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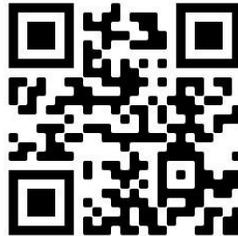
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Biological, Biochemical and Histopathological Alterations by Lemon Tree Leaves and Lemon Fruit Peels in Therapeutic Feeding of Diabetic Rats

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Abstract:

This investigation aimed to evaluate the effect of lemon tree leaves, lemon fruit peel and mixture of both on male diabetic 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): Diabetic rats fed on basal diet and lemon tree leaves (4%). Group (4): Diabetic rats fed on basal diet and lemon fruit peel (4%). Group (5): Diabetic rats fed on basal diet and mixture of both plants (4%). At the end of experiment, after 28 days of feeding, all serum samples were analyzed for biological, biochemical and histopathological parameters. Injection with alloxan caused a significant decreases in the levels of HDL, BWG, FI & FER while significant increases recorded in TC, TG, VLDL, LDL, U.A, Creatinine, Urea, GOT, GPT, ALP & Glucose for diabetic rats treated with various experimental diets, the results showed the improvement in all previous parameters. The best diet was that of the basal diet and lemon fruit peel (4%). Nevertheless the lemon tree peel diets improved also parameters of diabetic rats, although at less extent.

Key words: Diabetes – lemon tree leaves - lemon fruit peel.

Introduction:

Citrus limon (L.) Burm. f. is a tree with evergreen leaves and yellow edible fruits from the family Rutaceae. In some languages, *C. limon* is known as lemon (English) (**Klimek-Szczykutowicz et al., 2020**).

The main raw material of *C. limon* is the fruit, particularly the essential oil and juice obtained from it. The *C. limon* fruit stands out as having well-known nutritional properties, but it is worth remarking that its valuable biological activities are underestimated in modern phytotherapy and cosmetology (**Goetz, 2014**).

C. limon fruit juice (lemon juice) has traditionally been used as a remedy for scurvy before the discovery of vitamin C (**Mabberley, 2004**). This common use of *C. limon*, known since ancient times, has nowadays been supported by numerous scientific studies. Other uses for lemon juice, known from traditional medicine, include treatment of high blood pressure, the common cold, and irregular menstruation. Moreover, the essential oil of *C. limon* is a known remedy for coughs (**Bhatia et al., 2015**).

In Romanian traditional medicine, *C. limon* essential oil was administered on sugar for suppressing coughs (**Papp et al., 2011**). Aside from being rich in vitamin C, which assists in warding off infections, the juice is traditionally used to treat scurvy, sore throats, fevers, rheumatism, high blood pressure, and chest pain (**Balogun & Ashafa, 2019**).

In Trinidad, a mixture of lemon juice with alcohol or coconut oil has been used to treat fever, coughs in the common cold, and high blood pressure. Moreover, the juice or grated skin, mixed with molasses, has been used to remove excess water from the body, and the juice mixed with olive oil has been administered for womb infection and kidney stones. According to Indian traditional medicine, *C. limon* juice can induce menstruation; the recommended dose for this is two teaspoons consumed twice a day (**Bhatia et al., 2015**).

Currently, valuable scientific publications focus on the ever wider pharmacological actions of *C. limon* fruit extract, juice and essential oil. They include studies of, for example, antibacterial, antifungal, anti-inflammatory, anticancer, hepatoregenerating and cardioprotective activities (Otang & Afolayan, 2016). The pharmacological potential of *C. limon* is determined by its rich chemical composition. The most important group of secondary metabolites in the fruit includes flavonoids and also other compounds, such as phenolic acids, coumarins, carboxylic acids, aminoacids and vitamins. The main compounds of essential oil are monoterpenoids, especially D-limonene. These valuable chemical components are the reason for the important position of *C. limon* in the food and cosmetics industries (Russo *et al.*, 2015).

The mechanism of action of citrus phytophenolics in models of diabetes suggest that naringenin is able to reduce glucose uptake and inhibit intestinal and renal Na⁺-glucose co-transporter (Li *et al.*, 2006) (and that both naringin and hesperidin significantly increased the glucokinase mRNA level, while naringin reduced the mRNA expression of phosphoenolpyruvate carboxykinase and glucose-6-phosphatase in the liver (Jung *et al.*, 2006).

Materials and Methods:

Materials:

Lemon tree leaves & lemon fruit peel were obtained dry from herb shop in Cairo, Egypt.

Chemicals:

Alloxan 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 (2015)**.

Induced diabetic for rats:

Rats were injected by Alloxan at 150 mg /kg body weight to induce male diabetic for rats. Injection repeated for 3 consecutive days then fed on basal diet for 7 days before determination of serum glucose. Rats with serum glucose near: 200 mg/dl considered diabetic.

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 C⁰, 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 diabetic rats were fed on basal diet.

Group (3): Diabetic rats fed on basal diet contained lemon tree leaves 4%.

Group (4): Diabetic rats fed on basal diet contained lemon fruit peel 4%.

Group (5): Diabetic rats fed on basal diet contained mixture of both 4%.

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 cuvette tubes and stored frozen at -20°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 phsphatase (ALP) was determined according to **Belfield and Goldberg (1971)**. Total cholesterol (TC) was determined according to **Allen (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)**, triglyceride determination carried out as **Fossati and Prencipe (1982)**. Serum glucose determined according to **Kaplan (1984)**. Biological parameter (BWG, FI & FER) were also calculated.

At the same time livers were removed, washed, and stored frozen in formalin solution 10% for histiopathololgal testing according to method mentioned by (**Drury and Wallington, 1980**).

