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The roles of Arabic Gum and Corn silk extracts to avoid hepato-nephro toxicity of Gentamicin in rats

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ABSTRACT

The effects of different concentration of Arabic Gum (AG) and corn silk (CS) extracts against hepato-nephro toxicity which induced by gentamicin (GM) in experimental rats were investigated. 25 bioactive constituents in the extract of CS were investigated by GC-MS analysis;Phytol (3.325 µg/g) was the major constituent with antioxidant properties and can reduce free-radical generation in an in-vitro experimental system.GM at a dose 80 mg/kg, intraperitoneal (ip) for 8 sequential days was used to induce nephrotoxicity, manifested biochemically by a significant increase in serum creatinine, blood urea and uric acid. In addition, liver enzymes, Total Bilirubinincreased and total protein decreased. All extracts showed a significant effect in improving kidney function, liver enzymes, total protein and Bilirubin. The histopathological investigation of liver and kidney in rats injected with GM showed that, the best improvement in liver enzymeswere obtained by using 20% Arabic Gum Extract (AGE) +5% Corn Silk Extract (CSE) and 10% AGE,while using 10% CSE, 10% AGE and 20% AGE improved kidney function compared with control (+) group.

Key words:Arabic Gum; Corn silk; Liver enzymes; Kidney function;Gentamicin; Histopathology; rats.

INTRODUCTION

Gentamicin is an antibiotic of the aminoglycosides group. It is an important antibacterial agent since its discovery in the 40th century (Oliveira *et al*., 2006). Gentamicin is a commonly used aminoglycoside antibiotic either alone or in combination with a cell wall-active drug in the management of dangerous and life-threatening infections caused by Gram-positive and Gram-negative aerobes (Choi *et al*., 2011). All aminoglycosides have the potential to induce nephrotoxicity; however, gentamicin, compared to other aminoglycosides, has the highest nephrotoxicity (Balakumar *et al.*, 2010). Nephrotoxicity of gentamicin in the proximal convoluted tubules results from its internalization by lysosomes and causes release of hydrolase enzymes, thereby causing cell necrosis and proximal tubule obstruction (Hanslik e*t al*., 1994). In this case, aminoglycosides endocytosis probably damages renal pathways processing amino acids and small peptides (Rougier *et al.*, 2003). The disorders in the cell membrane structure caused by Gentamicin (Valipour *et al.*, 2016), cellular debris deposition, simultaneously, may block nephrons (Neugarten *et al*., 1983). As a result changes in glomerular permeability with decreased glomerular ultrafiltration coefficient may be found (De-Barros-e- Silva *et al*., 1992).

Gentamicin has limited clinical benefits due to its side effects. Major side effects include liver damage, which is a major cause of liver insufficiency in a large number of people who take the drug. Therefore, taking these drugs is constrained by the fact that one of the main side effects of gentamicin is the creation of hepatic toxicity (Masakazu *et al.*, 2014). Increasing the production of reactive oxygen species (ROS), which can be seen after the use of gentamicin in cells, is

effective in causing toxic effects of this drug on tissue structure and function (Wojciech and Vincen, 2005).

Medical plants have been recognized as potential sources of a new compound of therapeutic values as a source of drug design and development (Bisi-Johnson *et al*, 2012). Corn silk is made up of long silk threads that are the stigma and styles of the maize plant that covers the corn. Corn silk is a waste material from corn cultivation (*Zea mays* L.) and is widely available all over the world (Maksimovic*et al*., 2005). Maize being the third most planted food crop and one of the major energy sources, it is also one of the essential cereals and edible grain the world possesses. Corn silk, a part from having proteins, vitamins, carbohydrates, also is an excellent source of fixed and volatile oils, steroids such as sitosterol, stigmasterol, alkaloids, saponins and other natural antioxidants like flavonoids (Josephine *et al*., 2015).Corn silk is a well-known traditional Chinese herbal medicine, which was reported to treat weight loss, urinary ailments (Maksimovic*et al*., 2004), and possess anti-fatigue (Hu *et al*., 2010), antitumor (Habtemariam, 1998), hypoglycemic (Guo *et al*., 2008), antioxidant (Ebrahimzadeh *et al*., 2008), and anti-fungal activities (El-Ghorab and El-Massry, 2007).

Flavonoids of corn silk (FCS) have been investigated and confirmed to own various pharmaceutical activities such as, antihypertensive, anti-inflammatory, anti-oxidative and antidiabetic (Liu *et al.*, 2011). Nephroprotective effect of corn silk extract was also reported along with gentamicin renal toxicity (Sepehri *et al.*, 2011).

Arabic Gum (AG) is an edible, dried sticky exudate from *Acacia seyal* and *Acacia senegal*, which is rich in non-viscous soluble fiber. It is commonly used in the food and pharmaceutical industries as emulsifier and preservative (Ali*et al*., 2009). In North Africa and the Middle East, it has been used as an oral hygiene agent by various societies for centuries (Tyler*et al*., 1977). AG is used in Arabic folk medicine to reduce both frequency and need of hemodialysis in patients suffering from chronic renal failure. It has strong antioxidant properties and is used to reduce the experimental renal toxicity against gentamicin (Al-Majed*et al*., 2002) and cisplatin (Al-Majed*et al*., 2003) and to ameliorate cardiotoxicity (Abd-Allah*et al*., 2002). Moreover, AG is reported to reduce oxidative and inflammation against adenine-induced chronic renal failure in rats (Ali*et al*., 2013).

