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RESEARCH ARTICLE

OMEGA 3 FATTY ACID AND SIDER HONEY ATTENUATE SODIUM VALPROATE -INDUCED LIVER INJURY IN FEMALE ALBINO RATS

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Abstract

Sodium valproate (SVP) is one of the most widely prescribed antiepileptic drugs; however, its clinical use is frequently limited by hepatotoxicity, which is primarily associated with oxidative stress and inflammatory mechanisms. This study aimed to investigate the potential protective effects of Omega 3 (O3) and Sider honey (SH) against SVP-induced liver injury in female rats. Thirty female albino rats were randomly divided into five groups (n=6): group I (control) received distilled water; group II received SVP 300mg/kg/day; group III received SVP +O-3 (300mg/kg/day); group IV received SVP +SH (5g/kg/day); and group V received SVP + O-3+ SH. All treatments were administered orally for 14 consecutive days. Serum malondialdehyde (MDA) and liver function enzymes (ALT, AST, and ALP) were assessed. The results revealed that SVP administration significantly increased serum MDA levels compared to the control group ($p < 0.004$). On other hand, group III, IV and V showed a significant reduction in serum MDA compared to SVP group. The liver enzymes (ALT, AST, and ALP) also were significantly increased by SVP ($p < 0.001$). Co-treatment with Omega-3, Sider honey, or their combination resulted in a significant reduction in liver enzyme levels compared to the SVP-treated group ($p < 0.05$). The combined treatment demonstrated the most pronounced hepatoprotective effect. Omega 3 and Sider honey effectively attenuated Sodium valproate-induced hepatotoxicity, possibly through the suppression of oxidative stress and improvement of liver enzymes. These findings suggest that Omega 3 and Sider honey may serve as hepatotoxicity protective agent, warranting further clinical research.

Keywords: Sodium valproate; Omega 3; Sider honey; Hepatoprotective.

1. Introduction

The liver is a vital organ that plays a central role in regulating various physiological processes including metabolism, detoxification, storage, and secretion. Liver injury represents a major clinical problem and half of cases of acute liver failure are related to liver injury that is frequently brought on by drug-induced toxicity. Hepatotoxic medications frequently induce oxidative damage and lipid peroxidation, resulting in hepatocellular dysfunction and structural injury.[1].

Liver injury can arise from multiple factors, including hepatotoxic chemicals, immunological responses, metabolic disorders, and oxidative stress [2]. Oxidative stress, characterized by the overproduction of reactive oxygen species (ROS), leads to hepatocyte damage primarily through lipid peroxidation, protein oxidation, and DNA damage.[3] [4]

Sodium valproate (SVP) is a widely prescribed antiepileptic drug that interacts with cell membrane, producing both therapeutic and adverse effects. Although the mechanism of SVP-induced hepatotoxicity is not completely understood [5]. However, it has been linked to drug-induced adverse reactions, including hemorrhagic pancreatitis, bone marrow suppression, and hepatic injury. Chronic dosing with (SVP) can lead to serum liver enzymes and lipid peroxidation, fatty liver as microvascular steatosis, and disruption of FA metabolism [6]. In 44% of patients, chronic (SVP) usage has been associated with increased blood liver enzymes and lipid peroxidation.[7] in severe cases, SVP can lead to permanent liver injury with failure, highlighting the

need for preventive and protective strategies during SVP therapy[8].

Omega 3 fatty acids or polyunsaturated fatty acids (PUFA) have hepatoprotective properties. These properties include the regulation of cell proliferation, the inhibition of fatty acid metabolism, and the reduction of inflammation [9]. They can also interfere with inflammatory molecules and have hepato-prophylactic, antioxidant, and anti-inflammatory properties [10]. By lowering inflammation, oxidative stress, and cytokine-induced damage, O3FAs protect the liver from SVP-induced toxicity [11]. Therefore, owing to their favorable safety profile, omega-3 fatty acids represent a promising therapeutic option for mitigating drug-induced hepatotoxicity [12].

Seder Honey is made from nectar. It has been shown to be helpful in preventing chronic illnesses brought on by oxidative damage, particularly liver damage. Honey is a good substitute for traditional antibiotics and antiseptics because of its acidity and sugar content, which promote healing and oxygenation [13]. By scavenging free radicals, honey reduces oxidative stress and cellular damage in hepatic tissue, leading to improvement in liver enzyme levels [4]. Recent findings suggest that Sider honey effectively reduces hepatotoxicity and enhances tissue repair following SVP-induced injury [14].

