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Effect Of Ethanolic Extract Of *Psidium Guajava* And *Moringa Oleifera* Leaves On Acute Renal Injury In Experimental Rats

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Abstract

This study was carried out to investigate the effect of ethanolic extracts of *Psidium guajava* and *Moringa oleifera* leaves on acute renal injury in experimental rats. Thirty albino rats weighing 200 ± 20 g used in this study and divided into two main groups, one was the first main group (5 rats) who kept as a control –ve group, while another was the second main group (25 rats) , was injected intraperitoneally(IP) with a single dose of cisplatin (CP) (7ml / kg B.Wt.) to induce acute renal

injury. After induction, the rats in the second main group were divided into five groups (each group consisted of 5 rats) , one group was kept as (+ ve) control group, while others given administration of ethanolic extract of *Psidium guajava* leaves (EEPGL) and ethanolic extract of *Moringa oleifera* leaves (EEMOL) (100 and 200 mg/kg) orally for six weeks. Biological evaluation including feed intake (FI), body weight gain % (BWG %) and feed efficiency ratio (FER) were carried out. Serum creatinine, Serum urea and serum uric acid were measured. Antioxidant levels in kidneys tissues (Super Oxide Dismutase (SOD) , Glutathione Peroxidase (GPX) , Catalase (CAT), Malondialdehyde (MDA) and Nitric oxide(No) were estimated. Blood glucose was determined . Also, histopathological changes for kidney, were examined. The obtained results concluded that using EEPGL and EEMOL improve FI, BWG % and FER, Serum creatinine, Serum

urea and Serum uric acid, antioxidant enzymes and blood glucose level. The best results found by using high doses (200mg / kg) of EEPGL and EEMOL . According to the results, EEPGL and EEMOL could be used for improving kidney functions and curing acute renal injury .

Introduction

Kidney is important organ in the body which play vital role in excretion (**Naqvi , 2017**). Acute kidney injury (AKI) is a common disorder that spread in hospital and associated with excess morbidity and mortality. AKI is major problem which is developed to increase the risk of chronic kidney disease (**Moore et al., 2018**). Cisplatin contributed with reactive oxygen species (ROS) causing renal cell death, and lead to acute kidney injury which represent one complication of cisplatin chemotherapy (**Sonia et al., 2018**).

Guava (*Psidium guajava* ,L.) leaves have been used for several diseases in traditional medicine . Vivo and vitro researches demonstrated the possible effect of the extracts from the leaves for the co-treatment of different diseases (**Díaz-de-Cerio et al., 2017**) . Guava (*Psidium guajava* , L.) is a tree with nutritional values and has phytochemical compounds which contains alkaloids, carotenoids , anthocyanins, vitamin-C, and triterpenes (**Jayachandran et al., 2018**) . Recent studies indicated that ethanolic extract of *Psidium guajava*, L. leaves has renal protective effects (**Mohan et al., 2014**).

Moringa oleifera, Lam. (*M. oleifera*) has nutritional value which high content in proteins, vitamin A, minerals, essential amino acids, antioxidants, flavonoids, and isothiocyanates. *M. oleifera* extracts have pharmacological activities including anti-inflammatory, antioxidant, anti-cancer, hepatoprotective, neuroprotective and hypoglycemic activity (**Kou et al., 2018**) . *Moringa oleifera* leaves extract play a vital role in reducing oxidative stress and kidney damage depending on its antioxidant compounds (**Arafat,Nagah et al.,2018**)

Therefore, this study aimed to investigate the potential effects of ethanolic extract of *Psidium guajava* leaves (EEPGL)

and ethanolic extract of *Moringa oleifera* leaves (EEMOL) against cisplatin – induced acute renal injury in male rats.

Meaterials And Methods

Plant Material

Dried leaves of *Moringa oleifera* and *Pesiduim guajava* were purchased from the local company for medicinal plants and herbs, Cairo Governorate, Egypt.

Extraction of Plant Material

The dried leaves were ground using a milling machine to obtain fine powder. The active ingredients were extracted by using 95% ethanol. Briefly, 100 g of each leaf powder was added to 900 ml of 95% ethanol. The mixture was covered and shaken every 30 min. for 6 h, and then allowed to stand for 48 h for extraction. The mixture was then separated by passing through Whatman's No 1 filter paper, after which the filtrate was evaporated to dryness under air pressure. The dried crude extracts were stored in the refrigerator (at 40 °C) under aseptic conditions for subsequent use (Eze *et al.*, 2013).

Drug and dose

Cisplatin, [cis-PtCl₂ (NH₃)₂], was obtained from Pharmacy in Tanta City (0.5 mg/ml cisplatin in 0.9% sodium chloride). Cisplatin was injected as single dose 7 mg/kg of body weight intraperitoneally (IP).

Animals:

Thirty male albino rats of Sprague Dawley strain (200 ± 20 g) were obtained from the animal colony, Helwan farm, Vaccine and Immunity Organization, Ministry of Health, Cairo Governorate, Egypt.

Experimental Design

A total of 30 matured male rats weighing between 180-220g were housed in clean metabolic cages. The rats adaption lasted for one week before the beginning of the experiment. The rats fed on basal diet (B. D.) according to Reeves *et al.* , (1993) and divided into two main groups as follow:

The first main group (5 rats)

This main group was fed on basal diet and kept as a control (- ve) group.

The second main group (25 rats)

This main group was fed on basal diet and injected with cisplatin as single dose (7 mg/kg b.wt.) to induce acute renal injury according to **Ozyurt *et al.*, (2004)**. After that, the rats in the second main group (25 rats) were divided into five groups (each group consisted of 5 rats) as a following:- **Group 1:** Fed on B.D. and treated with cisplatin and Kept as control (+ ve) group. **Group 2:** Fed on B.D. and treated with one dose oral daily of 100 mg/kg b.w EEMOL.