These were mainly focused on the use of various antioxidantsextracts of medicinal plants or other agents having antioxidant properties sothe present investigation illustrates the effects of Arabic Gum and Corn silk extracts on some biochemical parameters in the serum of young male albino rats associated with liver and kidney functionstoavoid hepato-nephrotoxicity of Gentamicin.

MATERIALS AND METHODS

Materials:

Arabic gum (AG) was obtained from El- Gomhoria Company for Chemicals, Drugs and Medicals supplies, Cairo, Egypt. Fresh sweet corns were collected from local market in Cairo. Corn silk was removed from them, shade dried and stored at room temperature for further analysis. Gentamicin (GM) was obtained from Memphis Company for Pharmaceutical and Chemical industries, Cairo, Egypt. The enzyme kits used for analysis were obtained from Biodiagnostic Company, Cairo, Egypt.

Methods:

Preparation of extracts:

The dried powder of corn silk (5 and 10 g) was extracted with 100 ml water at 100◦C. After cooling down to room temperature, the whole extract was filtered and centrifuged at 3000 rpm for 15 min to obtain a clear solution. Arabic gum extracts (10 and 20%) were prepared using boiled water. The solutions centrifuged

after cooling down to room temperature at 3000 rpm for 15min to obtain clear solution.

Proximate analysis:

Nutritional composition for Arabic Gum and corn silk (moisture, protein, lipid and ash) was determined according to AOAC (2012) as follow: Moisture content of samples was determined using oven-dry technique. Protein content was determined using the Kjeldahl method (Gerhardt, Germany) and the nitrogen content of the samples was multiplied by 6.25. Lipid content was determined using a Soxhlet with petroleum ether as the extraction solvent. Total carbohydrate was calculated by difference. Also, the amounts of elements sodium (%Na) and potassium (%K) were determined by atomic absorption spectrometry ICP (optima 2000 DV – Perkin Elmer) according to AOAC (2012).

Gas Chromatography-mass Spectrometry (GC-MS) Analysis:

Isolation, identification of phenolic and flavonoid compounds were performed using a gas chromatograph (Agilent Technology 7890A) interfaced with a polar Agilent HP-5ms (5%-phenly methyl poly siloxane) capillary column (30m X 0.25 mm i.d. and 0.25 µm film thickness) Column temperature began at 550ºC and held for 5 min, increased 20ºC per minute to 1700ºC, and finally increased 10ºC per minute to 230ºC and kept at this temperature for 10 min. The constant column flow was 1 ml/min, using helium as carrier gas.

Biological experiment

Animal, housing and diets:

Fortyeightmale Albino rats weighing about 150±5 g were obtained from Agricultural Research Center, Giza, Egypt. The animal groups were placed in an atmosphere of filtered, pathogen-free air,water and maintained at a temperature between 20-25ºC for 8weeks with a 12 h light/dark cycle and light cycle (8-20 h) and relative humidity of 50%. The animals acclimatized for one week as an adaptation period. The animals were randomly divided into two main groups. The first group of rats control (-) (6 rats) was fed onstandard diet, while the second group (42 rats) was fed onstandard diet and received GM at adose rate of 80 mg / kg, ip for 8 consecutive days to induce nephrotoxic (Reddy *et al*., 2011), then rats were divided into seven groupssix rats each, and treated by different concentrations of Arabic Gum and corn silk extracts by epi gastric tubeas seen in Table (1) for 8 weeks. The rats were weighed weekly and at the end of the experimental feeding period, the animals were fasted overnight, anesthetized with ether and sacrificed for analysis.The followed steps by Schermer, (1967) were done in 6 rats after 8 weeks of treatment in each group:

* Animals were fasted for 12 h, blood samples were withdrawn from orbital plexus venous by using fine capillary glass tubes and were collected into plain tubes without anticoagulant and allowed to clot. Blood samples were centrifuged at 3000 rpm for 10 min at 4°C, to obtain clear serum that was frozen at -18^{o}C until analyzed.

*Animals were anesthetized with ether and sacrificed, quickly dissected to excise the liver, kidney.These organs were weighed and then kept in 10% formaldehyde until histological investigations.

Table (1): Experimental diet of rats used in the biological study.

Groups	Experimental diets
Control (-)	Standard diet (-)
Control (+)	*GM (control +) + Standard diet
10% AGE +10% CSE	*GM + Standard diet + (10% Arabic Gum extract +10% corn silk extract by epi gastric tube)
20% AGE +5% CSE	*GM + Standard diet + (20% Arabic Gum extract +5% corn silk extract by epi gastric tube)
5% CSE	*GM + Standard diet + (5% corn silk extract by epi gastric tube)
10% CSE	*GM + Standard diet + (10% corn silk extract by epi gastric tube)
10% AGE	*GM + Standard diet + (10% Arabic Gum extract by epi gastric tube)
20% AGE	*GM + Standard diet + (20% Arabic Gum extract by epi gastric tube)

*Intraperitoneal injection

Biological procedure:

Biological evaluation of the different animal groups was carried by determination of initial body weight (IBW), final body weight (FBW) and body weight gain% (BWG %) and organs weight / body weight% according to Chapman*et al*. (1959).

BWG% = [(Final weight-Initial weight) / (Initial weight)] X 100

Organ weight/ body weight % =(Organ weight / Final weight) X 100

Biochemical analysis:

Serum creatinine was determined at 495 nm as given by Bartles *et al*.,(1972).Serum urea nitrogenwas determined at 550 nm according to the method described by Fawcett and Soctt (1960). Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities were determined colorimetrically using spectrophotometer (HITACI, ü-1900) at 505 nm according to the method of Reitman and Frankel (1957).Total protein was determined at 550 nm according to the method described Gornal *et al*., (1949). Total bilirubin was determined at 535 nm according to the method described Walter and Gerade (1970).

