الدور المساهم لبذور الكرفس وقشور الرمان في استعادة الحالة العادية البيولوجية والكيماوية الحيوية والهستولوجية للفئران المصابة بارتفاع الكوليسترول

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الدور المساهم لبذور الكرفس وقشور الرمان في استعادة الحالة العادية البيولوجية والكيماوية الحيوية والهستولوجية للفئران المصابة بارتفاع الكوليسترول

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المستخلص العربي

يهدف هذا البحث إلى تقييم تأثير بذور الكرفس وقشر الرمان والخليط منهما علي ذكور الفئران المصابة بارتفاع الكوليسترول. تم تقسيم ثلاثون فأر من الذكور البالغين سلالة سبراغ داولي إلى خمس مجموعات. مجموعة (1): وهي المجموعة الضابطة السالبة (–) تغذت على الوجبة الأساسية ، المجموعة (2): وهي المجموعة الضابطة الموجبة (+) وهي الفئران المصابة بارتفاع الكوليسترول وتغذت على الوجبة الأساسية. المجموعة (3): الفئران المصابة بارتفاع الكوليسترول التي تغذت علي بذور الكرفس بنسبة 5%. المجموعة (4): الفئران المصابة بارتفاع الكوليسترول التي تغذت على قشر الرمان بنسبة 5 %. المجموعة (5): الفئران المصابة بارتفاع الكوليسترول التي تغذت على الاثنين معا بتركيز 5%. في نهاية التجربة ، بعد 28 يومًا من التغذية ، تم تقدير الاختبارات البيوكيميائية للدم. ارتفاع الكوليسترول سبب ارتفاع في مستويات الجلوكوز واليوريا والكرياتينين واليوريك اسيد و AST و ALT و ALP ومستوى الكوليسترول الكلي وجلسريدات ثلاثية والليبوبروتين منخفض الكثافة والليبوبروتين منخفض الكثافة جدا وانخفاض مستويات الليبروتين مرتفع الكثافة مع زيادة الوزن المكتسب في الفئران المصابة بارتفاع الكوليسترول وتحسنت النتائج باستخدام الأغذية المعالجة.

الكلمات المفتاحية: مرض ارتفاع الكوليسترول – بذور الكرفس – قشر الرمان والخليط من الاثنين معا.

Contribution Role of Celery Seeds and Pomegranate Peel diets in Restoration the Normal, Biological, Biochemical & Histological Status of Hypercholesterolemic Rats

Abstract

This investigation aimed to evaluate the effect of celery seeds, pomegranate peel and mix diets on male hypercholesterolemic rats. Thirty (30) adult male Sprague Dawley rats were divided into five groups. Group (1): Normal rats fed on basal diet as control negative (C-), Group (2): Control positive (C+) (untreated group). Group (3): Hypercholesterolemic rats fed on basal diet and celery seeds (5%). Group (4): Hypercholesterolemic rats fed on basal diet and pomegranate peel (5%). Group (5): Hypercholesterolemic rats fed on basal diet and mix diets (5%). At the end of experiment, after 28 days of feeding, all serum samples were analyzed for biochemical parameters. Hypercholesterolemia caused a significant decrease in HDL while a significant increase was recorded in BWG, TC, TG, VLDL, LDL, U.A, creatinine, urea, AST, ALT, ALP and glucose. Hypercholesterolemic rats treated with various diets, showed the improvement in all previous parameters.

Keywords: Hypercholesterolemia, Celery Seeds, Pomegranate Peel and Mixture of both.

Introduction

Apium plants belong to the family Apiaceae which are mostly aromatic plants. This genus consists of about 20 species of flowering plants that are distributed worldwide (Sowbhagya *et al*., 2010). The most prominent of this genus is the *Apium graveolens L*., popularly known as celery. There are three main varieties which are: *Apium graveolens viz. A. graveolens* var. *dulce* (Mill.) Pers which is known as cultivated celery or simply celery, A. *graveolens* var. rapaceum (Mill.) DC. also known as celeriac, root celery or turnip-rooted celery, and *A. graveolens* var. secalinum Alef. which is called leaf celery (Roslon *et al*., 2010; Mezeyova *et al*., 2018).

Celery (*A. graveolens*) is a rich source of vitamins, carotene, protein, cellulose along with some secondary metabolites including phenolic acids, flavonoids (mainly quercetin, apigenin, chrysoeriol, luteolin, and their glycosides), and terpenoids (Sellami *et al*., 2012).

Celery seeds contain 2 to 3% essential oil. Its oil contains mostly limonene (usually 60 percent), selinene (10 %), frocoumarin and frocoumarin glycosides and their flavonoids. Photochemistry tests of celery seeds approve the presence of flavonoid apigenin (as main component), and vitamins A and C. A total of 16 combinations of seed extract have been identified in celery which make up 98.7% of the whole extract whose main components are D. limonene and myrcene (Al-Snafi, 2014).

Pomegranate is the well-established fruit of a shrub (*Punica granatum L*.) that is particularly cultivated in west Asia and in the region around the Mediterranean, as well as other parts of the world, including America, where the climate is suitable for its growth (Pagliarulo *et al*., 2016).

Pomegranate peels are characterized by an interior network of membranes comprising almost 26-30 per cent of the total fruit weight and are characterized by substantial amounts of phenolic compounds, including flavonoids (anthocyanins, catechins, and other complex flavonoids) and hydrolyzable tannins (punicalin, pedunculagin, punicalagin, galic and ellagic acid). These compounds are concentrated in pomegranate peel and juice which account for 92 per cent of the antioxidant activity associated with the fruit (Negi *et al*., 2003).

Pomegranate fruits peel can be used as functional ingredient as a good source of crude fibers which provide numerous health benefits such as their ability to decrease serum LDL-Cholesterol level, improve glucose tolerance and the insulin response, reduce hyperlipidemia and hypertension, contribute to gastrointestinal health and the prevention of certain cancers such as colon cancer (Lansky and Newman, 2007; Viuda-Martos *et al*., 2010a, b).

Materials and Methods

Materials:

Celery seeds, pomegranate peel were obtained dry from herb shop in Cairo, Egypt.

Chemicals:

Cholesterol obtained from El-Gomhoria Company, Cairo, Egypt.

Animals:

Thirty (30) adult male Sprague Dawley rats, average body weight (150± 10 g) were used in this study. Rats were obtained from Research Institute of Ophthalmology, Medical Analysis Department, Giza, Egypt.

Methods:

Basal diet composition of tested rats:

The basal diet in the experiment consisted of casein (12%), corn oil (10%), mineral mixture (4%), vitamin mixture (1%),

cellulose (5%), chorine chloride (0.2%), methionine (0.3%) and the remained is corn starch (67.5%) according to AIN (1993).

Preparation of materials:

All materials were milled to soft powder by using electric grinder and kept in dusky stoppered glass bottles in a cool and dry location till use according to Russo (2001).

Induced hypercholesterolemia for rats:

Rats were fed on standard diet + 1.5% cholesterol + 0.5 % bile salts for 21 days to induce hypercholesterolemia.

Experimental design and animal groups:

Rats were housed in wire cages under the normal laboratory condition, and were fed on basal diet for a week as an adaptation period. The rats were divided into 5 groups each of 6 rats. All groups of rats were housed in wire cages at room temperature 25 C^0, and kept under normal healthy condition. Rats were divided into the following groups:

Group (1): Control negative group (-), in which normal rats were fed on basal diet.

Group (2): Control positive group (+), in which hypercholesterolemic rats were fed on basal diet.

Group (3): Hypercholesterolemic rats fed on celery seeds 5%.

Group (4): Hypercholesterolemic rats fed on pomegranate peel 5%.

Group (5): Hypercholesterolemic rats fed on mix diets5%.

Determination of Biochemical Blood Parameters:

Blood samples were collected after 12 hours fasting at the end of experiment using the abdominal aorta. The rats were scarified under ether anaesthesia. Blood samples were received into in clean dry centrifuge tubes, in which blood was left to clot at room temperature, and then centrifuged for 10 minutes at 3000 r.p.m to separate the serum. Serum was carefully aspirated and transferred into clean tubes and stored frozen at-20^{o}C for biochemical analysis as described by Schermer (1967). All serum samples were analyzed for determination the following parameters:

Urea was determined according to the enzymatic method of Patton and Crouch (1977), creatinine was determined according to kinetic method of Henry (1974) and uric acid was according to the enzymatic colorimetric test of Fossati and Prencipe (1980). Aspartate amino transaminase (AST) and alanine amino transferase (ALT) were carried out according to the method of Yound (1975) and Tietz (1976). Alkaline phosphatase (ALP) was determined according to Belfield and Goldberg (1971). Total cholesterol (TC) was determined according to Allain (1974), and high density lipoprotein cholesterol (HDL-c) according to Lopez (1997). The calculation of low density lipoprotein cholesterol (LDL-c) was carried out according to the method of Lee and Nieman (1996), atherogenic index (AI) was calculated according to Kikuchi *et al*., (1998) and triglycerides as Fossati and Prencipe (1982). Serum glucose determined according to Kaplan (1984).