The antioxidant capacity of honey was highlighted by the National Honey Board in 2005, which reported that darker varieties of honey exhibit higher antioxidant activity compared to lighter types [15]. Despite these promising properties, the hepatoprotective capacity of Sider honey particularly in combination with omega-3 fatty acids, remains insufficiently investigated.

Du to the limited availability of experimental studies in Yemen addressing the hepatoprotective effects of omega-3 in and Sider honey against SVP- induced hepatic injury, especially in female albino rats, the present study was designed to assess their potential hepatoprotective roles.

2. Methodology

2.1. Study design

The type of design was an experimental study using female albino rats after one week acclimation period.

2.2. Study Duration and area

The duration of this study was from April to June 2025.and was carried out in animal laboratory -Faculty of Pharmacy – University of Aden, Yemen.

2.3. Drugs and materials used for experimental

The drugs used in this study were Depakine oral solution-Sanofi- avent is France (200 mg per/ ml) purchased from Turkey Manufacturer, Omega Fit (omega-3 Sachets 1000 mg) Manufactured by :Dulex Lab Pharmaceutical purchased from Egypt sample preparation was written dissolved in distal water before experimental for preparation 300 mg \ kg\d\ b. w of each rate, Seder honey purchased from Hadhramaut marketing, which were available in Aden pharmacies and were bought from there and Ketamine was used for anesthesia of rats.

2.4. Instruments and Equipment

In order to accomplish the investigations of this study, the instruments and equipment used were Electronic balance (Spanish LABORCOM), Sensitive Electronic balance (Spanish – P SELECTA), Centrifuge (Spanish – P SELECTA) Screen master plus - Biochemical system international SrI (Italy- IVD), Eliza (USA - Star Fax 4700), micropipettes, oral gavage, Anatomy Dissection Kit, Test Tubes, Syringes, Spectrophotometer and kits, Centrifuge, were used.

2.7. Treatment of animals

Albino rats were housed in cages under standard laboratory condition (temperature-controlled environment (20 -25°C) with a 12:12-hour cycle for light and dark with relative humidity (55-60%). They were handled according to animal ethics guide. Standard diet and tap water ad libitum were available to them without charge. And they were adapted to this condition for 1 week before starting the procedure. The housing was in the pharmacology animal house at the Faculty of Pharmacy - Aden University, Yemen.

2.8. Methods

2.8.1 Experimentation

The study was carried out on 30 rats. The animals were randomly divided into 5 groups each group containing 6 rats as the following: rats in the group I (control group) were administered distal water throughout the experimentation orally for 14 days[9]. Group II (Valproate group) was treated with oral Sodium valproate 300 mg\kg\day for 14 days. [7]Group III (combination group, Sodium valproate 300 mg/kg/day and Omega 3 300mg \kg\day) through oral route for 14 days. Group IV (Sodium valproate 300 mg/kg/day with Seder honey 5 g\kg\day by oral route for 14 days. Group V (combination group) Sodium valproate 300 mg/kg/day with Omega 3 300mg/kg/day and honey Seder 5 g\kg\day orally for 14 days. Then after 24 hours (on 15 th day), blood samples were drawn from eyes of the female albino rats for analysis.

2.8.2. Experimental methods

2.8.2.1. Eliza Test

2.8.2.1.1 Determination of oxidative stress markers

Serum malondialdehyde (MDA) was measured following the steps of the instruction manual supplied by

the manufacturer after buying by using a spectrophotometer (BT- LAB ELISA kits), [9].

2.8.2.2. Spectrophotometer Test

2.8.2.2.1 Measurement of serum enzymatic activity (L F T)

Serum activities of Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST) and Alkaline Phosphatase (ALP) and were measured following the steps of the instruction manual supplied by AGAPPE Lab by using a spectrophotometer. Samples of venous blood were drawn via a capillary tube from the orbital-sinus capillary vein. The blood was put into the test tubes, allowed to clot for 20 minutes, and then centrifuged at 4000 g for 20 minutes. The (ALP), (ALT), and (AST) enzyme levels in the serum were analyzed later after collection and storage at 4°C. The unit of measurement for enzyme activity is the international unit per liter (IU/L).

2.9. Statistical analysis

Data processing and analysis were done by using the Statistical Package for the Social Sciences (SPSS) version 27. Means and standard deviation were calculated and the statistical difference between the groups were determined by using one-way analysis of variance (ANOVA). P value of ≤ 0.05 was determined as statistically significant for all tests. The percentage of changes (reduction or increment) was calculated.

2.10. Ethical consideration

This study was approved by the Animal Ethical Committee at Faculty of Medicine and Health Sciences University of Aden (REC-252-2025). Animal handling was done according to The Norwegian National Research Ethics Committees. Ethical Guidelines for the Use of Animals in Research. 1st edition, 2018. Available at: www.etikkom. After scarify, the animal's body were buried.