Group 3: Fed on B.D. and treated with one dose oral daily of 200 mg/kg b.w EEMOL.

Group 4: Fed on B.D. and treated with one dose oral daily of 100 mg/kg b.w EEPGL.

Group 5: Fed on B.D. and treated with one dose oral daily of 200 mg/kg b.w EEPGL.

Biological evaluation

Body weight& feed consumption were measured twice a week and total feed intake of the experimental period (6 weeks) calculated according to (**Chapman *et al.*, 1959**). The feed efficiency ratio was calculated according to the following equation as mentioned by **Hosoya (1980)**.

Kidney functions parametrs

Serum creatinine, serum urea and serum uric acid were determined according to **Murray and Kaplan, (1984); Kaplan, (1984) and Fossati *et al.*, (1980)**, respectively.

Blood glucose

Blood glucose was determined according to **Brăslasu *et al.*, (2007)**.

Antioxidant enzymes

Glutathione peroxidase (GPx), Malondialdehyde (MDA), (Super Oxide Dismutase (SOD), Catalase (CAT), and Nitric oxide (No) were determined acoording to the methods of **Paglia and Valentine, (1967) ; Ohkawa *et al.*, (1979); Nishikimi *et al.* ,**

(1972); Aebi, (1984) and Montgomery and Dymock, (1961), respectively .

Histopathology investigation

The rat kidney was fixed in 10% buffered neutral formalin immediately following excision from animals. Fixed tissues were subsequently processed for histopathology examinations as previously described by Adeyemi and Akanji, (2012).

Statistical analysis

Statistical analysis was carried out using one way analysis of variance (ANOVA) test followed by Duncan test through the program of statistical packages for the social science (SPSS) version 16. Results were expressed as mean \pm SD. The differences among means at $p \leq 0.05$ are considered significant (Snedecor and Cochran, 1989).

Results

Results

Table (1) results show the changes in feed intake, body weight gain % and feed efficiency ratio in control and experimental groups of rats. These parameters deteriorated in cisplatin (+ control) while improved in treatment groups specially high dose. The highest improvement recorded for the group which treated with 200 mg/kg b.wt. EEMOL followed by the group treated with 200 mg /kg b.wt. EEPGL.

Table (2) result show the non- significant changes in relative kidney weight in cisplatin (+ control) group, as compared to the negative control group and all treated groups. However, group treated with EEMOL at dose 200 mg/kg b.wt. was closed to normal control group.

Table (3) results show the high significant increase in kidney function parameters (creatinine, urea and uric acid) in cisplatin (+ control) group. On the other hand, these parameters decreased in all treated groups specially at high extract doses. The highest improvement was recorded for the groups which treated with 200 mg/kg b.wt. of EEMOL followed by the group treated with 200 mg /kg b.wt. of EEPGL.

Table (4) results indicated that cisplatin (+ control) showed a significant increase in blood glucose, while, all treated groups observed significant decreases compared to control positive group . The best results were recorded for high doses from EEMOL and EEPGL 200mg/kg b.wt. which improved blood glucose level and were closed to normal control.

Data presented in table (5) indicated that SOD, GPX and CAT levels diminished in control (+) group. While, MDA and NO levels were increased control (+) group. However , the reverse recorded for treated rats, in particular for EEMOL 200 mg/kg group , followed by that of EEPGL 200 mg/kg group. Histopathological investigation (Figure 1) confirmed all biological and biochemical results (Tables 1 – 5).

The results obtained from histological sections of kidney illustrated in (Fig. 1). Kidney, shows normal histological picture of glomeruli and tubules in Normal (- control) group (A). However, kidney from Cisplatin (+ control) group showed shrunken glomeruli (thick arrow), hydropic degeneration in tubular epithelium (arrowheads) and tubular necrosis (thin arrow) (B) ,while mild hydropic degeneration in tubular epithelium (arrowhead) observed in Cisplatin + EEMOL(100mg/kg) group (C), and congested blood vessels (arrow) observed in Cisplatin + EEMOL(200mg/kg) group and Cisplatin +EEPGL (200 mg/Kg) groups (D&F). While , retained normal histological picture of glomeruli and tubules observed in Cisplatin +EEPGL (100 mg/Kg) group (E) . H&E

Table (1) : Effects of ethanolic extracts of MOL and PGL on feed intake, body weight gain and feed efficiency ratio in nephrotoxic rats induced by cisplatin (mean±SD, n=5)

Groups	FI(g)	BWG(%)	FER
Normal (- control)	929±6.72 ^a	5.14±1.19 ^a	0.01±0.003 ^a
Cisplatin (+ control)	495±3.00 ^f	-35.30±2.22 ^c	-0.17±0.009 ^d
Cisplatin+ EEMOL(100mg/kg)	772±1.82 ^d	-33.47±4.15 ^c	-0.11±0.007 ^c
Cisplatin + EEMOL (200 mg/kg)	827±2.30 ^b	-19.01±2.89 ^b	-0.05±0.006 ^b
Cisplatin +EEPGL (100 mg/Kg)	738±2.70 ^e	-32.91±5.13 ^c	-0.10±0.014 ^c
Cisplatin + EEPGL (200 mg/kg)	792 ± 4.15 ^c	-23.44± 5.77 ^b	-0.07± 0.013 ^b

Means in the same column with completely different letters are significantly different at $p \leq 0.05$.

Table (2): Effects of ethanolic extracts of MOL and PGL on relative kidney weight in nephrotoxic rats induced by cisplatin (mean±SD, n=5)

Groups	Relative kidney weight %
Normal (- control)	0.72±0.2 ^c
Cisplatin (+ control)	0.79±0.1ab ^c
Cisplatin + EEMOL(100mg/kg)	0.88±0.09 ^a
Cisplatin + EEMOL (200 mg/kg)	0.77±0.04b ^c
Cisplatin +EEPGL (100 mg/Kg)	0.80±0.04 ^{abc}
Cisplatin + EEPGL (200 mg/kg)	0.85±0.08 ^{ab}

Means in the same column with completely different letters are significantly different at $p \leq 0.05$.

