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The possible ameliorative role of *Phoenix dactylifera* seed extracts against hepatotoxicity induced by Acetaminophen in rats

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ABSTRACT

Acetaminophen, known commercially as paracetamol, is used as a pain reliever and antipyretic drug. It is very safe if taken in appropriate doses (4 grams/ day), but when taken in excessive dosages, it may lead to some health problems. This work aims to establish the possible protective role of *Phoenix dactylifera* seed extracts against hepatotoxicity that may be caused by acetaminophen in rats. The bioactive compounds of *P. dactylifera* seeds have been identified using gas chromatography-mass spectrometry (GC/MS). Rats were divided into three groups of ten rats each: Gp1 (the -ve control group); Gp2 (+ve control group), which received acetaminophen orally (750 mg/kg daily); and Gp3 was injected with *P. dactylifera* seed extracts (200 mg/kg) after acetaminophen ingestion for a month (750 mg/kg daily). During this work, the initial and final rat body weights, hepatic function tests, and the antioxidant enzyme activities were measured; also, histological and immunohistochemical studies were examined. GC-MS analysis results showed the presence of various phytochemical components with potent antioxidants and anti-inflammatory activities. Administration of acetaminophen resulted in a significant decrease in the rats' final body weight. In contrast, treatment of rats by *P. dactylifera* extracts displayed a small percentage increase in their body weight. For biochemical tests, acetaminophen administration caused significant alterations in hepatic functions and antioxidant enzymes, while the group treated with *P. dactylifera* improved both. Histological and immunohistochemical staining supported these results. In conclusion, treatment with *p. dactylifera* seed extracts showed a potent therapeutic and protective effect against acetaminophen hepatotoxicity in rats.

Introduction

Liver is a crucial organ that is responsible for metabolization and detoxification of the toxic elements, particularly at high drug doses, where most acute hepatic failure cases are associated with extensive administration **(Cinar et al., 2024).** Acetaminophen is the most commonly used antipyretic medication; it is also used for back pain relief and headache. It can also be used together with other medicines to mitigate pain in cancer patients **(Pendo, 2021).** While acetaminophen is considered appropriately safe when taken in therapeutic doses, supratherapeutic, accidental use, and intentional taking may all result in liver injuries **(Adio, 2022).** Hepatotoxicity of acetaminophen is contributed to by its metabolization into N-acetyl benzoquinone imine (NAPQI) via the cytochrome P-450 enzyme, which triggers hepatotoxicity by depleting glutathione **(Turgut et al., 2023).** Presently used synthetic drugs against liver diseases are ineffectual and may cause adverse side effects. As a result, natural extracts from medicinal plants have lately gained scientific attention as a potentially effective treatment for liver damage **(Bouhlali, 2021) .**

Phoenix dactylifera (date palm) is vernacularly an ancient plant that belongs to the Arecaceae species **(Manda et al., 2022)** and is a globally popular tree that is widely planted in the world's arid regions, especially in North Africa and the Arab world, particularly in Egypt **(Radwan et al., 2022).** Because of the abundance of nutritious and bioactive ingredients, it is employed as the conventional treatment of a wide range of diseases, involving memory troubles, fever, loss of awareness, inflammation, paralysis, and nervous problems **(Tiwari et al., 2022).** It has previously been shown to protect against damage caused by a variety of toxicants, including CCl_4, trichloroacetic acid, acetaminophen, and dimethoate **(Abdeen et al., 2021).** Phoenix fruits and their seed extract can both prevent the toxicity of acetaminophen by enhancing antioxidant capacity, preventing membrane lipid peroxidation, and suppressing CYP formation, hence inhibiting NAPQI generation **(Badr et al., 2023).** Thus, the current study was designed to investigate the possible protective effect of *Phoenix dactylifera* seed extracts against pathophysiological and histopathological hepatic changes induced by acetaminophen in rats.

Materials and methods

The drug

Acetaminophen was obtained as Cetal drops 100 mg/ml and administered orally through gastric gavage. A dose of 750 mg/kg body weight is equivalent to 75 mg/100 g body weight, which is the maximum therapeutic dose for humans **(El Morsey et al., 2019).**

Plant materials

The plant samples were obtained from a local market in Tanta city, Egypt, and were identified by taxonomists at the Botany Department, Faculty of Science, Tanta University.

Preparation of plant extract

The seeds were collected and dried in the shade before being finely ground in a mortar and dissolved in cold distilled water (1:3) for 48 hours at 4°C, then centrifuged at 4°C for 20 minutes at 4000 rpm. Finally, the supernatant has been collected and kept at -80°C till use.