3. Results

3.1. Body weights of the rats

A total of thirty female albino rats were enrolled in this in vivo experiment. Following a one-week acclimatization period, each rat's body weight was measured on three separate occasions, and the average value was calculated prior to beginning the study. The overall mean body weight of the animals was 218.6 ± 7 g, with individual weights ranging between **203 g** and **232 g**. The average weights for the different experimental groups are summarized in Table (1)

Table (1): Mean ± SD of the body weights of the rats in the experimental groups (n=30)

Groups No	Groups	Body weight Mean ± SD (gram)
I	Control group	215±11.4
II	SV 300mg\kg	218±6.6
III	SV 300mg\kg +O3 300mg\kg	220±6.1
IV	SV 300mg\kg +SH 5g\kg	220±7.1
V	SV 300mg\kg +SH 5g\kg + O 3 300mg\kg	216±7.7

Note: All data are expressed as Mean ± SEM (n=6)

3.2. Effect of omega 3 and Sider honey on Sodium valproate -Induced the Oxidative Stress Biomarker serum MDA.

The levels of serum MDA was significantly increased in group II (3.01±0.17mmol/ml P < 0.004) by 69.1 % more than those in group I (1.78±0.49 mmol/ml). Group III, produced a reduction in levels of MDA by (2.65±0.76 mmol/ml), made 12 %, with *P* = 0.76 as compared to group II. Similarly, group IV insignificantly reduced MDA (2.83±0.67 mmol/ml) by 6 %, with *P* = 0.97 compared to group II. On the other hand, group V showed a substantial significant reduction in levels of MDA (2.08±0.33 mmol/ml) by 30.9%, (*P* = < 0.04) as compared to group II, Table (2).

Table (2): Effect of omega 3 and Seder honey on Sodium valproate -induced serum MDA

Groups no	Groups	MDA (mmol/ml) Mean ±SD	P Value
I	Control group	1.78±0.49	
II	SV 300mg\kg	3.01±0.17	0.004
III	SV 300mg\kg +O3 300mg\kg	2.65±0.76	0.76
IV	SV 300mg\kg +SH 5g\kg	2.83±0.67	0.97
V	SV 300mg\kg +SH 5g\kg + O 3 300mg\kg	2.08±0.33	< 0.04

Note: All data are expressed as Mean ± SEM (n=6/group). p = 0.004 of Group II vs Group I, P <0.04 of group V vs group II, MDA= Malonaldehyde.

3.3. Effect of omega 3 and seder honey on Sodium valproate -induced serum ALT and AST

The serum levels of ALT and AST were significantly elevated in Group II, which received Sodium Valproate compared to the control group (p < 0.001 with group II vs Group I). On other hand, group III, IV and V produced a significant reduction in serum ALT and AST compared to SVP group II in a dose dependent manner, Table (3)

Table (3): Effect of omega 3 and Seder honey on Sodium valproate-induced serum ALT and AST.

Groups no	Groups	ALT (IU/L) Mean ±SD	P Value	AST (IU/L) Mean ±SD	P Value
I	Control group	22.66±4.76		81.5 ±2.07	
II	SV 300mg\kg	46.16±10.16	< 0.001	133.33±37.0	< 0.001
III	SVP 300mg\kg +O3 300mg\kg	32.33±3.50	0.010	98±12.23	0.030
IV	SVP 300mg\kg +SH 5g\kg	30.00±6.44	0.002	98.50±17.40	0.033
V	SVP 300mg\kg +SH 5g\kg + O 3 300mg\kg	24.50±5.89	< 0.001	95.50±6.41	0.018

Note: All data are expressed as Mean ± SEM (n=6). p < 0.001 of group II vs Group I, p= 0.010, 0.002 and < 0.001 of group III, IV and V respectively vs Group II; p < 0.001 of group II vs Group I ; p= 0.030, 0.033, and 0.018 of group III, IV and V respectively vs Group II. Alanine aminotransferase= ALT; Aspartate aminotransferase =AST; Aspartate aminotransferase = AST.