Table (3): Effects of ethanolic extracts of MOL and PGL on kidney functions in nephrotoxic rats induced by cisplatin (mean±SD, n=5)

Groups	Creatinine (mg/dl)	Urea (mg/dl)	Uric acid (mg/dl)
Normal (- control)	0.39±0.01 ^d	15.67±2.16 ^d	1.39±0.02 ^f
Cisplatin (+ control)	1.80±0.24 ^a	94.67±15.20 ^a	2.90±0.16 ^a
Cisplatin+ EEMOL(100mg/kg)	0.96±0.06 ^{bc}	48.67±5.31 ^b	2.10±0.016 ^c
Cisplatin + EEMOL (200 mg/kg)	0.74±0.04 ^d	21.33±3.49 ^d	1.64±0.05 ^e
Cisplatin +EEPGL (100 mg/Kg)	1.06±0.15 ^b	53±9.90 ^b	2.27±0.015 ^b
Cisplatin + EEPGL (200 mg/kg)	0.89±0.05 ^d	37.67±1.78 ^c	1.86±0.03 ^d

Means in the same column with completely different letters are significantly different at $p \leq 0.05$.

Table (4) : Effects of ethanolic extracts of MOL and PGL on blood glucose in nephrotoxic rats induced by cisplatin (mean±SD, n=5)

Groups	Glucose (mg/dl)
Normal (- control)	91.4±10.85 ^o
Cisplatin (+ control)	114.8±13.88 ^d
Cisplatin + EEMOL(100mg/kg)	103±13.62 ^{ab}
Cisplatin + EEMOL (200 mg/kg)	88.4±11.41 ^o
Cisplatin +EEPGL (100 mg/Kg)	102.8±17.41 ^{ab}
Cisplatin + EEPGL (200 mg/kg)	91.4 ± 8.32 ^o

Means in the same column with completely different letters are significantly different at p≤0.05.

Table (5) : Effects of ethanolic extracts of MOL and PGL on antioxidant levels in kidneys tissues of nephrotoxic rats induced by cisplatin (mean±SD, n=5)

Groups	SOD (U/gT)	GPX (U/gT)	CAT (U/g)	MDA (nmol /gT)	NO (Mmol/L)
Normal (- control)	25.55±1.41 ^a	51.42±1.53 ^a	0.59±0.02 ^a	9.06±0.45 ^e	2.80±0.21 ^d
Cisplatin (+ control)	15.58±2.26 ^c	33.68±1.15 ^d	0.38±0.01 ^c	19.68±1.00 ^a	4.97±0.14 ^a
Cisplatin + EEMOL(100mg/kg)	21.98±2.57 ^b	41.46±0.95 ^c	0.49±0.01 ^c	13.06±0.61 ^c	3.80±0.03 ^b
Cisplatin + EEMOL (200 mg/kg)	25.64±0.68 ^a	47.24±0.82 ^b	0.53±0.01 ^b	10.06±0.43 ^d	3.31±0.04 ^c
Cisplatin +EEPGL (100 mg/Kg)	17.20±1.11 ^c	40.35±1.39 ^c	0.47±0.01 ^d	13.98±0.58 ^b	4.02±0.10 ^b
Cisplatin + EEPGL (200 mg/kg)	22.34±1.07 ^b	47.8±2.46 ^b	0.52±0.01 ^b	10.74±0.51 ^d	3.09±0.41 ^c

Means in the same column with completely different letters are significantly different at p≤0.05.

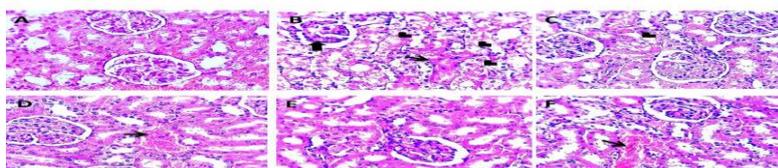


Figure (1): Microscopic images hematoxylin and eosin (H & E) -. (A) Normal (- control). (B) Cisplatin (+ control). (C) Cisplatin + EEMOL(100mg/kg) (D) Cisplatin + EEMOL (200 mg/kg) , (E) Cisplatin +EEPGL (100 mg/Kg) (F) Cisplatin + EEPGL (200 mg/kg) .

Discussion

Cisplatin is effective chemotherapy widely used for treatment many types of cancers, although it is restricted due to its side effects especially on kidneys. It can be accumulated in kidney tissues and caused acute renal injury as demonstrated by **Kim^a et al., (2015)**. In the present study, the authors indicated that cisplatin was leading to a decrease in appetite and subsequently to weight loss according to **Hesketh et al., (2003)**. These results supported by **Garcia et al., (2013)** who reported that cisplatin-induced appetite, body weight and feeding efficiency decreases. Also, **Malik et al., (2006)** reported that cisplatin-induced anorexia ,gastrointestinal tract disorders including vomiting, nausea, stomach distension, and gastric stasis may result in decreased food intake. In harmony with these findings, **Yamamoto et al., (2007)** observed that anorexia nervosa is one of the most common gastrointestinal side-effects associated with cisplatin and is, therefore, used as an index of patient quality of life. **Cabezos et al ., (2008)** demonstrated that cisplatin has highly emetic effect. Cisplatin led to a decrease gastric motility (**Gong et al., 2017**) .