Histopathology technique

The tissues of liver and kidney were fixed immediately after dissection in 10% neutral formalin for 24 h, then dehydrated in ascending concentration of alcohol, cleaned in xyline and embedded in paraffin wax. Tissues were sectioned at a thickness of 3 micron and stained with hematoxylin and fosin stains (Banchroft *et al*.,1996). All tissues were examined by the light microscope for detection of any histopathological alteration.

Statistical Analysis

The obtained data were exposed to analysis of variance. Duncan's multiple range test at 5% level of significance was used to compare between means. The analysis was carried out using the PROC ANOVA procedure of Statistical Analysis System (SAS, 1999).

RESULTS AND DISCUSSION

Proximate analysis:

Nutritional compositions of Arabic Gum and corn silk powder are shown in Table (2). The proximate composition of AG powder consists of 13.29% moisture and 3.17% ash, and this result within the 13-15 & 2-4% range specified by FAO (1990).Protein, lipids, ash and total carbohydrates contents of AG were 2.65, 0.2, 3.17 and 80.70%, respectively. These results were in agreement with data reported by Ali and Daffalla, (2018). On the other hand, proximate composition of corn silk powder shown in table (2) is similar to that reported by Wanrosli *et al*., (2011). Minerals Na and K were 0.023 and 1.17%, respectively in corn silk powder. Nurhanan and Rosli, (2014) reported that

Na and K were 2.63 and 0.019% in immature silk and 3.57 and 0.026% in mature silk, respectively.

Table (2): Proximate composition (%) of Arabic Gum and corn silk powder.

Samples	Moisture	Protein	Lipid	Ash	Total Carbohydrate
Arabic gum	13.29±0.39	2.65±1.05	0.2±0.01	3.17±0.29	80.70±1.13
Corn silk	4.02±0.13	12.85±0.81	0.98±0.28	5.36±0.13	76.78±0.38

Data expressed as Means ± SD (*n=3*).

Gas Chromatography-mass Spectrometry (GC-MS) Analysis:

GC-MS method was employed for the ethanolic extract of corn silk powder for testing availability of phytochemical constituents.The amount (µg/g) of different compounds identified in the ethanolic extract of corn silk powder was listed in Table (3).

Table (3): Phytocomponents identified in the ethanolic extract of the corn silk powder by GC-MS.

No.	RT* (min)	Compound name	Peak area (%)	Amount (µg/g)
1	5.03	3,4,5-trimethoxycinnamic acid	0.25	0.040
2	9.30	Bergenin	1.20	0.191
3	11.56	Esculin	0.29	0.046
4	12.7	Isovitexin	0.38	0.060
5	13.78	4′,6-Dimethoxyisoflavone-7-O-β-D-glucopyranoside	7.19	1.143
6	13.87	Palmitic acid, ethyl ester	7.03	1.118
7	14.70	Ethyl linoleate	1.14	0.181
8	14.87	Linoelaidic acid	14.96	2.379
9	14.91	E,E-2,13-Octadecadien-1-ol	13.54	2.153
10	15.10	Arachidic acid	2.50	0.398
11	15.46	E,E-3.13-Octadecadien-1-ol	0.70	0.111
12	15.86	Flavone, 3,5-dihydroy-3′,4′,7-trimethoxy	1.27	0.202
13	15.95	Luteolin 6,8-C-diglucoside	2.31	0.367
14	16.80	Geranylisovalerate	3.42	0.544
15	17.09	n-Heptacosane	1.82	0.289
16	17.90	2-Butenedioic acid, 2-methyl-,(E)-	1.69	0.269
17	18.12	5,7,2′-Trimethoxyflavone	1.33	0.211
18	18.61	cis-Vaccenic acid	1.74	0.277
19	19.26	2-Hexadecanol	2.00	0.318
20	20.22	Phytanic acid	1.01	0.161
21	20.70	2-Decanol	8.42	1.339
22	21.08	3,6,3′,4′-Tetramethoxyflavone	1.05	0.167
23	21.62	Kampferol-3,4′-dimethyl ether	1.56	0.248
24	21.78	Isomyristic acid	2.28	0.363
25	23.00	Phytol	20.91	3.325

*RT= Retention time (min)

The extract revealed the presence of 25 compounds. The major bioactive constituents in the extract of corn silk included, Palmitic acid, ethyl ester (peak area 7.03%), 4′,6-Dimethoxy-isoflavone-7-O-β-D-glucopyranoside (peak area 7.19%), 2-Decanol (peak area 8.42%), E,E-2,13-Octadecadien-1-ol (peak area 13.54%), Linoelaidic acid (peak area 14.96%) and phytol (peak area 20.91%). These six compounds were detected at different retention times (13.87, 13.78, 20.70, 14.91, 14.87 and 23 min) and high amounts as; 1.118, 1.143, 1.339, 2.153,

2.379 and 3.325 µg/g, respectively.Kumar *et al*., (2010) and Santos *et al*., (2013) reported that Phytol has been to possess antioxidant properties and to reduce free-radical generation in an in-vitro experimental system.

Corn silk (CS) is rich in phenolic compounds, such as anthocyanins, p-coumaric acid, vanillic acid, protocatechuic acid, derivatives of hesperidin and quercetin, and hydroxycinnamic acid derivatives consisting of p-coumaric and ferulic acid (Ebrahimzadeh *et al.*, 2008). It also contains flavonoid mysin, rutin, flavon-4-ols, chlorogenic acid, phytosterols, tannin and glycosylflavones (Elliger *et al*., 1980; El-Ghorab *et al*., 2007).