Experimental design

Rats were divided into 3 groups of ten rats each. **Gp1** (-ve control group) will receive vehicle-distilled water. **Gp2:** (+ve control group) will receive acetaminophen daily at 750 mg/kg body weight for a month **(Cemek et al., 2010). Gp3:** Will receive acetaminophen at 750 mg/ kg body weight, followed by 200 mg/kg body weight of *P. dactylifera* seed extracts daily for a month **(Cemek et al., 2010).**

Animals and Ethical Approval

Thirty male Wistar albino rats weighing 150–160 g and aged 7-9 weeks were purchased from Helwan University and allowed to acclimatize for 2 weeks under the animal house conditions. Then, they were divided and used according to the experiment plan (n = 10 per group). They were kept on a consistent light and dark cycle and fed a conventional pellet diet with unlimited tap water. The number of the ethically approved committee is **"IACUC-SCI-TU-0280 ".**

Gas Chromatography/ Mass Spectrometry (GC/ MS) analysis

The GC model was equipped at National Research Centre, and Cairo, Egypt. Separation was achieved using a Zebron ZB-FAME column Analyses were carried out using hydrogen as the carrier gas. The lipids of the sample were extracted by the biphasic 3:2 Hexane/Isopropanol (v/v) extraction method .

Determination of body weight changes

The starting and final body weights were measured; the difference between them was calculated to determine the percentage of the changes in the rat's body weight.

Assessment of liver enzymes

Serum levels of alanine transaminase (ALT) and aspartate transaminase (AST) were measured following **Thefeld et al. (1994)**, while alkaline phosphatase (ALP) was measured by using the **Jose and Purinergic (2006)** technique.

Assessment of biochemical parameters

Blood samples were collected by direct cardiac puncture of each rat from all groups using light anesthesia to measure total bilirubin **(Water and Gerard, 1980).** But total protein and albumin were followed **(Tietz, 1994)** technique.

Measurements of antioxidant enzyme activities and oxidative stress markers

(Wheeler et al., 1999) The method was applied to determine superoxide dismutase (SOD) activity, and catalase (CAT) was measured, followed **(Johansson and Borg, 1988),** while malonaldehyde (MDA) was determined using **(Sulochana et al., 1999)** technique.

Histological investigation

Using a microtome, 3-4 µm-thick sections of liver were taken from the paraffin blocks and stained with Hematoxylin-Eosin **(Azırak and Özgöçmen, 2023).**

Immunohistochemical (IHC) investigation

According to **(Rahadianiet al., 2023),** p53 antibodies were applied for immunohistochemical labeling of liver sections, and the immunoreactivity was recorded according to their intensity in brown color.

Statistical analysis

The data were analyzed by Excel 2021. Data were presented as mean ± standard deviation (SD) in at least triplicate. A one-way analysis of variance (ANOVA) was used to assess the significant differences between means in different groups, followed by a post-hoc Tukey multiple comparison test. All statistical

tests had p-values <0.05, indicating statistical significance.

Results

Chromatographic profile of seeds

As demonstrated in **Table (1)** the composition of *P. dactylifera* seed extracts was analyzed by GC–MS that identified 4 known fatty acids which are Hexadecanoic acid-methyl ester (100%), Dodecane, 2,6,10-trimethyl (9.51%), Methyl stearate (82.45%), and Phenol,2,4-bis(1,1-dimethylethyl)-phosphite (3:1) (69.34%).

Effect of seed extracts on the body weight

In comparison to the control group **(Gp1),** the acetaminophen group's final body weight **(Gp2)** was significantly decreased ($p < 0.05$). While the *P. dactylifera*-treated group **(Gp3)** showed a noticeable change in body weight when compared to the acetaminophen group **(Gp2) Table (2).**

Table (1): GC–MS analysis of *P.dactylifera* seed extracts

peak	RT (min)	Name	M. F.	Area	Area (%)
1	25.808	Hexadecenoicacid-methyl ester	$C_{17}H_{34}O_2$	3743495.59	100%
2	26.941	Dodecane, 2,6,10-trimethyl	$C_{15}H_{32}$	356163.36	9.51%
3	27.72	Methyl stearate	$C_{19}H_{38}O_2$	3086384.68	82.45%
4	36.886	Phenol,2,4-bis(1,1-dimethylethyl)-,phosphite (3:1)	$C_{42}H_{63}O_3P$	2595910.45	69.34%

RT: Retention time; M.F: Molecular formula.