Statistical Analysis:

The data were statistically analyzed using a computerized Costat Program by one way ANOVA using a Completely Randomized Factorial Design (SAS, 1988) when a significant mean effect was detected, the means were separated with the Duncan's Multiple Range Test. Differences between treatments at $P \leq 0.05$ were considered significant. The results are presented as mean ± SD.

Results and Discussion

Data presented in table (1) illustrate the effect of celery seeds, pomegranate peel and mix diets on BWG, FI and FER of hypercholesterolemic rats. It could be observed that the mean value of (BWG) of control (+) group was higher than control (-) group, being 2.43±0.005 and 0.98±0.001 g respectively. The best (BWG) level was showed for groups 5 (rats fed on basal diet containing 5% mix diets) when compared to control (+) group.

It could be noticed that the mean value of FI of control (+) group was higher than control (-) group, being 22.09±0.001 and 20.95±0.009 g respectively. The best (FI) level was showed for

group 5 (rats fed on basal diet + 5% mix diets) when compared to control (+) group.

Also, data of table (1) observed that the mean value of (FER) of control (+) group was higher than control (-) group, being 0.110±0.0001 and 0.047±0.0004 respectively. The best FER was shown for group 5 (rats fed on basal diet + 5% mix diets) when compared to control (+) group.

It seems possible that the combination of both celery seeds and pomegranate peel revealed a synergistic action.

Hossin, (2009) reported that pomegranate peel powder reduced body weight gain ratio comparing with control positive group acting on lipids metabolism in hypercholesterolemic male rats.

Al-Sa'aidi *et al*., (2012) found that n-butanol extract of celery (*Apium graveolens*) seeds reduced body weight gain in streptozotocin-induced diabetic rats.

Table (1): Effect of celery seeds, pomegranate peel and mix diets on body weight gain (BWG), feed intake (FI) and feed efficiency ratio (FER) of hypercholesterolemic rats

Parameters / Groups	BWG (g) Mean ± SD	FI (g) Mean ± SD	FER Mean ± SD
G1: Control –ve	0.98^{e}±0.001	20.95^{b}±0.009	0.047^{e}±0.0004
G2: Control +ve	2.43^{a}± 0.005	22.09^{a}± 0.001	0.110^{a}± 0.0001
G3: Celery seeds (5%)	1.71^{b}± 0.008	19.41^{d}± 0.004	0.088^{b}± 0.0005
G4: Pomegranate	1.53^{c}± 0.006	19.99^{c}± 0.002	0.077^{c}± 0.0003

peel (5%)			
G5: Mix diets (5%)	1.30^{d}± 0.009	18.11^{e}± 0.008	0.072^{d}± 0.0008
LSD	0.012	0.01	0.0009

Values in each column with different letters are significantly different (P<0.05).

Data presented in table (2) show the effect of celery seeds, pomegranate peel and mixture of both on organs weight of hypercholesterolemic rats. It could be observed that the mean value of liver of control (+) group was higher than control (-) group, being 9.6±0.05 and 7.5±0.07g respectively. The best liver weight showed for groups 5 (rats fed on basal diet containing 5% mixture of both) when compared to control (+) group.

It could be observed that the mean value of heart weight of control (+) group was higher than control (-) group, being 1.60±0.08 and 0.80±0.03 g respectively. The best heart weight was shown for group 5 when compared to control (+) group.

The same table indicated that the mean value of lungs weight of control (+) group was higher than control (-) group, being 2.30±0.05 and 1.40±0.08 g respectively. The best lungs weight was showed for group 3 (rats fed on basal diet + 5% celery seeds) when compared to control (+) group.

Also, data of table (2) noticed that the mean value of spleen weight of control (+) group was higher than control (-) group, being 1.70±0.04 and 0.80±0.05 g respectively. The best spleen weight was shown for group 5 (rats fed on basal diet + 5% mixture of both) when compared to control (+) group.

It could be noticed that the mean value of kidneys weight of control (+) group was higher than control (-) group, being 3.40±0.01 and 2.70±0.09 g respectively. The best kidneys weight

was showed for group 3 (rats fed on basal diet + 5% celery seeds) when compared to control (+) group.

Table (2): Effect of celery seeds, pomegranate peel and mixture of both on organs weight (g) of hypercholesterolemic rats

Parameters / Groups	Liver (g) Mean ±SD	Heart (g) Mean ±SD	Lungs (g) Mean ±SD	Spleen (g) Mean ±SD	Kidneys (g) Mean ±SD
G1: Control –ve	7.5^{e}±0.07	0.80^{d}±0.03	1.40^{d}±0.08	0.80^{e}±0.05	2.70^{b}±0.09
G2: Control+ve	9.6^{a}±0.05	1.60^{a}±0.08	2.30^{a}±0.05	1.70^{a}±0.04	3.40^{a}±0.01
G3: Celery seeds (5%)	8.9^{b}±0.02	1.40^{b}±0.07	1.50^{c}±0.06	1.30^{b}±0.06	2.40^{d}±0.07
G4: Pomegranate peel (5%)	8.6^{c}±0.09	1.30^{bc}±0.01	1.70^{b}±0.04	1.10^{c}±0.02	2.50^{cd}±0.03
G5: Mixture of both (5%)	8.4^{d}±0.04	1.20^{c}±0.08	1.70^{b}±0.01	0.90^{d}±0.03	2.60^{bc}±0.08
LSD	0.11	0.11	0.097	0.077	0.12

Values in each column with different letters are significantly different (P<0.05).

Data presented in table (3) indicate the effect of celery seeds, pomegranate peel and mix diets on total cholesterol and triglycerides of hypercholesterolemic rats. It could be observed that the mean value of total cholesterol (TC) of control (+) group was higher than control (-) group, being 235±2.43 and 95±2.15 mg/dl respectively. The best serum (TC) level was showed for groups 5 (rats fed on basal diet containing 5% mix diets) when compared to control (+) group.

It could be noticed that the mean value of triglycerides TG of control (+) group was higher than control (-) group, being 147±1.25 and 89±0.99 mg/dl respectively. The best serum (TG) level was showed for group 5 (rats fed on basal diet + 5% mix diets) when compared to control (+) group.

Mansi *et al*., (2009) reported that oral administration of ethanol extract of *A. graveolens* seeds showed a significant decrease ($p<0.05$) of serum total cholesterol and triglycerides in hypolipideamic adult male albino rats.

Ramzy (2019) investigated the effects of different concentrations of pomegranate peels (5, 10, and 15%) for 28 days reduced serum total cholesterol and triglycerides in rats having diabetes and hypercholesterolemia.

Table (3): Effect of celery seeds, pomegranate peel and mix diets on total cholesterol (TC) and triglycerides (TG) of hypercholesterolemic rats

Parameters / Groups	TC Mean ± SD	TG Mean ± SD
G1: Control –ve	95^{d}± 2.15	89^{d}± 0.99
G2: Control +ve	235^{a}± 2.43	147^{a}± 1.25
G3: Celery seeds (5%)	122^{b}± 2.32	112^{b}± 1.43
G4: Pomegranate peel (5%)	117^{c}± 2.68	109^{c}± 1.61
G5: Mix diets (5%)	99^{d}± 2.93	87^{d}± 1.86
LSD	4.58	2.65

Values in each column with different letters are significantly different ($P<0.05$).

Data presented in table (4) show the effect of celery seeds, pomegranate peel and mix diets on HDLc, LDLc, VLDLc & AI of hypercholesterolemic rats.

It could be observed that the mean value of ($VLDL_C$) of control (+) group was higher than control (-) group, being 29.4±0.08 and 17.8±0.01 mg/dl respectively. The best serum VLDLc was shown for group 5 (rats fed on basal diet + 5% mix diets) when compared to control (+) group.

It could be showed that the mean value of (HDLc) of control (-) group was higher than control (+) group, being 56±1.11 and 35±0.48 mg/dl respectively. The best serum HDLc was shown for group 5 (rats fed on basal diet containing 5% mix diets) when compared to control (+) group.