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 \pm SD.

Results and Discussion:

Data presented in table (1) illustrate the effect of lemon tree leaves, lemon fruit peel and mixture on BWG, FI and FER of diabetic rats. It could be observed that the mean value of (BWG) of control (-) group was higher than control (+) group, being 0.864 ± 0.0005 and 0.136 ± 0.0003 g respectively. The best (BWG) level showed for groups 3 (rats fed on basal diet containing 4% lemon tree leaves) when compared to control (+) group.

It could be noticed that the mean value of FI of control (-) group was higher than control (+) group, being 17.7 ± 0.04 and 17.11 ± 0.002 g respectively. The best (FI) level showed for group 5 (rats fed on basal diet + 4% mixture) 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 0.0482 ± 0.00004 and 0.0079 ± 0.00001 respectively. The best FER was shown for group 3 (rats fed on basal diet +4% lemon tree leaves) when compared to control (+) group.

Table (1): Effect of lemon tree leaves, lemon fruit peel and mixture on body weight gain (BWG), feed intake (FI) and feed efficiency ratio (FER) of diabetic rats

Parameters Groups	BWG (g) Mean \pm SD	FI (g) Mean \pm SD	FER (%) Mean \pm SD
G1: Control -ve	$0.864^a \pm 0.0005$	$17.7^d \pm 0.04$	$0.0482^a \pm 0.00004$
G2: Control +ve	$0.136^c \pm 0.0003$	$17.11^e \pm 0.002$	$0.0079^c \pm 0.00001$
G3: Lemon tree leaves (4%)	$0.429^b \pm 0.0007$	$17.99^c \pm 0.009$	$0.0238^b \pm 0.0003$
G4: Lemon fruit peel (4%)	$0.071^d \pm 0.0004$	$18.73^b \pm 0.007$	$0.0038^e \pm 0.00004$
G5: Mixture (4%)	$0.136^c \pm 0.0008$	$19.33^a \pm 0.006$	$0.0070^d \pm 0.00007$
LSD	0.001	0.034	1.22

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

Data presented in table (2) show the effect of lemon tree leaves, lemon fruit peel and mixture on serum glucose of diabetic rats. It could be noticed that the mean value of glucose of control (+) group was higher than control (-) group, being 259 ± 0.19 and 91 ± 0.14 (mg/dl) respectively. The best serum glucose was observed for group 4 (basal diet containing 4% lemon fruit peel) when compared to control (+) group.

Lv et al., (2018) found that hydroalcohol extract of lemon peel (LP) for 35 days significantly reduced blood glucose levels in diabetic rats due to the function of flavonoids found to be involved in the maintenance of glucose homeostasis, gastrointestinal glucose absorption, insulinotropic actions, and promoting pancreatic β -cell regeneration.

Kumar et al., (2019) showed that indicated that oral administration of methanol leaves extract of *citrus pseudolimon* (200 mg/kg) and ethyl acetate fraction (100 mg/kg) for 21 days decreased the fasting blood glucose level in diabetic rats due to both hesperidin and hesperetin which considered an important flavonoids.

Table (2): Effect of lemon tree leaves, lemon fruit peel and mixture on glucose of diabetic rats

Groups	Parameters	Glucose Mean \pm SD
G1: Control -ve		$91^c \pm 0.14$
G2: Control +ve		$259^a \pm 0.19$
G3: Lemon tree leaves (4%)		$124.4^b \pm 0.04$
G4: Lemon fruit peel (4%)		$111.25^d \pm 0.007$
G5: Mixture (4%)		$122.3^c \pm 0.29$
LSD		0.21

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

Data presented in table (3) show the effect of lemon tree leaves, lemon fruit peel and mixture on organs weight of diabetic rats. It could be observed that the mean value of liver of control (+) group was higher than control (-) group, being 8 ± 0.18 and 6.2 ± 0.07 g respectively. The best liver weight showed for groups 4 (rats fed on basal diet containing 4% lemon fruit peel) 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 1.7 ± 0.08 and 0.7 ± 0.04 g respectively. The best heart weight was showed for group 4 (rats fed on basal diet + 4% lemon fruit peel) 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 ± 0.016 and 1 ± 0.11 g respectively. The best lungs weight was showed for group 4 (rats fed on basal diet + 4% lemon fruit peel) when compared to control (+) group.

Also, data of table (3) noticed that the mean value of spleen weight of control (+) group was higher than control (-) group, being 1.3 ± 0.001 and 0.98 ± 0.008 g respectively. The best spleen weight was shown for group 4,5 (rats fed on basal diet + 4% lemon fruit peel and mixture) 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 2.6 ± 0.03 and 1.5 ± 0.06 g respectively. The best kidneys weight was showed for group 4 (rats fed on basal diet + 4% lemon fruit peel) when compared to control (+) group.