Medicinal plants have been used in traditional medicine due to their antioxidant activities. In the present study, the body weight of adult male rats treated with *Moringa oleifera* leaf extract improved as compared to cisplatin group due to this extract enhancing growth according to **Akudu et al., (2014)**. In contrast to **Adedapo et al ., (2009)** suggested that supplementation of *moringa* extract at 200mg/kg and 400mg/kg are capable of preventing body weight gain. It is may be dependent on dose of extract it mean that, high doses decrease the body weight. This findings agree with **Bernadier, (2004)** who suggested that *moringa* extract may affect some regulation signals of feed intake and metabolism of the animals. In the study treatment with *Pesiduim guajava* extract lead to improvement in FI, BWG% as compared to positive group, the results agree with **Amer, Afaf, (2014)** who revealed that diet supplemented with *Pesiduim guajava* extract showed significantly increase in feed intake and body weight gain % as compared to the

positive group. On the other hand *Pesiduim guajava* extract reduce body weight according to **Houmard et al ., (2011)**.

The obtained results indicated that there are no significant differences in relative kidney weight among all groups. However group treated with EEMOL at dose 200 mg/kg b.wt. was closed to normal control. This result agree with **Adeyemi and Elebiyo (2014)** reported that *M. oleifera* addition to diet has improved relative kidney weight and protected from exposer to toxicants. Also, agree with **Ezejindu et al., (2016)** who reported that ethanolic leaf extract of *Moringa oleifera* has antioxidant and anti-inflammatory properties .

In the current study cisplatin group was increased in creatinine, urea and uric acid .These results are in agreement with earlier reports which reported by **Ilic et al., (2014)**. Also, matching with **Kim^a et al., (2015)** who indicated that increasing the levels of blood urea nitrogen and serum creatinine in cisplatin group caused by increasing in oxidative stress in kidney tissues. Injection of cisplatin increased serum urea, uric acid, and creatinine as indicators of nephrotoxicity (**Sen et al., 2018 and Singh et al., 2018**). Administration of ethanolic extract of *Moringa oleifera* and *Pesiduim guajava* leaves at high dose (200 mg/kg b.wt.) significantly caused decrease in creatinine, urea and uric acid. In line with these results, **Adeyemi and and Elebiyo** stated, **(2014)**; **Onah et al., (2016)**; **Suleiman et al.,(2017)**; **Nnadiukwu et al., (2017)**; **Kou et al., (2018)** and **Saleh, Nahed et al., (2018)** stated that *Moringa oleifera* has renoprotective effect and lowering effect on kidney functions parameters duo to bioactive compounds as beta-carotene, vitamin C, vitamin E, and polyphenols and are a good source of natural antioxidants which can protect against oxidative damage.

Similarity, the ethanolic extract of *Pesiduim guajava* leaves, in the present study, lowered creatinine, urea and uric acid, these results agree with **Talubmook and Buddhakala, (2013)** who reported that *Pesiduim guajava* leave extract decreased blood urea nitrogen (BUN), and creatinine duo to antioxidant properties.

Similar finding to our results suggested by **Abd EL-khalik, Dalia (2016)** who reported that *Psidium guajava* leaves led to significant decrease in kidney functions parameters. Guava-purees contain polyphenol, antioxidant capacity responsible for decreasing the levels of urea and creatinine (**Yolanda et al., 2017**). Also, the results matching with **Innih, and Omage, (2018)** who showed that the aqueous extract of *P. guajava* restored the levels of kidney functions to normal.

In the obtained findings, it found that cisplatin group was increased in blood glucose. These findings supported by **Sarangarajan and Cacini, (2004)** who reported that cisplatin increased plasma glucose. In harmony with these findings, **Nora et al., (2014)** observed that cisplatin caused an increase in blood glucose levels, due to oxidative stress which lead to alteration in glucose concentration. Also, cisplatin increased secretion of urinary glucose as demonstrated by **Patel et al., (2012)** and **Boroushaki et al., (2015)**.

Treating with ethanolic extract of *Moringa oleifera* and *Psidium guajava* leaves at high dose (200 mg/kg b.wt.) significantly caused decrease in blood glucose. The present findings were in accordance with **Kumar and Mandapaka (2013)** who declared that hypoglycemic effect of *Moringa oleifera* leaves. **Basyony et al., (2016)**; **Rahman et al., (2018)** and **Saleh, Nahed et al., (2018)** concluded that oral administration of *Moringa oleifera* leaf extract decreased the glucose level due to it contains antidiabetic isolated compounds, and its ability to stimulate insulin release from the pancreatic beta cells and so reduced the blood glucose level.

On the other hand, the lowering effect of glucose levels by extract of *P. guajava* may be due to the high content of antioxidant this results agree with **Atawodi and Muazu (2003)** and **Banu et al., (2012)** who showed marked decrease in glucose in groups treated with *P. guajava*. Due to *P. guajava* increase of glucose utilization and inhibition reabsorption glucose in the kidney. **Jiao et**

al., (2018) explained the causes of decreasing blood glucose by *P. guajava* when they reported that guava polysaccharides act as an α -glucosidase inhibitor which reducing blood glucose level. In harmony with our findings **Kangogo, (2018)** showed that guava leaves extracts significantly reduced blood glucose in rats due to bioactive compounds which responsible for hypoglycemic activity, and recommended using higher doses of the extracts.

The current investigation revealed that a significant ($p \leq 0.05$) decrease in of SOD, GPx, Catalase while increase in MDA and NO levels in cisplatin (+ control) compared to the normal control group. The decreased levels of SOD, GPx, CAT and increased levels of MDA and NO in kidney imply that the CP generate excessive amount of reactive oxygen species which combat tissue antioxidant defense. The obtained results agree with **Lee *et al.*, (2017)** who reported that cisplatin induced high levels of oxidative stress, as accompanied by an increased level of MDA, and decreased activities of glutathione S-transferase, superoxide dismutase, and catalase in kidney tissues and caused acute kidney damage.