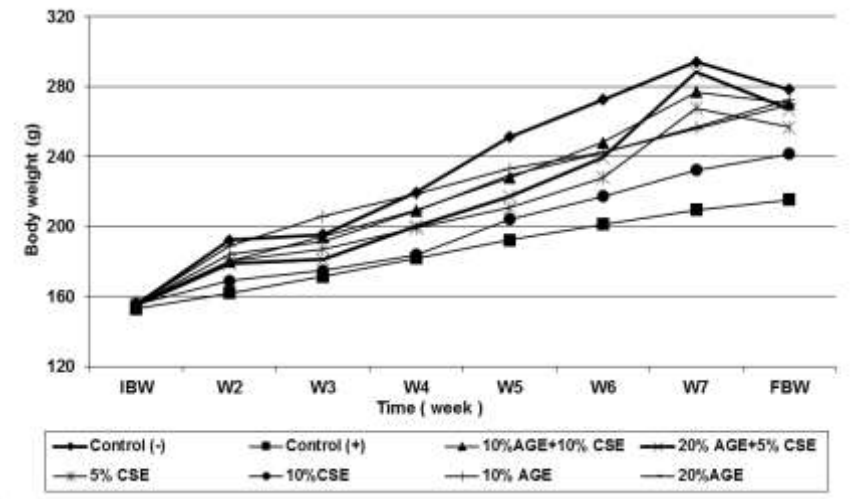
Biological evaluation:

General signs in the rats:

No rats in among groups died during the experimental period (8 weeks) and some of rats in groups exhibited abnormal signs throughout the test period.

Body and organs weights:

Body weight change is often a very sensitive indicator of animal well-being. It integrates many other parameters and often, in particular, food consumption. Increase in weight gain compared with control may not be due to an adverse effect; but due to enrich dietary palatability or a nutritionally richly balanced diet due to concern incorporation of the test material in the animal feed. The final body weights (FBW) of rats for different groups are given in Figure (1).



IBW= Initial body weight; FBW= Final body weight; BWG= Body Weight gain

Fig. (1): Growth curve of experimental rats injected by gentamicin and fed on different concentration of Arabic Gum and corn silk extracts.

There were significant differences ($P \leq 0.05$) in the final body weights of rats in the control (+) group (215.3 g) and the remaining treatment groups (control (-), 10% AGE +10% CSE, 20% AGE +5% CSE, 10% CSE, 10% AGE, and20% AGE) were 278.3, 270.3, 267.0, 256.8, 241.5, 272.2 and269.7, respectively.

The body weight gain per week was recorded highest value (79.6g) for theControl (-) group, while the body weight gain per week for the remaining treatment groups with different concentration of Arabic gum and corn silk extracts ranged between 55.6 to75.5g. The lowest rates of body weight gain per week occurred in control (+) group (40.7g) (Fig. 2).

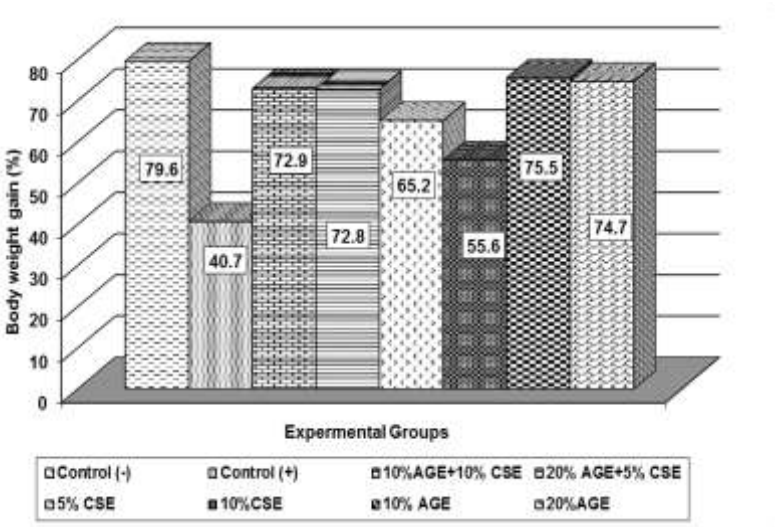


Fig. (2): Mean body weight gain (g) of experimental rats injected by gentamicin and fed on different concentration of Arabic Gum and corn silk extracts.

The weights of the various organs / body weight % of the rats treated by different concentration of Arabic Gum and corn silk extracts are shown in Table (4).A significant decrease ($P \leq 0.05$) can be observed in the weight of liver and kidney in the treatment groups {control (-), 10% AGE +10% CSE, 20% AGE +5% CSE} as compared with the control (+) group. The remaining groups (10% CSE, 10% AGE, and 20% AGE) were either show low ratio of decrease weight organ compared with other groups.It was found an increase in kidney/body weight ratio in animals that were treated with GM, which is in accordance with Ali *et al*.(2009). This change is due to edema in the inflammatory process that occurs during the implementation phase of renal failure in renal toxicity caused by gentamicin (Valipour *et al*., 2016).This results agree with data shown in Tables (5 and 6) which have presented higher significant of liver enzyme (ALT and AST) and kidney function in Control (+) group and histopathology examination which illustrate liver and kidney damage.

Table (4):Mean organ weight/body weight (%) of experimental rats injected by gentamicin and fed on different concentration of Arabic Gum and corn silk extracts.

