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Studythe Effectof Papaya Lwaves And Seeds On Liver Disordersincarbon Tetrachloride-Inducedhepatic Rat

Yousif A. El-Hassaneen , Esraa N. A. Matter
Department of Nutrition and Food Science, Faculty of Home Economics, Menoufia University, Shebin El-Kom, Egypt

Abstract

This study was conducted to investigate the Effect of Papaya(Leaves and seeds) on Liver Disorders in Carbon Tetrachloride-Induced Hepatic Rat. Rats weighing (140±10) g were used in this study. The animals were divided into two main groups. The first main group (n=6) was kept as a control (-ve) group, while rats in the second main group (n=42) were injected by carbon tetrachloride (CCL_4**)** to induce liver disorder. Rats a themwas kept as a control (+) group and the other six groups treated with differentpapaya leaves and seedsand mixture of them (2.5% and 5%) from the basil diet. At the end of experimental period (28 days), rats were fasted over night before slaughtering and blood was collected then centrifuged to separate the serum and estimate liver functions (AST,ALT and ALP) kidney functions (urea, creatinine and uric acid) serum lipid profile (TC, TG and HDL-c) while LDL-c and VLDL-c were calculated and blood analysis (HB,RBCs,HCT,WBCs and PLT). The obtained results revealed thattreated groups by CCL_4 led to significant ($P\leq 0.05$)decrease in body weight gain (%)HDL, total protein,albumin and globulin and increased AST, ALT and ALP, cholesterol, triglycerides, LDL-c, VLDL-c, uric acid, urea, creatinine.Treating groups which fed onPapaya (Leaves and seeds) and their mixture showed significantly ($P\leq 0.05$) decreased levels of AST, ALT and

ALP, LDL, VLDL , cholesterol, triglycerides , urea, creatinine and uric acid and increase HDL, total protein , albumin and globulin . It could be concluded that papaya leaves and seedswere effective in protecting against hepatic rats not only decreased the level of AST,ALT and ALP but also has beneficial effect on lipidsserum profile and renal function .

Keywords: Hepatoprotective, Papaya,leaves,seeds,Liver function, kidney function,serumlipid profile.

Introduction

Liver is the largest glandular organ of the bodywhich plays a pivotal role to regulate whole metabolic process and homeostasis of the body.Itis the most important Site of intermediary metabolism and accountable for detoxifying any foreign one of the Most vital organs due to handling the metabolism of carbohydrates, lipid, protein, Secretion of bile, storage of vitamins and production of a variety of coagulation factors. Thus, the maintenance of healthy liver is imperative for human health **Haidry and Malik.,(2014).**Also,Liver an important organ actively involved in metabolicfunctions is a frequent Target of number oftoxicants1. In absence of a reliable liver protective drug in the modern Medicine, there are number of medicinal preparations in Ayurveda recommended for theTreatment of liver disorders and other xenobiotics by converting and excreting waste And toxin It is considered as hepatoprotective property by improving antioxidant status. The liver is necessary for survival there is currently no Way to compensate. The principle causes of carbon tetrachloride (CCL_4) induced hepatic Damage is lipid peroxidation and decreased activities of antioxidant enzymes and Generation of free radicals **Castro *et al.*,(*1974*)** .The antioxidant activity or the inhibition of thegeneration of free radicals is important in providing protection against hepatic Damage.

Many plant products have been evaluated for their possible antioxidant and Hepatoprotective effects that might make them suitable for treatment chemical-induced Liver damage in experimental animals. Phenolic compounds are widely distributed in Medicinal plants, spices, vegetables, fruits, grains, pulses and other seeds are an Important group of natural antioxidants with possible beneficial effects on human health. They

can participate in protection against the harmful action of reactive oxygen free Radicals, which are involved in the development of most chronic degenerative diseases Such as cardiovascular diseases and cancer. These reactive oxygen metabolites can also be regarded as central players in the pathophysiology of the gastrointestinal tract **Block*etal*., (1992).**