The same table indicated that the mean value of (LDLc) of control (+) group was higher than control (-) group, being 170.6±2.52 and 21.20±2.11 mg/dl respectively. The best serum LDLc was shown for group 5 (rats fed on basal diet +5% mix diets) when compared to control (+) group.

Also, data of table (3) observed that the mean value of (AI) of control (+) group was higher than control (-) group, being 5.71±0.007 and 0.70±0.001 respectively. The best AI was shown for group 5 (rats fed on basal diet + 5% mix diets) when compared to control (+) group.

Al-Kurdy (2016) found that hydroalcoholic extract of celery (*Apium graveolens*) seed on blood & biochemical parameters of adult male rats reduced low density lipoprotein (LDL) and increased high density lipoprotein (HDL).

El-Hadary and Ramadan (2019) indicated that administration of hydro-methanol pomegranate (*Punica granatum* L.) peel extract MPE 200 mg/kg to both diabetic and hyperlipidemic rats decreased LDL-C, and very low-density lipoprotein cholesterol levels, while increased high density lipoprotein cholesterol levels.

Table (4): Effect of celery seeds, pomegranate peel and mix diets on (VLDLc), (HDLc), (LDLc) (mg/dl) and Atherogenic index (AI) of hypercholesterolemic rats

Parameters / Groups	VLDL (mg/dl) Mean ± SD	HDL (mg/dl) Mean ± SD	LDL (mg/dl) Mean ± SD	AI Mean ± SD
G1: Control –ve	17.8^{d}±0.01	56^{a}±1.11	21.20^{e}±2.11	0.70^{e}±0.001
G2: Control +ve	29.4^{a}± 0.08	35^{e}±0.48	170.6^{a}± 2.52	5.71^{a}±0.007
G3: Celery seeds (5%)	22.4^{b}± 0.05	48^{d}±0.25	51.6^{b}±2.35	1.54^{b}±0.005
G4: Pomegranate peel (5%)	21.8^{c}± 0.02	51^{c}±0.62	44.2^{c}± 2.38	1.29^{c}±0.008
G5: Mix diets (5%)	17.4^{e}± 0.04	54^{b}± 0.74	27.6^{d}± 2.94	0.83^{d}±0.004
LSD	0.085	1.27	4.50	0.01

Values in each column with different letters are significantly different (P<0.05).

Data of table (5) show the effect of celery seeds, pomegranate peel and mix diets on serum levels of AST, ALT, ALP enzymes & (AST/ALT) ratio of hypercholesterolemic rats.

It could be observed that the mean value of AST enzyme of control (+) group was higher than control (-) group, being 150±1.48 and 76±1.16 (U/L) respectively. The best treatment was observed for group 5 (basal diet containing 5% mix diets) when compared to control (+) group.

It could be noticed that the mean value of ALT enzyme of control (+) group was higher than control (-) group, being 45±1.28 and 27±1.41 (U/L) respectively. The best treatment was observed for group 5 (basal diet containing 5% mix diets) when compared to control (+) group.

Data of the same table (4) show the mean value of ALP enzyme of control (+) group was higher than control (-) group, being 285±0.7 and 139±0.2 (U/L) respectively. Group 5 showed

the lowest mean value of ALP enzyme level as compared to control (+) group which and recorded the best result**.**

It could be noticed that the mean value of (AST/ALT) of control (+) group was higher than control (-) group, being 3.33±0.003 and 2.82±0.001 respectively. The best treatment was observed for group 5 when compared to control (+) group.

Tashakori-Sabzevar *et al*., (2016) investigated the effects of celery seed extract on different biochemical factors and histopathological changes in normal and streptozotocin (STZ)-induced diabetic rats reduced serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST).

Faddladdeen and Ojaimi (2019) found that pomegranate peel extract (PPE) against diabetic-induced hepatic complication reduced alanine aminotransferase, alanine phosphatase, and aspartate aminotransferase levels in rats.

Table (5): Effect of celery seeds, pomegranate peel and mix diets on AST, ALT, AST/ALT and ALP (U/L) of hypercholesterolemic rats

Parameters / Groups	AST (U/L) Mean ± SD	ALT (U/L) Mean ± SD	AST/ALT Mean ± SD	ALP (U/L) Mean ± SD
G1: Control –ve	76^{d}±1.16	27^{d}± 1.41	2.82^{b}±0.001	139^{e}±0.2
G2: Control +ve	150^{a}± 1.48	45^{a}± 1.28	3.33^{d}±0.003	285^{a}±0.7
G3: Celery seeds (5%)	95^{b}± 1.64	39^{b}± 1.37	2.44^{c}±0.009	176^{b}±0.5
G4: Pomegranate peel (5%)	84^{c}± 1.29	36^{c}± 1.64	2.33^{a}±0.004	150^{c}±0.4
G5: Mix diets (5%)	78^{d}± 1.38	34^{c}± 1.86	2.29^{e}±0.005	142^{d}±0.4
LSD	2.55	2.78	0.009	0.85

Values in each column with different letters are significantly different (P<0.05).

Results of table (6) show the mean value of serum creatinine, urea and uric acid (mg/dl) on hypercholesterolemic rats fed on various diets.

It could be observed that the mean value of uric acid of control (+) group was higher than control (-) group, being 2.93±0.005 and 1.12±0.003 mg/dl respectively. Group 5 (basal diet containing 5% mixture of both) recorded the best result as compared to control (+) group.

The same table (6) results illustrate that mean value of creatinine of control (+) group was higher than control (-) group, being 0.92±0.001 and 0.60±0.006 mg/dl respectively. In concern to creatinine the best treatment was recorded for the group 5 (rats fed on basal diet +5% mixture of both) when compared to control (+) group.

It could be noticed that the mean value of urea of control (+) group was higher than control (-) group, being 51.20±0.003 and 18.11±0.007 mg/dl respectively. Group 5 recorded the best result as compared to control (+) group.

Ibrahium (2010) indicated that pomegranate peel extract decreased serum levels of urea, uric acid, and creatinine in hypercholesterolemic rats.

Hijazi & Mouminah (2017) showed that oral pretreatments with celery leaves extracts in gentamicin intoxicated rats for 6 weeks induced significant ($P< 0.05$) decreases in serum urea nitrogen, uric acid and creatinine when compared with GM-intoxicated rats.

Table (6): Effect of celery seeds, pomegranate peel and mixture of both on uric acid (U.A), creatinine and urea (mg/dl) of hypercholesterolemic rats

Parameters / Groups	U.A (mg/dl) Mean ± SD	Creatinine (mg/dl) Mean ± SD	Urea (mg/dl) Mean ± SD
G1: Control –ve	1.12^{e}±0.003	0.60^{e}±0.006	18.11^{e}±0.007
G2: Control +ve	2.93^{a}±0.005	0.92^{a}±0.001	51.20^{a}±0.003
G3: Celery seeds (5%)	1.38^{b}±0.002	0.80^{b}±0.002	25.61^{b}±0.006
G4: Pomegranate peel (5%)	1.26^{c}±0.009	0.76^{c}±0.005	23.50^{c}±0.009
G5: Mixture of both (5%)	1.14^{d}±0.004	0.65^{d}±0.008	19.22^{d}±0.002
LSD	0.009	0.009	0.01

Values in each column with different letters are significantly different (P<0.05).

Data presented in table (7) show the effect of celery seeds, pomegranate peel and mix diets on serum glucose of hypercholesterolemic rats. It could be noticed that the mean value of glucose of control (+) group was higher than control (-) group, being 134±0.5 and 70±0.2 (mg/dl) respectively. The best serum glucose was observed for group 3 (basal diet containing 5% Celery seeds) when compared to control (+) group.

Niaz, (2013) reported that celery seeds extract treatment caused a statistically significant decrease in the elevated serum glucose levels in diabetic rats.

Çam *et al*., (2014) found that extracts of pomegranate peel reduced blood glucose significantly compared with the control diabetic rats group.

Table (7): Effect of celery seeds, pomegranate peel and mixture of both on serum glucose (mg/dl) of hypercholesterolemic rats

Parameters / Groups	Glucose (mg/dl) Mean ± SD
G1: Control –ve	70^{d}±0.2
G2: Control +ve	134^{a}±0.5
G3: Celery seeds (5%)	89^{b}±0.9
G4: Pomegranate peel (5%)	74^{c}±0.6
G5: Mixture of both (5%)	71^{d}±0.8
LSD	1.18

Values in each column with different letters are significantly different (P<0.05).