Groups	Mean ±SDM of Organs Weight*	
	Liver	**Kidney**
Control (-)	3.28^{c}±0.32	0.79^{bc}±0.08
Control (+)	5.10^{a}±0.37	1.06^{a}±0.19
10% AGE +10% CSE	3.46^{c}±0.31	0.79^{bc}±0.14
20% AGE +5% CSE	3.33^{c}±0.50	0.80^{bc}±0.07
5% CSE	3.40^{c}±0.22	0.75^{c}±0.05
10% CSE	4.39^{b}±0.43	0.92^{b}±0.07
10% AGE	4.27^{b}±0.63	0.86^{bc}±0.09
20% AGE	4.17^{b}±0.23	0.86^{bc}±0.06

* Data are presented as means ± SDM ($n=6$). Data in a column with different superscript letters are statistically different ($P \leq 0.05$).

Biochemical Analysis:

Results of serum total bilirubin, total protein and liver enzymes for all tested groups are presented in Table (5). The results of rats administered with gentamicin control (+) showed a significant increase (P≤0.05) in total bilirubin and a significant decrease (P≤0.05) in total protein (0.56and 3.80 g\dl, respectively) compared with control (-) group (0.34and 5.19 g\dl, respectively). While all groups injected by gentamicin and fed on different concentration of Arabic Gum and corn silk extracts (10, 20%AGE, 20% AGE +5% CSE, 10% AGE +10% CSE, 5% CSE and 10% CSE) showed a significant decrease (P≤0.05) as compared with control (+).Also, a significant increase (P≤0.05) in (10% AGE +10% CSE, 20% AGE +5% CSE, 10% CSE, 20% AGE, 5% CSE and 10%AGE,) groups was observed (Table 5) as compared with control (+)..

Bilirubin is a breakdown product of hem (a part of haemoglobin in red blood cells). The liver is responsible for removing bilirubin blood. The total level of serum bilirubin is the sum of the conjugated (direct) and unconjugated (indirect) bilirubin. Normally, the unconjugated bilirubin makes up 70% to 85% of the total bilirubin. If direct bilirubin is high, the liver is naturally associated with bilirubin but is unable to secret it. Bile duct obstruction by gallstones, hepatitis or cancer should be suspected (Nyblom *et al*., 2004).

Table (5): Liver enzymes (U/I),serum total bilirubin and total protein (mg\dl) of rats injected by gentamicin and fed on different concentration of Arabic Gum and corn silk extract.

Groups	Parameters*			
	Total Bilirubin (mg\dl)	Total Protein (g\dl)	Liver enzymes	
			ALT(U/I)	AST(U/I)
Control (-)	0.34^{bcd}±0.09	5.19^{b}±0.67	34.67^{e}±1.97	47.83^{c}±2.93
Control (+)	0.56^{a}±0.06	3.80^{c}±1.31	77.67^{a}±2.66	80.67^{a}±3.01
10% AGE +10% CSE	0.37^{bc}±0.13	7.48^{a}±0.52	50.67^{c}±2.42	49.33^{c}±1.97
20% AGE +5% CSE	0.32^{cd}±0.07	7.23^{a}±0.47	34.33^{e}±1.37	46.83^{c}±2.48
5% CSE	0.42^{abc}±0.12	6.76^{a}±0.29	49.67^{c}±1.51	48.17^{c}±2.04
10% CSE	0.47^{ab}±0.23	7.14^{a}±0.30	68.33^{b}±2.34	68.83^{b}±3.13
10% AGE	0.21^{d}±0.06	6.72^{a}±0.41	45.33^{d}±2.73	46.83^{c}±2.04
20% AGE	0.26^{cd}±0.07	6.95^{a}±0.56	33.17^{e}±0.98	46.50^{c}±2.66

* Data are presented as means ± SDM (*n=6*). Data in a Colum with different superscript letters are statistically different (P ≤ 0.05).

Table (5) indicated a remarkable significant increase (P≤0.05) in serum ALT activityfor all groupsinjected by gentamicin and fed on standard diet and different concentration of Arabic Gum and corn silk extracts as compared with the control group (-) 34.67U/I, but (20% AGE +5% CSE and 20% AGE) groups recorded high significantly decreased (P < 0.05), respectively as compared with the control (+) group. The increase in ALT is the result of a pathogenic malignancy that destroys liver cells by releasing these circulating enzymes in agreement with Tameda *et al.* (2005) who considered increased ALT activity to be sensitive to liver cell injury. However, ALT is more specific to liver damage than AST. While AST recorded a significant decreased in all groups injected by gentamicin and fed on standard diet and different concentration of Arabic Gum and corn silk extracts as

compared with the control group (+) (80.67 U/I) in the same Table (5).The damage or death of liver cells usually results in leaks of enzymes in infected tissues into the bloodstream (Obi *et al*., 2001). Serum or plasma enzyme levels have been used as markers for monitoring chemically induced tissue damages. The enzymes Alanin aminotransferase (ALT), Aspartate aminotransferase (AST) and Gamma glutamate transferase (GGT) are important enzymes that are often used to assess liver injury (Obi *et al*., 1998).

This results agreed with Mohamed *et al*. (2012) who showed addition of tested plant parts corn cob silk (*Zea maize*) by 5 and 10% of the diet intake in the presence of CCl_4 induced significant improvements in all liver functions. And the same results in accordance with that observed by Ebtihal, (2017) who showed the addition of gum Arabic (GA) to the all suggested diets leads to significant decreasing in the AST, ALT and ALP activities.Urea is formed in the liver as the end product of protein metabolism. During ingestion, protein is broke down into amino acids. In the liver, these amino acids are catabolized and free ammonia is formed. The ammonia is combined to form urea. Urea, the main product of protein catabolism measuring urea is the most popular laboratory procedure for evaluating kidney function (Bennett *et al*., 1995). Creatinine is a metabolite of creatinine phosphate, which is used in skeletal muscle concentration (Pagana *et al.,* 1997).