Table (3): Effect of lemon tree leaves, lemon fruit peel and mixture on organs weight (g) of diabetic rats

Parameters Groups	Liver (g) Mean \pm SD	Heart (g) Mean \pm SD	Lungs (g) Mean \pm SD	Spleen (g) Mean \pm SD	Kidneys (g) Mean \pm SD
G1: Control -ve	6.2 ^c \pm 0.07	0.7 ^d \pm 0.04	1 ^c \pm 0.11	0.98 ^b \pm 0.008	1.5 ^d \pm 0.06
G2: Control+ve	8 ^a \pm 0.18	1.7 ^a \pm 0.08	2 ^a \pm 0.16	1.3 ^a \pm 0.001	2.6 ^a \pm 0.03
G3: Lemon tree leaves (4%)	6.6 ^b \pm 0.09	0.93 ^b \pm 0.002	1.4 ^b \pm 0.07	1.1 ^{ab} \pm 0.005	1.99 ^b \pm 0.007
G4: Lemon fruit peel (4%)	6.2 ^c \pm 0.01	0.83 ^c \pm 0.006	1.1 ^c \pm 0.04	1 ^b \pm 0.009	1.1 ^e \pm 0.02
G5: Mixture (4%)	6.4 ^c \pm 0.05	0.91 ^b \pm 0.009	1.3 ^b \pm 0.09	1 ^b \pm 0.004	1.92 ^c \pm 0.009
LSD	0.19	0.07	0.19	0.13	0.058

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

Data presented in table (4) illustrate the effect of lemon tree leaves, lemon fruit peel and mixture on total cholesterol and triglycerides of diabetic rats. It could be observed that the mean value of total cholesterol (TC) of control (+) group was higher than control (-) group, being 228 \pm 0.17 and 168 \pm 0.12 mg/dl respectively. The best serum (TC) level was showed for groups 4 (rats fed on basal diet containing 4% lemon fruit peel) 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 63 \pm 0.16 and 41 \pm 0.13 mg/dl respectively. The best serum (TG)

level was showed for group 5 (rats fed on basal diet + 4% mixture) when compared to control (+) group.

Dinesh and Hegde (2016) found that the oral administration of *Citrus maxima* leaves extract (200 and 400 mg/kg BW) in obese rats determined reduction total cholesterol and triglycerides which may be content of hesperidin (flavonoid).

Abdelhaliem and Sheha (2018) indicated that treatment with lemon peels powder significantly reduced total cholesterol and triglycerides in hyperlipidemic rats, may be the flavonoids contained which considered antioxidant and anti-inflammatory effects in hyperlipidemia.

Afifi and Abd El Rahman, (2021) found that *Annona* (*Annona Squamosa*) and lemon (*Citrus Aurantifolia*) leaves powder reduced total cholesterol and triglycerides in hyperlipidemic rats.

Table (4): Effect of lemon tree leaves, lemon fruit peel and mixture on total cholesterol (TC) and triglycerides (TG) of diabetic rats

Parameters	TC Mean \pm SD	TG Mean \pm SD
G1: Control –ve	168 ^e \pm 0.12	41 ^e \pm 0.13
G2: Control +ve	228 ^a \pm 0.17	63 ^a \pm 0.16
G3: Lemon tree leaves (4%)	204 ^c \pm 0.15	53 ^b \pm 0.11
G4: Lemon fruit peel (4%)	200 ^d \pm 0.19	48 ^c \pm 0.14
G5: Mixture (4%)	206 ^b \pm 0.13	45 ^d \pm 0.18
LSD	0.28	0.27

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

Data presented in table (5) show the effect of lemon tree leaves, lemon fruit peel and mixture on HDLc, LDLc, & VLDLc of diabetic rats.

It could be observed that the mean value of (VLDL_c) of control (+) group was higher than control (-) group, being 12.6 ± 0.09 and 8.2 ± 0.04 mg/dl respectively. The best serum VLDLc was shown for group 5 (rats fed on basal diet + 4% mixture) when compared to control (+) group.

It could be showed that the mean value of (HDLc) of control (-) group was higher than control (+) group, being 61 ± 0.22 and 42 ± 0.7 mg/dl respectively. The best serum HDLc was shown for group 4 (rats fed on basal diet containing 4% lemon fruit peel) when compared to control (+) group.

The same table indicated that the mean value of (LDLc) of control (+) group was higher than control (-) group, being 173.4 ± 0.07 and 98.8 ± 0.04 mg/dl respectively. The best serum LDLc was shown for group 4 (rats fed on basal diet +4% lemon fruit peel) when compared to control (+) group.

Dinesh and Hegde (2016) found that the oral administration of *Citrus maxima* leaves extract (200 and 400 mg/kg BW) in obese rats determined reduction low density lipoprotein, very low density lipoprotein and increased high density lipoprotein.

Abdelhaliem and Sheha (2018) indicated that treatment with lemon peels powder significantly reduced low density lipoprotein, very low density lipoprotein and increased high density lipoprotein in hyperlipidemic rats.

Afifi and Abd El Rahman, (2021) found that *Annona* (*Annona Squamosa*) and lemon (*Citrus Aurantifolia*) leaves powder reduced low density lipoprotein, very low density lipoprotein and increased high density lipoprotein in hyperlipidemic rats.

Table (5): Effect of lemon tree leaves, lemon fruit peel and mixture of both on (VLDLc), (HDLc) and (LDLc) (mg/dl) of diabetic rats

Parameters Groups	VLDL (mg/dl) Mean \pm SD	HDL (mg/dl) Mean \pm SD	LDL (mg/dl) Mean \pm SD
G1: Control -ve	8.2 ^e \pm 0.04	61 ^a \pm 0.22	98.8 ^e \pm 0.04
G2: Control +ve	12.6 ^a \pm 0.09	42 ^d \pm 0.7	173.4 ^a \pm 0.07
G3: Lemon tree leaves (4%)	10.6 ^b \pm 0.07	43 ^c \pm 0.3	150.4 ^b \pm 0.05
G4: Lemon fruit peel (4%)	9.6 ^c \pm 0.06	61 ^a \pm 0.9	129.4 ^d \pm 0.01
G5: Mixture (4%)	9 ^d \pm 0.01	51 ^b \pm 0.26	146 ^c \pm 0.32
LSD	0.11	0.99	0.27

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

Data of table (6) illustrate the effect of lemon tree leaves, lemon fruit peel and mixture on serum levels of AST, ALT and ALP enzymes of diabetic rats.