The obtained other hand, all treated groups improved previous parameters as compared to cisplatin (+ control). The best result was found in treated groups with high doses of EEMOL and EEPGL. Our results corresponding to **Karthivashan *et al.*, (2016)** who demonstrated that EEMOL increases the capability of antioxidant system and showed a modulatory effect on specific inflammatory cytokines in kidney tissues that evidence by elevated SOD, CAT and GPx activities and decreased the levels of MDA in the groups treated with MO leaf extract. These results indicate that MO leaf extracts effectively regulate and restore the antioxidant status of acetaminophen -intoxicated mice kidney.

The extract of *M. oleifera* leaves scavenged NO and inhibited MDA production due to gallic acid, chlorogenic acid, quercetin, and kaempferol were the most abundant phenolic compounds identified in the leaf extract which play important role in development antioxidant potential (**Oboh *et al.*, 2015**).

Also, our results agreement with **Mohan *et al.*, (2014)** who suggested that ethanolic extract of *Psidium guajava* leaves has nephroprotective activity against doxorubicin. The animals treated with *Psidium guajava* showed a significant increase in SOD, GPX, CAT levels and decreased level of lipid peroxidation (LPO). The ethanolic extract of *Psidium guajava* leaves possess antioxidant and free radical scavenging activity.

Histopathological examination of kidney tissues in cisplatin group showed shrunken glomeruli, hydropic degeneration in tubular epithelium and tubular necrosis these results are supported by **Ilić *et al.*, (2014)**. The toxic effects of cisplatin in our study were similar to those shown by **Kim^a *et al.*, (2015)** who reported that cisplatin caused histological changes in kidney tissues, increased generation of (ROS) and reduced antioxidant enzymes. The obtained results were in agreement with the finding of **Sonia *et al.*, (2018)** who demonstrated that cisplatin-induced nephrotoxicity by promoting oxidative renal tubular cell death.

Administration of EEMOL at two dose (100 and 200 mg/kg b.wt.) and EEPGL at dose (200 mg /kg b.wt.) improved to some extent the histopathological picture but some microscopical lesions were still apparent including mild hydropic degeneration in tubular epithelium and congested blood vessels. These results are supported by **Adeyemi and Elebiyo, (2014)** and **Karthivashan *et al.*, (2016)**. who stated the renoprotective effect of *Moringa oleifera* against kidney damage through enhancement of antioxidant system. In harmony with our results **Saleh, Nahed *et al.*, (2018)** when observed that *Moringa* leaf extract improved the histopathological picture but some lesions were still apparent. The best results which retained kidney tissues to normal histological picture is *Psidium guajava* (100 mg/ kg b.wt.) duo to antioxidant activity, inhibition of oxidative stress and scavenger of free radical as reported by **Udemezue *et al.*, (2014)**; **Innih and Oimage, (2018)** and **Wu *et al.*, (2018)**.

Conclusion

Cisplatin has side effects on body organs specially kidneys. It caused acute kidney injury and nephrotoxicity . In the light of biochemical results and histological findings, EEPGL and EEMOL be suggested as neuroprotective plants duo to antioxidant activity . Therefore, this can be used for improvement kidney functions and protection from renal injury .

References

- Abd EL-khalik, Dalia, M.T. (2016):** Effect of *Psidiumguajava* leaf and its aqueous extract on rats suffering from diabetes and acute renal failure, and its practical application in the production of bread. Egyptian Journal of Food Science, 44 :153-173.
- Adedapo, A.A.; Mogbojuri, O.M. and Emikpe, B.O.(2009):** Safety evaluations of the aqueous extract of the leaves of *Moringaoleifera* in rats. Journal of Medicinal Plants Research, 13 (8):586–591.
- Adeyemi, O.S. and Elebiyo , T.C. (2014) :** *Moringaoleifer*-asupplemented diets prevented nickel-induced nephrotoxicity in Wistar rats. Journal of Nutrition and Metabolism, 1-8. <http://dx.doi.org/10.1155/2014/958621>.
- Adeyemi, O.S. and Akanji, M.A. (2012) :** *Psidiumguajava* leaf extract effects on rat serum homeostasis and tissue morphology. Comparative Clinical Pathology, 21(4): 401–407.
- Aebi, H. (1984):** Catalase in vitro. Methods Enzymol, 105: 121-126
- Akudu, L. S.; Ezejindu, D. N.; Nnama, T. N. and Ezejindu, C. N.(2014):** evaluation of protective potentials of *Moringaoleifer* leaf extract on testes of adult male Wistar rats . International Journal of Research , 1 (10):793-800.
- Amer, Afaf, B. (2014):** Effect of guava leaves (*Psidiumguajava*) as a source of antioxidants on hepatotoxic rats. J. Food and Dairy Sci., Mansoura Univ., 5 (10): 679 – 688.
- Arafat, Nagah; Awadin, Walaa. F. ; El-Shafei, Reham ,A.; Farag, Virginia. M.E. and Saleh, Rasha M.(2018):** Protective Role of *Moringaoleifer* leaves extract against

gentamicin -induced nephro -and hepato-toxicity in chickens. *AJVS.*, 58 (1): 173-185.