Table (6) illustrated the serum urea, creatinine and uric acid levels:Gentamicin treatment for eight days resulted significantly increased ($P < 0.05$) urea, creatinine and uric acid levels in relation to control (+) groups. The previous parameters were significantly decreased ($P < 0.05$)byfed on different concentration of Arabic Gum and corn silk extracts. The high significantly decreased ($P < 0.05$) observed in (20% AGE +5% CSE and 20% AGE) groups, respectively as compared with the control (+) group.

Table (6): Kidney function (mg/dl) of rats injected by gentamicin and fed on different concentration of Arabic Gum and corn silk extracts.

Groups	Parameters*		
	Urea(mg/dl)	**Uric Acid(mg/dl)**	**Creatinine(mg/dl)**
Control (-)	30.55^{d}±9.76	1.17^{cd}±0.16	0.61^{c}±0.08
Control (+)	70.34^{a}±11.89	2.02^{a}±0.38	2.01^{a}±0.22
10% AGE +10% CSE	66.17^{a}±14.96	1.42^{bcd}±0.26	0.98^{b}±0.18
20% AGE +5% CSE	29.74^{d}±6.28	1.00^{d}±0.55	0.56^{c}±0.38
5% CSE	69.87^{a}±3.20	1.55^{abc}±0.73	0.83^{bc}±0.22
10% CSE	47.84^{bc}±3.97	1.18^{cd}±0.14	1.01^{b}±0.17
10% AGE	54.92^{b}±11.66	1.81^{ab}±0.24	1.02^{b}±0.40
20% AGE	40.10^{cd}±5.65	1.00^{d}±0.43	0.68^{bc}±0.41

* Data are presented as means ± SDM ($n=6$). Data in a Colum with different superscript letters are statistically different ($P \leq 0.05$).

In the skeletal muscle serum, creatinine levels are elevated by renal disease and dehydration. Moreover, the AG was taken with the diet has been shown to increase output of fecal nitrogen and decrease serum urea nitrogen concentration in patients with CKD, and this has been shown to depend on increased bacterial growth and activity in the intestines (Bliss *et al*., 1996). Colonic

bacteria produce ureases that hydrolyze urea to ammonia and carbon dioxide. The resultant ammonia can then be incorporated into bacterial proteins, which are subsequently excreted in the bacterial mass portion of the feces (Ali *et al*., 2010).

Corn silk tea has the function to increase urinary output, which can help remove the toxins and wastes out, thus reducing the level of creatinine. In addition, it also helps remove excess fluid, which can help relieve swelling. High blood pressure, being the most prominent symptom, is reduced with the help of corn silk tea (Elin *et al*., 2013).

Histopathological Examination:

Liver, and kidney were examined and the photomicrographs are illustrated inFigures (3 to 4). Table (7) shows the degrees of histopathological alteration in liver and kidney sections of rats in different experimental groups.

Liver

Histopathological examination of the liver sections from control (-) (normal rats fed on commercial diet only) showed no histopathological alteration and the normal histological structure of the central vein and surrounding hepatocytes in the parenchyma (Fig.3A). While in the control (+) group (normal rats fed on commercial diet + injection with GM thickening was observed in the Glissons capsule, while the underlying hepatocytes showed atrophy and shrinkage,fatty change was noticed in the hepatocytes at the periphery of the hepatic lobules with appearance of intracytoplasmic signet ring,sever dilatation and congestion was observed in the central vein. The portal area showed inflammatory cells infiltration (Fig. 3B).

Liver of animals affected by GM and fed on (10% AGE +10% CSE) showed mild dilatation in the central vein (Fig.3C1). In contrast, no histopathological alteration in liver was observed in the animals affected by GM and fed on (20% AGE +5% CSE)(Fig. 3C2), while animals affected by GM plus fed on (5% CSE) (Fig. 3D1), fatty change was detected in some of their liver hepatocytes. Liver of injected rat by GM plus fed on (10% CSE) showed dilatation in the portal vein with oedema and few inflammatory cells infiltration in the periductal tissue surrounding the dilated hyperplastic bile ducts(Fig. 3D2). In contrast, no histopathological alteration were observed in the animals affected by GM plus fed on (10% AGE) and (20% AGE) as seen in Figure(3E1, E2).