3.4. Effect of omega 3 and Seder honey Sodium valproate -induced serum ALP

The serum ALP levels were significantly higher in group II (183.50±89.97 IU/L, P <0.001), making154.9 % increase over than those in the group I (72.0±3.74 IU/L). Interestingly, administration of Omega 3 300 mg/Kg alone or Sider honey 5g/Kg to Sodium valproate 300mg/kg/d revealed a significant reduction in serum ALP levels, P=0.022 and P=0.010, respectively, as comparing to rats treated with Sodium valproate 300mg/Kg/d. But a combination of both Omega 3 300mg/Kg/d and Sider honey 5g/Kg showed a highly significant reduction in ALP levels, (P <0.001), Table (4)

Table (4): Effect of omega 3 and seder honey on Sodium valproate -induced serum ALP

Groups No	Groups	ALP (IU/L) Mean ±SD	P Value
I	Control group	72.0±3.74	
II	SVP 300mg\kg\d	183.50±89.97	< 0.001
III	SVP 300mg\kg\d +O3 300mg\kg\d	103.66±10.23	0.022
IV	SVP 300mg\kg\d+ SH 5g\kg\d	95.83±23.18	< 0.010
V	SVP 300mg\kg +SH 5g\kg + O 3 300mg\kg\d	70.33±7.68	< 0.001

Note: All data are expressed as Mean ± SEM (n=6). P<0.001 of group II vs Group I, P = 0.022, < 0.010 and < 0.001 of group III, IV and V respectively vs Group II; ALP=Alkaline phosphatase.

4. Discussion

Long-term Sodium valproate (SVP) use has been associated with a spectrum of liver injuries that can range from mild hepatotoxicity to severe hepatic failure and even death. One proposed mechanism involves oxidative stress induced by generation of free radicals and reactive oxygen species (ROS) [16], leading to DNA damage and apoptosis, which ultimately results in hepatocellular necrosis. Additionally, the hepatotoxicity of SVP has been linked to the formation of its toxic metabolites.[17].

The present study was conducted to assess the hepatoprotective effect of omega 3 and Seder honey or their combination on SVP-induced hepatic toxicity in female albino rats by biochemical testing. The results of these study showed that the rats which received SVP had a significant induced liver injury manifested as raised serum levels of liver enzymes. This result is parallel with Ibrahim et a.l from Egypt [18].

SVP is an anticonvulsant with a therapeutic range of 60 mg/kg/day; however, despite possible organ toxicity, especially to the liver, greater dosages may be required in some severe instances. In this investigation, adult rats were used as liver function models, and SVP was given orally for 14 days at a dose of 300 mg/kg/day. Hepatocellular injury was indicated by the considerably higher levels of liver enzymes AST, ALT, and ALP in SVP-treated rats when compared to controls. These results are consistent with other studies that linked elevated blood liver transaminases to VPA-induced hepatic damage, indicating that oxidative stress or direct hepatocyte damage may be involved in cell death.[19].

The leakage of proteins from injured hepatocytes into the bloodstream has been the main basis for the investigation of a number of serum protein biomarkers for evaluating liver injury. Nevertheless, these biomarkers are not yet ready for clinical application and are still in the early stages of development. Since ALT1 is found in human hepatocytes, renal tubular epithelial cells, and salivary gland epithelial cells, recent research indicates that evaluating the isozymes of alanine aminotransferase, ALT1 and ALT2, may help distinguish the site of injury [20].

The main metric used to evaluate liver disease is the concentration of serum alanine aminotransferase (ALT). However, ALT testing frequently fails to detect patients with minimal to mild necro inflammatory activity in chronic hepatitis C virus (HCV) infections. Due to out-of-date reference populations that include people with nonalcoholic fatty liver disease, current ALT thresholds, which were established in the 1980s, may underestimate the prevalence of chronic liver disease. A recent 4-year study assessed first-time blood-donation candidates to identify low-risk populations for subclinical liver disease and tested the sensitivity and specificity of new ALT

ranges in assessing anti-HCV-positive individuals with or without chronic liver damage, highlighting the need for a critical reevaluation of ALT limits that focuses on defining "healthy ranges" rather than just updating "normal ranges."[21].

For noninvasive liver disease monitoring, clinical chemistry data—specifically, alanine aminotransferase (ALT) levels—are essential. When hepatocellular damage occurs, ALT, which is mostly present in the liver, trans aminates alanine leaks into the bloodstream. It has a half-life of roughly 42 hours and a delayed clearance. Although liver cell injury is indicated by elevated ALT, extrahepatic injuries such as muscle damage can also cause elevated ALT levels.[22]. In the present study, the administration of SVP (300 mg/kg. b w) into rats of group II showed a significantly elevation in ALT levels, with a mean value of 46.16 IU/L that is statistical significant (P<0.001). This finding is in line with [19], who reported high ALT levels. This finding reflects the induction of liver toxicity with SVP.

