

PROTECTIVE EFFECT OF STRAWBERRY LEAVES AGAINST NEPHROTOXICITY OF MALE RATS

**Nourelhouda M. Moustafa* ; Maysa M. El-Mallah
and Haggag M. Hamdy**

Nutrition and Food Science Department, Faculty of Home Economics,
Helwan University, Cairo, Egypt

*E-mail - medoelmasrawy48@gmail.com

Key Words: strawberry, leaves, nephrotoxicity, kidney functions, silymarin, rats

ABSTRACT

Nephrotoxicity refers to kidney dysfunction or kidney damage that is associated with an overload of drugs or xenobiotic. Agents with recognized nephrotoxicity include molds and fungi, cancer therapeutics such as cisplatin. In this study determine of the protective effect of strawberry leaves against nephrotoxicity of male rats was evaluated. Thirty five adult male albino rats (Sprague-Dawley strain), weighing about (150±10g) were divided randomly into seven groups (5rats of each) as follow; -ve and +ve control groups which fed on basal diet. Groups 3 and 5 fed on basal diet supplemented with 5% and 10% strawberry leaves powder (SLP), respectively. Groups 4 and 6 were orally administered with 5% and 10% strawberry leaves water extract (SLWE), respectively. Also group 7 was orally administered with 50ml of diluted silymarin /Kg body weight of rats. At the end of the experiment 28 days +ve control and groups 3-7 were intraperitoneally injected with a single dose of cisplatin 5mg/kg of body weight for four days. Rats were weighed daily and feed intake and feed efficiency ratios were calculated. At the end of the experimental period rats were sacrificed and serum was collected for biochemical analysis. The result showed that SLP and SLWE improving serum blood lipids and markers of kidney function and liver function as compared to the positive control group, decreased malondialhyde (MDA) level and increased the activity of antioxidant enzymes, glutathione (GSH) in the nephrotoxic rats. The high concentration of SLP and SLWE ameliorated histopathological and biochemical alterations that caused by cisplatin administration. According to above findings this research recommended that a strawberry leaf has a potential to be used as a functional health food ingredient with beneficial effects on kidney damage.

INTRODUCTION

Nephrotoxicity is the most common kidney problems occur when the body is exposed to a drug or toxin. When kidney damage occurs, body

unable to get rid of excess urine and wastes from the body and blood electrolytes. **Konam and Yalamuri, (2014).**

Cisplatin is a clinically advanced and highly effective anticancer drug used in the treatment, it has only a limited use in clinical practice due to its severe adverse effects, particularly nephrotoxicity; 20%–35% of patients develop acute kidney injury (AKI) after Cisplatin administration. Recent in vitro and in vivo studies show that numerous natural products (flavonoids, saponins, alkaloids, polysaccharide, phenylpropanoids, etc.) have specific antioxidant, anti-inflammatory, and anti-apoptotic properties that regulate the pathways associated with Cisplatin-induced kidney damage **Fang et al., (2021).**

Herbal drugs are being in use for the management of human health and for prevention as well as to cure human diseases since ancient civilization. In recent days, the use of herbal drugs has been increased significantly in various forms such as herbal formulations, dietary supplements, and nutraceuticals in the global market. This growing demand undoubtedly proves the therapeutic claims of herbal drugs as biomedicines and/or functional foods **Rudrapal and Chetia, (2021).**

Strawberry tree water leaf extract showed high biocompatibility with kidney tissue. It did not impair DNA integrity of renal cells and kidney function, either in male or female rats **Jurica et al., (2020).** There is a long list of other effects reported in folk medicine: as a diuretic, to strengthen sight and dentition, to expel kidney stones and intestinal worms, to treat anaemia and hepatitis, to strengthen the nervous, Strawberry leaves extract can be considered a very promising phytochemical for treating the neurotoxicity due to lead toxicity **Issa et al., (2018).**

Strawberry leaves as an abundant source of ellagitannins (ETs) can be considered as a valuable biomaterial for industrial application such as food ingredients, dietary supplements, pharmaceuticals and cosmetics .In addition, strawberry leaves particularly rich in monomeric ETs have potential application as a raw material for preparing the formulations for controlling plant pathogens **Karlińska et al.,(2021).**

MATERIALS AND METHODS

Materials

Strawberry leaves of (*Fragaria*) in the rose family (*Rosaceae*) were obtained from Agriculture Research Center, Cairo, Egypt. Chemical and kits Cisplatin, Casein, cellulose, choline chloride, D-L methionine, vitamins mixture and minerals mixture were purchased from Gomhoriya

Pharmaceutical Company, Cairo, Egypt. Starch, corn oil, and sucrose were obtained from the Egyptian local market.

Methods:

Preparation of Leaves Water Extract:

Dried Strawberry leaves were grounded and submerged in distilled water and allowed to soak overnight, 50 gm of leaves were added to 950ml water (5%) concentration, 100 gm of leaves were dissolved to 900 ml water (10%) concentration, then the water extract is administered orally to rats.

- Induction of nephrotoxicity:

Intraperitoneally (i.p.) injected of male albino rats with a single dose of Cisplatin 5mg/kg of body weight for four days **Mansour et al., (2006)**.