It could be noticed that the mean value of AST enzyme of control (+) group was higher than control (-) group, being 206 ± 0.7 and 105 ± 0.2 (U/L) respectively. The best treatment was observed for group 4 (basal diet containing 4% lemon fruit peel) when compared to control (+) group.

It could be observed that the mean value of ALT enzyme of control (+) group was higher than control (-) group, being 43.5 ± 0.04 and 29.4 ± 0.09 (U/L) respectively. The best treatment was observed for group 4 (basal diet containing 4% lemon fruit peel) when compared to control (+) group.

Data of the same table (6) show the mean value of ALP

enzyme of control (+) group was higher than control (-) group, being 250 ± 0.17 and 130 ± 0.06 (U/L) respectively. Group 4 showed the lowest mean value of ALP enzyme level as compared to control (+) group which and recorded the best result.

Green et al., (2013) investigated that citrus ortanique peel polymethoxylated flavones extract (PMF^{ort}) reductions the activities of aspartate aminotransferase and alkaline phosphatase in hypercholesterolemic rats.

Soji-Omoniwa et al., (2014) indicated that leaf essential oil of *C. sinensis* reduced alkaline phosphatase (ALP), alanine transaminase (ALT) and aspartate transaminase (AST) activity on diabetic rats. This may be attributed to the presence of monoterpenes, a major component of the plant essential oil which has been reported to have hepatoprotective property.

Table (6): Effect of lemon tree leaves, lemon fruit peel and mixture of both on GOT, GPT and ALP (U/L) of diabetic rats

Parameters Groups	GOT (AST) (U/L) Mean \pm SD	GPT (ALT) (U/L) Mean \pm SD	ALP (U/L) Mean \pm SD
G1: Control -ve	$105^e \pm 0.2$	$29.4^e \pm 0.09$	$130^e \pm 0.06$
G2: Control +ve	$206^a \pm 0.7$	$43.5^a \pm 0.04$	$250^a \pm 0.17$
G3: Lemon tree leaves (4%)	$162.8^b \pm 0.05$	$36.3^b \pm 0.08$	$177^b \pm 0.12$
G4: Lemon fruit peel (4%)	$152^d \pm 0.4$	$33^d \pm 0.25$	$171^d \pm 0.22$
G5: Mixture (4%)	$161.3^c \pm 0.01$	$34.5^c \pm 0.06$	$174^c \pm 0.29$
LSD	0.68	0.23	0.34

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

Results of table (7) show the mean value of serum creatinine,

urea and uric acid (mg/dl) on diabetic 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 5.04 ± 0.008 and 1.38 ± 0.003 mg/dl respectively. Group 4 (basal diet containing 4% lemon fruit peel) recorded the best result as compared to control (+) group.

The same table (7) results illustrate that mean value of creatinine of control (+) group was higher than control (-) group, being 0.84 ± 0.005 and 0.58 ± 0.01 mg/dl respectively. In concern to creatinine the best treatment was recorded for the group 4 (rats fed on basal diet +4% lemon fruit peel) when compared to control (+) group.

It could be noticed that the mean value of urea of control (+) group was higher than control (-) group, being 45 ± 0.12 and 37 ± 0.97 mg/dl respectively. Group 4 (rats fed on basal diet +4% lemon fruit peel) recorded the best result as compared to control (+) group.

Soji-Omoniwa et al., (2014) indicated that leaf essential oil of *C. sinensis* reduced serum urea and creatinine on diabetic rats.

Sridharan et al., (2016) found that citrus lemon peel aqueous methanol extract reduced urea and creatinine induced urolithic rats because of its content of bioflavonoids like hesperidin, eriocitrin, narigenin, rutin, etc.

Table (7): Effect of lemon tree leaves, lemon fruit peel and mixture of both on uric acid (U.A), creatinine and urea (mg/dl) of diabetic rats

Parameters Groups	U.A (mg/dl) Mean \pm SD	Creatinine (mg/dl) Mean \pm SD	Urea (mg/dl) Mean \pm SD
G1: Control -ve	1.38 ^e \pm 0.003	0.58 ^d \pm 0.01	37 ^c \pm 0.97
G2: Control +ve	5.04 ^a \pm 0.008	0.84 ^a \pm 0.005	45 ^a \pm 0.12
G3: Lemon tree leaves (4%)	3.79 ^b \pm 0.002	0.70 ^b \pm 0.002	39 ^b \pm 0.21
G4: Lemon fruit peel (4%)	2.3 ^d \pm 0.05	0.62 ^c \pm 0.006	35 ^e \pm 0.09
G5: Mixture (4%)	2.99 ^c \pm 0.004	0.69 ^b \pm 0.009	36 ^d \pm 0.8
LSD	0.041	0.013	0.68

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

Results of histological examination of diabetic rats:

Examination of liver sections of control negative rats showed normal histological structure of hepatic cells, control veins, and portal areas (Photo 1). While, livers of diabetic control positive rats showed marked histological alterations as; marked vacuolar degeneration, necrosis, and severely dilated hepatic sinusoids with mild leukocytosis (Photo 2). The portal areas in liver of diabetic control positive rats severe congestion of the portal vessels, edema and mononuclear inflammatory cells infiltration (Photo 3) with severely dilated sinusoids (Photo 4). Regarding the treated groups, livers of diabetic control positive rats which treated with lemon leaves showed moderate degree of hepatocellular vacuolar degeneration and some necrosis (Photo 5) with mild congestion of the portal vessels (Photo 6). Livers of

diabetic control positive rats which treated with lemon peels showed good degree of protection of the hepatic parenchymal cells with still some degree of hepatic sinusoidal dilation (Photo 7). Restoration of the portal areas was observed, only very few inflammatory cells infiltration and very mild necrobiotic changes of the hepatic cells were noticed (Photo 8). Liver of diabetic control positive rats which treated with mix diets showed moderate vacuolar degeneration and scattered necrosis of the hepatic cells with mild dilatation of some hepatic sinusoids (Photo 9 and 10).

