدهيد، الإنزيمات المضادة للأكسدة، انزيمات الكبد.