Table (2): The percentage of the changes in the rat's body weight

Groups	I. B. wt. (g)	F. B. wt. (g)	Change in B. wt (%)
Control (Gp1)	152.8 ± 1.1^{a}	163.8 ± 1.39^{a}	59.32 ± 4.6^{a}
Acetaminophen (Gp2)	152.65 ± 1.15^{a}	156.6 ± 2.8^{c}	43.27 ± 3.9^{b}
Treated with *P. dactylifera* (Gp 3)	152.85 ± 0.85^{a}	161.3 ± 1.05^{b}	$47.06\pm4.03^{a,b}$

The values represented mean±SD; I. B. wt: Initial body weight; F. B. wt: final body weight. a and b: the statistical diff erence between groups with diff erent letters in the same column is significant ($p < 0.05$).

Treatment with *P. dactylifera* seeds ameliorated hematological parameters

As depicted in **(Figs. 1, 2)** administration of acetaminophen to rats **(Gp2)** resulted in a significant increase ($p\leq0.05$) in the serum activities of ALT, AST, and ALP as well as total bilirubin with a noticeable reduction in albumin and the total protein when compared to the normal control **(Gp1)**. Treatment with *P. dactylifera* **(Gp3)** protected against the increase in hepatic enzyme levels ALT, AST, and ALP as well as total bilirubin and significantly ameliorated the reduction in total proteins and albumin levels.

Treatment with *P. dactylifera* seeds protects against acetaminophen-induced oxidative stress.

When compared to their control **(Gp1)**, a single dose of acetaminophen **(Gp2)** reduced SOD and CAT activities while increasing MDA levels significantly. Treatment with *P. dactylifera* seeds **(Gp3)** resulted in an increase in SOD and CAT with a reduction in MDA concentration when compared with the acetaminophen group **(Fig. 3).**

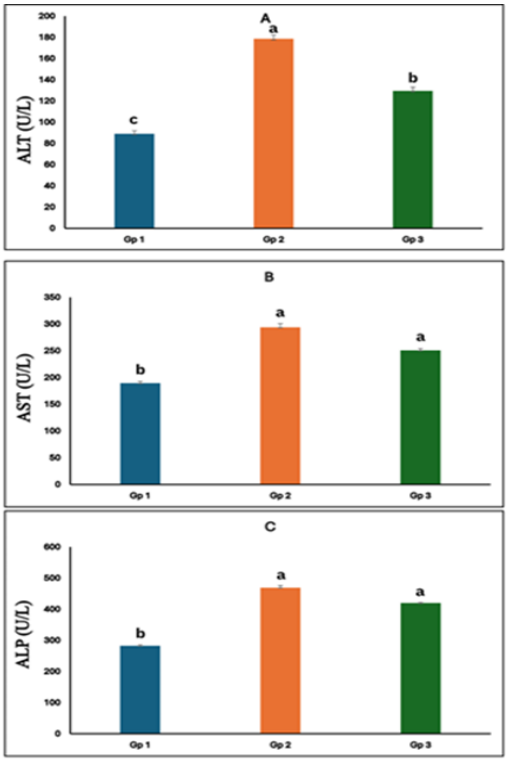

Fig. (1) (A- C): Serum levels of ALT, AST, and ALP in different groups.

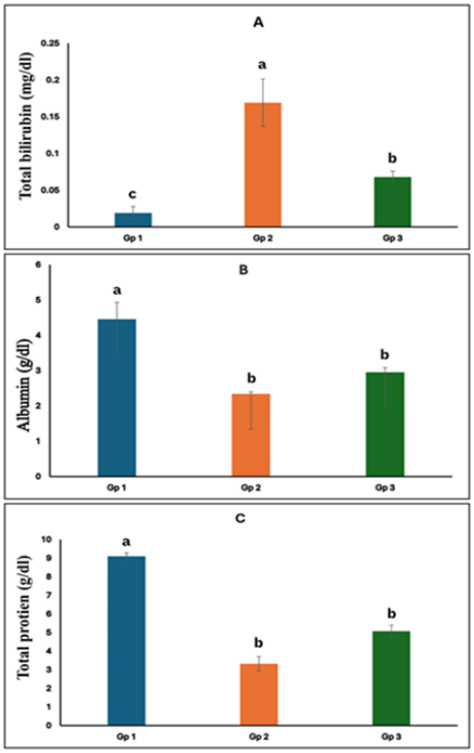

Fig. 2 (A- C): Total bilirubin, Albumin, and Total protein levels in different groups.