Histopathological observations were in line with that of biochemical parameters.

The reason for improvement of rats suffering from diabetes mellitus may be the constituents of lemon fruit peel and lemon tree leaves mainly phenol, flavonoids, Vit C, fibers and others (Russo *et al.*, 2015)

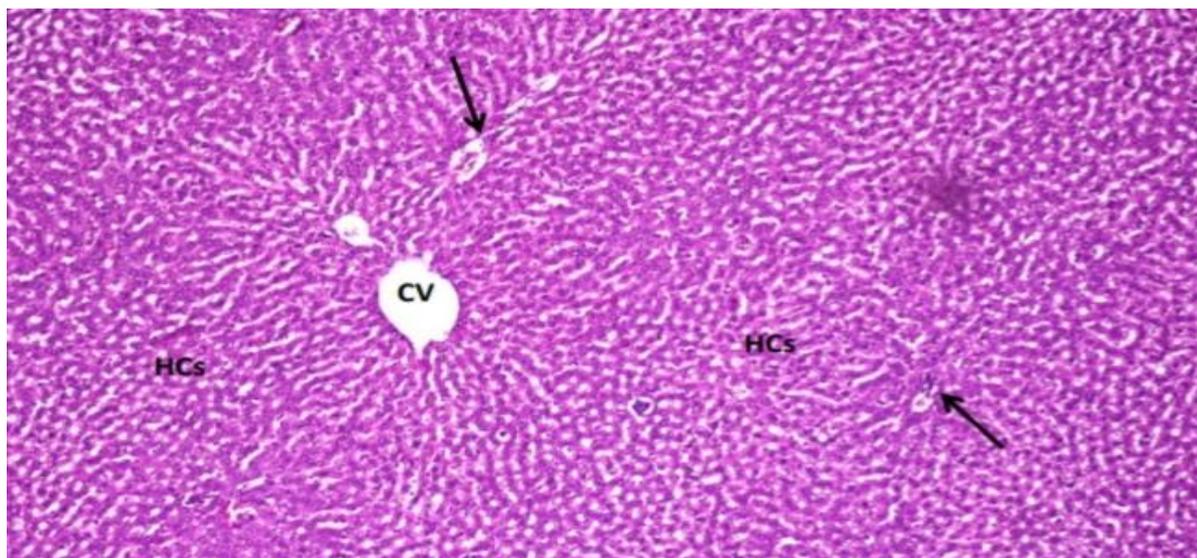


Photo (1): Liver of control negative rat showing normal central vein (CV), normal hepatic cells (HCs) and portal areas (arrow). (H&E, X200).

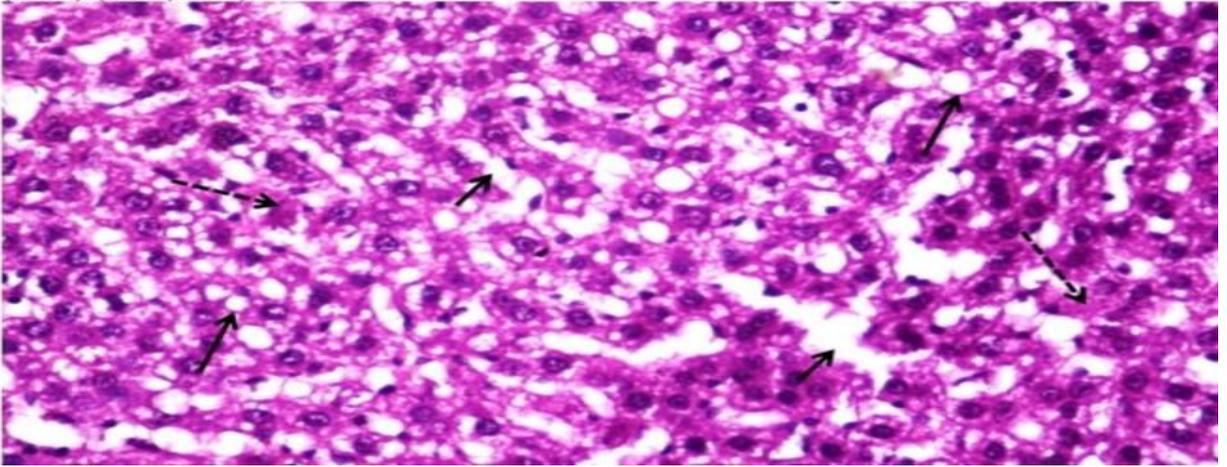


Photo (2): Liver of diabetic control positive rat showing marked vacuolar degeneration (arrow), necrosis (dashed arrow), and severely dilated hepatic sinusoids (short arrow) with mild leukocytosis. (H&E, X400).