Papaya (*Carica papaya)* a member of the family *Caricaceae*, is a tropical fruit rich in dietary antioxidants (vitamin C, tocopherols, total phenols, and β-carotene) and bioactive phytochemicals with antioxidant activity **Ali*et al*.,(2011).**Different parts of *C. papaya* (leaves, barks, roots, latex, fruit, flowers, and seeds) are used in folk medication to treat a broad range of diseases **Jaiswal*et al*., (2010).**Papaya extract used contained some active compounds that can heal the liver damage this assumption is further confirmed by decrease in serum bilirubin treated with the extract compared to the untreated group. The increase in serum bilirubin may result from the decrease in liver uptake, conjugation or increase bilirubin production from hemolysis and administration of the extract leads to reduction in transaminase level and subsequently healing of the liver damage caused by alloxan. found**Demerdash*et al*., (2005)** that flavonoids, alkaloids, saponin, tannin, anthraquinones, and an-thacyanosides in medicinal plants extract like Carica papaya possess hepato-protective actions, which is mediated via antioxidant and free radicals scavenging activities of the compound. Its fresh leaves are also efficacious in the treatment of gonorrhea, syphilis and amoebic dysentery the milky juice of the unripe fruit is a powerful abortifacient, anthelmintic for roundworms, stomach disorders and enlargement of liver and spleen. The seeds are also used as a vermifuge**(Gill, 1992).** The unripe fruit is used traditionally for the treatment of various human and veterinary diseases including malaria, hypertension, diabetes mellitus, hypercholesterolemia, jaundice, and sickle cell anemia . **Ogunyemi*etal*., (2008)** Medicinal uses of papaya seed are carminative, anti-fertility agent in males, counter irritant, as a paste in the treatment of ringworm, psoriasis, emmenagogue, vermifuge, liver cirrhosis and abortifacient. Seed juice is used for bleeding piles, enlarged liver and pectoral properties. These properties mainly depend on the antioxidant activity of some secondary metabolites present in the *C. papaya*

organs. The studies of the antioxidant nutrients in *C. papaya* have led to the identification of the main compounds that differ in the different organs. Whole fruit extract contains ferulic, p-coumaric, and caffeic acid, carotenoids, and vitamin C that collectively protect human cells from oxidative stresses, promote wound healing, and skin repair **Ajlia*et al.*(*2010*).**

Leaves extract contains folic acid, vitamins B_{12}, A, and C, alkaloids, saponins, glycosides, tannins, and flavonoids with anticancer activity and protection against the alcohol-induced oxidative damage to the gastric mucosa **Otsuki*et al*. (2010).**Aqueous leaf extract of *papaya* as medicine in the treatment of some forms of liver diseases traditionally is a common practice in the south western part of Nigeria and some other part of Africa. Based on perceiving use of the leaves and seeds of this plant in the treatment of liver related disease and oral safety on acute safety, a number of studies have been conducted in recent times to validate or invalidate these claims. In studies by **Pandit*et al*. (2013),***Carica papaya* leaves extracts had an ameliorative effect on drug-induced hepatotoxicity. Hepatoprotective activity of leaves of *Carica papaya* was evident by significant reduction in levels of all serum markers in both experimenter models. Extracts significantly increased levels of superoxide dismutase, glutathione and total protein with the corresponding decrease in the levels of thiobarbituric acid reactive substance and corresponding improvementsin the histopathology of liver. Papaya extract used contained some active compounds that can heal the liver damage this assumption is further confirmed by decrease in serum bilirubin treated with the extract compared to the untreated group. The increase in serum bilirubin may result from the decrease in liver uptake, conjugation or increase bilirubin production from hemolysis and administration of the extract leads to reduction in transaminase level and subsequently healing of the liver damage caused by alloxan. This is in agreement with previous finding that flavonoids, alkaloids, saponin, tannin, anthraquinones, and an-thacyanosides in medicinal plants extract like *Carica papaya* possess hepato-protective actions, which is mediated via antioxidant and free radicals scavenging activities of the

compounds**Demerdash*et al*.,(2005)**the present study was conducted to evaluate the Effect of Papaya
(Leaves and seeds) on Liver Disorders in Carbon Tetrachloride-Induced Hepatic Rat

Materialsand methods

Papaya (Leaves and seeds) was par chased from herbs merckantsdants,Shibin El-Kom City, Menoufia Governorate, Egypt.Carbon tetrachloride was obtained fromAlGomhoriyacompany for trading drugs chemicals and medical instranelDru,CairoEgypt as 10%liquid solution. It was dispensed in white plastic bottles each containing one liter as atoxic chemical material for liver poisoning according to **Passmore and Eastwood(1986*)*** in the same time it is mixed with olive oil by equal volumes and used for liver disorders induction.