The effect of Omega 3 300 mg/kg with sodium valproate (SVP) on liver enzymes was evaluated. The mean ALT level in Sodium valproate 300 mg/kg and Omega 3 300 mg/kg group III was 32.33 ± 3.50 IU/L, which was significantly reduced compared with the SVP-only group (P = 0.010). In addition, serum levels of other liver markers, including ALP and γ-GT, were also decreased. This suggests that Omega 3 (DHA) may exert a protective effect against SVP-induced hepatotoxicity, potentially by preserving hepatocyte integrity and supporting normal biliary outflow. These findings are consistent with previous studies demonstrating the hepatoprotective effects of DHA [23].

Testing Sider honey 5 g /kg group IV with SVP showed a statistically significant reduction in the ALT level (30.00 ± 6.44 IU/L) compared with the VPA-only group II (P = 0.002). This indicates that Sider honey co-administration mitigates the hepatotoxic effects of SVP. Similar hepatoprotective effects of honey have been reported in other studies [24]. [13], which attributed these effects to its antioxidant and cytoprotective properties.

Aspartate aminotransferase (AST) is a crucial pyridoxal 5′-phosphate (PLP) -dependent enzyme that catalyzes the reversible conversion of L-aspartate and α-ketoglutarate into oxaloacetate and L-glutamate through a ping-pong mechanism (Toney, 2015). AST is predominantly located in the liver, kidney, skeletal muscle, and heart. Elevations in serum AST are indicative of tissue damage, making it a valuable diagnostic marker for myocardial infarction, hepatobiliary diseases, and muscle necrosis [25]. Specifically, AST levels exceeding 400 IU/L indicate hepatocellular damage, while values above 1000 IU/L are associated with severe conditions such as drug-induced toxicity or viral hepatitis. Moderate increases are observed in liver cancer, cirrhosis, and cholestasis.

In the present study, administration of SVP (300mg/kg) to rats revealed a significant elevation in serum AST levels (Group II) compared with the control group. The same effect has been showed by Abdel-Dayem et al from Egypt [6] and Mahesh et al. from india[24].

Co-administration of hepatoprotective agents attenuated elevated AST levels. Group III (SVP + Omega 3) and Group IV (SVP + Sider honey) exhibited reductions in AST levels by 26.5% and 26.1% (P = 0.030 and 0.033, respectively) compared with Group II. Similarly, Group V showed a significant decrease in AST levels to 95.50 ± 6.41 IU/L, representing a 28.4% reduction (P = 0.018) relative to Group II. These reductions align with the hepatoprotective effects reported in prior studies (Abdel-Dayem et al., 2014; Mahesh et al., 2009), supporting the protective role of Omega 3 and Sider honey against VPA-induced liver injury.

Alkaline phosphatases (ALP), called glycoproteins, are widely distributed across prokaryotes and higher eukaryotes, excluding certain higher plants. ALPs are dimeric enzymes that are mainly found on the cell surface. At high pH, they hydrolyze monophosphate esters and release inorganic phosphate. Zinc is present in these metalloenzymes; two Zn2+ and one Mg2+ ions are essential for their structural conformation and enzymatic activity, which affects subunit interactions.[26].

Tissue-nonspecific alkaline phosphatase (TNAP), the main ALP isoenzyme, has been extensively studied as a potential biomarker in neurological disorders, particularly stroke, with both preclinical and clinical data supporting its diagnostic and therapeutic relevance[27].

The current study showed significant higher ALP levels in rats treated with SVP. This increase made about 54.9 % over than those in the control group. Interestingly, administration of Omega 3 300mg/Kg alone, or Sider honey 5g/Kg to rats treated with Sodium valproate 300mg/Kg revealed a significant reduction in serum ALP levels, P=0.022 and P=0.010, respectively, as comparing to rats treated with Sodium valproate alone. More than that, a combination of both Omega 3 and Sider honey showed a highly significant reduction in ALP levels, (P <0.001), . This is in line with Omidipour et al. from Iran [23].

When compared to the control and other groups, the SVP group had the highest MDA level. On the other hand, group IV showed the lowest MDA level, indicating less peroxidation and cell death, while receiving the largest amount of honey.

Reduced antioxidant enzyme activity and elevated oxidative stress are thought to be important contributors to cellular death [23], [14]. According to studies, omega-3 fatty acids have hepatoprotective benefits because they can change liver marker levels that are impacted by hepatocellular injury caused by Acetaminophen (APAP),

resulting in a near-normalization of blood ALT, AST, ALP activity, and overall hepatic function, as reported by Elsafty et al. from Egypt [28]. This study supports our finding.