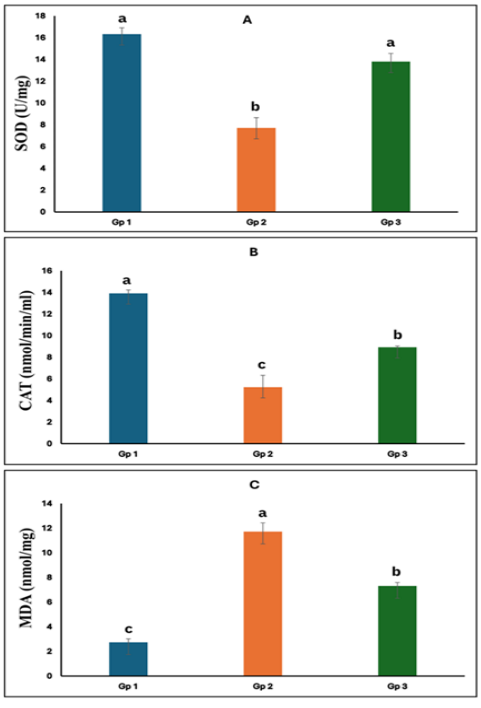

Fig. 3 (A-C): levels of SOD, CAT, and MDA

Treatment with *P. dactylifera* seed extracts ameliorated the histopathological changes

Examination of control liver sections showed the normal hepatic architecture with no histopathological changes: a normal central vein, a normal portal area, and normal radiating hepatic cords. Blood sinusoids separating hepatic cords were lined by flat endothelial cells and Kupffer cells. The polygonal hepatocytes had granular cytoplasm with central, rounded, and vesicular nuclei. Some cells appeared binucleated **Fig. (4a).** Branches of the hepatic artery, portal vein, and bile ductules could be seen at the portal tracts **Fig. (4b).**

Liver sections of the acetaminophen group exhibit severe damage in the hepatic architecture, where most hepatocytes are swollen with highly vacuolated cytoplasm and shrunken, irregular, and darkly stained nuclei surrounding the congested central vein. Blood sinusoids are hardly visible and deteriorate between the ballooned hepatocytes with interstitial hemorrhage **Fig. (4c).** The portal vein and hepatic artery are congested with oedema, and a light mixed inflammatory cell infiltrate. Vacuolated hepatocytes around the portal area are also seen **Fig. (4d)**

The treated rat group with *P. dactylifera* extracts showed slight improvement in the liver tissue, represented by reduced dilated central vein. Some hepatocytes are still affected by karyolitic or karyorrhetic nuclei and separated by slightly elongated blood sinusoids **Fig. (4e).** Portal veins appeared mildly congested, hepatocytes are regenerated in most areas with radical shape arrangement, but some still affected with pyknotic nuclei **Fig. (4f).**