Rats:

Total of 48 male Albino rats of weight ranges between (140-150 g) were obtained from Vaccine and Immunity Organization, Ministry of Health, Helwan Farm, Cairo, Egypt.

Methods

Preparation of papaya Seeds

Chemicals and buffers in analytical grade were produced from AlGomhoriyaCompanyFruits were washed thoroughly under running tap water, then took the seeds and dried it in oven at low temperature 50^0c for60 minutes, and ground to a fine powder using an air mill.

Preparation of papaya leaves

Papaya leaves obtained from local market then removed the impurities from it and dried it in oven at low temperature for 10 minutes then put papaya leaves in the blender to get the powder.

Biological Experiments

Basal Diet

The basal diet prepared according to the following formula as mentioned by (AIN, (1993) as follow: casein (12%), Sunflower oil (10%), vitamin mixture (1%), mineral mixture (4%), choline chloride (0.2%) and the remained is

cornstarch (56.5%). The used vitamin and minerals mixture component was that recommended by **AOAC, (1990).**

Induction of liverDisorders in rats

On day 0, rats were injected subcutaneously at a dose of 0.2 ml/100 g body weight of 40 ml/LCCl_4 dissolved in paraffin oil **(Diao*et al.*, 2011).**$CCL_4$was injected two times per week for 2 consecutive weeks. Induction process wascontinued in rats by determine a the liverunction

Experimental design

The experiment was done in the Faculty of Home Economics, Menoufia University, Shebin El-Kom. Rats were housed in wire cages in a room temperature $25c^0$ and kept under normal healthy condition.

The rats will be divided into two main groups as following:

-**The first main group** :(n=6) fed on the basal diet as control negative.

-**The second main group**: (n = 42) hepatic rats. In this group rats were injected by CCL4 then divided into the following subgroups:-

Group (2): Hepatic rats + Basel diet (positive control).

Group (3):Hepatic rats + 2.5% from Papaya seeds

Group (4):Hepatic rats + 5% from Papaya seeds

Group (5):Hepatic rats + 2.5% from Papaya Leaves

Group (6): Hepatic rats + 5% from Papaya Leaves

Group(7): Hepatic rats + 2.5% from mixture of Mixture (leaves and seeds)

Group (8): Hepatic rats + 5% from mixture of Mixture (leaves and seeds)

Blood sampling

After fasting for 12 hours, blood samples in initial times were obtained from retro orbital vein, while it obtained from hepatic portal vein at the end of each experiment. Two kinds of blood samples were taken. The first parts of blood samples were collected into a dry clean centrifuge glass tubes and left to clot in water bath (37°C) for 28 minutes, then centrifuged for 10 minutes at 4000 rpm to separate the serum, which were carefully aspirated and transferred into clean cuvette tube and stored frozen at -20°C till analysis according to the method described by **Schermer, (1967).**

Biochemicalanalysis

Different tested parameters in serum were determination using specific methods as follow: cholesterol (**Thomas ,1992)**, triglycerides(T.G) (**Young, 1975) and (Fossati, 1982) ,** high density lipoprotein(HDL-C)**(Friedewaid, 1972) and (Grodon&Amer, 1977),** low density lipoprotein(LDL-C) **(Lee and Nieman, 1996),** very low density lipoprotein(VLDL-C) **(Lee and Nieman, 1996);** alanine amino transferase (ALT) **(ClinicaChimicaActa, 1980),** aspartate amino transferase (AST) **(Hafkenscheid, 1979)**, alkaline phsphatase (ALP) **(Moss ,1982);** urea **(Patton and Crouch, 1977)**,creatinine**(Henry, 1974)**, uric acid **(Schuntz, 1984),** serum Proteins **(Henry, 1974) ,** Serum Albumin **(Doumas *et al.*, 1971)** andserum Globulin (**Chary and Sharma, 2004**)

Statistical analyses

The data were analyzed using a completely randomized factorial design **(SAS, 1988)** when a significant main effect was detected; the means were separated with the Student-Newman-Keuls Test. Differences between treatments of ($P \leq 0.05$) were considered significant using Costat Program. Biological results were analyzed by One Way ANOVA.