Diet Composition and Experimental Animal Design:

The basal diet was formulated according to AIN-93M diet (**Reeves et al., 1993**). Thirty five adult male albino rats (Sprague-Dawley strain), weighing about (150±10g) were divided randomly into -ve and +ve control groups were fed on basal diet throughout the experiment. Groups 3-7 were fed basal diet with 5 & 10% SLP; 5 & 10% SLWE; 50ml silymarin, respectively. Positive and all tested groups (3-7) were i.p. injected with a single dose of cisplatin 5mg/kg b.w of rats in the end of the experiment (4 weeks). After 2 days rats were fasted overnight before scarifying and blood samples were collected from each rat and were centrifuged at 3000 rpm for 15 min to obtain serum for biochemical analysis.

Biological Evaluation: feed intake (FI), body weight gain (BWG%) and feed efficiency ratio (FER) were determined according to **Chapman et al., (1959)**.

Serum Biochemical Analysis:

Serum total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C) were determined according to **Richmond, (1973); Wahlefeld, (1974) and Albers et al., (1983)**, respectively. Regarding to serum low density lipoprotein cholesterol (LDL-C) and very low density lipoprotein cholesterol (VLDL-C) were calculated according to **Friedewald et al., (1972)**. Serum level of creatinine was determined colorimetrically using the method described by **Burtis and Ashwood, (1999) and Young, (2001)**. Serum albumin level was determined as described by **Young, (1995)**. Blood urea nitrogen was determined as described by **Schrier, (2008)**. Urea concentration was determined according to method of **Tabacco, (1979)**.

Serum uric acid was determined using the enzymatic colorimetric method as described by **Fossati et al., (1980)**. Aspartate aminotransaminase (AST) and Alanine aminotransaminases (ALT) were determined according to the method described by **Young, (2001)**. Malondialdehyde (MDA) and Glutathione peroxidase (GPx) were determined according to **Young, (2001)**.

Histopathological Examination: Specimens from the kidney were dissected out, washed and placed in 10% neutral buffered for histopathological according to **Bancroft and Stevens, (1996)**. Histopathological examination was done in Veterinary medicine, Cairo University.

Statistical Analysis: Results were expressed as the mean standard error \pm SE. Data were statistically analyzed for variance "ANOVA" test at $P \leq (0.05)$ using SPSS statistical software, version 20 was used for these calculations (**Armitage and Berry, 1987**).

RESULTS AND DISCUSSION

Table (1) showed that strawberry leaves contained protein, fat, ash, moisture, fiber and carbohydrate at 13.45, 5.38, 9.22, 3.80, 12.35 and 55.80%, respectively and ascorbic acid at 113.15 mg/100g. Results in Table (2): revealed that strawberry leaves powder had more powerful in phenolic and flavonoid compounds. The result revealed that **SLP** contained high amount of benzoic acid, hydroxy benzoic acid and rutin with the value 718.13, 606.18 mg and 458.52 mg, respectively. As well as Table (3) showed that antioxidant activities were recorded 94.37 % for SLP and 95.77 for SLWE. Similar results was obtained by **Shalaby,(2018)**. Also results showed that the high content of vitamin C was found in strawberry leaves **Oliveira et al., (2009)**. Another study by **Zhong et al., (2016)** confirmed that the content of vitamin C in strawberry leaves, these results were in agreement with **Šic Žlabur et al., (2020)**. These results agree with **Kårlund et al., (2014)** who detected those 21 different ellagitannins constituted the largest group of compounds in the strawberry leaves. These results in the same line with **Buricova et al., (2011)**.

Table (1): Chemical composition and of strawberry leaves

Strawberry Leaves	
Protein	13.45%
Fat	5.38%
ASH	9.22 %
Moisture	3.80%
Fiber	12.35%
Carb	55.80%
vitamin C Ascorbic acid	113.15 Mg/100g

Table (2): Polyphenolic Compounds Concentration of strawberry leaves powder and its water extract

Polyphenolic Compounds	Concentration of Polyphenolic Compounds(mg/kg)	
	Strawberry Leaves Powder	Strawberry Leaves Water Extract
3-Hydroxytyrosol	-	241.23485
Catechol	-	2.97130
Gallic acid	111.42381	56.23273
p-Hydroxybenzoic acid	606.18149	119.21654
Catchin	35.92478	10.00669
Chlorogenic	33.96632	1.35904
Vanillic acid	145.44196	15.03163
Caffeic acid	28.39657	7.78022
Syringic acid	44.40879	8.64853
p- Coumaric acid	46.09581	1.99560
Benzoic acid	718.13003	177.11228
Ferulic acid	23.96767	110.07631
Rutin	458.52870	146.52750
Ellagic	45.96542	32.07249
o- Coumaric acid	78.72518	45.25717
Resvertol	34.27319	60.59034
Cinnamic acid	34.04893	3.48184e-1
Quercetin	67.96691	17.85518
Rosemarinic	--	14.73611
Myricetin	15.16239	--
Quinol	43.53554	59.37174
Kampherol	2.08206	7.59562e-1
Total	2574.22556	1139.14579

Table (3): The antioxidant activity in strawberry leaves powder and its water extract

Sample	%DPPH Radical-Scavenging Activity					
	0.05%	0.125%	0.2%	0.25%	0.5%	1%
strawberry leaves powder	74.65	86.20	-	94.37	-	-
strawberry leaves water extract	-	-	73.52	-	87.61	95.77