- Atawodi, S.E. and Muazu, A.(2003):** Effect of aqueous extract of *Psidiumguajava* on glucose levels in normoglycaemic and alloxan-induced diabetic rats. *Nigeria Journal of Biochemistry and Molecular Biology*,13(2):125-128.
- Banu, M.S.; Sujatha, K.; Kamala, M. and Kumar, K.V. (2012):**Hypoglycaemic and hypolipidaemic potentials of isolated fraction of *Psidiumguajava* leaf in alloxan-induced diabetic rats. *International Journal of Pharmaceutical Innovations*, 2(2):16-22.
- Basyony, M. A.; El-Desouki, N. I.; Hegazy, M. M. and El-Aama, M. S. I. (2016):** Evaluation of anti- hyperglycemic effect of *Moringaoleifera* leaves Extract on some physiological parameters of diabetic rats induced apoptosis in the pancreas. *International Journal of Scientific & Engineering Research*, 7(3): 1461-1481.
- Berdanier, C. D. (2004):** Gastrointestinal system and metabolism. In: *The Laboratory Mouse*. Hedrich, H.J. and Bullock, G. (eds.) Amsterdam: Elsevier, 245-259.
- Boroushaki, M.T.; Rajabian, A.; Farzadnia, M.; Hoseini,A.; Poolashkari, M.; Taghavi, A.; Dolati , K.andBazmandegan, G. (2015):** Protective effect of pomegranate seed oil against cisplatin-induced nephrotoxicity in rat. *Renal Failure*, 37(8): 1338–1343.
- Brăslasu, M.C ;Brăslasu, E.D. and Brădălan, C. (2007):** Experimental studies regarding the diabetes mellitus induced in white wistar rats. *Lucrări Stiințifice Medicină Veterinară*, 11:109–116.
- Cabezos, P.A. ; Vera, G. ; Castillo, M. Fernández-Pujol, R.; Martin, M.I. and Abalo,R (2008):** Radiological study of gastrointestinal motor activity after acute cisplatin in the rat. Temporal relationship with pica. *AutonNeurosci* .,141:54-65.
- Chapman, D.G.; Castilla, R. and Cambell, A.J. (1959):** Evaluation of protein in food. In *Method for the Documentation of protein Efficiency Ratio*.*Can. J. Biochem. Physiol.*, 37; 679-686.

- Díaz-de-Cerio, E.; Verardo, V.; Gómez-Caravaca, A. M.; Fernández-Gutiérrez A, . and Segura-Carretero, A.(2017):** Health effects of *Psidiumguajava* L. leaves: An overview of the last decade". *Int. J. Mol. Sci.*, 18, 897; doi:10.3390/ijms18040897.
- Eze, E. A. ;Oruche, N .E. ; Onuora V. C and Eze, C.N.(2013):** Antibacterial screening of crude ethanolic leaf extracts of four medicinal plants . *Journal of Asian Scientific Research*, 3(5):431-439.
- Ezejindu, D.N.; Anibeze, C.I. and Nduwe, G.U. (2016):** The histological effects of ethanolic leaf extract of *Moringaoleifera* potassium bromate induced renotoxicity in adult Wistar rats. *Journal of Medicine, Physiology and Biophysics*, 23: ISSN 2422-8427.
- Fossati, P.; Prencipe, L. and Berti, G. A. (1980):** New direct colorimetric procedure for uric acid in serum and urine. *Clinical Chemistry*, 26(2):227-231.
- García ,J.M. ; Scherer, T. and Chen , J.A. et al.(2013):** Inhibition of cisplatin induced lipid catabolism and weight loss by ghrelin in male mice. *Endocrinology*, 154:3118-3129.
- Gong, Y.; Liu, Y. ; Liu, F. et al. (2017):** Ghrelin fibers from lateral hypothalamus project to nucleus tractus solitaries are involved in gastric motility regulation in cisplatin-treated rats. *Brain Res.*,1659:29-40.
- Hesketh, P.J. ;Belle,V. S. ; Aapro, M. ;Tattersall, F.D;. Naylor, R.J. ; Hargreaves, R. and Horgan, K.J . (2003):**Differential involvement of neurotransmitters through the time course of cisplatin-induced emesis as revealed by therapy with specific receptor antagonists. *Eur J Cancer*, 39:1074–1080.
- Hosoya, N. (1980):** Determination of feed efficiency ratio . Cited in Hosoya, N .; Inami , S. and Goto , S., eds. *Nutrition Experiments Using Small Animals*. Daiichi Shuppan, Tokyo, Japanese, pp:71.
- Houmard , J.A;. Pories ,W.J. and Dohm, J.L. (2011):** Is there a metabolic program in the skeletal muscle of obese individuals ? *Journal of Obesity* , 240496.

- Ilić, S.; Stojiljković, N.; Veljković, M.; Veljković, S. and Stojanović, G. (2014):** Protective effect of quercetin on cisplatin-induced nephrotoxicity in rats. *Medicine and Biology*, 16 (2): 71-75.
- Innih, S.O. and Omage, S.O. (2018):** *Psidium guajava* leaves elicit mild protection on the liver and kidneys of rats exposed to ciprofloxacin. *Annals of Biomedical Sciences*, 17(1).
- Jayachandran, M.; Vinayagam, R.; Ambati, R.; Xu, B. and Chung, S. (2018):** Guava leaf extract diminishes hyperglycemia and oxidative stress, prevents β -cell death, inhibits inflammation, and regulates NF- κ B signaling pathway in STZ induced diabetic rats. *Bio. Med. Research International*, 14 pages. <https://doi.org/10.1155/2018/4601649>.
- Jiao, Y.; Hua, D.; Huang, D.; Zhang, Q. and Yan, C. (2018):** Characterization of a new heteropolysaccharide from green guava and its application as an α -glucosidase inhibitor for the treatment of type II diabetes. *Food Funct.*, 9: 3997-4007.
- Kangogo, G. K. (2018):** Phytochemical composition, safety and hypoglycemic activity of purple tea and guava extracts in a mouse model of diabetes mellitus. Jomo Kenyatta University of Agriculture and Technology. <http://hdl.handle.net/123456789/3898>.
- Kaplan, A. (1984):** Urea. *Clin Chem.*, 1257- 1260 and 437 and 418.
- Karthivashan, G.; Kura, A.U.; Arulselvan, P.; Md Isa, N. and Fakurazi, S. (2016):** The modulatory effect of *Moringa oleifera* leaf extract on endogenous antioxidant systems and inflammatory markers in an acetaminophen-induced nephrotoxic mice. model". *PeerJ* 4:e2127 <https://doi.org/10.7717/peerj.2127>.
- Kim^a, E.S.; Leeb, J.S.; Akrama, M.; Kima, K. A.; Shina, Y. J.; Yua, J.H. and Baea, O.N. (2015):** Protective activity of dendropanax morbifera against cisplatin-induced acute kidney injury. *Kidney Blood Press Res.*, 40:1-12.
- Kou, X.; Li, B.; Olayanju, J.; Drake, J. and Chen, N. (2018):** Nutraceutical or Pharmacological Potential of *Moringa oleifera* Lam. *Nutrients*, 10 (3) 343.