Results of histopathological examination:

Examination of liver sections of control (-) rats showed normal histological structure of the central vein and hepatic cells and portal areas (Photo 1), kidneys' tissue of control (-) rats showed normal histological structure of the renal glomeruli and renal tubules (Photo 2). While examination of liver sections of control positive rats showed congested central vein, diffuse vacuolar degeneration and necrosis of the hepatic cells (Photo 3) as well as scattered lytic necrosis of the hepatic cells (Photo 4). Portal areas in livers of control positive rats showed congested portal vessels, proliferated bile duct epithelial linings, edema and few inflammatory cells infiltration (Photo 5). The kidney of control positive rats showed congested inter-tubular and glomerular capillaries, diffuse vacuolar degeneration of the renal tubular epithelium and necrosis (Photo 6), also swelling of the glomerular tuft with vacuolation of the glomerular capillary

epithelium, vacuolar degeneration, necrosis and nuclear pyknosis (Photo 7).

Regarding the treated groups, the treatment with (Mix of PP+CS and that of PP diets) had marked protective effect than (CS diet). (CS: celery seeds diet; PP: Pomegranate peel; CS+PP= Mix).

Livers of control positive rats which treated with (cs + pp diet) showed good protection of the hepatic parenchymal cells with mild degeneration and scattered necrosis and congested central vein (Photos 8 and 9). Kidneys of control positive rats which treated (celery seeds diet) showed mild degenerative and necrotic changes of the renal tubular epithelial linings with few pyknotic nuclei and congested inter-tubular hemorrhage (Photo 10). Generally, good restoration of the kidney tissue with mild degeneration and scattered necrosis of the tubular epithelium were all observed as well as some congested inter-tubular vessels considering celery diet (Photo 11). Livers of control positive rats which treated with (pp diet) showed normal portal areas, moderate degree of vacuolar degeneration and few necrotic cells (Photo 12). Liver of control positive rat which treated with pp diet showing few scattered degenerated and necrotic cells as well as mild portal edema (Photo 13). Kidneys of control positive rats which treated with (pp diet) showed moderate degree of tubular epithelial vacuolar degeneration, necrosis and some pyknotic nuclei (Photos 14 and 15) .

Livers of control positive rats which treated with (cs + pp diet) showed good restoration of the hepatic parenchyma with near to normal appearance (Photo 16).

Livers of control positive rats which treated with (cs + pp diet) showing good restoration of the hepatic parenchyma with near to normal appearance (Photo 17). Kidneys of control positive rats which treated with (cs + pp diet) showed near to normal appearance of the kidney tissue, notice the normal renal glomeruli

and tubules (Photo 18). Kidneys of control positive rats which treated with (cs +pp diet) showing near to normal appearance of the kidney tissue, notice the renal glomeruli and tubules, with few necrotic cells (Photo 19).

The results indicate the synergism observed when celery seeds and pomegranate peel combined in on diet. Nevertheless only celery seeds diet showed also some improvement of the histological structure of liver and kidney.

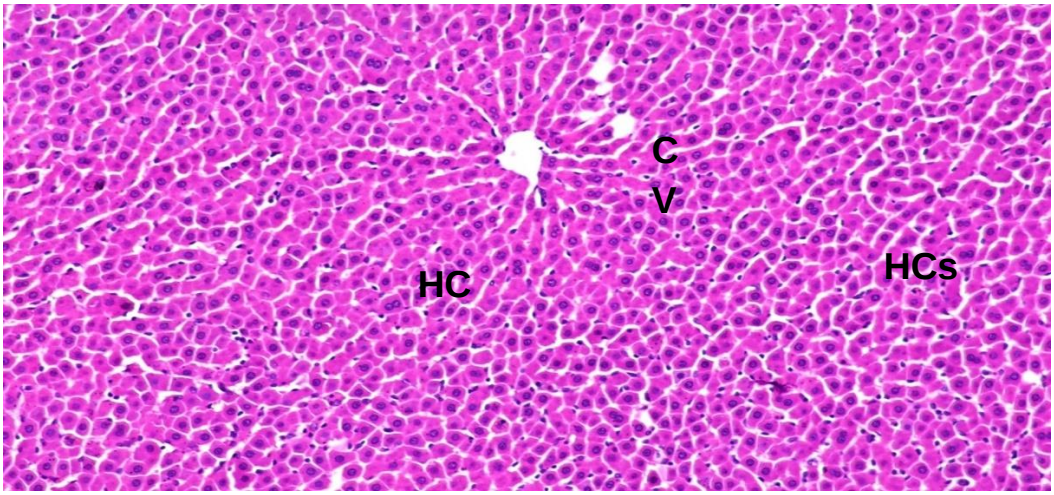

Photo (1): Liver of control (-) rat showing normal histological structure of the central vein (CV) and hepatic cells (HCs). **(H&E, X200).**

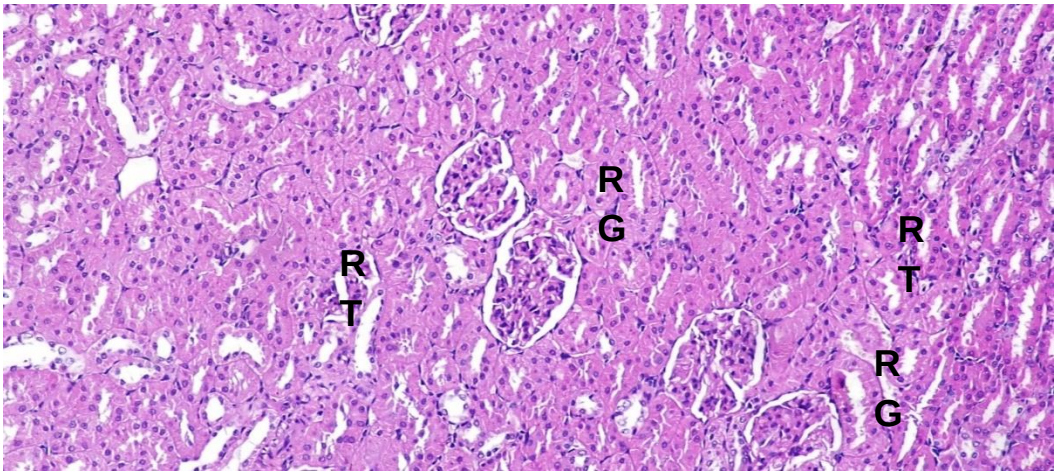

Photo (2): Kidney of control (-) rat showing normal histological structure of the renal glomeruli (RG) and renal tubules (RT). **(H&E, X200).**

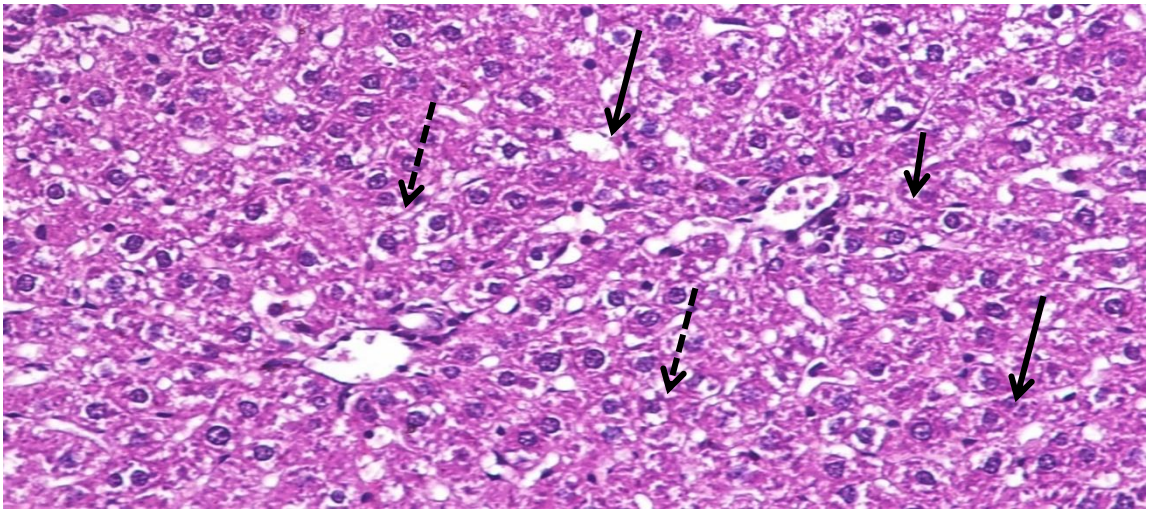

Photo (3): Liver of control positive rat showing congested central vein (short arrow), diffuse vacuolar degeneration (arrow) and necrosis (dashed arrow) of the hepatic cells. **(H&E, X400).**