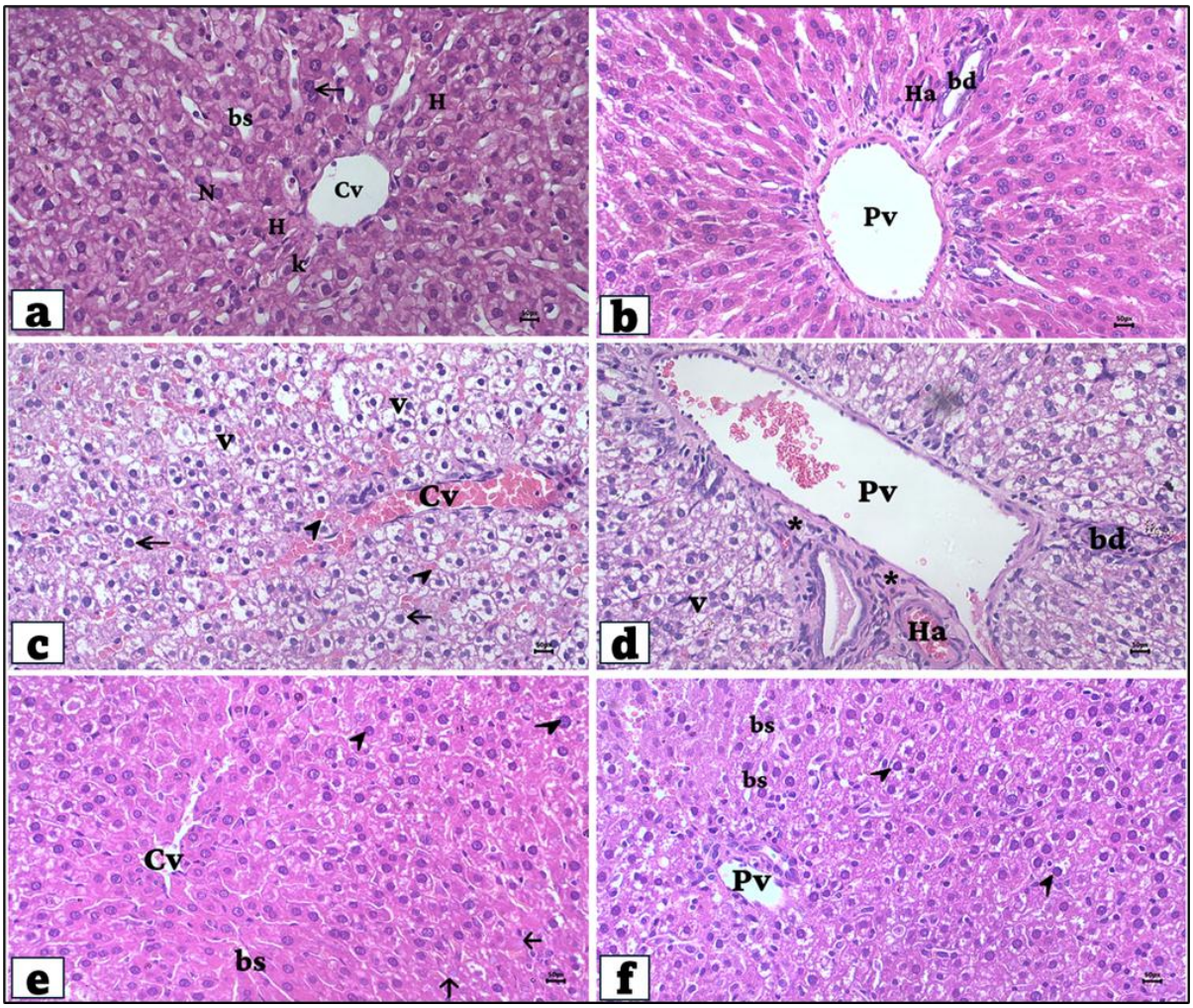

Fig. (4): Photomicrograph of liver sections of different experimental animal groups stained with H&E(X400). **a,b:** high magnified sections of control rat liver showing central vein (Cv), cords of polygonal hepatocytes (H), granular cytoplasm and central, rounded, vesicular nuclei (N). Some cells appear binucleated (arrow). Blood sinusoids (bs) are lined by flat endothelial cells and Kupffer cells (k), and the portal area shows branches of the portal vein (Pv), hepatic artery (Ha), and bile ductule (bd). **c, d:** High magnified liver sections of acetaminophen group showing disorganization of the hepatic structure, dilated and congested central vein (Cv), mostly hepatocytes are swollen with highly vacuolated cytoplasm(v) others with pyknotic nuclei (arrows), interstitial hemorrhage (arrowhead) and blood sinusoids are deteriorated, portal tract exhibits dilated and congested portal vein (Pv), congested hepatic artery (Ha). Note oedema with a light mixed inflammatory cell infiltrate (*).**e,f :** High magnified sections of liver of P. dactylifera treated group showing improvement of the hepatic structure: mild congested central vein (Cv), mostly hepatocytes are organized with normal central nuclei (N), few ones with karyolitic nuclei (arrows) and pyknotic ones (arrowheads), regular blood sinusoids (bs) and normal portal tract was observed.

Treatment with P. dactylifera seed extracts ameliorated the immunohistochemical changes

In the control group, liver sections demonstrated no reaction with P53 immuno-stain or few scattered cells exhibiting faint light brown granules in their cytoplasm **Fig. (5a-b).** In contrast, the acetaminophen group displayed strong p53 immunoreactivity in almost all hepatocytes **Fig. (5c-d) .**

P. dactylifera-treated group exhibited a weak to moderately positive reaction for p53 immunostain in the cytoplasm of some hepatocytes. **Fig. (5e-f).**