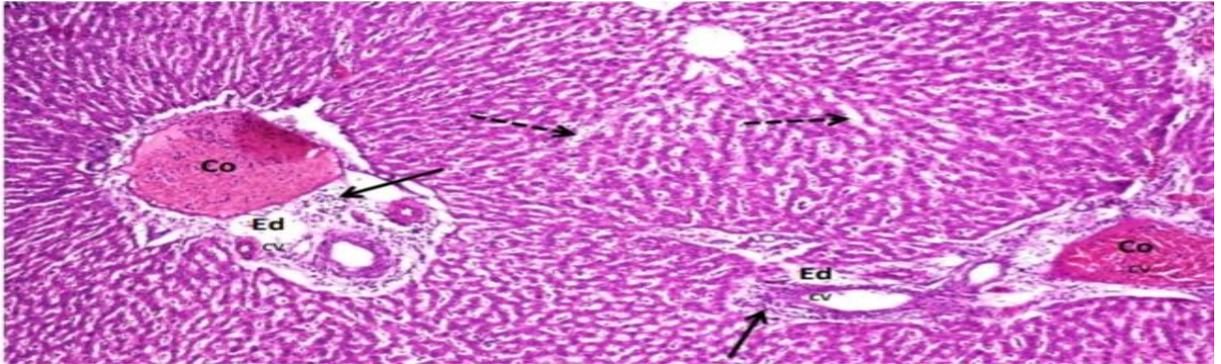


Photo (3): Portal areas in liver of diabetic control positive rat showing severe congestion of the portal vessels (Co), edema (Ed) and mononuclear inflammatory cells infiltration (arrow), notice the severely dilated sinusoids (dashed arrow). (H&E, X200).

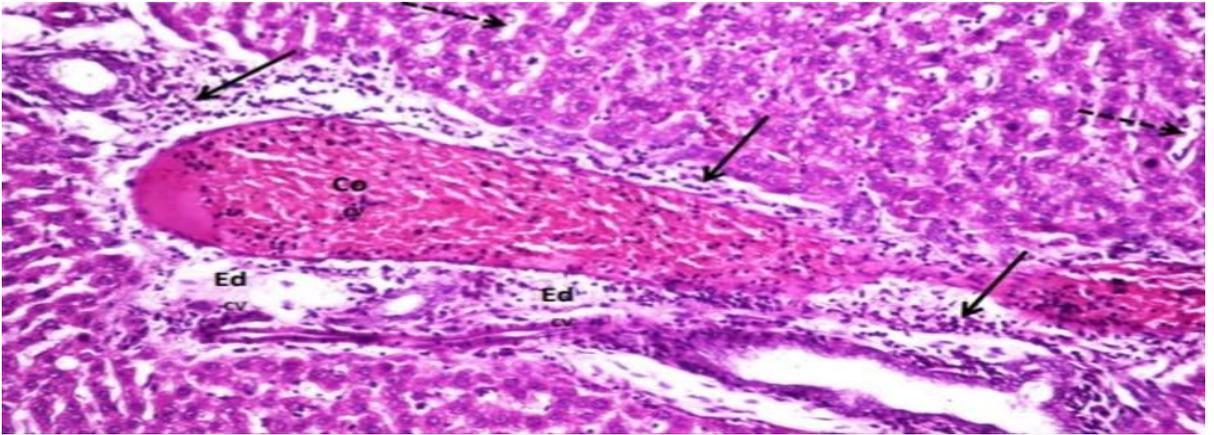


Photo (4): Portal area in liver of diabetic control positive rat showing severe congestion of the portal vessels (Co), edema (Ed) and mononuclear inflammatory cells infiltration (arrow), notice the severely dilated sinusoids (dashed arrow). (H&E, X200).

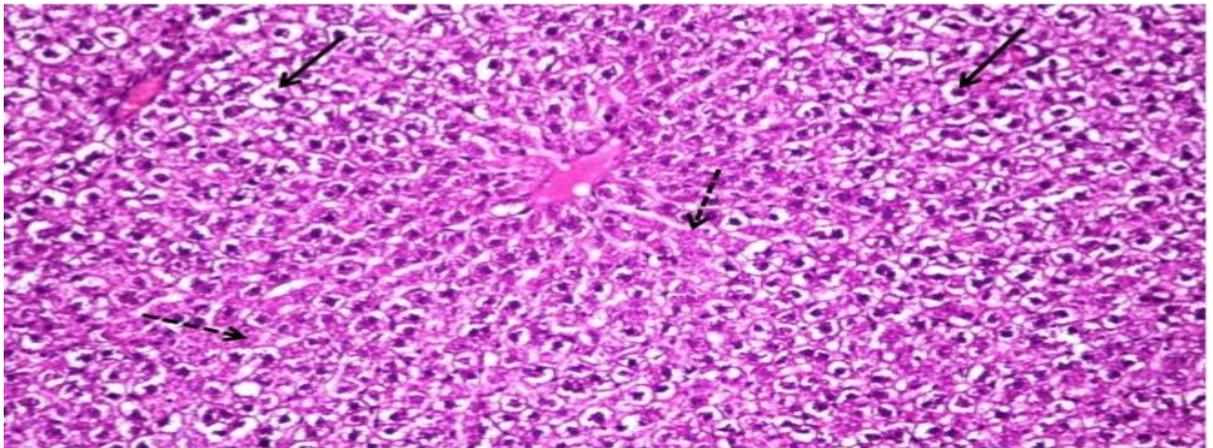


Photo (5): Liver of diabetic control positive rat which treated with lemon leaves showing moderate degree of hepatocellular vacuolar degeneration (arrow) and some necrosis (dashed arrow). (H&E, X200).