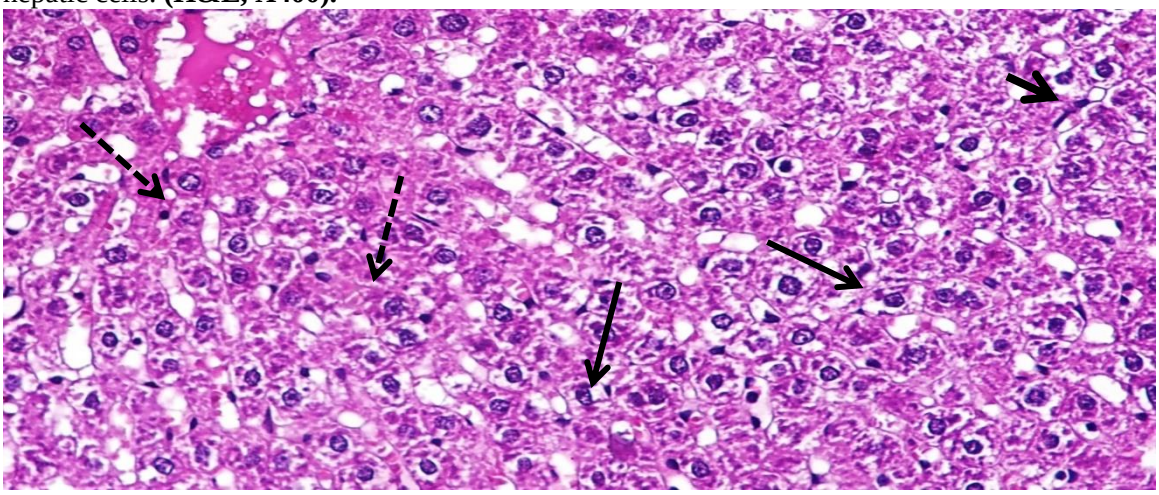

Photo (4): Liver of control positive rat showing diffuse vacuolar degeneration (arrow), necrosis (dashed arrow) and scattered lytic necrosis (short arrow) of the hepatic cells. **(H&E, X400).**

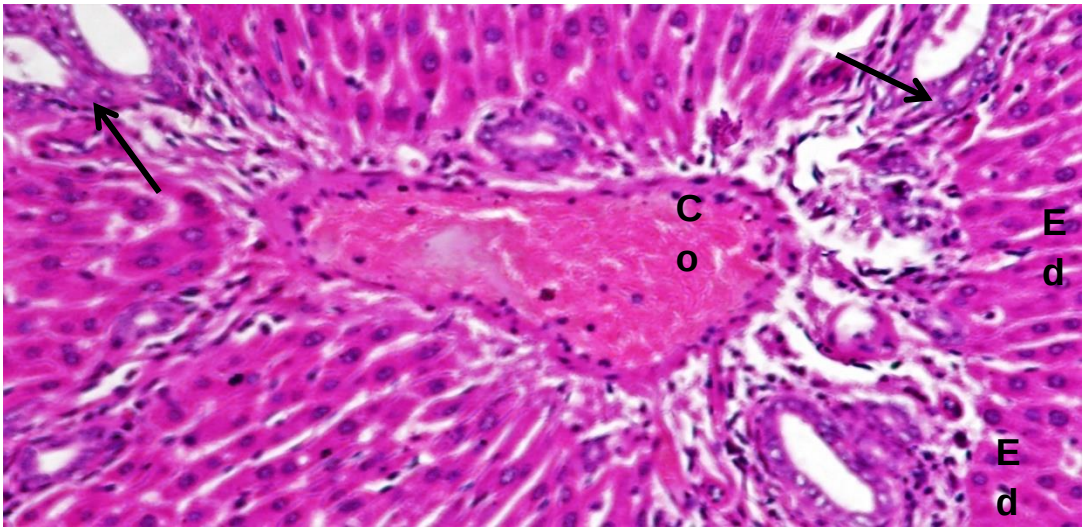

Photo (5): Portal area in liver of control positive rat showing congested portal vessels (Co), proliferated bile duct epithelial linings (arrow), edema (Ed) and few inflammatory cells infiltration (dashed arrow). **(H&E, X400).**

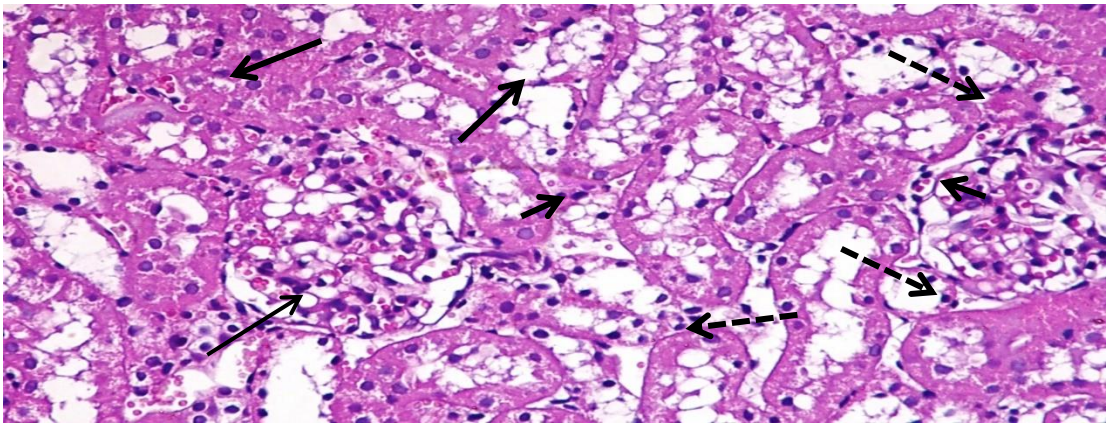

Photo (6): Kidney of control positive rat showing congested inter-tubular (arrow) and glomerular capillaries (thin arrow), diffuse vacuolar degeneration of the renal tubular epithelium (dashed arrow) and necrosis (short arrow). **(H&E, X400).**

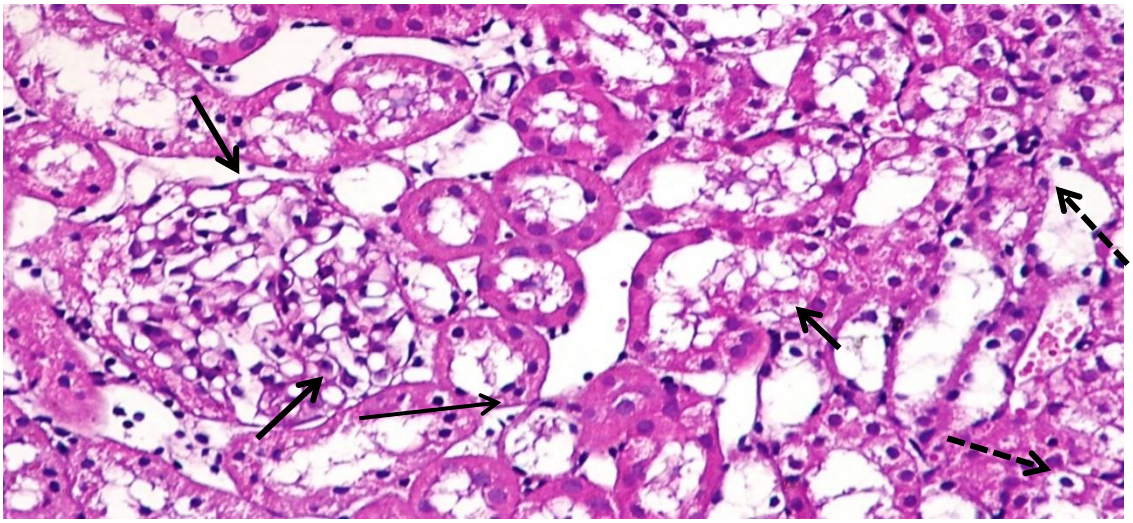

Photo (7): Kidney of control positive rat showing swelling of the glomerular tuft with vacuolation of the glomerular capillary epithelium (arrow), vacuolar degeneration (dashed arrow), necrosis (short arrow) and nuclear pyknosis (thin arrow). **(H&E, X400).**