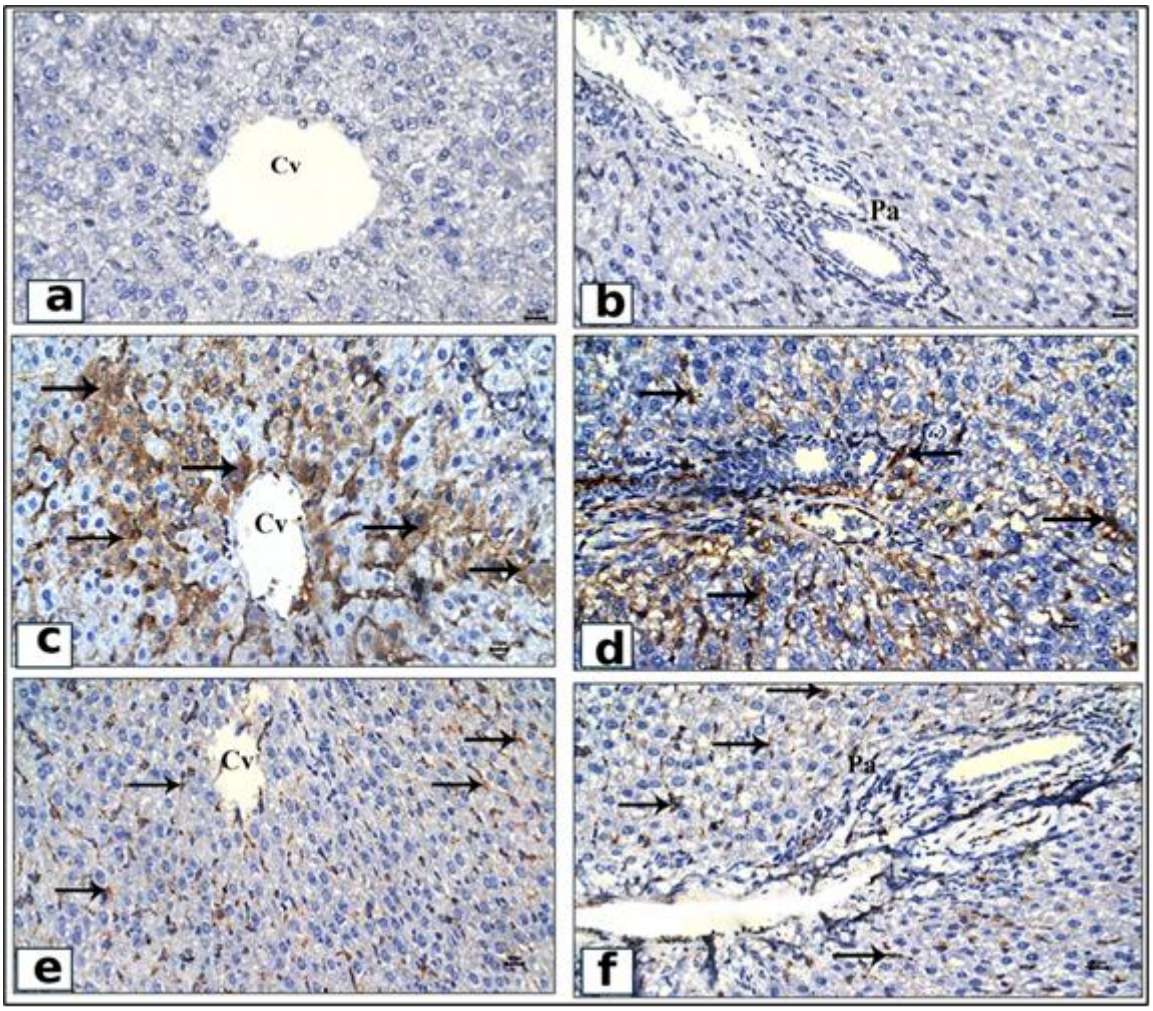

Fig. (5): Photomicrographs of liver sections stained with p53 immunostain, Hematoxylin is a counter stain (X400). **(a-b)** sections of the liver control group showing faint and few cytoplasmic reactions for p 53 immunostaining in the hepatocytes. **(c-d)** Sections of the liver of acetaminophen group showing a strong positive immunoreaction to P 53 as a dark brown in the cytoplasm of many hepatocytes (arrows). **(e-f)** p53-immunostained liver sections of P. dactylifera-treated group reveals a weak to moderate positive reaction for P 53 expression (arrows) in the cytoplasm of the hepatocytes.

Discussion

Acetaminophen is one of the safest medications available today. Due to its high consumption and being an easily accessible drug, the incidence of toxicity is quite high if taken in doses more than recommended. The primary pathway for acetaminophen toxicity is its metabolism to N-acetyl benzoquinone imine (NAPQI) via the cytochrome p-450 enzyme, which triggers hepatotoxicity by depleting glutathione. As a result, it leads to cellular necrosis in hepatocytes and sinusoidal endothelial cells, as well as inflammatory cell infiltration **(Turgut et al., 2023) .**

The preventive impacts of various natural products against acetaminophen hepatotoxicity have recently been elaborated because of their anti-inflammatory and antioxidant as well as their damage-reparative actions **(Al-Doaiss, 2020).** Dates are used in traditional medicine to treat some health problems such as gastroenteritis, cough, hypertension, tiredness, asthma, diabetes, hepatic failure, and chest pains. Date seeds are a great source of antioxidants due to their high phenolic and flavonoid content as well as vitamin C concentration **(Moni et al., 2024).** The current study was performed to appraise phytochemicals of *P. dactylifera* seed extracts by using the GC-MS technique and assessing its protective effect against hepatotoxicity induced by acetaminophen in rats .

Date seeds contain essential phytochemicals, such as fiber, phenolics, fatty acids, and amino acids **(Alkatheri et al., 2024).** GC-MS analysis results showed the presence of various phytochemical components like hexadecenoic acid-methyl ester and methyl stearate, which have potent antioxidants and anti-inflammatory activities **(Shahin et al., 2022).** The results were parallel to the tests by **Alkhalidy (2023)** who found that date seed oil contains some alkanes, fatty acids, aldehydes, fatty alcohols, and amides.