Results and Discussion

Effect of papaya leaves and seeds on liver functions of hepatic rats

Data given in Table (1) show the effect of papaya leaves and seeds on liver functions levels (ALT, GOT and GPT) of hepatic rats. It is clear to mention that the higher ALT liver enzyme levels recorded for positive control group, while negative control group recorded the lower value with significant differences. The mean values were 92.4 and 30.80 U/L, respectively. On the other hand, the highest ALT liver enzyme of treated groups (hepatic groups) recorded for 2.5% papaya seeds, while the lowest value recorded for 5% papaya (leaves and seeds) with significant differences. The mean values were 71, 70 and 44.25 U/L, respectively. In case of GOT liver enzyme, the higher levels recorded for positive control group, while negative control group recorded the lower value with significant($P \leq 0.05$) differences. The mean values were 75.20 and 20.00 U/L, respectively.On the other hand, the highest GOT liver enzyme of treated groups (hepatic groups) recorded for 2.5% papaya seeds, while the lowest value recorded for 5% mixture of papaya leaves and seeds with

significant differences. The mean values were 46.90 and 26.10 U/L, respectively.In case of GPT liver enzyme; the higher levels recorded for positive control group, while negative control group recorded the lower value with significant differences. The mean values were 19.70 and 5.50 U/L, respectively.On the other hand, the highest GPT liver enzyme of treated groups (hepatic groups) recorded for 2.5% papaya seeds, while the lowest value recorded for 5% mixture of papaya leaves and seeds with significant differences. The mean values were 9.93 and 5.00 U/L, respectively**.**

These results are in agreement with**Demerdash*et al.*, (2005)**,**reported that treatment of the rats treated with aqueous extracts of papaya showed reduction at the activities of liver enzymes (AST and ALP) when compared to the treated group and consequently alleviated liver damage.

Table (1): Effect ofpapaya leaves and seeds on liver functions of hepatic rats

Groups	ALT (U/L)	GOT (U/L)	GPT (U/L)
Group (1) control (-)	$30.80^{h} \pm 1.40$	$20.00^{f} \pm 1.11$	$5.50^{d} \pm 0.80$
Group (2) control (+)	$92.40^{a} \pm 1.31$	$75.20^{a} \pm 1.20$	$19.70^{a} \pm 0.40$
Group (3) 2.5%Papaya seeds	$71.70^{b} \pm 1.70$	$46.90^{b} \pm 1.10$	$9.93^{b} \pm 0.90$
Group (4) 5% Papayaseeds	$64.80^{c} \pm 1.50$	$40.80^{c} \pm 1.40$	$8.20^{c} \pm 1.20$
Group (5) 2.5%Papaya leaves	$60.00^{d} \pm 1.20$	$41.45^{c} \pm 1.20$	$7.81^{c} \pm 0.50$
Group (6) 5% Papaya leaves)	$55.75^{e} \pm 1.10$	$39.25^{c} \pm 1.30$	$5.50^{d} \pm 0.80$
Group (7) 2.5% Mixture (leaves and seeds)	$49.70^{f} \pm 1.21$	$29.25^{d} \pm 1.40$	$5.30^{d} \pm 0.40$
Group (8) 5% of Mixture (leaves and seeds)	$44.25^{g} \pm 1.40$	$26.10^{e} \pm 1.22$	$5.00^{d} \pm 0.60$
LSD	**2.33**	**2.20**	**1.15**

Each value represents the mean value three replicates ±SD

Mean under the same column bearing different superscript letters are different significantly ($P \leq 0.05$)

Effect of papaya leaves and seeds on serum triglycerides and serum total cholesterol levels of hepatic rats:

Data presented in Table (2) show the effects of papaya (leaves and seeds) on serum triglycerides and serum total cholesterol levels of hepatic rats.The obtained results indicated that the higher serum triglycerides levels recorded for positive control group, while negative control group recorded the lower value with significant differences. The mean values were 131.8 and 69.9 mg/dl, respectively.On the other hand, the highest serum triglycerides levels of treated groups (hepatic groups) recorded for 2.5% papaya leaves, while the lowest value recorded for5% papaya leaves and seeds with no significant differences. The mean values were 93.30 and71.10mg/dl, respectively. In case of serum total cholesterol levels, it could be concluded that the highest serum total cholesterol levels recorded for positive control group, while negative control group recorded the lowest value with significant differences. The mean values were 147.85 and 70.15 mg/dl, respectively.

On the other hand, the highest serum cholesterol levels of treated groups (hepatic groups) recorded for 2.5% papaya leaves, while the lowest value recorded for 5% papaya (leaves and seeds) with significant differences. The mean values were 101, 90 and 78.15 mg/dl, respectively. These results are in agreement with **Banerjee *et al.*, (2006)***Carica papaya* extract has also been shown to reduce total cholesterol by interfering with their biosynthesis. That treatment with C. papaya extract decreased serum cholesterol of HD rats. Previous reports from our laboratory have shown that *C. papaya* leaf contains sterols among their main components. It is known that phytosterols with analogue structure to cholesterol may decrease cholesterol absorption displacing it from bile salt micelles and competing for intestinal absorption **Vijayaraj*et al.*, (2013).** Also, these results are in agreement with **Chaiyasut*et al.*, (2011).** Our results demonstrated that triacylglycerol levels decreased in diabetic rats with the administration of *C. papaya* extract. The hyperlipidemia associated with diabetes may result

from an accelerated hepatic triglyceride biosynthesis and the release of VLDL without an increase in its rate of clearance from the blood by lipoprotein lipase, which is dependent on the insulin/glucagon ratio .Furthermore, these results are in agreement with **Proninet *al.*, (2014)** shown that *C. papaya* leaf contains sterols among their maincomponents.

It is known that phytosterols with analogue structure to cholesterol may decrease cholesterol absorption displacing it from bile salt micelles and competing for intestinal absorption. Intestinal absorption plays a main role in the regulation of cholesterol homeostasis. It has been suggested that transporters can affect its intestinal absorption.In addition, these results are in agreement with **Ezikeet *al.*, (2009)** the results showed that extract of *Carica papaya* seeds significantly lowered the total cholesterol, serum triglyceride, fasting blood glucose and significantly reduced the density of lipoprotein cholesterol in a dose dependent

Table (2) Effect of papaya leaves and seeds on serum triglycerides and serum total cholesterol of hepatic rats

Groups	Triglycerides (TG, mg/dl)	Total cholesterol
Group (1)control (-)	69.90 ^{e} ±0.32	70.15 ^{g} ±0.50
Group (2)control (+)	131.80 ^{a} ±0.60	147.85 ^{a}±0.30
Group (3)2.5%Papaya seeds	86.10 ^{c} ±0.40	95.55 ^{c} ±0.20
Group (4)5% Papayaseeds	75.45 ^{b} ±0.50	90.65 ^{d} ±0.10
Group (5)2.5%Papaya leaves	93.30 ^{b} ±0.10	101.90 ^{b} ±0.13
Group (6) 5% Papaya leaves	88.80 ^{c} ±0.20	90.10 ^{d} ±0.40
Group (7) (2.5% Mixture leaves and seeds	80.50 ^{d} ±0.11	85.10 ^{e} ±0.40
Group (8) (5% of Mixture leaves and seeds	71.10 ^{e} ±0.30	78.15 ^{f} ±0.22
LSD	**3.50**	**3.82**

Each value represents the mean value three replicates ±SD

Mean under the same column bearing different superscript letters are different significantly (P≤ 0.05)

Effect of papaya leaves and seeds on serum lipid profile levels of hepatic rats:

Data presented in Table (3) show the effects of papaya (leaves and seeds) on lipid profile (HDL-c, LDL-c and VLDL-c) levels of hepatic rats. The obtained results indicated that the higher HDL-c levels recorded for positive control group, while negative control group recorded the lower value with significant differences. The mean values were 48.15 and 28.20 mg/dl, respectively.On the other hand, the highest HDL-c levels of treated groups (hepatic groups) recorded for 5% of Mixture (leaves and seeds), while the lowest value recorded for 2.5% papaya leaves with no significant differences. The mean values were 45.14 and37.25mg/dl, respectively. In case of LDL-c, the obtained results showed that the higher LDL-c levels recorded for positive control group, while negative control group recorded the lower value with significant differences. The mean values were 93.29 and 8.02 mg/dl, respectively.On the other hand, the highest LDL-c levels of treated groups (hepatic groups) recorded for 2.5% papaya seeds, while the lowest value recorded for5% mixture papaya leaves and seeds with significant differences. The mean values were 44.30 and18.79mg/dl, respectively. On the other hand, the obtained results showed that the higher VLDL-c levels recorded for positive control group, while negative control group recorded the lower value with significant differences. The mean values were 26.36 and 13.98 mg/dl, respectively.On the other hand, the highest VLDL-c levels of treated groups (hepatic groups) recorded for 2.5% papaya leaves while the lowest value recorded for5% mixture papaya leaves and seeds with significant differences. The mean values were 18.66 and14.22 mg/dl, respectively. These results are in agreement with **Geetha*et al.*, (2011)**showed significant (P<0.05) increase in HDL-c by Carica papaya leave extracts (methanol and ethanol). This could possibly be due to increasing activity of lecithin-cholesterol acyl transferase (LCAT), an enzyme responsible for incorporating free cholesterol into HDL-c.Also, **Banerjee *et al.*, (2006)**reported thatCarica papaya extract has also been shown to reduce total cholesterol by interfering with their biosynthesis.

Furthermore,**Johnson et al., (2015)**reported thatthe results of the phytochemical analysis of Carica papaya extract showed the presence of saponin which is known to elicit serum cholesterol lowering activity by causing resin-like action, thereby reducing the enterohepatic circulation of bile acids.

Table (3): Effect of papaya leaves and seeds on serm lipid profile of hepatic rats

Groups	Parameters		
	(VLDL-c) (mg/dl)	**(HDL-c) (mg/dl)**	**(LDL-c) (mg/dl)**
Group (1) control (-)	13.98^{c}± 0.69	48.15^{a} ± 2.80	8.02^{h}± 0.93
Group (2) control (+)	26.36^{a}± 1.20	28.20^{d} ± 1.71	93.29^{a}± 1.58
Group(3) 2.5% Papaya seeds	17.22^{b} ± 1.72	37.25^{c} ±1.38	41.08^{c}± 1.91
Group (4)5% Papaya seeds	15.09^{c} ± 0.90	40.50^{b}±0.50	35.06^{d}±0.83
Group (5)2.5% Papaya leaves	18.66^{b}± 1.60	39.94^{b}± 0.90	44.30^{b}±2.41
Group (6) 5% Papaya leaves	17.76^{b}±2.20	41.40^{b} ±1.9	30.94^{e}±2.15
Group (7) 2.5% Mixture (leaves and seeds)	16.10^{c}± 1.60	42.50^{b} ±1.9	26.50^{f} ±2.15
Group (8) 5% of Mixture (leaves and seeds	14.22^{c}± 1.60	45.14^{a} ±1.9	18.79^{g}±2.15
LSD	**2.40**	**3.10**	**3.00**

Each value represents the mean value three replicates ±SD

Mean under the same column bearing different superscript letters are different significantly ($P \leq 0.05$)

Effect of papaya leaves and seeds on kidney functions levels of hepatic rats:

Data presented in Table (4) show the effects of papaya leaves and seeds on kidney functions(urea, uric acid and creatinine) levels of hepatic rats.The obtained results indicated that the higher urea levels recorded for

positive control group, while negative control group recorded the lower value with significant differences. The mean values were 68.10 and 35.50 mg/dl, respectively.On the other hand, the highest urea levels of treated groups (hepatic groups) recorded for 2.5% papaya seeds, while the lowest value recorded for5% mixture of papaya leaves and seeds with significant differences. The mean values were 55.03 and38.25mg/dl, respectively. In case of uric acid, the obtained results showed that the higher uric acid levels recorded for positive control group, while negative control group recorded the lower value with significant differences. The mean values were 3.50 and 1.50 mg/dl, respectively.On the other hand, the highest uric acid levels of treated groups (hepatic groups) recorded for 2.5% papaya seeds, while the lowest value recorded for5% mixture of papaya leaves and seeds with significant differences. The mean values were 2.50 and1.66 mg/dl, respectively. On the other hand, the obtained results showed that the higher creatinine levels recorded for positive control group, while negative control group recorded the lower value with significant differences. The mean values were 8.10 and 3.30 mg/dl, respectively.While, the highest creatinine levels of treated groups (hepatic groups) recorded for 2.5% papaya seeds, while the lowest value recorded for5% mixture of papaya leaves and seeds with significant differences. The mean values were 5.60 and 3.60 mg/dl, respectively. These results are in agreement with **Gheith and ElMahmoud, (2018)** who reported thataqueous extract of *C. papaya* leaves has a strong potential of Nephroprotection based on its antioxidant activity and its content of beneficial phytochemical constituents. The leaves of C. *papaya* plant, thus, could be a good pharmaceutical source of natural nephroprotective medicines

Table (4): Effect of papaya leaves and seeds on kidney functions of hepatic rats

Parameters / Groups	Urea (mg/dl)	Uric acid (mg/dl)	Creatinine (mg/dl)
G_1 control (-)	$35.50^{e} \pm 1.10$	$1.50^{b} \pm 0.10$	$3.30^{c} \pm 0.27$
G_2 control (+)	$68.10^{a} \pm 2.20$	$3.50^{a} \pm 0.60$	$8.10^{a} \pm 1.56$
Group (3) 2.5%Papaya seeds	$55.03^{b} \pm 1.10$	$2.50^{ab} \pm 0.40$	$5.60^{b} \pm 0.21$
Group (4) 5% Papayaseeds	$53.27^{b} \pm 0.50$	$2.20^{b} \pm 0.20$	$4.73^{b} \pm 0.70$
Group (5) 2.5%Papaya leaves	$45.96^{c} \pm 1.30$	$2.30^{ab} \pm 0.50$	$4.72^{b} \pm 0.53$
Group (6) 5% Papaya leaves	$41.25^{d} \pm 0.30$	$2.00^{b} \pm 0.20$	$4.00^{c} \pm 0.14$
Group (7) 2.5% Mixture (leaves and seeds)	$40.96^{d} \pm 1.30$	$1.83^{b} \pm 1.20$	$3.90^{c} \pm 0.53$
Group (8) 5% of Mixture (leaves and seeds)	$38.25^{d} \pm 0.30$	$1.66^{b} \pm 0.10$	$3.60^{c} \pm 0.14$
LSD	**3.36**	**1.18**	**1.21**

Each value represents the mean value three replicates ±SD
Mean under the same column bearing different superscript letters are different significantly ($P \leq 0.05$)

Effect of papaya leaves and seeds on glucose levels of hepatic rats:

The effect of papaya leaves and seeds on glucose levels of hepatic rats are shown in Table (5) it is clear to notice that the higher glucose levels recorded for positive control group, while negative control group recorded the lower value with significant differences. The mean values were 177.60 and 96, 00 mg/dl, respectively. On the other hand, the highest glucose levels of treated groups (hepatic groups) recorded for 2, 5 % papaya leaves, while the lowest value recorded for 5% papaya (leaves and seeds) with significant differences. The mean values were 146.25 and 122.10 mg/dl, respectively. Standl and Schnell, (2012) they reported that papaya markedly decreased glucose levels when compared with high fat diet, this action due to papaya sterols which may delay glucose absorption by blocking enzymes at

intestinal which hydrolyzed carbohydrates with the concomitant lower glycemia. In addition, these results are in agreement with **Juárez-Rojop*et al*., (2012**) they showed that oral administration of different parts of papaya to alloxan- induced diabetic rats significantly reduced the glucose levels.
This reduction effect of glucose due to described to the ability of papaya seed and leaf to decrease the rate of intestinal glucose absorption and raised peripheral glucose utilization.