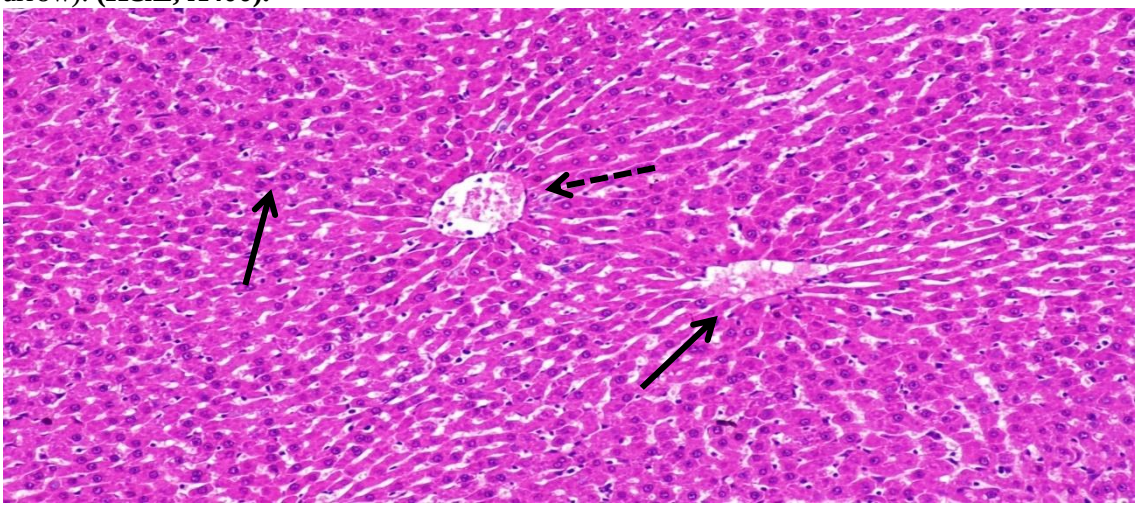

Photo (8): Liver of control positive rat which treated with (celery seeds "cs" diet) showing good protection of the hepatic parenchymal cells with mild degeneration and scattered necrosis (arrow) and congested central vein (dashed arrow). **(H&E, X200).**

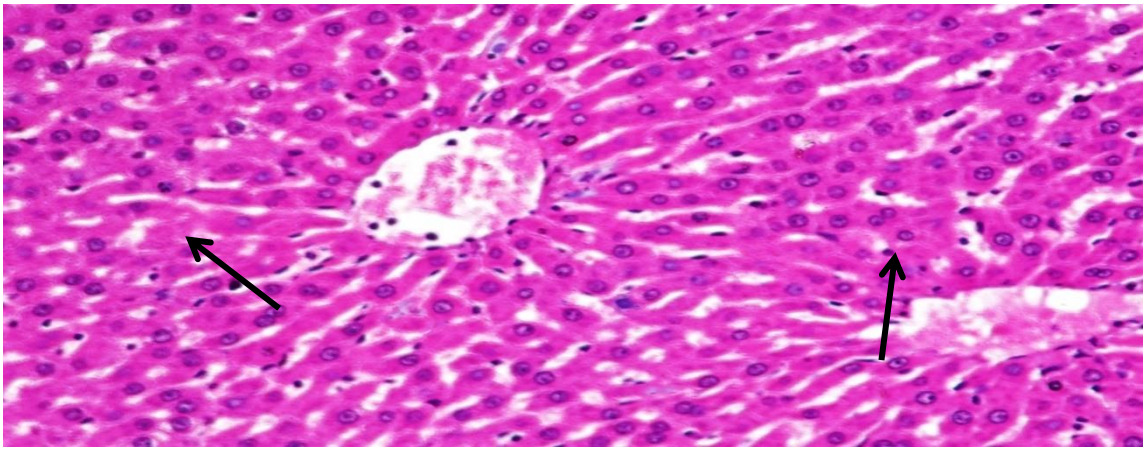

Photo (9): Higher magnification of liver of control positive rat which treated with (celery seeds diet) showing few scattered necrotic cells (arrow). **(H&E, X400).**

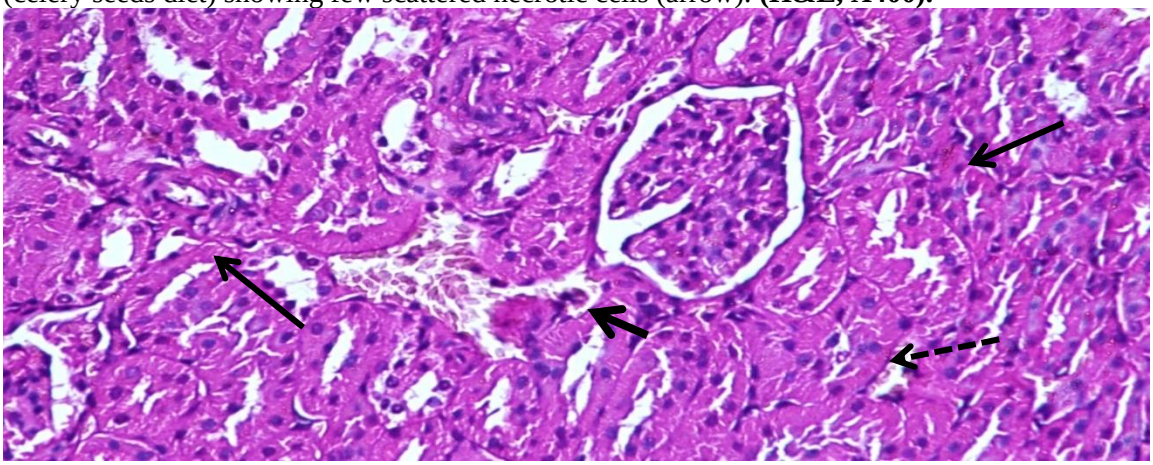

Photo (10): Kidney of control positive rat which treated with (celery seeds diet) showing mild degenerative and necrotic changes (arrow) of the renal tubular epithelial linings with few pyknotic nuclei (dashed arrow) and congested inter-tubular hemorrhage (short arrow). **(H&E, X200).**

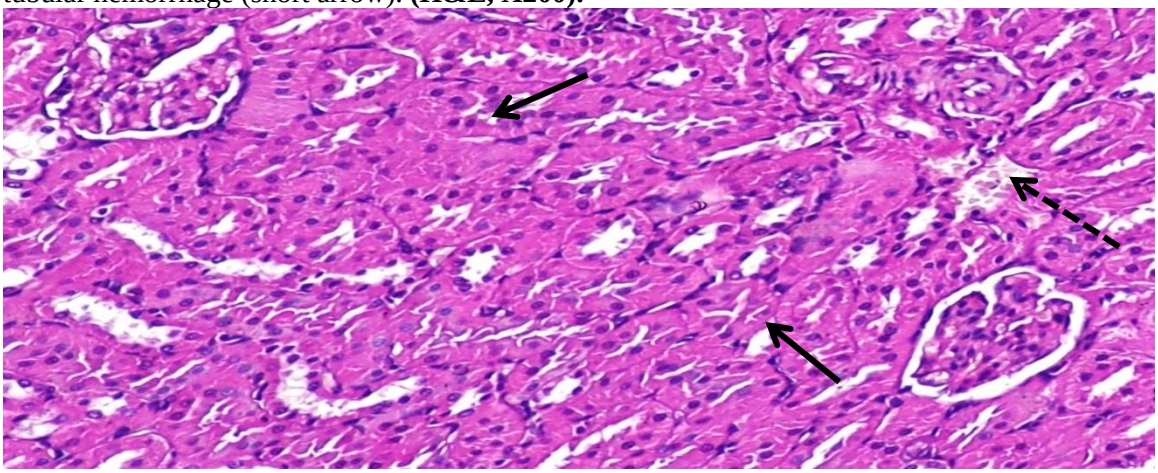

Photo (11): Kidney of control positive rat which treated with (celery seeds diet) showing good restoration of the kidney tissue with mild degeneration and scattered

necrosis (arrow) of the tubular epithelium as well as some congested inter-tubular vessels (dashed arrow). **(H&E, X200).**