Compared with the normal control group, administration of acetaminophen resulted in a decrease in the rats' body weight. These findings agreed with the previous study conducted by **Abd-Elrahman and Abd Allah (2020).** The decrease might be due to oxidative stress and reactive oxygen species generated from hepatotoxicity, altered liver metabolism, and other liver diseases. Also, it turns out that liver diseases led to anorexia, early satiety, nausea, maldigestion, malabsorption, and abnormalities in the metabolism and storage of macro- and micronutrients, which finally resulted in marked malnutrition **(Fuente, 2022) .**

The treated group's body weight significantly improved, which could be attributed to the fact that *P. dactylifera* seeds may operate as antioxidants, free radical scavengers, and anti-inflammatory agents **(Eltahir, 2024).** The findings were consistent with **(Abd El Latif et al., 2021),** who investigated treatment with natural products that protect experimental animals from losing weight.

In the current study, administration of acetaminophen resulted in a significant increase in the following hepatic enzymes (ALT, AST, ALP), besides an increase in total bilirubin when compared to the healthy control group. On the other hand, acetaminophen administration caused a decrease in total protein and albumin together. The elevated levels of hepatic enzymes may

be attributed to their leakage from the cells through the blood to adjust the transport functions and membrane permeability **(Abdel-Fatah and El-Sayed, 2023).** While the disturbance of protein synthesis due to altered hepatic functions or inflammation leads to increased levels of total bilirubin with reduced total protein and albumin levels **(Salah and El-Sayed, 2023).** Similar findings were mentioned by **Fakher Eldeen et al. (2022)** and **Eltahir et al. (2023)**

Treatment with *p. dactylifera* extracts efficiently protected the rats against acetaminophen toxicity by lowering ALT, AST, and ALP enzyme levels and total bilirubin while raising albumin and total protein levels. Normalization of serum biomarkers may be attributed to the possibility of Phoenix extracts to maintain the hepatocellular membrane's structural integrity, which prevents intracellular enzyme leakage **(Bouhlali et al., 2021).** Our results are consistent with **El-Naggar et al., (2023)** and **Eltahir et al., (2023).**

SOD and CAT are significant antioxidant enzymes that operate as the first line of defense against oxidative damage, scavenging reactive oxygen species, reducing hydrogen peroxide, and preserving redox balances in biological systems. MDA is a typical biomarker for assessing oxidative stress levels in cells and tissues, where elevated levels imply increased oxidative damage to cell membranes and lipids **(Yener et al., 2024).** Based on the current investigation, rats that received acetaminophen experienced a major decrease in CAT and SOD activities, together with a critical increase in MDA concentration in comparison to the control group. The decreased activities of CAT and SOD enzymes were related to their increased utilization in scavenging and neutralizing free radicals and lipid peroxides **(Abd-Elrahman and Abd Allah, 2020).** Meanwhile, reactive oxidative stress assaults polyunsaturated fatty acids and disrupts cell membranes, which induce oxidative lipids and form MDA **(Abd El Fadil et al., 2019).** Similar findings were mentioned by **Amer et al. (2023),** who observed that the administration of acetaminophen caused a reduction of antioxidant enzymes (CAT and SOD) while increasing MDA .

The results demonstrated that the administration of *P. dactylifera* seed extracts displayed an increase in CAT and SOD activities with a reduction in MDA concentration when compared with the acetaminophen group, which could be attributed to its phytochemical contents that act both intracellularly and extracellularly to combat free radical damage **(Agbon et al., 2025).** These results were also consistent with (**Ghania and Djahra, 2023),** who studied the antioxidant capacity of *P. dactylifera* seeds on hepatotoxicity in rats.

Histopathological assessment is a strong diagnostic tool with a wide scope of use in pretty much every area of life sciences and allows the proof of the changes to the living tissues and possibly their etiological agent that can’t be recognized or affirmed with the unaided eye **(Johnson, 2022).** Histopathologic studies were consistent with the results of the biochemical parameters measured in our study. Histological examination of rat liver receiving acetaminophen showed significant hepatic injury as

indicated by vacuolar degeneration of hepatocytes, sinusoidal disorganization with interstitial hemorrhage, dilated, congested central vein, and portal venule with nearby inflammatory cell infiltration. These pathological alterations were similar to the findings of **El-Araby et al. (2022)** and **Nouioura et al. (2023),** who studied the impact of acetaminophen on liver toxicity .

