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# The Impact of *Aqueous Ethanol Extract of Acacia Pennata* Leaves on Fructose-Induced Fatty Liver in Rats

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## Abstract

NON-ALCOHOLIC fatty liver disease (NAFLD) affects nearly 50% from globe; from both adults and children due to wrong nutritional practices and lack of awareness. Untreated NAFLD can be worsened to end in liver cancer. However fatty liver can be reversed by lifestyle modifications. The aim of our study was to evaluate the efficacy of *Acacia pennata* leaves extract (APLE) in improving liver insults due to NAFLD induced in rats by feeding them high fructose diet for 12 weeks. Thirty male adult rats were divided into 5 groups of 6 rats each. Oral daily intervention for treating induced NAFLD started from the 9$^{th}$ week till the end of the experiment using APLE (250 mg/kg); that was compared with metformin (100 mg/kg) or combination of metformin (100 mg/kg) with APLE (250 mg/kg). At the end of the experiment rats were anaesthesized and serum was separated. Different biochemical parameters in serum were measured spectrophotometrically. Combinatory intervention of APLE with metformin was the best in preventing the progression of NAFLD. Significant improvements in serum glucose, insulin, insulin resistance and lipid profile (TG, TC, LDL-c and HDL-c) were noticed. Liver enzymes were also significantly decreased relative to the diseased group. Serum uric acid and liver contents of TG, TC and MDA (lipid peroxidation product) were significantly decreased; while superoxide dismutase was significantly increased. Other groups showed significant improvements but less than the group that received combinatory intervention. Histopathological examination of liver tissue confirmed the biochemical results.

**Keywords:** glucose, insulin, lipids, antioxidants and *Acacia pennata*.

## Introduction

Liver is the largest organ in the body and the main organ in metabolism. Fatty liver (Bright liver) can be diagnosed due to the yellow fat accumulation in it; in which fat represents more than 5% of the liver content. Non-alcoholic fatty liver disease (NAFLD), recently renamed metabolic dysfunction-associated steatotic liver disease, affects almost 38% of adults and around 13% of adolescents and children. Excess fat accumulation in liver if not reversed; can affect liver efficiency, progress to steatosis, then inflammation seen in non-alcoholic steatohepatitis then fibrosis, cirrohosis and may ultimately end up to hepatic cancer [1,2]. Fructose overconsumption was proven to induce fatty liver. Fructose is a lipogenic sugar, that elevates blood lipid profile and contributes to fatty liver. Since the liver is the main organ in lipid metabolism and fructose metabolism, then the deposition of lipid droplets in hepatocytes is the main step in the pathogenesis of NAFLD. Fructose is widely used in food industries [3]. People used to eat a lot of fruits and honey may also at risk of developing fatty liver. Over the past decades, fructose, which was thought to be beneficial in diabetic diets [4], has been reevaluated based on the results of experimental and clinical research. Fructose has been studied in the context of various

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liver diseases in rodents over many years. Fructose is involved in the pathogenesis and severity of NAFLD and its associated features of metabolic syndrome (MS) such as hyperglycemia, hyperinsulinemia, insulin resistance, hyperlipidemia, low HDL-C, hyperuricemia, and oxidative stress [5,6].

Remedy from food sources is preferred to complement drug action; helping in decreasing drug dose and side effects. *Acacia pennata*, recently renamed as *Senegalia pennata*, is a species that belongs to the Fabaceae family [7] and is a wild leafy vegetable with a wide variety of macro and micronutrients. Additionally, it has been cultivated in home gardens for culinary, medicinal, and cultural purposes [8]. Different activities of *A. pennata in-vitro* and *in-vivo* studies have been determined, including anti-inflammatory, reducing lipid digestion, lowering blood pressure, antioxidant, anticancer and antidiabetic [9, 10]. However, to the best of our knowledge, there are no studies on the effect of the plant in treatment of NAFLD. Our investigation aimed to evaluate the efficacy of APLE in the treatment of fatty liver in rats induced by feeding them a high fructose diet.

## Material and Methods

### *Animals*

Thirty adult male albino rats (Sprague Dawley strain), weighing about (118 – 156g) were housed in polypropylene cages at ambient temperature 25°C ± 2, with 12h light/dark cycle. As bedding material, clean wood shaving is given. Food and water were supplied *ad libitum* and left to acclimatize for one week before starting the experiment.