Key byproducts of lipid peroxidation include malondialdehyde (MDA), 4-hydroxy-nonenal (HNE), and F2-isoprostane 15 (S) -8-iso-prostaglandin F2a, which are produced from polyunsaturated fatty acids (PUFAs) via chemical and enzyme-catalyzed processes. Arachidonic acid is the unique source of 15 (S) -8-iso-PGF2a, whereas MDA and HNE can come from a wider variety of PUFAs. All three of these chemicals are known to be important indicators of oxidative stress, and MDA is a standard for thiobarbituric acid reactive substances (TBARS). Biological samples from sick people frequently show higher levels of MDA, HNE, and 15 (S) -8-iso-PGF2a than those from healthy people.[29].

In the present study, the administration of SVP significantly increased the levels of serum MDA (3.01±0.17mmol/ml $P < 0.004$) by 69.1 % more than those in the control (1.78±0.49 mmol/ml). Group III produced a reduction in levels of MDA by 12 and group IV insignificantly by 6 % compared to group II. On the other hand, group V showed a substantial significant reduction in levels of MDA by 30.9 % ($P = < 0.04$) as compared to group II, The antioxidant qualities combination of Omega 3 with Sider honey may be responsible for such decrease in MDA levels. Omega-3's ability to scavenge free radicals and reduce lipid peroxidation may be probably what gives it its anti-inflammatory and antioxidant properties. Abdullah and Othman from Iraq showed the same significant effect, which supprout the results of the present study.[30].

In Conclusion, the study showed that Sodium valproate induced hepatotoxicity in female albino rats by increasing oxidative stress biomarker (Malonaldehyde), and liver enzymes. Omega 3 and Sider honey effectively attenuated Sodium valproate-induced hepatotoxicity, possibly through the suppression of oxidative stress and improvement of liver enzymes. These findings suggest that Omega 3 and Sider honey may serve as hepatotoxicity protective agent, warranting further clinical research.

References

[1] H. A. Hameed and A. F. Hassan, “The Hepatoprotective Effect of Omega-7 Against Paracetamol-Induced Hepatotoxicity in Male Rats, ” *Iraqi J. Pharm. Sci.*, vol. 32, no. 3, pp. 85–94, 2023, doi: 10.31351/vol32iss3pp85-94.

[2] P. D.. SAHAR ATREES, Ph.D., SAHAR ATREES, “Review Article Drug Impairment and Liver Disease, ” *Med. J. Cairo Univ.*, vol. 89, no. 6, pp. 911–917, doi: 10.21608/mjcu.2021.184505.

[3] T. Santh Rani and Y. Chandravadana, “Pharmacologyonline 2: 265-281 (2008) Rani and Chandravadana INFLUENCE OF SPIRULINA FUSIFORMIS ON THE SODIUM VALPROATE INDUCED HEPATOTOXICITY AND OXIDATIVE STRESS, ” vol. 281, pp. 265–281, 2008.

[4] S. Srinivasan *et al.*, “Therapeutic Potential of Honey Against Hepatotoxicity and Renal Toxicity: Insight into Its Mechanisms of Action, ” *Honey Food Sci. Physiol.*, pp. 389–410, 2024, doi: 10.1007/978-981-97-3565-5_17.

[5] A. M. Jassim, “Protective Effect of Petroselinum crispum (parsley) extract on histopathological changes in liver, kidney and pancreas induced by Sodium Valproate- In male Rats, ” *Kufa J. Vet. Med. Sci.*, vol. 4, no. 1, pp. 20–27, 2013, doi: 10.36326/kjvs/2013/v4i13922.

[6] M. A. Abdel-Dayem, A. A. Elmarakby, A. A. Abdel-Aziz, C. Pye, S. A. Said, and A. M. El-Mowafy, “Valproate-induced liver injury: Modulation by the omega-3 fatty acid DHA proposes a novel anticonvulsant regimen, ” *Drugs R D*, vol. 14, no. 2, pp. 85–94, 2014, doi: 10.1007/s40268-014-0042-z.

[7] A. M. El-Mowafy, M. M. Katary, C. Pye, A. S. Ibrahim, and A. A. Elmarakby, “Novel molecular triggers underlie valproate-induced liver injury and its alleviation by the omega-3 fatty acid DHA: role of inflammation and apoptosis, ” *Heliyon*, vol. 2, no. 7, 2016, doi: 10.1016/j.heliyon.2016.e00130.

[8] O. Oztopuz *et al.*, “Melatonin ameliorates sodium valproate-induced hepatotoxicity in rats, ” *Mol. Biol. Rep.*, vol. 47, no. 1, pp. 317–325, 2020, doi: 10.1007/s11033-019-05134-6.