Mean values in Table (4) showed the effect of strawberry leaves and its water extract and silymarin (as a drug) on feed intake (FI), body weight gain (BWG) and feed efficiency ratio (FER) of nephrotoxic rats. Feed intake was decreased in positive control group compared to negative control group, while treated groups with 5 and 10% of strawberry leaves (powder or its water extract) or silymarin were close to negative control group. Cisplatin caused significant decrease ($P \leq 0.05$) in BWG and FER for the positive control group compared to the negative control group, while pretreated groups with 5% and 10% strawberry leaves (powder or water extract) or silymarin were significantly increased in BWG compared to +ve group, also

there were no significant differences in FER of treated groups compared to the positive control group. Similar observation was obtained by **Lin et al., (2018)**. Gastrointestinal tract disorders including vomiting, nausea, stomach distention and gastric stasis may result in decreased food intake **Malik et al., (2006)**. Pre-treatment with strawberry leaves powder or extract showed enhanced feed intake, body weight gain and relative organ weight for nephrotoxic pretreated rats. These results are in the same line with **Galal et al., (2014)**. While disagree with **Duru, (2013)** who found SL had no effect on feed intake and feed conversion ratio.

Table (4): Effect of dried strawberry leaves and its water extract on Feed Intake (FI), Body Weight Gain (BWG) and Feed Efficiency Ratio (FER) of Nephrotoxicity rats

Parameters	FI (g/d)	BWG %	FER
G1: -ve control	16.00	19.38±1.24 ^a	0.120±0.080 ^a
G2: +ve control	14.00	16.64±1.12 ^c	0.041±0.003 ^b
G3: 5% STLP	15.00	17.48±.60 ^b	0.0412±0.0026 ^b
G4: 5% STWE	15.00	17.52±1.23 ^b	0.041±0.003 ^b
G5: 10% STLP	15.40	17.70±0.77 ^b	0.041±0.002 ^b
G6: 10% STWE	15.50	18.00±0.75 ^b	0.041±0.002 ^b
G7: Silymarin 50 ml/k	15.40	17.92±0.43 ^b	0.041±0.001 ^b

*Mean values are expressed as means ± SE.

*Mean values at the same column with the same superscript letters are not statistically significant at $P \leq 0.05$.

Data illustrated in Table (5) showed that cisplatin caused an increase in serum levels of TC, TG, LDL-C and VLDL-C levels and decrease in high density lipoprotein cholesterol (HDL-C) of +ve control group compared to -ve control. On the other hand all groups that treated with strawberry leaves powder or water extract were decreased significantly ($P \leq 0.05$) in serum TC, TG, LDL-C and VLDL-C levels compared to the positive control group. Regarding serum HDL-C level, results showed a significant ($P \leq 0.05$) increase in serum HDL-C level of the pretreated groups with strawberry leaves. Therefore the high concentration of strawberry leaves water extract had the best effect on improving blood lipid profile, which was close to the effect of silymarin. This research is in agreement with **Abdel-Gayoum and Ahmida, (2017)**. In this study pretreatment of rats with strawberry leaves powder or extract that could be attributed to enhanced lipid profile. In the same line, hypolipidaemic action may be due to polyphenols and antioxidants present in strawberry leaves powder or extract, the same effect of strawberry leaves extract on lipid profile was confirmed by **Forbes-Hernández et al., (2017)**. Also in agreement with **El-Hawary et al., (2021)**.

Table (5) : Effect of dried strawberry leaves , its water extract and silymarin on serum total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and very low density lipoprotein cholesterol (VLDL-C) of nephrotoxicity rats

Parameters Groups	TC	TG	HDL-C	LDL-C	VLDL-C
	mg/dl				
G1:-ve control	68.58±.65 ^d	39.90±.56 ^c	40.10±.51 ^a	20.50±.50 ^d	7.98±.11 ^c
G2: +ve control	81.60±.68 ^a	62.50±.92 ^a	20.40±.51 ^c	48.70±.37 ^a	12.50±.18 ^a
G3: 5% STLP	76.26±.74 ^b	54.30±.37 ^b	31.70±.54 ^b	33.70±.54 ^b	10.86±.07 ^b
G4: 5% STWE	73.40±.40 ^c	52.50±.71 ^b	31.50±.55 ^b	31.40±.60 ^b	10.50±.14 ^b
G5: 10% STLP	72.88±.96 ^c	51.40±.53 ^b	31.50±.50 ^b	31.10±.51 ^b	10.28±.11 ^b
G6:10% STWE	73.60±.67 ^c	50.50±.50 ^b	33.70±.54 ^b	29.80±.37 ^c	10.10±.10 ^b
G7:Silymarin 50 ml/kg b.wt	72.88±.09 ^c	53.40±.98 ^b	34.70±.37 ^b	27.50±.81 ^c	10.68±.11 ^b

*Mean values are expressed as means ± SE.

*Mean values at the same column with the same superscript letters are not statistically significant at P≤ 0.05.