### *Methods*

#### *Plant Identification*

*Acacia Pennata* leaves were identified by Mrs. Therese Labib Youssef; an expert in plant taxonomy at Ministry of agriculture and El-orman Botanical garden Herbarium; Egypt.

#### *Extract preparation*

*Acacia pennata* hydro-alcohol extract; water/ethanol (30/70 by volume) was prepared according to previous method [11]. Powdered dried leaves (500 g) were soaked overnight in 1.5 L aqueous ethanol. The suspension was filtered and the residue was re-suspended for 48 hours in another 1.5 L aqueous ethanol and then filtered. The two extracts were pooled and the solvents were evaporated in a rotary evaporator at 40℃ under reduced pressure to obtain a dark green thick extract.

#### *Extract and drug preparation for animals' administration*

APLE and metformin drug solutions were freshly prepared by dissolving in distilled water each time before oral dosing using stomach tube. Control groups were given only distilled water as a vehicle.

#### *Diets formulation*

Two diets were prepared, a basal diet and a high fructose diet (HFD) as shown in Table (1). HFD used for NAFLD induction was prepared according to Nakagawa et al. by adding 60% fructose [12]. The diets were prepared each week and stored at a temperature of 3–4°C.

#### *Experimental design*

After adaptation period, animals were divided into five groups of six rats each, G (1) served as the normal control (NC), was fed on the basal diet for 12 weeks, and was given the daily oral dose of the vehicle for the last 4 weeks; All the other groups were fed on HFD for 12 weeks but received different interventions for the last 4 weeks for comparative study: G (2) served as the positive control (PC), was given the vehicle; G (3) received per oral metformin (100 mg/kg/day) as an insulin sensitizer [13]; G (4) received per oral APLE (250 mg/kg/day) according to Maulana et al. [14]. G (5) received a combinatory intervention as a per oral metformin drug (100 mg/kg/day) followed by APLE (250 mg/kg/day).

#### *Samples collection*

At the end of the experimental period (12 weeks), rats were fasted overnight and blood samples were withdrawn from light ether inhaled rats and serum was separated by centrifugating blood at 3000 r.p.m for 15 min. Serum glucose was measured at the same day. Rats were euthanized by cervical decapitation and dissected; portions of livers were kept in 10% formalin for histopathological examination [15]. Other liver portions were manually homogenized in 5 ml cold buffer (i.e., 50 mM potassium phosphate, pH 7.5)/1g tissue, centrifuged at 4000 r.p.m for 15 min, then both the supernatant and the rest of serum were kept at temperature –20° C for further biochemical analysis.

#### *Serum Biochemical Analysis*

Serum glucose; insulin (rat-specific ELISA kit from RayBio® (Norcross, GA, USA), lipid profile (Triglycerides (TG), Total cholesterol (TC), Low density lipoprotein-cholesterol (LDL-c) and high density lipoprotein cholesterol (HDL-c)), liver enzymes (Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), and Alkaline phosphatase (ALP)) and uric acid were determined spectrophotometrically according to the manufacturer's instructions (Biodiagnostic®; Egypt).

Insulin resistance was calculated using the homeostasis Model Assessment of insulin resistance (HOMA-IR) according to Matthews et al. [16]:

$$\text{HOMA-IR} = \frac{\text{Serum glucose (mmoL/L)} \times \text{Serum insulin (μIU/mL)}}{22.5}$$

*Hepatic Biochemical Testing*

Hepatic TG and TC were determined colorimetrically using commercial kits purchashed from . Malondialdehyde (MDA) and superoxide dismutase (SOD) activities were estimated according to Yoshioka et al.[17] and Minami and Yoshikawa [18], respectively.

*Statistical analysis*

*Re*sults were reported as Mean ± standard error (SE). SPSS software (version 27) was used and one-way analysis of variance (ANOVA) test was performed followed by LSD test to determine the statistical significance of the difference according to Snedecor and Cochran [19]. The significance level was set at $P<0.05$.