Table (5): Effect of papaya leaves and seeds on glucose of hepatic rats

Groups	**Glucose (mg/dl)**
G1 C control (-)	96.00 ^{g}±0.30
G2 C control (+)	177.60 ^{a}±0.21
Group (3) 2.5% Papaya seeds	142.40 ^{b}±0.60
Group (4) 5% Papaya seeds	138.20 ^{d}±0.11
Group (5)(2.5% Papaya leaves	146.25 ^{b}±0.50
Group (6) 5% Papaya leaves	140.40 ^{c}±0.20
Group (7) 2.5% Mixture leaves and seeds	128.15 ^{e}±0.10
Group (8)5% of Mixture (leaves and seeds)	122.10 ^{f}±0.50
LSD	**4.28**

Each value represents the mean value three replicates ±SD
Mean under the same column bearing different superscript letters are different significantly ($P \leq 0.05$) ≤ 0.05).

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تأثيرأوراق وبذورالباباظ على الخلل الحادث في كبد الفئران المستحث برابع كلوريدالكربون

يوسف عبد العزيزالحسانين،اسراء نصرعلي مطر
قسم التغذية وعلوم الاطعمة ،كليةالاقتصادالمنزلي،جامعة المنوفية،شبين الكوم ،مصر.

الملخص العربى:

تم اجراء الدراسة الحالية لمعرفة تأثير استخدام أوراق وبذور البابايا على الخلل الحاد ثفي كبد الفئران المستحث برابع كلوريد الكربون. أجريت الدراسة علي٤٨ فأر البينو ذكور تتراوح اوزانهم من ١٤٠ -١٥٠ جم، تم تغذيتهم على الوجبة الأساسية لمدة اسبوع، ثم قسمت بعد ذلك الي مجموعتين أساسيتين،المجموعة الأولى ٦ فئران (المجموعة الضابطة السالبة) حيث تم تغذية هذه المجموعةعلى الوجبة الأساسية طوال فترة التجربة. ثم تم حقن ٧ مجموعات وعددهم ٤٢ فأر برابع كلوريد الكربون بمقدار ٢ ملجم/ كجم من وزن الجسم بمادة رابع كلوريد الكربون بهدف احداث خلل في وظائف الكبد ثم تم تقسيمهم الى مجموعات فرعية كالتالي: المجموعة الضابطة الموجبة حيث تم تغذيتها على الوجبة القياسية طوال مدةالتجربة. - بينما الست مجموعات الأخرى تم اضافة أوراق وبذور البابايا ومخلوط من كليهما بنسب ٢.٥ , ٥% من الوجبة الأساسية. وفي نهاية التجربة ثم وزن الفئران ثم ذبحهم وتجميع عينات الدم وتم قياسدرجه نشاط انزيمات الكبد (ALP،ALT ، AST)، الكولسترول الكلي، الجلسريدات الثلاثية، ووظائف الكلي (اليوريا،الكرياتين، حمض اليوريك)، (البروتين،الجلوبيولين،الألبومين). وقدأظهرت نتائج هذه الدراسة أن مجموعه الكنترول الموجبةأظهرت الي ارتفاعفي الدهون الثلاثية وانزيمات الكبد والجلوكوز والكوليسترول والجلسريدات الثلاثية بينما المجموعات المعالجة بأوراق وبذور البابايا انخفض فيها درجه نشاط انزيمات الكبد والدهون والجلوكوز والكوليسترول والجلسريدات الثلاثية. وقد اظهرت هذه الدراسةأن التغذية على أوراق وبذور البابايا نتج عنها تحسن في وظائف الكبد والكلي ودهون الدم وانخفاض مستوى الجلوكوز بالدم لدى الفئران المصابة بمرض الكبد.

الكلمات المفتاحية: - التأثير الوقائي للكبد، أوراق، بذور، الباباظ ،وظائف الكبد، وظائف الكلي، صوره دهون الدم