As seen in Table (6), serum concentrations of creatinine, urea, blood urea nitrogen (BUN), and uric acid were significantly ($P \leq 0.05$) elevated and reduced in serum Albumin by cisplatin administration (positive control group) compared with negative control group. It was observed significant ($P \leq 0.05$) reduce in serum creatinine, urea, Blood urea nitrogen (Bun), uric acid and elevated in serum Albumin for all groups treated with strawberry leaves powder and its water extract or silymarin compared to positive control group. Results indicated that strawberry leaves water extract at 10% concentration had the best effect on enhancing kidney functions.

Sen et al., (2013) concluded that cisplatin administration produced a significant increase in serum creatinine and BUN accompanied by significant decrease in total proteins and albumin. These results were confirmed by current study the results. Cis injected rats that received strawberry leaves powder or extract had significant ($P \leq 0.05$) lower levels of urea, creatinine, blood urea nitrogen, uric acid and accompanied by significant decrease in albumin compared to positive control. In the same line **Mohamed and Ashour,(2019)** who confirmed that Both doses of strawberry leaves extract caused the decrease in urea level, creatinine level. Also **Sato et al., (2019)** suggested that the strawberry leaf extract may exert a potent hypouricemic effect. Natural phenolics, alkaloids, coumarins and flavonoids such as hesperidin, rutin, silymarin and carotenoids were shown to ameliorate cis-mediated nephrotoxicity **Sahu et al., (2013)**. Moreover, **Pattanayak et al., (2017)** who reported that Ellagic Acid binds to human serum albumin, the major transport protein in blood serum that caused reduce serum albumin.

Table (6): Effect of dried strawberry leaves powder, its water extract and silymarin on serum albumin creatinine, urea, blood urea nitrogen (BUN), and uric acid

Parameters Groups	Creatinine	Urea	Albumin	BUN	Uric acid
	(mg/dl)				
G1:-ve control	0.51±.01 ^d	18.06 ±0.52 ^c	4.30±.09 ^a	8.10±0.18 ^d	1.26±0.05 ^c
G2:+vecontrol	0.99±.05 ^a	44.00±1.00 ^a	2.50±0.22 ^c	17.62±0.53 ^a	2.93±0.07 ^a
G3: 5%STLP	0.69±.00 ^b	22.00±1.00 ^b	3.30±0.07 ^b	10.30±0.44 ^b	2.30±0.04 ^b
G4: 5%STWE	0.65±.02 ^c	21.30± 0.58 ^b	3.74±0.07 ^a	10.00±0.23 ^b	2.18±0.012 ^b
G5:10%STLP	0.69±.01 ^b	21.90± 0.90 ^b	3.86±0.07 ^a	10.37±0.35 ^b	1.97±0.016 ^c
G6:10%STE	0.61±.02 ^d	19.00± 0.45 ^c	3.92±0.06 ^a	8.90±0.16 ^c	1.66±0.09 ^d
G7:Silymarin50 ml/kg b.wt	0.58±.02 ^d	21.40±1.03 ^b	4.02±0.06 ^a	9.17± 0.20 ^c	1.89±0.05 ^c

*Mean values are expressed as means ± SE.

*Mean values at the same column with the same superscript letters are not statistically significant at P≤ 0.05.

Data revealed in Table (7) that serum concentrations of aspartate aminotransferase (AST), alanine aminotransferase (ALT) were significantly (P≤ 0.05) increased by cisplatin administration (+ve group) compared with -ve control group, while pretreated rats with strawberry leaves (powder or water extract) at doses 5% and 10% concentrations and silymarin 50 ml/kg b.wt caused a significant decrease (P≤ 0.05) in the activity of AST , ALT enzymes compared to the positive control group. Also it was observed that strawberry leaves water extract at 5, 10% concentrations had the best effect on improving liver functions. In the present study, induced with cis of rats was confirmed by a significant elevation of AST and ALT. this agreement with *Mir et al., (2015)*.The results of this study showed that, nephrotoxic rats pretreated with strawberry leaves powder or water extract effective improvement in liver function and afforded a protection against cis toxicity. These results were in accordance with those reported by *Jurica et al., (2020)* who showed that strawberry tree water leaf extract acceptable biocompatibility with liver tissue both in male and female rats. As well as *Shalaby, (2018)* who confirmed that strawberry leaves powder greatly reduces high levels of serum ALT and AST.

Table (7): Effect of dried strawberry leaves, its water extract and silymarin on aspartate aminotransferase (AST), alanin aminotransferase (ALT) of nephrotoxicity rats

Parameters Groups	AST	ALT
	U/L	
G1: -ve control	7.00±0.45 ^c	8.00±0.45 ^{cd}
G2: +ve control	37.60±2.16 ^a	26.00±1.00 ^a
G3: 5% STLP	14.50±1.34 ^b	14.50±0.57 ^b
G4: : 5% STWE	8.80±0.58 ^c	10.60±0.51 ^c
G5: 10% STLP	11.00±0.71 ^b	14.10±0.33 ^b
G6: : 10% STWE	8.50±0.50 ^c	9.70±0.44 ^c
G7:Silymarin50ml/kg b.wt	11.30±0.86 ^b	14.00±1.61 ^b

*Mean values are expressed as means ± SE.

*Mean values at the same column with the same superscript letters are not statistically significant at P≤ 0.05.