## Results

*Serum glucose, insulin and insulin resistance (HOMA-IR)*

Rats in G2 showed significantly higher fasting serum glucose and insulin levels and severe insulin resistance than all other groups. Those on HFD who were treated with metformin and *A. pennata* extract, each alone or combined in the last month, had obviously lower levels in the aforementioned biomarkers compared to those on HFD alone. The glucose levels of all treated rats and IR value of rats on combinatory intervention were statistically similar to those of the NC (Table 2).

*Serum and Hepatic lipid profile*

Table 3 showed that fructose intake significantly affected all levels of the serum lipid profile after 12 weeks, such that rats fed on high-fructose diet alone (PC) had significantly higher TG, TC and LDL-C and lower HDL-C concentrations compared to NC on normal feed and all HFD-treated groups. Treatment with metformin and APLE, either alone or combined, induced amelioration noticeably in these biomarkers (with different degrees in some) relative to PC. From shown results, the best improvement was achieved in the combinatory intervention. Hepatic TG and TC were markedly higher in the rats that were fed a fructose-rich diet (PC) compared to (NC) after 12 weeks. Significant decreases in hepatic TG and TC levels were observed in all treated groups compared to the PC. This improvement in the treated groups was statistically gradual as noticed in TG levels, and TC was the best in the last treated group.

*Oxidative/antioxidant stress markers*

Regarding the lipid peroxidation state in the liver, High-fructose diet in (PC) induced a significant elevation in the hepatic MDA content relative to NC. *Acacia* extract, metformin and a combination of them prevented fructose-induced oxidative stress by reducing MDA levels as compared to the non-treated HFD group. Conversely, rats in PC showed significantly lower hepatic SOD activity than NC. Rats on all treatments had obviously higher activity of SOD compared to non-treated HFD rats. The best improvement in hepatic antioxidant status belonged to treatment with metformin plus *Acacia* extract. Serum uric acid was significantly elevated in all HFD fed rat groups compared to NC. However there was a significant difference in serum uric acid levels among HFD fed rat groups themselves. PC group had the highest uric acid levels; while treatment with metformin plus *Acacia* extract significantly decrease uric acid levels than all other groups (Table 4).

*Liver enzymes*

Addition of 60% fructose to the diet for 90 days significantly increased rats' AST, ALP and ALT as compared to NC. Rats on the treatments (metformin and *Acacia* extract, each alone or combined) had marked improvement in all the mentioned parameters than the untreated group. The best beneficial effect on hepatorenal parameters was reached at the treatment with combined metformin and *acacia* extract (Table 5).

*Histopathological examination of liver*

Our histopathological results indicated that the combinatory intervention of metformin with APLE was the best in prevention of hepatic steatosis and inflammation, and alleviation of most of the liver lesions induced by high-fructose diet, thus protecting from the development and progression of NAFLD. Histopathological examination of liver tissue confirmed the biochemical results.

## Discussion

This study investigated the potential beneficial role of the hydroethanolic APLE on NAFLD induced by feeding HFD to rats. Feeding of a 60% fructose diet to rats for 12 weeks resulted in the development of hepatic insults; resulted from significantly higher levels of metabolites: serum glucose, insulin, TG, TC, LDL-C, AST, ALT, ALP, uric acid, hepatic fat and MDA content, and IR. While hepatic SOD activity and serum HDL-C were significantly lower than normal control rats. Conversely, amelioration of all these serum/hepatic biochemicals was much seen as HFD rats treated with metformin + APLE > metformin = APLE. While, histologically, improvement was as follows: HFD rats treated with metformin + APLE > metformin > APLE. Overall, we found that treating NAFLD rats with metformin plus APLE produced pronounced therapeutic effect.

Although fructose intake does not trigger insulin release from pancreatic beta-cells, resulting in lesser postprandial insulin than glucose, it eventually, over time, causes a decrease in insulin sensitivity, hyperinsulinemia, hyperglycemia, and insulin resistance. Insulin resistance is a state where body needs more insulin to maintain normal blood glucose levels. Long-term (> 4 weeks) consumption of a high-fructose (60%) diet caused marked increases in fasting glucose and insulin levels and HOMA-IR, which were well documented in earlier studies [20] and confirmed in the present study. Nonetheless, other studies have shown no significant change was found in glucose [21] and insulin [22] levels of HFD groups related to the control group, while HOMA-IR was indicated in all these studies.