- Kumar, P.K. and Mandapaka, R.T. (2013):** Effect of *Moringaolifera* on blood glucose,LDL levelsin types II diabetic obese people. Innovative Journal of Medical and Health Science, 3(1):23 – 25.
- Lee , I.C.; Ko, J.W.; Park, S.H .; Shin, N.R.; Shin , I.S.; Kim ,Y.B. and Kim, J.C. (2017):** Ameliorative effects of pine bark extract on cisplatin-induced acute kidney injury in rats. Ren. Fail.,39(1):363-371.
- Malik, N.M. ; Moore, G.B. ; Smith, G. ; Liu, Y.L.;Sanger, G.J. and Andrews, P.L.(2006):** Behavioural and hypothalamic molecular effects of the anti-cancer agent cisplatin in the rat: A model of chemotherapyrelated malaise? PharmacolBiochem Behav.,83:9-20.
- Mohan,M.; Shashank, B. and Priya, A.V.(2014):** Protective effect of *Psidiumguajava* L . leavesethanolic extract on doxorubicin-induced nephrotoxicity in rats. Indian Journal of Natural Products and Resources , 5(2): 129-133.
- Montgomery, H. A. C. and Dymock, J. F., (1961):** Colorimetric determination of nitrite. Analyst, (86): 414.
- Moore, P.K.; Hsu, R.K. and Liu, K.D.(2018):** Management of acute kidney injury: Core curriculum. AJKD., 27(1):136-148.
- Murray, R. L. and Kaplan, A. (1984):** Creatinine. Clin Chem., 1261- 1266 and 418.
- Naqvi, R. (2017):** Acute kidney injury from different poisonous substances . World J. Nephrol., 6(3): 162-167.
- Nishikimi, M.; Roa, N.a. and Yogi,K.(1972):** Biochem. Bioph. Res. Common, 46:849-854.
- Nnadiukwu, T. A.; Monago, C. C. and Chuku, L.C. (2017):** Synergistic effect of ethanol extracts of *Moringaoleifera*and pleurotusostreatus on liver enzymes and some renal functions of alloxan-induced diabetic Wistaralbino Rats. International Journal of Biochemistry Research & Review,16(1):1-11.
- Nora, C.D.; Danelli, D.; Souza ,L.F.; Rios, a.D.O.; Jong, E.V.D. and Flôres, S.H.(2014):** Protective effect of guabiju (*Myrcianthespungens* (O. Berg) D. Legrand) and red guava (*Psidiumcattleyanum* Sabine) against cisplatin-induced

hypercholesterolemia in rats. Brazilian Journal of Pharmaceutical Sciences, 50(3): 484-491.

- Oboh, G.; Ademiluyi, A.O.; Ademosun, A.O.; Olasehinde, A.T.; Oyeleye, S. I.; Boligon, A.A. and Athayde, M.L. (2015):** Phenolic extract from *Moringaoleifera* leaves inhibits key enzymes linked to erectile dysfunction and oxidative stress in rats' Penile Tissues. Biochemistry Research International ,Volume 2015, Article ID 175950, 8 pages. <http://dx.doi.org/10.1155/2015/175950>.
- Ohkawa,H.; Ohishi, W. and Yagi, k.(1979):** Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Anal.Biochem., 95(2): 351.
- Onah, C.E.; Meludu, S. C.; Dioka,C.E.; Onuegbu, A.J.; Onah, C.F.; Ajaghaku, D.L.; Nnodim, J.K. and Ejeatuluchukwu, O. (2016):** Amelioratory effect of methanol leaf extract of *Moringaoleifera* on some liver and kidney function and oxidative stress markers in lead-intoxicated rats. European Journal of Medicinal Plants, 12(4): 1-12.
- Ozyurt, H.; Yildirim, Z.; Kotuk , M.;Yilmaz, H.R.; Yağmurca, M.; Iraz ,M.; Söğüt, S. and Gergerlioglu, S.(2004):** Cisplatin-induced acute renal failure is ameliorated by erdosteine in a dose-dependent manner. J. Appl. Toxicol.;24(4):269-75.
- Paglia, D.E. and Valentine,W.N.(1967):** Studies on quantitative and qualitative characterization of erythrocyte glutathione peroxidase. J. Lab.Clin. Med.,70:158-169.
- Patel, N.M.; BM, V.S.; Swamy, A.P. and Ravirala, R. (2012):** Nephroprotective activity of *Psidiumguajava* Linn. leaves extract against cisplatin induced nephrotoxicity in rats. Research Journal of Pharmaceutical, Biological and Chemical Sciences, 3(4):1237.
- Rahman, M.; Hafizur, Maryam, K.; Hameed, A.; Zaheer, L.; Bano,S. et al.,(2018):** Insulin releasing effect of some pure compounds from *Moringaoleifera* on mice islets. Medicinal Chemistry Research , 27:1408-1418.