[9] Z. A. El-Gendy *et al.*, “Hepatoprotective effect of Omega-3 PUFAs against acute paracetamol-induced hepatic injury confirmed by FTIR, ” *Hum. Exp. Toxicol.*, vol. 40, no. 3, pp. 526–537, 2021, doi: 10.1177/0960327120954522.

[10] N. O. Ayaz, “Protective Mechanisms of Omega-3 Fatty Acids Against Hepatotoxic Impact of Cadmium Exposure in Rats, ” *Pages*, vol. 8, no. 5, pp. 25–34, 2017, [Online]. Available: http://www.pharmacophorejournal.com

[11] R. A. Maheshwari, D. Khemani, A. K. Sen, R. Balaraman, R. Velmurugan, and D. B. Sen, “Protective Effects of Silymarin and/or Omega-3 Fatty Acids against Paracetamol-initiated Liver Toxicity in Rats, ” *Indian J. Pharm. Educ. Res.*, vol. 56, no. 1, pp. S81–S88, 2022, doi: 10.5530/ijper.56.1s.46.

[12] M. Meganathan *et al.*, "Evaluation of hepatoprotective effect of Omega 3-fatty acid against paracetamol induced liver injury in albino rats, " *Glob. J. Pharmacol.*, vol. 5, no. 1, pp. 50–53, 2011.

[13] N. M. Meligi, S. A. Ismail, and N. S. Tawfik, "Protective effects of honey and bee venom against lipopolysaccharide and carbon tetrachloride-induced hepatoxicity and lipid peroxidation in rats, " *Toxicol. Res. (Camb).*, vol. 9, no. September, pp. 693–705, 2021, doi: 10.1093/TOXRES/TFAA077.

[14] E. M. A. Alshailabi and N. I. Al-zail, "Wijdan E. MOHAMMED 3, " 2024.

[15] R. Adolph, "**済無**No Title No Title No Title, " vol. 15, no. 1, pp. 1–23, 2016.

[16] M. Ibrahim, R. Abdel-Karim, H. Tamam, A. Mohamed, and F. Wani, "Protective effect of silymarin and ascorbic acid in valproic acid-induced hepatic toxicity in male albino Rats, " *Mansoura J. Forensic Med. Clin. Toxicol.*, vol. 25, no. 2, pp. 33–49, 2017, doi: 10.21608/mjfmct.2018.47251.

[17] C. Journal, *aft*. 2020.

[18] S. Arabia, "Anti-inflammatory and protective effects of royal jelly against hepatic and renal damage induced by valproic acid in rats, " vol. 22, no. 1, pp. 1–17, 2023.

[19] R. H. Abdel-Kareem and S. E. Tawfeek, "Evaluation of dose related structural changes in sodium-valproate-induced hepatotoxicity and a possible protective role of Vitamin E in adult albino rats, " *Egypt. J. Histol.*, vol. 43, no. 2, pp. 585–597, 2020, doi: 10.21608/ejh.2019.16176.1161.

[20] X. Yang, W. F. Salminen, and L. K. Schnackenberg, "Current and emerging biomarkers of hepatotoxicity Current and emerging biomarkers of hepatotoxicity, " vol. 2492, 2012, doi: 10.2147/CBF.S27901.

[21] D. Prati *et al.*, "Article Updated Definitions of Healthy Ranges for Serum Alanine Aminotransferase Levels, " no. September 1995, pp. 1–10, 2002.

[22] I. T. O. Liver, "Hepatic toxicity biomarkers, " 2014, doi: 10.1016/B978-0-12-404630-6.00013-0.

[23] R. Omidipour, L. Zarei, M. B. Boroujeni, and A. Rajabzadeh, "Protective Effect of Thyme Honey against Valproic Acid Hepatotoxicity in Wistar Rats, " vol. 2021, 2021.

[24] A. Mahesh, J. Shaheetha, D. Thangadurai, and D. M. Rao, "Protective effect of Indian honey on acetaminophen induced oxidative stress and liver toxicity in rat, " *Biologia (Bratisl).*, vol. 64, no. 6, pp. 1225–1231, 2009, doi: 10.2478/s11756-009-0205-5.

[25] P. E. Posch, I. Cruz, D. Bradshaw, and B. A. Medhekar, "Novel polymorphisms and the definition of promoter ' alleles ' of the tumor necrosis factor and lymphotoxin a loci : inclusion in HLA haplotypes, " vol. 724, pp. 547–558, 2003, doi: 10.1038/sj.gene.6364023.

[26] U. Sharma, D. Pal, and R. Prasad, "Alkaline Phosphatase : An Overview, " vol. 29, no. 3, pp. 269–278, 2014, doi: 10.1007/s12291-013-0408-y.