Results in Table (8) showed a significant decrease ($P \leq 0.05$) in serum GPx activity of the +ve control group compared with the negative control group. It was clear that, there was significant ($P \leq 0.05$) increase in serum GPx activity for all treated groups with strawberry leaves or silymarin compared to the positive control group. Concerning to serum malondialdehyde (MDA) level, results showed that serum MDA level was significantly increased ($P \leq 0.05$) in the +ve control group compared with the -ve control group, whereas, all treated groups with strawberry leaves or silymarin significantly decreased ($P \leq 0.05$) compared to the positive control group. It was also observed that rats were administrated with 10% strawberry leaves water extract considered the best group for increasing the serum GPx and reducing serum MDA levels. Lipid peroxidation closely related to Cis-induced toxicity **Somani, (2000)**. The result of the present study supported the findings of the previous studies as there was an increase in serum lipid peroxidation (MDA), and decrease in GPx. The observed increase in MDA in the current study could be because cisplatin induced formation of free radicals and also through exhaustion of antioxidants leading to oxidative stress **Verma et al., (2016)**. In this study, it was found that strawberry leaves Provides great protection against nephrotoxicity CIS effects. The strawberry leaves were too able to significantly reduce MDA production and increase GSH levels in the blood Similarly. These results strongly support that Strawberry leaves are strong antioxidant, anti-inflammatory and protective effects against cis-induced toxicity. **Ibrahim and Abd El-Maksoud, (2019)** suggested that strawberry leaf extract might be used as an antioxidant, anti-inflammatory and anti-apoptosis to improve brain damage caused by diabetes. These result agree with **Zhang et al., (2020)**. The presence of Ellagic acid in strawberry leaves could have been the cause for the observed protection of kidney from Cisplatin induced toxicity **Aslan et al., (2020)**.

Table (8): Effect of dried strawberry leaves, its water extract silymarin on serum glutathione peroxidase (GSH) and malondialdehyde (MDA) of nephrotoxicity rats

Parameters	GSH ($\mu\text{mol/dL}$)	MDA ($\mu\text{mol/dL}$)
G1: -ve control	19.66 \pm .38 ^a	3.44 \pm .16 ^d
G2: +ve control	10.50 \pm .50 ^d	7.67 \pm .54 ^a
G3: 5% SLP	14.80 \pm .29 ^d	5.01 \pm .17 ^b
G4: 5% STWE	16.06 \pm .12 ^c	3.82 \pm .19 ^d
G5: 10% STLP	17.02 \pm .17 ^b	5.26 \pm .16 ^b
G6: 10% STLWE	17.92 \pm .15 ^b	3.65 \pm .19 ^d
G6: Silymarin	15.84 \pm .29 ^d	4.18 \pm .18 ^c

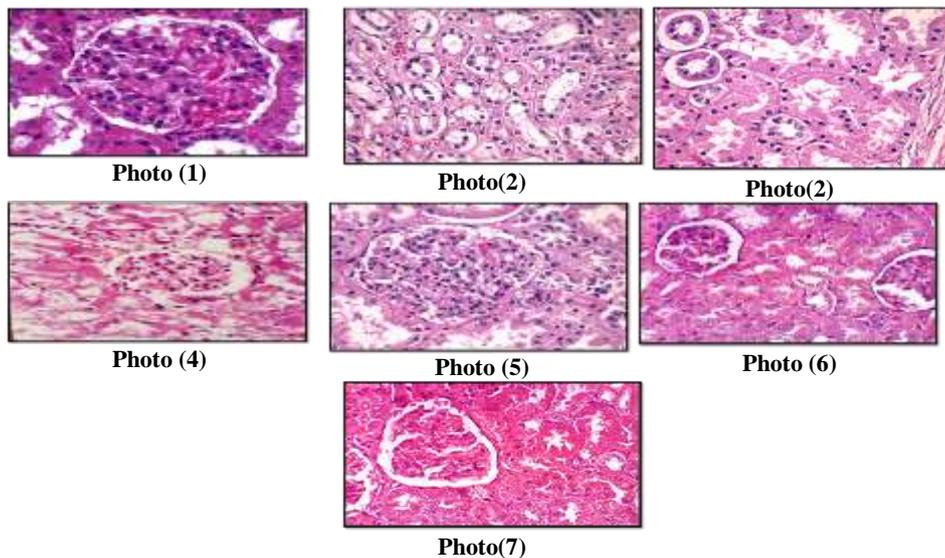
*Mean values are expressed as means \pm SE.

*Mean values at the same column with the same superscript letters are not statistically significant at $P \leq 0.05$.

The histopathological examinations of kidney are shown the effect of strawberry leaves powder or extract from Photos 1 - 7. All histopathological

findings were in harmony with serum biochemical parameters. Results of the histological examination of previous studies demonstrated changes in kidney structure due to Cis treatment. In several studies, glomerular and tubular modifications were found to be a result of Cis **Ravindra et al., (2010)**. In this study, pretreated with strawberry leaves reduced the Severity of cis-induced renal histological changes. These histological findings agreed with the study of **Zhang et al., (2020)**.