The results reported therapeutic effects of *P. dactylifera* extracts, represented by improvement of hepatic structure, slightly widening blood sinusoids, and less congestion of the portal and central veins, but fewer numbers of hepatocytes were still affected with karyolitic and pyknotic nuclei. Along those lines, P. dactylifera extracts influence the histological alterations, as they are rich in amino acids, vitamins, minerals, and phytochemicals like rutin, flavonoids, and phenolic substances that have antioxidant activity. Similarly, these phytochemicals were demonstrated to have hepato- and nephroprotective properties in animal models **(Al-Asmari et al., 2020). (Gad El-Hak et al., 2022)** reported the same effect of P. dactylifera seeds extract ameliorating cisplatin-induced hepatic injury in male rats.

Histological evaluation with hematoxylin and eosin stains and many others is important. However, histological assessment alone cannot provide a definitive diagnosis in some circumstances. So, in this instance, the immunohistochemical technique is used due to its diverse applications, ease of performance and evaluation, and affordability **(Takahashi et al., 2021).** p53 IHC is now a commonly utilized diagnostic technique as it is frequently applied in clinical cases **(Aswathi et al., 2024).** In the current investigation, examination of control liver sections showed a few to the absence apoptotic cells and very little cytoplasmic p53 expression. In contrast, the acetaminophen group displayed strong p53 immunoreactivity in almost all hepatocytes .

P53 immunoreactivity in liver sections of rats treated with *P. dactylifera* showed modest positive responses in the cytoplasm of some cells. The results agreed with **Diab et al. (2020),** who noticed that the restitution of the liver's architecture has been correlated with decreasing the p53 expression, explaining that natural extracts manifested their hepatoprotective impact through the suppression of inflammation and oxidative stress .

Conclusion

In conclusion, these results showed that treatment with *P. dactylifera* seeds significantly ameliorated acetaminophen side effects.

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الدور التحسيني المحتمل لمستخلصات بذور البلح ضد السمية الكبدية الناجمة عن الأسيتامينوفين في الجرذان

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الأسيتامينوفين أو ما يعرف تجاريًا بإسم الباراسيتامول هو عقار يستخدم كمسكن للألم وخافض للحرارة.على الرغم من أن الأسيتامينوفين يُعتبر آمنًا جدًا عند تناوله بجرعات مناسبة (٤ غرامات يوميًا)، إلا أنه قد يؤدي إلى بعض المشاكل الصحية عند تناوله بجرعات زائدة مثل الإجهاد التأكسدى أو تسمم الكبد والكلى. تهدف هذه الدراسة إلى تحديد الدور الوقائي المحتمل لمستخلصات بذور البلح ضد الُسمية الكبدية التي قد يسببها الأسيتامينوفين فى الجرذان . وتم التعرف على المركبات النشطة بيولوجيًا لبذور البلح باستخدام تقنية كروماتوغرافيا الغاز-مطياف الكتلة .قُسِّمت الجرذان إلى ثلاثة مجموعات، كل مجموعة تضم عشرة جرذان: المجموعة الأولى (المجموعة الضابطة) ، المجموعة الثانيه تم حقنها بالأسيتامينوفين يوميًا (٧٥٠ ملغ/كغ). أما المجموعة الثالثة فقد حُقِنت بمستخلصات بذور البلح (٢٠٠ ملغ/كغ) بعد حقنها بالأسيتامينوفين لمدة شهر (٧٥٠ ملغ/كغ يوميًا). أثناء الدراسة تم قياس كل من: وزن جسم الجرذان المبدئى والنهائى، وظائف الكبد،ونشاط الإنزيمات المضادة للأكسدة. أظهرت نتائج كروماتيغرافيا الغاز لدى مستخلصات بذور البلح الى وجود مكونات كيميائية نباتية مختلفة لها مضادات أكسدة قوية وأنشطة مضادة للالتهابات. أدى إعطاء الأسيتامينوفين الى انخفاض الوزن النهائي لجسم الجرذان، بينما المجموعة المعالجة بواسطه بذور البلح فقد ازداد وزنها بشكل طفيف. أما بالنسبة للإختبارات الكيميائية الحيوية فقد أدى إعطاء الأسيتامينوفين الى حدوث تغيرات ملحوظة فى كلًا من وظائف الكبد ونشاط الإنزيمات المضادة للأكسدة بينما شهدت المجموعة المعالجه بالبلح تحسنًا فى كليهما.وقد دعم الفحص النسيجي والفحص النسيجي الكيميائي المناعي النتائج السابقة.وأشارت الدراسة فى النهاية إلى ان مستخلصات بذور البلح لها تأثيرًا علاجيًا ووقائيًا فعالًا ضد سمية الكبد الناتجة عن الأسيتامينوفين لدى الجرذان.