- Reeves, P.G., Nielsen, F.H. and Fahmy, G.C. (1993):** Final report of American Institute of Nutrition adhoc writing committee on the reformulation of AIN-76A rodent diet. *Journal of Nutrition*, 123: 1939-1951.
- Saleh, Nahed, S. ;Allam, T.S.; El-Rabeaie, Riham, M. and El-Sabbagh, H.S. (2018):** Protective effect of some egyptianmedicinal plants against oxidative stress in rats. *Alexandria Journal of Veterinary Sciences*, 58 (1): 1-14.
- Sarangarajan, R. and Cacini, W. (2004):** Early onset of cisplatin-induced nephrotoxicity in streptozotocin –diabetic rats treated with insulin. *Basic & Clinical Pharmacology & Toxicology*, 95: 66–71.
- Sen,S .; Chakraborty, R. and Kalita, p. (2018):** Dilleniaindica fruit prevents cisplatininduced kidney injury in experimental rats through modulation of oxidative stress, marker enzyme, and biochemical changes.*Nutr.*, 43:15.
- Singh, M.P.; Chauhan, A.K. and Kang, S.C. (2018):** Morin hydrate ameliorates cisplatin-induced ER stress, inflammation and autophagy in HEK-293 cells and mice kidney via PARP-1 regulation. *International Immunopharmacology*, 56:156-167.
- Sneddecor, George, W. and Cochran, William, G. (1989):** *Statistical Methods*. Eighth Edition, Iowa State University Press.
- Sonia, H.; Kaminskib, D.; Gangarajub, R. and Adebिया, A.(2018):** Cisplatin-induced oxidative stress stimulates renal Fas ligand shedding. *Renal failure*, 40(1): 314–322.
- Suleiman,N.; Ibrahim,B.; Ahmed, B.I. and Zayyanu, A. (2017):** Effect of *Moringaoleifera* aqueous leaf extract on hepato-renal changes of albino rats induced with *Salmonella typhimurium*. *International Journal of Basic & Clinical Pharmacology*, 6 (4): 734.
- Talubmook, C. and Buddhakala, N. (2013):** Hypoglycemic and hypolipidemicproperties of leaf extracts from *phyllanthusacidus* (L.) Skeels.,*Leucaenaleucocephala* (Lam.) de Wit. and*Psidiumguajava* (L.) in Streptozotocin induced

diabetic rats. *International Journal of BioSciences* , 2 (2): 30-34.

- Udemezu, O.O.; Ukoha, U.; Ezejindu, D. N.; Okafor, J.I. and Obilor, A.D. (2014):** The histological effects of guava leaf aqueous extract on kidneys of adult Wistar rats. *International Journal of Research In Medical and Health Sciences*, 4 (3): 1-6.
- Wu, T.K.; Liu, H.C.; Lin, S.Y.; Yu, Y.L. and Wei, C.W. (2018):** Extracts from guava fruit protect renal tubular endothelial cells against acetaminophen-induced cytotoxicity. *Molecular Medicine Reports*, 17(4):5544-5551.
- Yamamoto, K. ; Nakai, M. ; Nohara, K. and Yamatodani, A. (2007):** The anti-cancer drug-induced pica in rats is related to their clinical emetogenic potential. *Eur J Pharmacol.*, 554:34–39.
- Yolanda, E.; Mendelev, E. and Verdã, B. (2017):** Nutritional characteristics and bioactive compound content of guava purees and their effect on biochemical markers of hyperglycemic and hypercholesterolemic rats. *Journal of Functional Foods*, 35: 447-457.



تأثير الستخلص الايثانولي لأوراق الجوافة والمورينجا على اصابة الكلى الحادة في فئران التجارب

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الملخص العربي:

أجريت الدراسة لمعرفة تأثير الستخلص الايثانولي لأوراق الجوافة والمورينجا على التهاب الكلى الحاد في فئران التجارب الذكور . أجريت الدراسة باستخدام ثلاثون من ذكور فئران الألبينو والتي تبلغ أوزانهم (200 ± 20 جم) وتم تقسيمهم الى مجموعتين رئيسيتين احدهما المجموعة الرئيسية الأولى (٥ فئران) وهي المجموعة الضابطة السليمة، بينما الأخرى هي المجموعة الرئيسية الثانية (٢٥ فأر) تم حقنها في الغشاء البريتوني مرة واحدة بمادة السيصبلائين بجرعة (٧ ملجم / كجم من وزن الجسم) لاحداث اصابة الكلى الحادة. بعد احداث الاصابة تم تقسيم المجموعة الرئيسية الثانية الى خمس مجموعات , بقيت احدي المجموعات كمجموعة ضابطة موجبة بينما المجموعات الأخرى تم اعطائهم عن طريق الفم المستخلص الايثانولي لأوراق الجوافة والمورينجا بجرعتين هما ١٠٠ و ٢٠٠ مجم / كجم من وزن الجسم. استمرت التجربة لمدة ست اسابيع. تم اجراء التقييم البيولوجي ويشمل النسبة المئوية لوزن الجسم المكتسب , المأخوذ الغذائي و معدل الاستفادة من كفاءة الغذاء . تم تقدير مستوى الكرياتنين واليوريا وحمض اليوريك في السيرم ، تم تقدير الانزيمات المضادة للأكسدة في انسجة الكلى (سوبر أكسيد ديسميوتيز , جلوتاثيون بيروكسيديز و الكتاليز) وقياس مؤشرات حدوث الأكسدة (المألون داي الدهيد , اكسيد النيتريك) وتم تقدير مستوى سكر الجلوكوز في الدم. وكذلك التغيرات الهستوباثولوجية في الكلى تم فحصها , ووجدت افضل النتائج في المجموعات المعالجة بالجرعات العالية لكلا المستخلصات النباتية (الجوافة والمورينجا) . وفقا لهذه النتائج يمكن استخدام المستخلصات الايثانولية لأوراق الجوافة والمورينجا في تحسين وظائف الكلى وكذلك معالجة اصابة الكلى الحادة .