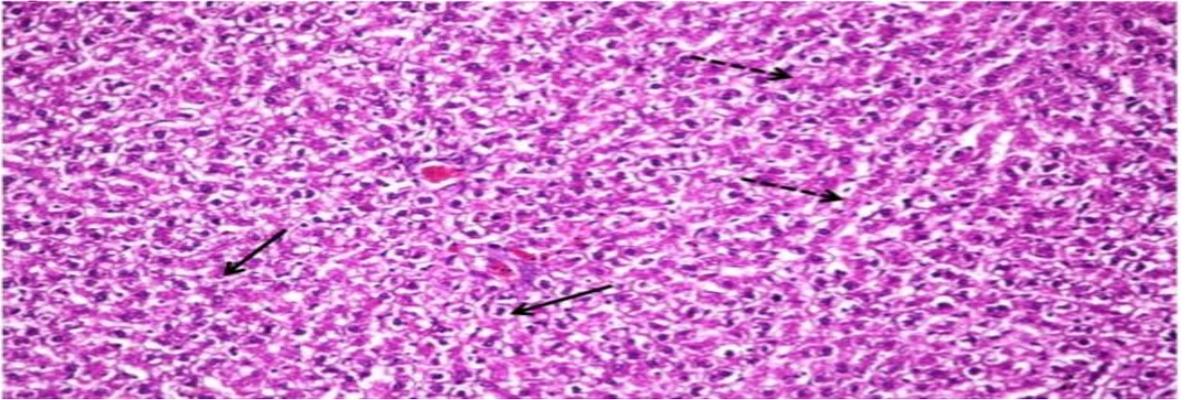


Photo (6): Liver of diabetic control positive rat which treated with lemon leaves showing moderate degree of hepatocellular vacuolar degeneration (arrow) and some necrosis (dashed arrow) with mild congestion of the portal vessels (short arrow).

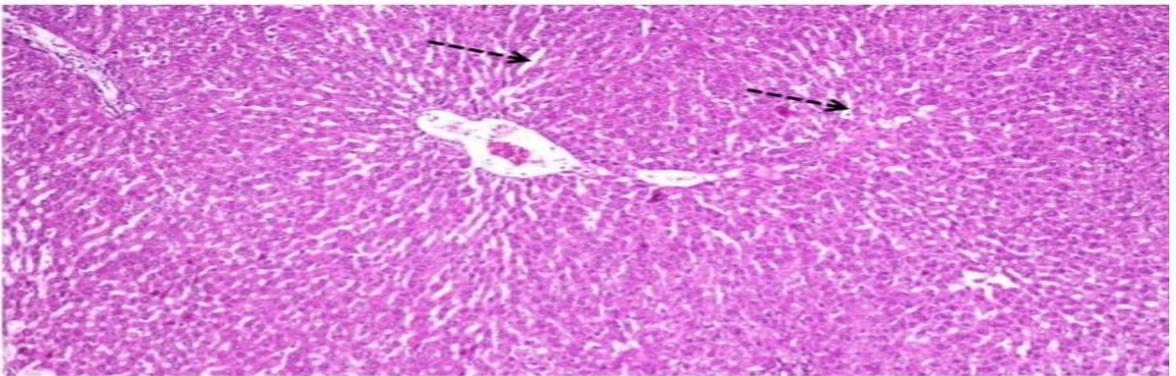


Photo (7): Liver of diabetic control positive rat which treated with lemon peels showing good degree of protection of the hepatic parenchymal cells with still some degree of hepatic sinusoidal dilatation (dashed arrow). (H&E, X200).

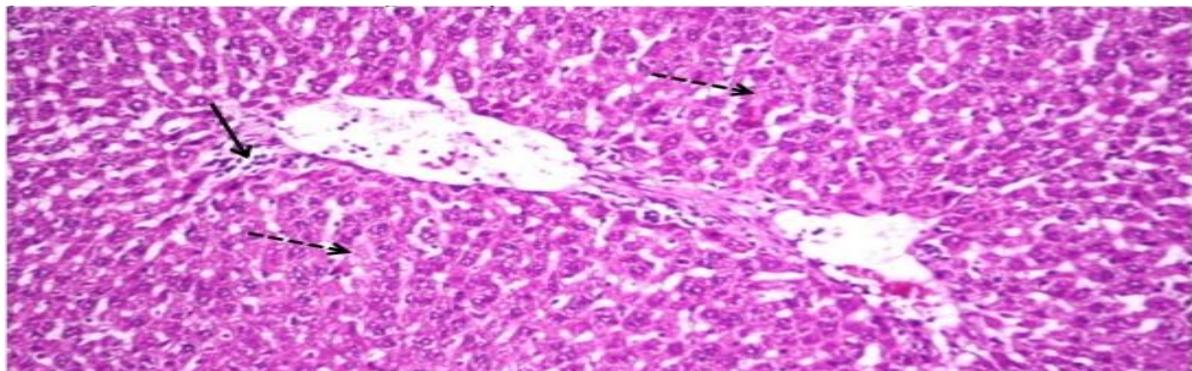


Photo (8): Liver of diabetic control positive rat which treated with lemon peels showing restoration of the portal areas with very few inflammatory cells infiltration (arrow) and very mild necrobiotic changes (dashed arrow) of the hepatic cells. (H&E, X200).