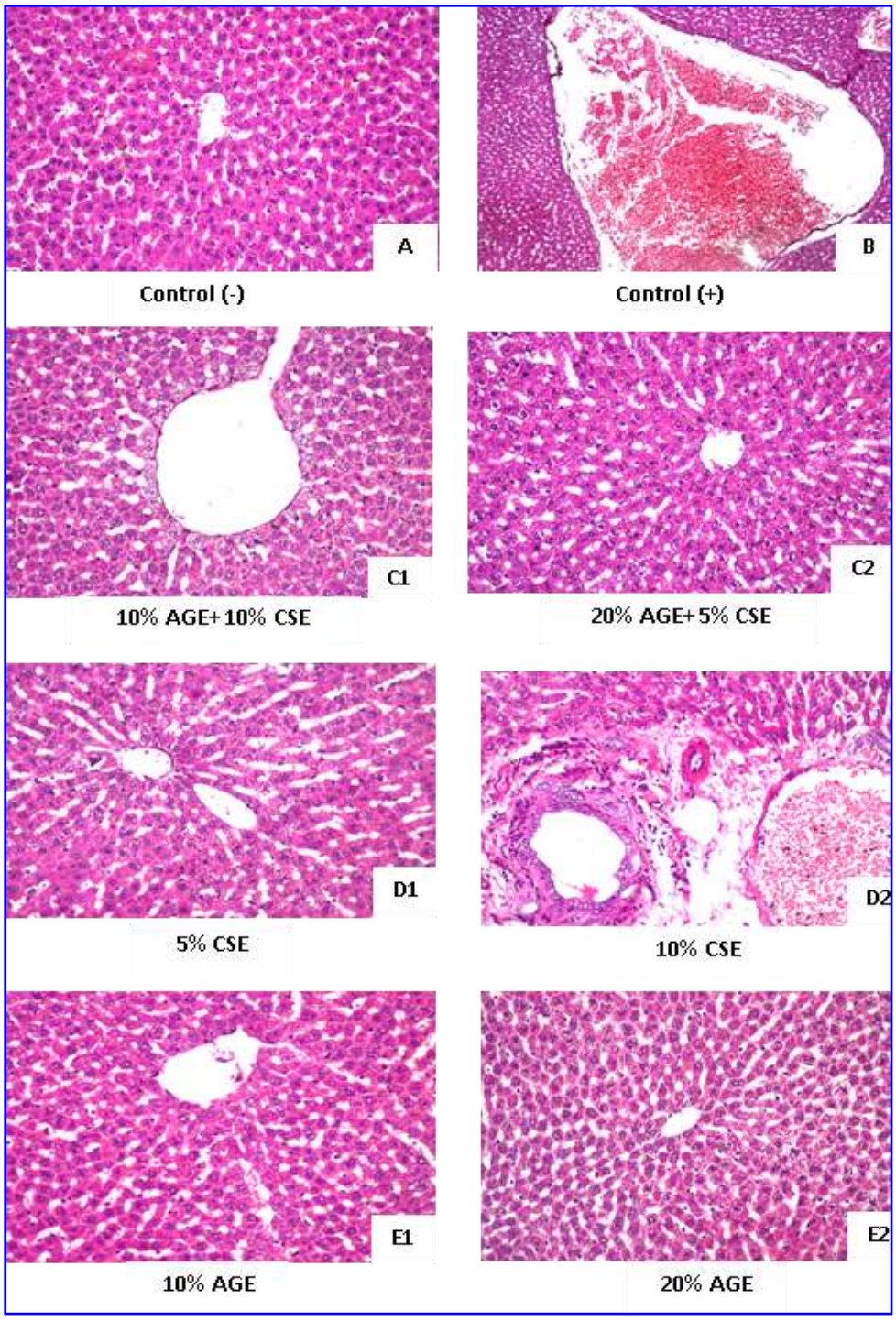
Kidney:

Rats fed on commercial diet only (control -) showed no histopathological alteration and the normal histological structure of the glomeruli and tubules at the cortex (Fig.4A). While animals fed on commercial diet plus injection with GM (control +) focal haemorrhage was detected underneath the capsule as well as in between the tubules at the cortex and There was congestion in the cortical blood vessels (Fig.4B). Furthermore, kidney of animals affected by GM plus fed on (10% AGE +10% CSE) and (20% AGE +5% CSE) showed congestion in the cortical blood vessels as seen in Figure (4C1). Smilar observation was given for animals affected by GM plus fed on (5% CSE) as seen in Figure (4D1). In contrast, animals affected by GM and fed (10% CSE) , (10% AGE) and (20% AGE) showed normal changes histopathological as seen in Figure (4D1, E1 and E2), respectivaly.

Gentamicin accumulates in epithelial cells mainly in nearby tubes, but also distal and aggregated for an extended period and leads to changes within the cells, causing damage that can range from loss of the brush limit to full tubular necrosis (Quiros *et al*., 2011). After drug uptake, a number of cellular processes are activated, culminating in apoptosis. This contributes to loss of the renal tubular epithelium and thus kidney dysfunction. In addition to tubular injury, persistent contraction of the glomerular mesangial cells, cellular apoptosis, proliferation and necrosis have all been described in the histopathological evidence of

aminoglycosides nephrotoxicity (Lopez-Novoa *et al*., 2011).

The observed improvement effect in the present study may be due to formation of short-chain fatty acids such as butyrate (Matsumoto *et al*., 2006), which is produced during AG degradation by intestinal bacteria (Bliss, 2004) and which have been shown to increase glomerular filtration rate and renal blood flow (Fioretto *et al*., 1987).



Fig(3):Photomicrograph of Sections of liver of different rats groups, stained with H & E, X 400.