On the other hand, since hepatic pathology can affect insulin action, hepatic *de novo* lipogenesis generates toxic metabolites that may induce insulin resistance [23]. This implies that hyperglycemia and hyperinsulinemia observed in the HFD rats are linked to IR, which was further indicated by the elevated HOMA-IR value.

Maulana et al. found that methanolic leaf extract of *A. pennata* at doses of 125, 250, and 500 mg/kg over 15 days has a hypoglycemic activity in diabetic male Sprague Dawley mice [14]. The best reduction was at the 250 mg/kg dose. They clarified that secondary metabolites in the extract attributed to the blood glucose lowering effect and acting as antioxidants that reduce oxidative stress, thereby delaying the disease complications. *A. pennata*, the leafy vegetable, has been reported as a good source of different bioactive compounds (identified/isolated) ranging from flavonoids like quercetin, to vanillin [10, 24]. In another study by Shao et al., diabetic rats treated with ethanolic (70%) extract of *A. pennata* aerial parts (100 and 400 mg/kg) for 4 weeks resulted in a dose-dependent and marked decrease in the fasting blood glucose levels [25]. Further, Abdallah et al. investigated *in-vitro* the antidiabetic effect of APLE and their findings demonstrated a great inhibitory activity against α-amylase and α-glucosidase which slow down the digestion of carbohydrates; thereby decreasing hyperglycemia, pointing out that this effect may be related to the phenolic content of the plant [10].

Previous studies showed that a fructose-enriched diet in rodents is associated with dyslipidemia, which is also indicated in our study [26, 27]. The relationship between high dietary fructose and hypertriglyceridemia has been revealed, showing different mechanisms [28, 29].

In this work, we have observed that APLE significantly lowered serum TG, TC and LDL-C, while HDL-C levels increased. These results agreed with Shao et al. [25]. Additionally, Muhlishah et al. found that giving hypercholesterolemic male mice APLE methanolic extract at various doses (100, 250, and 500 mg/kg body weight) for two weeks significantly reduced TC, supposing that the mechanism of action was via its antioxidant ability due to presence of flavonoids, tannins, and saponins [30].

In our study, 60% fructose diet fed to rats resulted in a significant liver fat deposition, which, by histological examination appeared as steatosis with other steatosis-related liver injuries (Table 6 & Fig. 1), along with a substantial increase in the hepatic TG and TC (Table 3). These findings agree with those of Ackerman et al. and Zaki et al., who used 60 and 55% high-fructose diets, respectively [21, 26].

Additionally, the other major cause of liver injury is oxidative stress (OS), a consequence of increased hepatic fat accumulation caused by fructose [31]. Crescenzo et al. clarified that long-term HFD in rats resulted in increased ectopic fat accumulation and hepatic oxidative damage along with a decrease in the antioxidant status [32]. This was confirmed in this study by the higher oxidant and lower antioxidant markers, respectively, MDA and SOD in the liver of HFD rats than those in the control group (Table 4), indicating OS. This result agrees with that of El-Mehi and Faried [33]. Uric acid is one of the metabolites; that result from frucotse intake and it can work as either pro-oxidant or antiooxidant (34, 35). Serum uric acid was significantly lower in all treated groups than fructose fed control group. This result was agreed with Zhang et al. who stated that natural compounds can decreased uric acid levels by suppression of enzymes in the uric acid synthetic pathway as xanthine oxidoreductases (36). However, in our study, treatment with metformin plus APLE showed beneficial and antioxidant effects on alleviating both hepatic fat content and OS, accompanied by significant improvements in the liver cell morphology (Table 6 & Fig. 1). According to earlier studies, *Acacia pennata* extracts showed antioxidant effects and noticeably protected liver cells in acetaminophen-treated rats and pancreas of diabetic rats from OS [25, 37]. Additionally, different antioxidant activity assays using *Acacia pennata* extracts were employed, displaying high antioxidant activity, which could be attributed to its high total phenolic content [9].

Polyphenols are associated with amelioration in various MS components associated with NAFLD through their antioxidant, anti-inflammatory effects, and improve metabolism of carbohydrate and lipid [38,39].