The histopathological examinations of kidney



- Photo (1)** Kidney of negative control group (1) rats showing that in normal kidney, the tubules are relatively uniform parallel arrangement and No leukocytes are present. **(H & E X 400)**
- Photo (2)** positive control group (2), the cisplatin-injected kidneys showed marked injury with sloughing of tubular epithelial cells, loss of brush border, and dilation of tubule **(H & E X 400)**
- Photo (3)** kidney of rat from group (3), fed on strawberry leaves powder 5% Showing normal appearance of tubules with loss of some brush border in so tubules. **(H & E X 400)**
- Photo (4)** kidney of rat from group (4), oral administrated of strawberry leaves extract 5% Showing normal appearance of kidney structure with infiltration of some inflammatory cells **(H & E X 400)**
- Photo (5)** kidney of rat from group (5), fed on strawberry leaves powder 10%) showing normal appearance of proximal convoluted tubule with some evidence of blood **(H & E X 400)**
- Photo (6)** kidney of rat from group (6), showed Normal appearance oral administrated of strawberry leaves extract at 10% **(H & E X 400)**
- Photo (7)** kidney of rat from group (7), oral administrated of Silymarin as drug showed Normal appearance **(H & E X 400)**

REFERENCE

- Abdel-Gayoum, A. and S. Ahmida (2017):** Changes in the serum, liver, and renal cortical lipids and electrolytes in rabbits with cisplatin-induced nephrotoxicity. *Turkish Journal of Medical Sciences*, 47(3): 1019-1027.
- Albers, N. ; V. Benderson and G. Warnick (1983):** Enzymatic Academic Press, Chapter, 5: 1831-1835.
- Armitage, Y. and G. Berry (1987):** Statistical methods 7th Ed. Ames., Iowa state university. Press. 39-63.
- Aslan, A. ; O. Gok ; S. Beyaz ; A. Ağca ; O. Erman and A. Zerek (2020):** Ellagic acid prevents kidney injury and oxidative damage via regulation of Nrf-2/NF-κB signaling in carbon tetrachloride induced rats. *Molecular Biology Reports*, 47(10): 7959-7970.
- Bancroft, J. and A. Stevens (1996):** Theory and practice of histological technique, Churchill, Livingston, Eden burgh, London, Melhourne and New York.
- Buricova, L. ; M. Andjelkovic ; A. Cermakova ; Z. Reblova ; O. Jurcek,; E. Kolehmainen, and F. Kvasnicka (2011):** Antioxidant capacities and antioxidants of strawberry, blackberry and raspberry leaves. *Czech Journal of Food Sciences*, 29 (2): 181-189..
- Burtis, C. and E. Ashwood (1999):** Tietz textbook of clinical chemistry. 3rd ed. Philadelphia: W.B. Saunders, 1999: 1840, 1841, 1844, 1845; 1799; 1834-5 Textbook of Clinical Chemistry, 3rd ed AACC.
- Chapman, G. ; R. Castillo and A. Campbell (1959):** Evaluation of protein in foods: 1. A method for the determination of protein efficiency ratios. *Canadian Journal of Biochemistry and Physiology*, 37(5): 679-686.
- Duru, M. (2013):** Effects of dietary strawberry (*Fragaria x ananassa* Duch.) leaf powder on egg yield, quality and egg yolk cholesterol in laying hens. *J Food Agric Environ*, 11: 477-480.
- El-Hawary, S. ; R. Mohammed ; M. El-Din ; H. Hassan ; Z. Ali ; M. Rateb and R. Abdelmohsen, (2021):** Comparative phytochemical analysis of five Egyptian strawberry cultivars (*Fragaria x ananassa* Duch.) and antidiabetic potential of Festival and Red Merlin cultivars. *RSC Advances*, 11(27): 16755-16767.

- Fang, Y. ; Y. Lou ; Q. Zhou ; C. Wang ; J. Yang and J. Weng (2021)** : Natural products: potential treatments for cisplatin-induced nephrotoxicity. *Acta Pharmacologica Sinica*, 1-19.
- Forbes-Hernández, Y. ; M. Gasparrini ; S. Afrin ; D. Cianciosi ; M. González-Paramás ; C. Santos-Buelga and S. Bompadre (2017):** Strawberry (cv. Romina) methanolic extract and anthocyanin-enriched fraction improve lipid profile and antioxidant status in HepG2 cells. *International journal of molecular sciences*, 18(6): 1149.
- Fossati, F. and L. Principe (1982):** Plasma triglycerides determined colorimetrically with an enzyme that produces hydrogen peroxide. *Clin. Chem.*, 28(10):2077-2080.
- Friedewald, T. ; I. Leve and S. Fredrickson (1972):** Graw Hill Book Company (U.K.) Limited
- Galal, F. ; A. El Menniawy ; H. Abo-Fadel and A. Khir (2014):** Some nutritional studies on using strawberry (*Fragaria ananas*) vine as hay in rabbit ration. *Journal of Animal and Poultry Production*, 5(12): 635-647.
- Abd El-Maksoud, M.A. and S. Ibrahim (2019):** Strawberry (*Fragaria x ananassa*) leaf extract reduces brain damage in diabetic male rats. *Egypt. J. Exp. Biol. (Zool.)*, 15(1): 39 – 43
- Issa, I. ; A. Abbas and I. Abdel-Gawad (2018):** Potential impact of strawberry leaves extract on neurotoxicity in rats . *International Journal of Innovative Science and Research Technology*, 2456-2165
- Jurica, K. ; V. Benković ; S. Sikirić ; I. Brčić Karačonji and N. Kopjar (2020):** The effects of strawberry tree (*Arbutus unedo* L.) water leaf extract and arbutin upon kidney function and primary DNA damage in renal cells of rats. *Nat Prod Res.*, 2020 34(16):2354-2357
- Karlińska, E. ; A. Masny ; M. Cieślak ; J. Macierzyński ; Ł. Pecio ; A. Stochmal and M. Kosmala (2021) :** Ellagitannins in roots, leaves, and fruits of strawberry vary with developmental stage and cultivar. *Scientia Horticulturae*, 275: 109665.
- Kårlund, A. ; P. Salminen ; P. Koskinen ; R. Ahern ; M. Karonen ; K. Tiilikkala and O. Karjalainen (2014):** Polyphenols in strawberry (*Fragaria x ananassa*) leaves induced by plant activators. *Journal of Agricultural and Food Chemistry*, 62(20): 4592-4600.