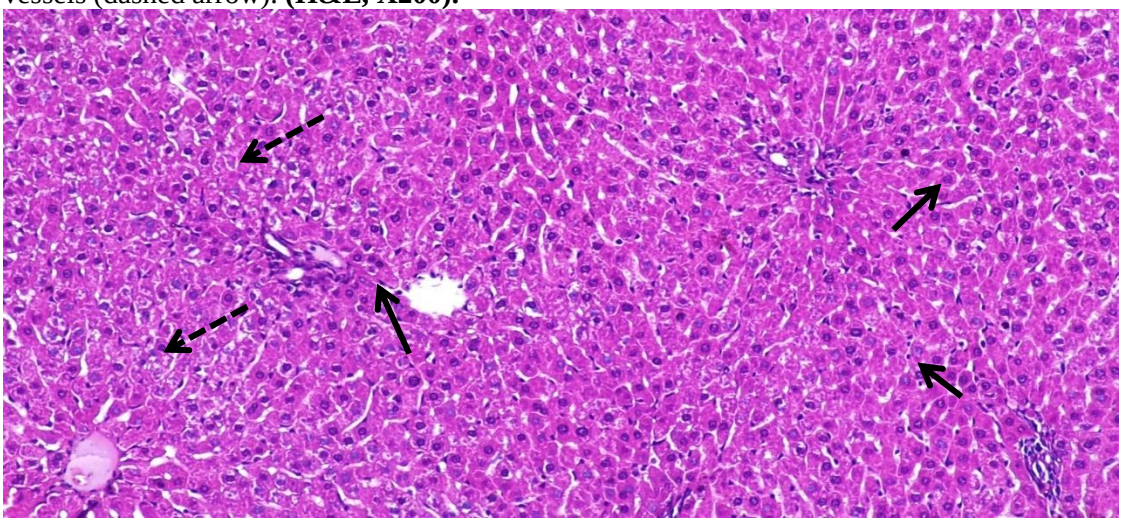

Photo (12): Liver of control positive rat which treated with (Pomegranate peel "pp" diet) showing normal portal areas (arrow), moderate degree of vacuolar degeneration (dashed arrow) and few necrotic cells (short arrow). **(H&E, X200).**

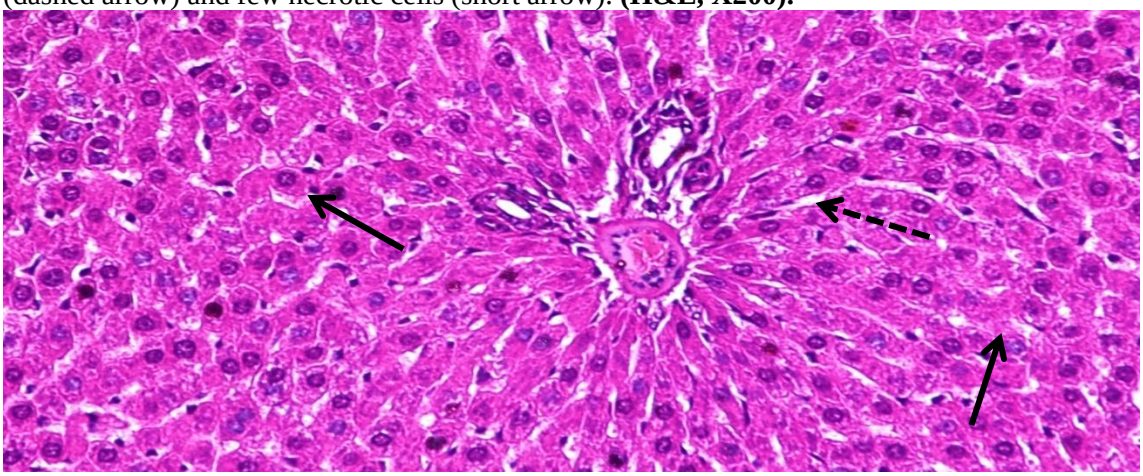

Photo (13): Liver of control positive rat which treated with (Pomegranate peel "pp" diet) showing few scattered degenerated and necrotic cells (arrow) as well as mild portal edema (dashed arrow). **(H&E, X400).**

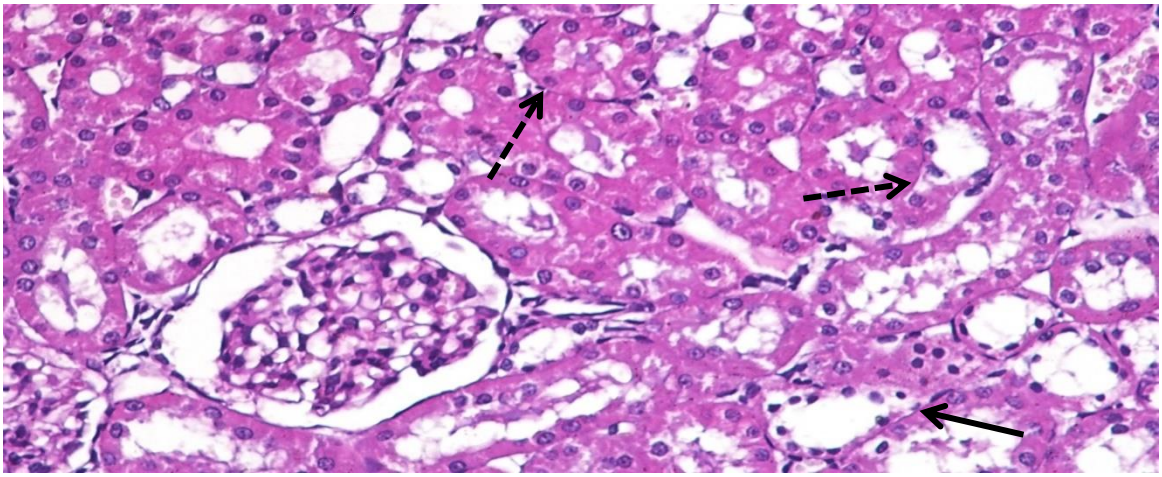

Photo (14): Kidney of control positive rat which treated with (Pomegranate peel "pp" diet) showing moderate degree of tubular epithelial vacuolar degeneration, necrosis (dashed arrow) and some pyknotic nuclei (arrow). **(H&E, X400).**

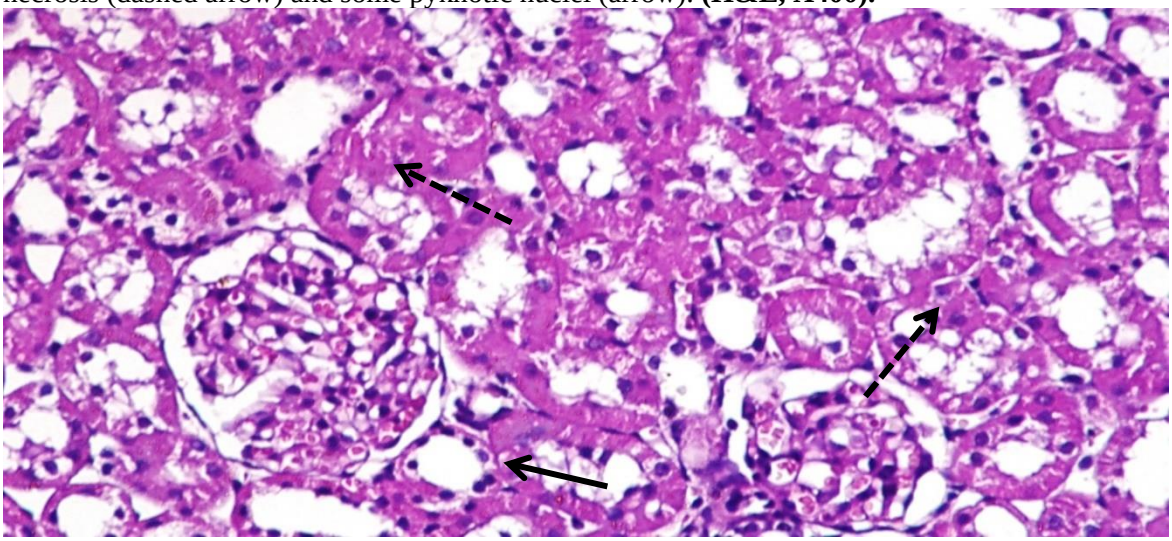

Photo (15): Kidney of control positive rat which treated with (Pomegranate peel "pp" diet) showing moderate degree of tubular epithelial vacuolar degeneration, necrosis (dashed arrow) and some pyknotic nuclei (arrow). **(H&E, X400).**