Combined treatment using polyphenols with medications, such as insulin sensitizing agents are promising in enhancing liver function in NAFLD. Additionally, the dose of the drug can be reduced [39], thereby reducing its adverse effects [27, 40]. Metformin, an insulin sensitizer, was able to reverse aspects of MS, decrease hepatic steatosis and apoptosis, and improve liver biochemistry in HFD rats. These results correlated with those of Karise et al. [40]. Taken together, this can account for our findings, which indicated that the treatment with metformin plus APLE, even in the constantly administrated HFD, showed the most pronounced therapeutic and protective effects. This combination effectively helps to prevent the progression of NAFLD to its more severe form.

## Conclusion

Our experimental data clearly showed that APLE was efficient in attenuating rats′ liver insults as seen in histopathological photomicrographs, as well as improving insulin sensitivity, hyperinsulinemia, and dyslipidemia induced by HFD. Liver oxidative stress markers and enzymes also significantly improved. More pronounced effect was seen when APLE was taken in adjunct to metformin.

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This study did not receive any external funds.

*Declaration of Conflict of Interest*

The authors declare that there is no conflict of interest.

*Ethical approval:*

This study was approved by Medical Research Ethics Committee, National Research Centre (NRC), Dokki, Egypt (**Approval No. 08420424**). Animal procedures were performed in accordance with the guidelines and recommendations of ethics Committee of NRC, Egypt, and Institutional Animal Care and Use Committee (IACUC).

**TABLE 1. Composition of experimental diets (g/100g).**

| Component | Basal diet | Fructose diet |
|---|---|---|
| Casein (80% protein) | 12.3 | 12.3 |
| Corn oil | 10 | 10 |
| Salt mixture | 3.5 | 3.5 |
| Vitamin mixture | 1 | 1 |
| Methionine | 0.18 | 0.18 |
| Choline chloride | 0.06 | 0.06 |
| Cellulose | 5 | 5 |
| Fructose | - | 60 |
| Corn starch | Up to 100 | Up to 100 |

**TABLE 2. Effect of APLE alone/ or with metformin on serum glucose and insulin in HFD fed rats.**

| Groups | Glucose (mmol/L) | Insulin (µIU/m) | HOMA-IR |
|---|---|---|---|
| **G1** | $3.22 \pm 0.34^{ac}$ | $80 \pm 0.73^{a}$ | $11.45^{a}$ |
| **G2** | $5.81 \pm 0.29^{b}$ | $130 \pm 0.81^{b}$ | $33.57^{b}$ |
| **G3** | $3.83 \pm 0.29^{a}$ | $101 \pm 1.17^{cd}$ | $17.19^{cd}$ |
| **G4** | $4.02 \pm 0.26^{a}$ | $103 \pm 1.27^{c}$ | $18.40^{d}$ |
| **G5** | $2.53 \pm 0.43^{c}$ | $99 \pm 1.01^{d}$ | $11.13^{ac}$ |

Values are expressed as mean± SE (n=6). Significance was calculated at $P<0.05$ within columns where different letters indicate statistical significance. (G1): normal control; (G2): positive control; (G3): group fed on HFD and treated with metformin (100mg/kg); (G4): group fed on HFD and treated with APLE (250mg/kg); (G5): group maintained on HFD and treated with both metformin (100mg/kg) and APLE (250mg/kg). (HOMA-IR) Homeostasis Model Assessment for Insulin resistance

**TABLE 3. Effect of APLE alone/ or with metformin on serum and hepatic lipids in HFD fed rats.**

| Parameter | G1 | G2 | G3 | G4 | G5 |
|---|---|---|---|---|---|
| **Serum lipid profile** (mg/dl) | | | | | |
| TG | 131 ± 1.65 [a] | 251 ± 1.12 [b] | 172 ± 1.27 [c] | 166 ± 1.51 [d] | 161 ± 1.09 [e] |
| TC | 136 ± 1.65 [a] | 214 ± 6.62 [b] | 174 ± 1.51 [c] | 172 ± 2.11 [c] | 169 ± 0.81 [c] |
| LDL-C | 64 ± 2.69 [a] | 134 ± 5.43 [b] | 107 ± 1.53 [c] | 106 ± 2.28 [c] | 99 ± 1.61 [c] |
| HDL-C | 46 ± 1.35 [a] | 27 ± 0.54 [b] | 33 ± 1.25 [c] | 32 ± 0.65 [c] | 37 ± 0.86 [d] |
| **Liver tissue** | | | | | |
| TG (mg/g tissue) | 9.12 ± 0.11 [a] | 13.98 ± 0.12 [b] | 12.08 ± 0.13 [c] | 11.63 ± 0.18 [d] | 10.63 ± 0.20 [e] |
| TC (mg/g tissue) | 5.02 ± 0.11 [a] | 8.85 ± 0.15 [b] | 6.32 ± 0.16 [c] | 6.45 ± 0.16 [c] | 5.78 ± 0.13 [d] |