- Konam, B. and C. Yalamuri (2014):** A review on nephroprotective activity of herbal plants. *J Compr Phar*; 1(4):95-107.
- Lin, M. ; J. Ko ; T. Liu ; P. Chao and C. Ou (2018):** Protective Effect of D-Methionine on Body Weight Loss, Anorexia, and Nephrotoxicity in Cisplatin-Induced Chronic Toxicity in Rats 17(3):813 –824.
- Malik, N. ; G. Moore ; G. Smith ; Y. Liu ; G. Sanger and P. Andrews (2006):** Behavioral and hypothalamic molecular effects of the anti-cancer agent cisplatin in the rat: a model of chemotherapy related malaise? *Pharmacol Biochem Behav*; 83:20.
- Mansour, H. ; F. Hafez and M. Fahmy (2006):** Silymarin modulates cisplatin-induced oxidative stress and hepatotoxicity in rats. *BMB Reports*, 39(6): 656-661.
- Mir, M. ; M. Arab ; M. Shahraki ; M. Mashhadi ; M. Salar ; F. Aval and M. Karimfar (2015):** Toxic Effects of Cisplatin on Hepatocytes and Liver Enzymes of Rats. *Journal Of Iranian Anatomical Sciences*, 12(4): 171 - 175.
- Mohamed, E. and E. Ashour (2019):** Influence of ethanolic extract of strawberry leaves for abrogating bromate hazards in male rats. *The Journal of Basic and Applied Zoology*, 80(1): 1-6.
- Oliveira, I. ; V. Coelho ; R. Baltasar ; J. Pereira and P. Baptista (2009):** Scavenging capacity of strawberry tree (*Arbutus unedo L.*) leaves on free radicals. *Food and Chemical Toxicology*, 47(7): 1507-1511.
- Pattanayak, R. ; P. Basak ; S. Sen and M. Bhattacharyya (2017):** An insight to the binding of ellagic acid with human serum albumin using spectroscopic and isothermal calorimetry studies. *Biochemistry and Biophysics Reports* 10: 88–93 peroxide. *Clin. Chem.*, 28(10):2077-2080.
- Ravindra, P. ; A. Bhiwgade ; S. Kulkarni ; P. Rataboli and C.Y. Dhume (2010) :** Cisplatin induced histological changes in renal tissue of rat. *Journal of Cell and Animal Biology*, 4(7): 108-111.
- Reeves, G.; H. Nielsen and C. Fahmy (1993):** AIN-93 purified diets for laboratory rodents: final reports of committee of reformulation of the AIN-76 A rodent diet. *J. Nutr.*,123: 1939-51.
- Richmond, N. (1973):** Colorimetric determination of total cholesterol and high density lipoprotein cholesterol (HDL-c). *Clin. Chem.*, 19: 1350-1356.

- Rudrapal, M. and D. Chetia (2021):** Herbal Drugs: Efficacy, Toxicity, and Safety Issues. In *Evidence Based Validation of Traditional Medicines*:537-553.
- Sahu, B. ; M. Kuncha ; G. Sindhura and R. Sistla (2013):** Hesperidin attenuates cisplatin-induced acute renal injury by decreasing oxidative stress, inflammation and DNA damage . *Phytomedicine*; 20: 453-460.
- Sato, T. ; Y. Ikeya ; I. Adachi ; K. Yagasaki ; I. Nihei and N. Itoh (2019):** Extraction of strawberry leaves with supercritical carbon dioxide and entrainers: Antioxidant capacity, total phenolic content, and inhibitory effect on uric acid production of the extract. *Food and Bioproducts Processing*, 117: 160-169.
- Schrier, W. (2008):** Blood urea nitrogen and serum creatinine: not married in heart failure. *Circulation: Heart Failure*, 1(1): 2-5.
- Sen, S. ; D. Biplab ; N. Devanna and R. Chakraborty (2013)** :cisplatin-induced nephrotoxicity in mice: protective role of *Leea asiatica* leaves. *Renal Failure*, 35 (10): 1412-1417.
- Shalaby, Hanan S. (2018):** Impact of Strawberry (*Fragaria x ananassa*) Leaves Powder on Induced Diabetic Rats. *Scientific Journal of the Faculty of Specific Education*,14 (1)1-2
- Šic Žlabur, J. ; Bogdanović, S., Voća, S. and Skendrović Babojelić, M. (2020):** Biological potential of fruit and leaves of strawberry tree (*Arbutus unedo* L.) from Croatia. *Molecules*, 25(21), 5102.
- Somani, M. ; K. Husain ; C. Whitworth ; L. Trammell ; M. Malafa and P. Rybak (2000)** :Dose-dependent protection by lipoic acid against cisplatin-induced nephrotoxicity in rats: antioxidant defense system. *Pharmacology & toxicology*, 86(5): 234-241.
- Tabacco, A. (1979):** Quntitative enzymatic colorimetric determination of blood urea nitrogen in serum or plasma. *Clin. Chem*, 25:336.
- Verma, P. ; R. Raina ; M. Sultana ; M. Singh and P. Kumar (2016):** Total antioxidant and oxidant status of plasma and renal tissue of cisplatin-induced nephrotoxic rats: protection by floral extracts of *Calendula officinalis* Linn. *Ren Fail*; 38(1): 142–150.
- Wahlefeld, A. (1974):** *Methods of Enzymatic Analysis*. Academic Press, Chapter, 5: 1831-1835.
- Young, Donald S. (1995):** *Effect of drugs on clinical lab Tests*, 4 th ed. Washington (D.C.) : AACC press
- Yousef, I. ; A. Saad and K. El-Shennawy (2009):**Protective effect of grape seed proanthocyanidin extract against oxidative stress induced by cisplatin in rats. *Food and Chemical Toxicology*, 47(6): 1176-1183.
- Young, D. (2001):** *Effect of disease on clinical lab Tests*, 4thed. AACC press. *Clin. Chem.*, 19: 1350-1356. colorimetrically with an