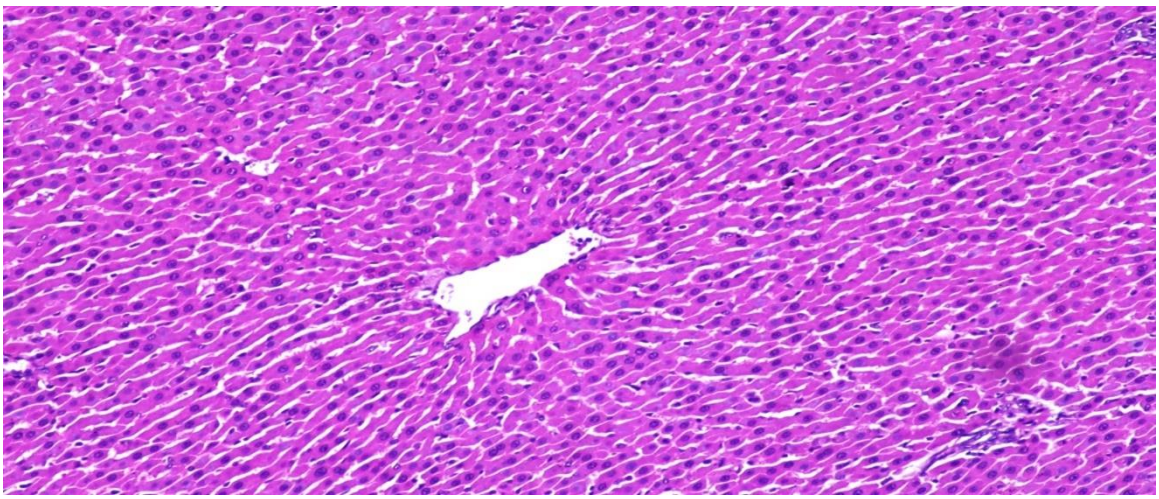

Photo (16): Liver of control positive rat which treated with (celery seeds + Pomegranate peel "cs+pp" diet) showing good restoration of the hepatic parenchyma with near to normal appearance. **(H&E, X200).**

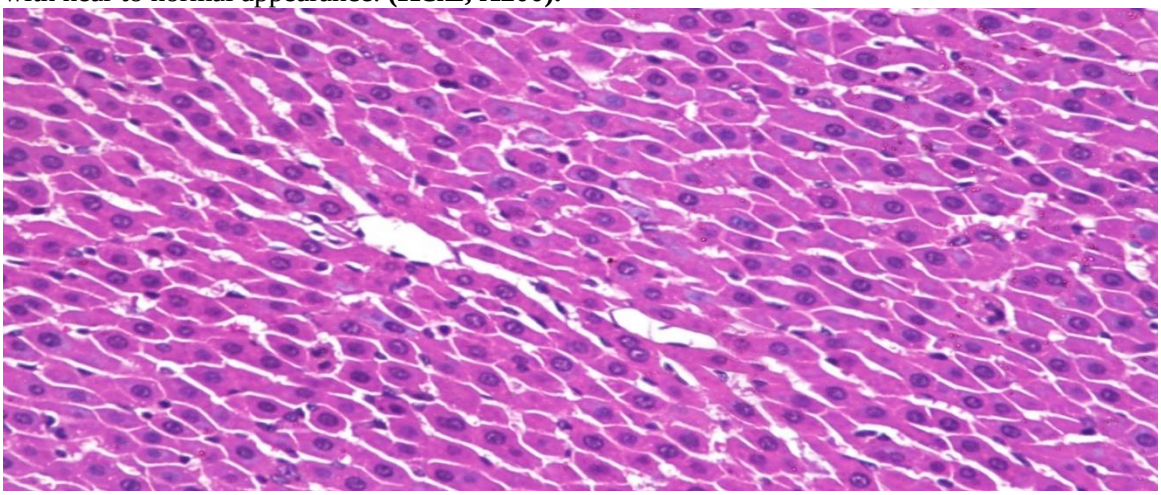

Photo (17): Liver of control positive rat which treated with (celery seeds + Pomegranate peel "cs+pp" diet) showing good restoration of the hepatic parenchyma with near to normal appearance. **(H&E, X400).**

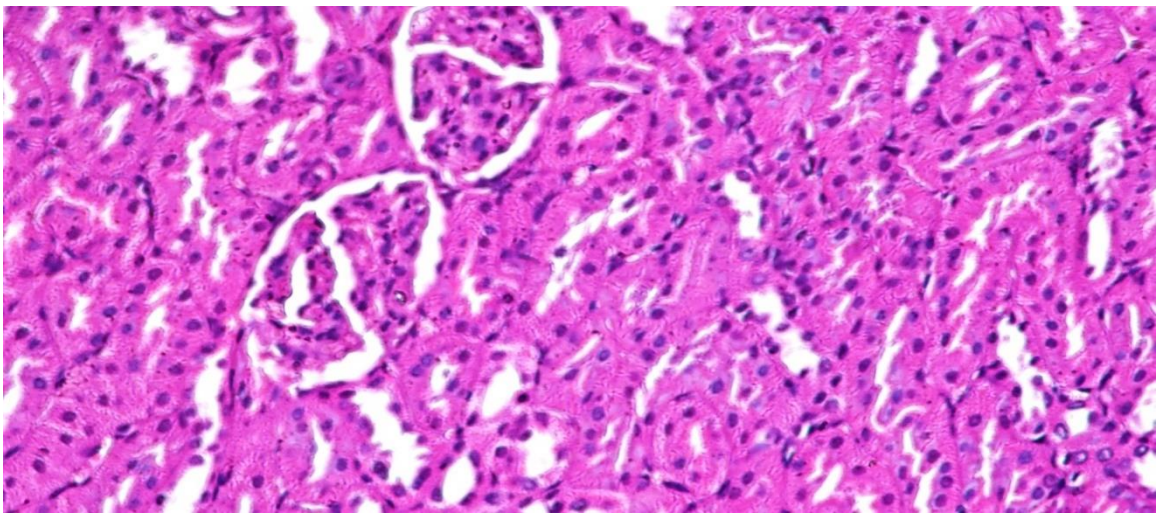

Photo (18): Kidney of control positive rat which treated with (celery seeds + Pomegranate peel "cs+pp" diet) showing near to normal appearance of the kidney tissue, notice the normal renal glomeruli and tubules. **(H&E, X400).**

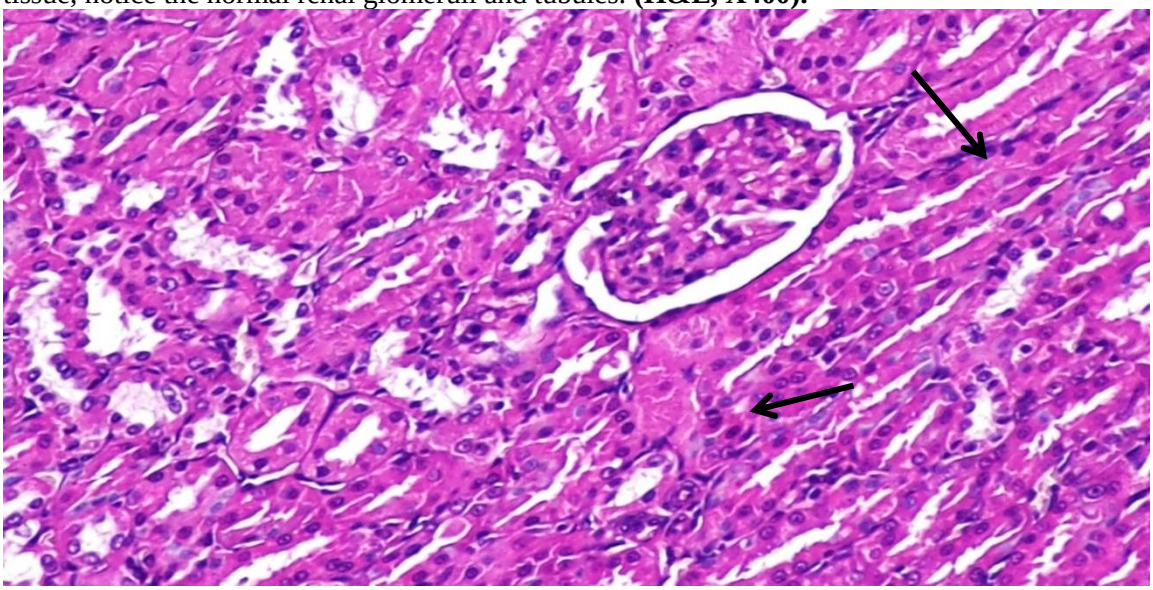

Photo (19): Kidney of control positive rat which treated with (celery seeds + Pomegranate peel "cs+pp" diet) showing near to normal appearance of the kidney tissue, notice the renal glomeruli and tubules, with few necrotic cells (arrow). **(H&E, X400).**

Conclusion

Quercetin has curative effect in rats inflicted with aspirin-induced gastric ulcer, being more pronounced as the dose increased.

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