Values are expressed as mean± SE (n=6). Significance was calculated at $P<0.05$ within rows where different letters indicate statistical significance. (G1): normal control; (G2): positive control; (G3): group fed on HFD and treated with metformin (100mg/kg); (G4): group fed on HFD and treated with APLE (250mg/kg); (G5): group maintained on HFD and treated with both metformin (100mg/kg) and APLE (250mg/kg). (TG) triglyceride; (TC) total cholesterol; (LDL-C) low density lipoprotein cholesterol; (HDL-C) high density lipoprotein cholesterol.

**TABLE 4. Effect of APLE alone/ or with metformin on oxidative stress markers in HFD fed rats.**

| Groups | MDA (ng/g tissue) | SOD (U/mg protein) | Uric acid (mg/dl) |
|---|---|---|---|
| **G1** | 87 ± 1.39 [a] | 84 ± 1.45 [a] | 2.6 ± 0.14[a] |
| **G2** | 137 ± 1.44 [b] | 52 ± 0.92 [b] | 4.3 ± 0.010 [b] |
| **G3** | 111 ± 2.00 [c] | 62 ± 0.72 [c] | 3.4 ± 0.12 [c] |
| **G4** | 113 ± 1.98 [c] | 63 ± 1.47 [c] | 3.3 ± 0.11 [cd] |
| **G5** | 108 ± 3.52 [c] | 71 ± 1.29 [d] | 3.0 ± 0.08 [d] |

Values are expressed as mean± SE (n=6). Significance was calculated at $P<0.05$ within rows where different letters indicate statistical significance. (G1): normal control; (G2): positive control; (G3): group fed on HFD and treated with metformin (100mg/kg); (G4): group fed on HFD and treated with APLE (250mg/kg); (G5): group maintained on HFD and treated with both metformin (100mg/kg) and APLE (250mg/kg). (MDA) malondialdehyde; (SOD) superoxide dismutase.

**TABLE 5. Effect of APLE alone/ or with metformin on Liver enzymes activity (IU/L) in HFD fed rats.**

| Groups | AST | ALP | ALT |
|---|---|---|---|
| **G1** | 29 ± 0.50 [a] | 65 ± 1.56 [a] | 24 ±1.09 [a] |
| **G2** | 46 ± 0.96 [b] | 100 ± 1.81[b] | 40 ± 0.61 [b] |
| **G3** | 36 ± 0.45 [cd] | 83 ± 1.55 [c] | 30 ± 0.77 [cd] |
| **G4** | 37 ± 0.48 [c] | 85 ± 1.76 [c] | 31 ± 0.52 [c] |
| **G5** | 35 ± 0.32 [d] | 80 ± 0.61 [c] | 28 ± 0.57 [d] |

Values are expressed as mean± SE (n=6). Significance was calculated at $P<0.05$ within columns where different letters indicate statistical significance. (G1): normal control; (G2): positive control; (G3): group fed on HFD and treated with metformin (100mg/kg); (G4): group fed on HFD and treated with APLE (250mg/kg); (G5): group maintained on HFD and treated with both metformin (100mg/kg) and APLE (250mg/kg). (AST) Aspartate aminotransferase; (ALP) Alkaline phosphatase; (ALT) Alanine aminotransferase.