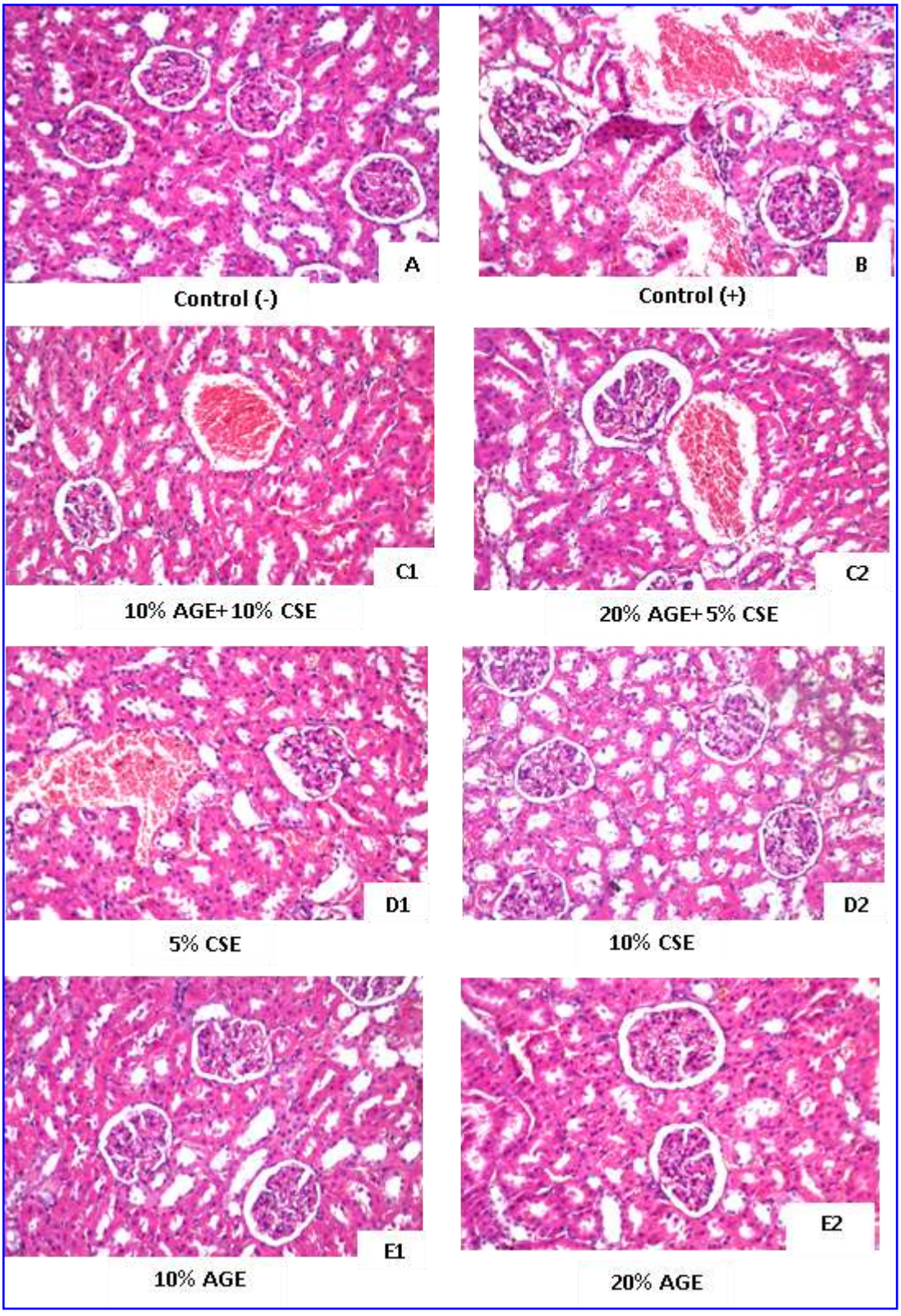


Fig. (4): Photomicrograph of Sections of kidney of different rats groups, stained with H and E, X 400.

Table 7: Degrees of histopathological alteration in liver and kidney sections of rats in different experimental groups

organs	Gp.No	Control (-)	Control (+)	10% AGE 10% CSE	20% AGE +5% CSE	5% CSE	10% CSE	10% AGE	20% AGE
liver	thickening in Glissons capsule	-	++	-	-	-	-	-	-
	Fatty change in hepatocytes	-	++	-	-	+	++	+	-
	congestion	-	+++	+	-	-	++	-	-
	Portal inflammatoryreaction	-	++	-	-	-	++	-	-
kidney	Focal haemorrhages	-	+++	-	-	-	-	-	-
	Congestion in the cortical blood vessels.	-	+++	+	+	+	-	-	-

+++ Sever, ++ Moderate, + Mild, - Nil

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دور مستخلص الصمغ العربي وحريرة الذرة لتفادي التسمم الكلوي للجنتاميسين في فئران التجارب

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المستخلص

تم دراسة التأثيرات المختلفة لمستخلصات الصمغ العربي (AG) وحرير الذرة (CS) علي فئران التجارب التي تعاني من التسمم الكلوي hepato-nephro المفتعل بواسطة الجنتاميسين (GM). وجد 25 مكونًا نشطًا بيولوجيًا في مستخلص حريرة الذرة CS بواسطة تحليل GC-MS ؛ وكان الفيتول (325,3 ميكروجرام / جرام) هو المكون الرئيسي الذي عرف بأنه يمتلك خصائص مضادة للأكسدة وتقليص تكوين الشقوق الحرة معمليا. تم حقن الفئران في الغشاء البريتوني بعقار الجنتاميسين بجرعة 80 ملجم / كلجم من وزن الجسم / يوم لثمانية ايام متتالية لاحداث التلف الكلوي الحاد . أظهرت النتائج ان الحقن بالجنتاميسين ازاد بدلالة احصائية مستويات اليوريا ، وحامض البوليك واليوريا كذلك نشاط انزيمات الكبد و ارتفع ايضا إجمالي البيليروبين وانخفض البروتين الكلي مقارنة بالمجموعة الضابطة السالبة وقد ادي التدخل بمستخلصات الصمغ العربي وحريرة الذرة الي تحسن (بدلالة احصائية) كل هذه القياسات الحيوية . وقد اظهر التحليل الهيستولوجى لعينات الكبد والكلى لفئران التجارب المحقونة بالجنتاميسين وبعد التدخل بالمستخلصات ان افضل التأثيرات في الكبد كانت 20%من مستخلص الصمغ العربي + 5% مستخلص حريرة الذرة ويليها ال 10% مستخلص الصمغ العربي ، بينما في الكلي كانت ال 10% مستخلص حريرة الذرة ثم 10 % مستخلص الصمغ العربي ويليهم ال 20 % مستخلص الصمغ العربي مقارنة بالمجموعة الكنترول الموجبة