enzyme that produces hydrogen determination of high density lipoprotein cholesterol, Selected Methods. Clin. Chem., 10: 91-99.

Zhang, L. ; Q. Ma and Y. Zhou (2020): Strawberry Leaf Extract Treatment Alleviates Cognitive Impairment by Activating Nrf2/HO-1 Signaling in Rats With Streptozotocin-Induced Diabetes. *Frontiers in Aging Neuroscience*, 12.

Zhong, F. ; L. Mazzoni ; F. Balducci ; L. Di Vittori ; F. Capocasa ; F. Giampieri and B. Mezzetti (2016): Evaluation of vitamin C content in fruit and leaves of different strawberry genotypes. In *VIII International Strawberry Symposium*, 1156: 371-77.

التأثير الوقائي لأوراق الفراولة ضد تسمم نفروونات الكلى في ذكور الفئران

نورالهدى محمد مصطفى ، مايسه محمد الشحات ، محمد حمدي حجاج

قسم التغذية وعلوم الأطعمة - كلية الاقتصاد المنزلي - جامعة حلوان

يشير التسمم الكلوي الى اختلال وظيفي أو تلف الكلى المرتبط بجرعة عالية من الادوية او الكائنات الحية الغريبة ومن اهم مسببات التسمم الكلوي العفن ،الفطريات وعلاجات السرطان مثل السيسبلاتين . كان هدف هذه الدراسة معرفة التأثير الوقائي لأوراق الفراولة ضد تسمم نفروونات الكلى في ذكور الفئران . حيث أجريت الدراسة علي خمسة وثلاثون فأراً من نوع الالبينو، تتراوح أوزانهم من (10 ± 150) جم) . تم تقسيم الفئران الي سبع مجموعات (5 فأر لكل منهم). مجموعة ضابطه سالبه تم تغذيتهم علي الغذاء الأساسي طوال فترة التجربة(4 اسابيع).المجموعة الضابطه الموجبه تم تغذيتهم علي الغذاء الأساسي و حقنهم تحت الجلد بجرعة واحدة من سيسبلاتين 5 ملجم / كجم من وزن الجسم في اخر التجربه لإحداث تلف حاد في الكلى. المجموعات من 3-7 تم تغذيتهم علي الغذاء الأساسي مضاف اليه 5 و 10% مسحوق أوراق الفراولة و 5 و 10% المستخلص المائي لأوراق الفراولة و 50 مل من سيليمارين فمويأ / كجم من وزن الجسم للفئران علي التوالي. وبعد يومين من الحقن بالسيسبلاتين تم تشريح الفئران والحصول على عينات الدم لاجراء التحاليل البيوكيميائية واجراء الفحوص التشريحية. كما تم وزن الفئران و حساب نسب زيادة الوزن وكفاءة التغذية . ولقد أظهرت النتائج ان مسحوق اوراق الفراولة والمستخلص المائي حسنوا من نسبة الدهون في الدم ووظائف الكلى وكذا وظائف الكبد مقارنة بالمجموعة الضابطة الإيجابية ، كما لوحظ انخفاض مستوى MDA وزيادة نشاط أنزيمات مضادات الأكسدة ، GSH. أدى التركيز العالي لـ SLP و SLWE إلى تحسين التغيرات النسيجية والكيميائية الحيوية التي يسببها السيسبلاتين. لذلك يمكن التوصية باستخدام أوراق الفراولة كمكون غذائي صحي وظيفي له آثار مفيدة على الوقايه من تلف الكلى.

كلمات مفتاحية: مسحوق أوراق الفراولة ، خلاصة ماء أوراق الفراولة ، وظائف الكلى ، فئران التجارب ، تسمم نفروونات الكلى