**TABLE 6. Liver Histopathological Scoring of the studied rats.**

| | Portal tract | | | | | Peri-venular area | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **PT** | **PV** | **Apoptosis** | **Steatosis** | **Inflamm infiltrate** | **CV** | **Apoptosis** | **Steatosis** | **Inflamm Infiltrate** |
| **G1** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **G2** | + | + | + | 0 | + | ++ | ++ | + | 0 |
| | + | 0 | + | ++ | + | 0 | + | ++ | 0 |
| **G3** | + | + | 0 | 0 | + | ++ | + | + | 0 |
| **G4** | + | + | + | + | + | ++ | + | + | 0 |
| **G5** | 0 | + | + | 0 | 0 | + | + | 0 | 0 |

(PT) portal tract: (0): Average, (+): Mildly edematous/mild inflammatory infiltrate, (++): Markedly edematous.
(PV) portal vein and (CV) central vein: (0): Average, (+): Mildly dilated/congested, (++): Markedly dilated/congested.
Apoptosis: (0): No, (+): Scattered/mild, (++): Moderate/marked.
Steatosis: (0): No, (+): Scattered/mild, (++): Moderate/marked.
Inflammatory infiltrate: (0): No, (+): Mild, (++): Moderate/marked.

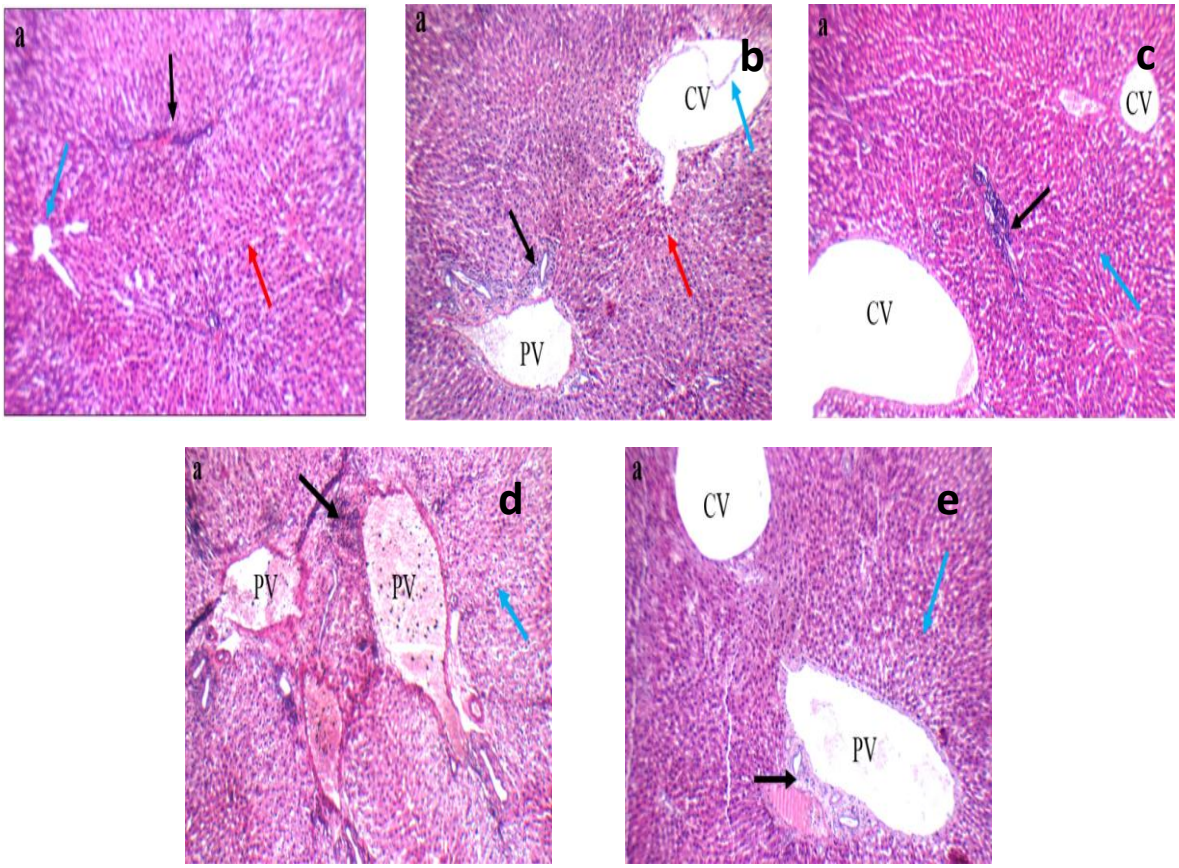


**Fig.1. Photomicrographs of hematoxylin and eosin stained sections of studied rats livers under 200X standard light magnification.**