[27] A. L. Brichacek, C. M. Brown, C. Biology, and C. Biology, "HHS Public Access, " vol. 34, no. 1, pp. 3–19, 2020, doi: 10.1007/s11011-018-0322-3.Alkaline.

[28] M. Elsafty, A. Abdeen, and M. Aboubakr, "Protective effect of allicin and omega-3 against paracetamol induced hepatic toxicity, " *Benha Vet. Med. J.*, vol. 43, no. 1, pp. 26–31, 2022, doi: 10.21608/bvmj.2022.154736.1569.

[29] D. Tsikas, "Assessment of lipid peroxidation by measuring malondialdehyde (MDA) and relatives in biological samples : Analytical and biological challenges, " *Anal. Biochem.*, vol. 524, pp. 13–30, 2017, doi: 10.1016/j.ab.2016.10.021.

[30] T. A. Abdullah and H. K. Othman, "Protective effects of omega3 on ccl4-induced oxidative stress and nephrotoxicity in female albino rats, " *Indian J. Public Heal. Res. Dev.*, vol. 10, no. 11, pp. 2275–2280, 2019, doi: 10.5958/0976-5506.2019.03900.7.

مقالة بحثية

يخفّف حمض أوميغا-3 الدهني وعسل السِّدر من الإصابة الكبدية المُستحثة بفالبروات الصوديوم لدى إناث الفئران البيضاء

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المُلخّص

يعد الصوديوم فالبروات أحد أكثر الأدوية المضادة للصرع التي يتم وصفها بشكل شائع؛ إلا أن استخدامه السريري غالبًا ما يكون محدودًا بسبب تأثيراته السامة على الكبد، والتي ترتبط بشكل رئيسي بالإجهاد التأكسدي والآليات الالتهابية. هدفت هذه الدراسة إلى التحقيق في التأثيرات الوقائية المحتملة للأوميجا 3 وعسل السدر ضد إصابة الكبد الناتجة عن الصوديوم فالبروات في إناث الفئران البيضاء. تم تقسيم 30 من الفئران البيضاء الإناث عشوائيًا إلى خمس مجموعات (6 فئران في كل مجموعة): المجموعة الأولى (التحكم) تلقت ماءً مقطرًا؛ المجموعة الثانية تلقت صوديوم فالبروات بجرعة 300 مجم/كجم/يوم؛ المجموعة الثالثة تلقت صوديوم فالبروات + اوميجا 3 بجرعة 300 مجم/كجم/يوم؛ المجموعة الرابعة تلقت صوديوم فالبروات + عسل السدر بجرعة 5 جرام/كجم/يوم؛ والمجموعة الخامسة تلقت صوديوم فالبروات + اوميجا 3+ عسل السدر. تم إعطاء جميع العلاجات عن طريق الفم لمدة 14 يومًا متتاليًا. تم تقييم مستوى المالونديالديهيد (**MDA**) في المصل وإنزيمات وظائف الكبد (**ALT**, **AST**, **ALP**). أظهرت النتائج أن إعطاء الصوديوم فالبروات أدى إلى زيادة كبيرة في مستويات **MDA** في المصل مقارنةً بمجموعة التحكم ($P < 0.004$). من ناحية أخرى، أظهرت المجموعات الثالثة والرابعة والخامسة انخفاضًا كبيرًا في مستوى **MDA** مقارنةً بمجموعة الصوديوم فالبروات. كما تم زيادة إنزيمات الكبد (**ALT**, **AST**, **ALP**) بشكل كبير بواسطة الصوديوم فالبروات ($P < 0.001$). أدى العلاج المشترك مع الأوميجا 3، عسل السدر، أو مزيج منهما إلى تقليل كبير في مستويات الإنزيمات الكبدية مقارنةً بمجموعة الصوديوم فالبروات ($P < 0.05$). أظهر العلاج المشترك التأثير الوقائي الأكثر وضوحًا على الكبد. قد تكون الأوميجا 3 وعسل السدر فعّالتين في تقليل التسمم الكبدي الناتج عن الصوديوم فالبروات، ربما من خلال تثبيط الإجهاد التأكسدي وتحسين إنزيمات الكبد. تشير هذه النتائج إلى أن الأوميجا 3 وعسل السدر قد يكونان عاملين وقائيين ضد التسمم الكبدي، مما يستدعي المزيد من البحث السريري.

الكلمات المفتاحية: الصوديوم فالبروات؛ الأوميجا 3؛ عسل السدر؛ الوقاية من التسمم الكبدي.

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