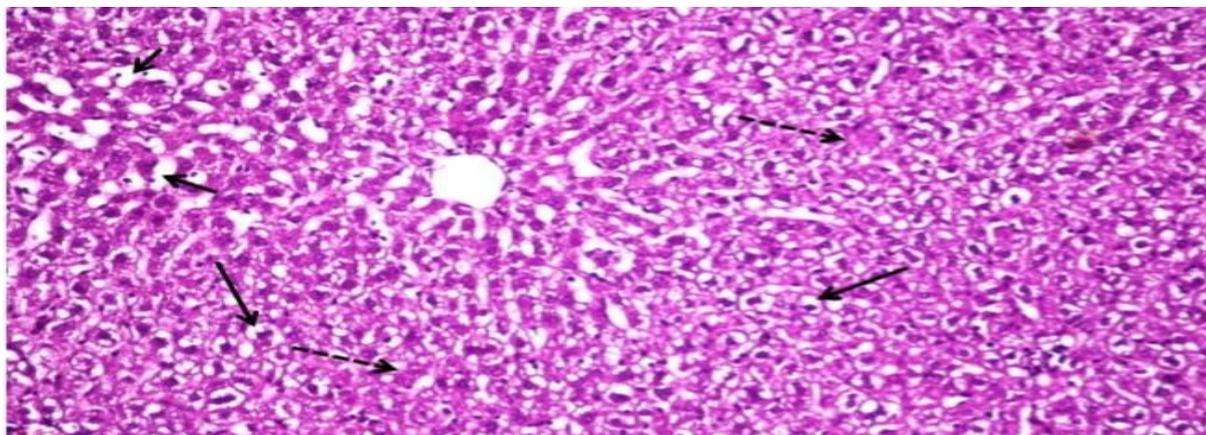


Photo (9): Liver of diabetic control positive rat which treated with mix diets showing moderate vacuolar degeneration (arrow) and scattered necrosis (dashed arrow) of the hepatic cells, notice dilatation of some hepatic sinusoids (short arrow). (H&E, X200).

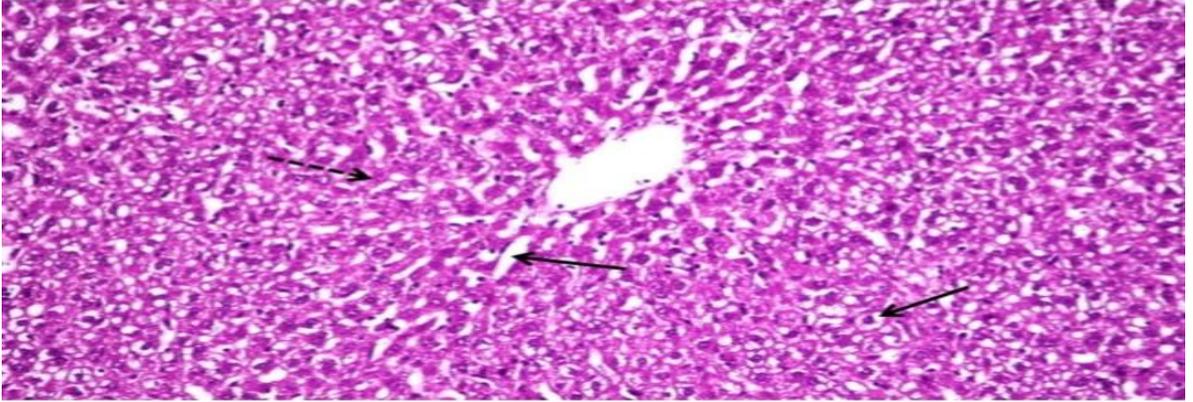


Photo (10): Liver of diabetic control positive rat which treated with mix diets showing moderate vacuolar degeneration (arrow) and scattered necrosis (dashed arrow) of the hepatic cells, notice dilatation of some hepatic sinusoids (short arrow). (H&E, X200).

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التغيرات البيولوجية والكيمائية والحيوية والنسجية بتأثير أوراق شجرة الليمون وقشور ثمرة الليمون عند استخدامها في التغذية العلاجية للفئران المصابة بالسكري

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الملخص العربي

يهدف هذا البحث إلى تقييم تأثير أوراق شجرة الليمون وقشور ثمرة الليمون والخليط منهما علي ذكور الفئران المصابة بالسكري. تم تقسيم ثلاثون فأر من الذكور البالغين سبراغ داولي إلى خمس مجموعات. مجموعة (1): وهي المجموعة الضابطة السالبة (-) تغذت على الوجبة الأساسية ، المجموعة (2): وهي المجموعة الضابطة الموجبة (+) وهي الفئران المصابة بالسكري وتغذت على الوجبة الأساسية. المجموعة (3): الفئران المصابة بالسكري التي تغذت علي اوراق شجرة الليمون بنسبة 4%. المجموعة (4): الفئران المصابة بالسكري التي تغذت على قشور ثمرة الليمون بنسبة 4%. المجموعة (5): الفئران المصابة بالسكري التي تغذت على الاثنين معا (أوراق الليمون وقشور الليمون) بتركيز 4%.. في نهاية التجربة ، بعد 28 يوماً من التغذية ، تم تقدير الاختبارات البيولوجية والبيوكيميائية والنسجية للدم. الحقن بالألوكسان سبب ارتفاع الجلوكوز واليوريا والكرياتينين وحامض اليوريك وAST وALT وALP ومستوى الكوليسترول الكلي والجلسريدات ثلاثية والليوبروتين منخفض الكثافة والليوبروتين منخفض الكثافة جدا وانخفاض الليوبروتين مرتفع الكثافة و وزن الجسم والمأخوذ من الغذاء ومعدل الاستفادة من الغذاء في الفئران المصابة بالسكر وتحسنت النتائج باستخدام الأغذية المعالجة كما تحسنت التغيرات النسجية للكبد. وقد كان أفضل غذاء هو المجهز من قشور ثمرة الليمون، غير أن الغذاء المحتوي علي أوراق الليمون قد حسن أيضا للكبد بدرجة أقل.

الكلمات المفتاحية: مرض السكري - اوراق شجر الليمون - قشور ثمرة الليمون.