Fig. 1. Representative liver sections from experimental groups stained with H&E (X200).
(a) G1: Liver showed normal hepatocytes; normal portal tracts, and normal central vein (CV).
(b) G2: Liver showed portal tracts with mild portal inflammatory infiltrate and mildly dilated portal vein (PV), markedly dilated CV with detached lining and markedly apoptotic hepatocytes.
(c) G3: Portal tracts with mild portal inflammatory infiltrate, markedly dilated CV and normal hepatocytes.
(d) G4: Portal tracts with mild portal inflammatory infiltrate, mildly dilated congested PV and normal hepatocytes.
(e) G5: Normal hepatocytes with normal portal tracts; mildly dilated PV and mildly dilated CV.

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# التأثيرات النافعة المحتملة لمستخلص الأكاسيا بيناتا على الكبد الدهني المُحدث بواسطة نظام غذائي عالي الفركتوز في الفئران

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**الملخص**

يصيب مرض الكبد الدهني غير الكحولي ما يقرب من 50% من سكان العالم من البالغين والأطفال على حد سواء، بسبب الممارسات الغذائية الخاطئة وقلة الوعي. وقد يتفاقم مرض الكبد الدهني غير الكحولي غير المُعالج مؤدياً في النهاية إلى سرطان الكبد. ومع ذلك، يُمكن علاج الكبد الدهني من خلال إجراء تعديلات فى نمط الحياة. هدفت هذه الدراسة إلى تقييم فعالية مستخلص أوراق الأكاسيا بيناتا في تحسين إصابات الكبد الناجمة عن مرض الكبد الدهني غير الكحولي، المُحدث في الفئران عن طريق إطعامهم باستخدام نظامًا غذائيًا عالي الفركتوز لمدة 12 أسبوعًا. تم تقسيم ثلاثين من ذكور الفئران البالغة إلى خمس مجموعات، تضم كل منها ستة فئران. بدأ التجريع الفموي اليومي للفئران لعلاج مرض الكبد الدهني غير الكحولي المُستحث من الأسبوع التاسع وحتى نهاية التجربة، باستخدام مستخلص أوراق الأكاسيا بيناتا بجرعة 250 مجم/كجم؛ وقد تم مقارنته بدواء الميتفورمين (100 مجم/كجم) أو بمزيج من الميتفورمين (100 مجم/كجم) والمستخلص (250 مجم/كجم). وقد كان العلاج المركب باستخدام مستخلص أوراق الأكاسيا بيناتا مع الميتفورمين هو الأكثر فعالية في منع تطور المرض. فقد لوحظ تحسن معنوي ذو دلالة إحصائية في مستويات الجلوكوز في مصل الدم، والأنسولين، ومقاومة الأنسولين، وصورة الدهون (الدهون الثلاثية، والكوليستيرول الكلي، وكوليسترول البروتينات الدهنية منخفضة الكثافة، وكوليسترول البروتينات الدهنية عالية الكثافة). حدث أيضاً انخفاض معنوي ذو دلالة إحصائية في إنزيمات الكبد مقارنةً بالمجموعة المصابة غير المعالجة. كما سجلت النتائج حدوث انخفاض معنوي ذو دلالة إحصائية في محتوى الكبد من ثلاثي أسيل الجليسرول، والكوليسترول الكلي، والمالون داي ألدهيد (أحد نواتج أكسدة الدهون)، بينما ازداد مستوى إنزيم السوبرأكسيد ديسميوتيز زيادة معنوية. وجدير بالذكر أن المجموعات الأخرى أظهرت تحسنًا معنويًا ذو دلالة إحصائية، ولكن بدرجة أقل من المجموعة التي تلقت العلاج المركب. بالإضافة إلى ذلك، أكد الفحص النسيجي للكبد نتائج التحاليل الكيميائية الحيوية. وختامًا، يجب إجراء دراسات سريرية لتوضيح دور مستخلص أوراق الأكاسيا بيناتا في تخفيف مرض الكبد الدهني غير الكحولي والتأكد من سلامته على الإنسان.

**الكلمات المفتاحية:** الكبد الدهني، الفئران، الفركتوز، الأكاسيا بيناتا، الميتفورمين.