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RESEARCH ARTICLE

EFFECT OF VITAMIN C AND VITAMIN B12 ON ACETAMINOPHEN INDUCED LIVER INJURY IN ALBINO RATS

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Abstract

Several vitamins, including vitamin C, and B12, have been recognized as antioxidants and have shown hepatoprotective effects against the liver injury caused by acetaminophen (APAP) overdose. The current study aimed to investigate the effect of vitamin C, and B12 in protecting the liver from APAP induced hepatotoxicity in rats. An experiment was carried out on female albino rats. There were five groups of animals: a control group that received normal saline (10 ml/kg), acetaminophen treated group (2000 mg/kg), vitamin C treated group (500 mg/kg), vitamin B12 treated group (10mg g/kg), and N-acetylcysteine (NAC) treated group (150mg/kg). All animals were given oral medications for six days. On the seventh day, all the animals except the control group were subjected orally to APAP and then were observed for 24 hours for blood sample collection before they were sacrificed. APAP treatment showed a significant elevation in lipid peroxidation confirmed by the results of liver tissue malondialdehyde (MDA), and elevation in serum liver enzymes levels, aspartate aminotransferase (AST) alanine aminotransferase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), and depletion in albumin levels, $p<0.001$, which all indicated hepatic injury. Pre-treatment with vitamin C, vitamin B12 and NAC significantly ($p<0.01$) reduced the elevated MDA, AST, ALT, and ALP, but slightly elevated albumin levels that was insignificant in case of vitamin B12 and NAC, with $P=0.09$ and $P=0.4$, respectively. Acetaminophen induced liver hepatocellular impairment through elevation of oxidative stress marker MDA and elevation of the liver function markers in the experimental rats. Vitamin C and vitamin B12 seem to have protective effects in rat hepatic toxicity that was comparable to those of N-acetylcysteine (NAC). Further studies are required to determine the mechanisms stand behind this effectiveness.

Keywords: Liver, Acetaminophen, Vitamin C, Vitamin B12.

1. Introduction

The liver is one of many organs in the body that is vital for maintenance of homeostasis; which is involved in chemical substance metabolism, biotransformation, secretion, storage and detoxification [1]. The continuous exposure of the liver to some factors such as drugs, viruses, alcohol, fat, and biotransformed metabolites can cause hepatotoxicity. Hepatotoxicity results in damage to the liver's tissues, cells, structure, or functionality. Acetaminophen and other substances may cause like this kind of liver damage. Healthcare providers and the pharmaceutical industry in general are at significant risk from drug-induced hepatotoxicity, particularly from idiosyncratic reactions [2].

Acetaminophen (N-acetyl-para-aminophenol, paracetamol, APAP)is a common over-the-counter pain reliever and fever reducer [3]. It inhibits cyclooxygenase (COX) activity quickly, reversibly, and noncompetitively and inhibits prostaglandin synthesis in the brain and central nervous system (CNS) respectively [4]. Acetaminophen continues to be a leading contributor to overdose, acute liver failure (ALF), and fatalities in the United States, the United Kingdom, and many other nations, including Saudi Arabia and Yemen[5].According to Blieden et al acute liver failure has been recorded after high dose of acetaminophen greater than 4 g/day [6].

At therapeutic doses, the majority of the administered dose is typically metabolized by the Phase II processes including glucuronidation and sulfonation reactions to produce inactive, harmless metabolites that are quickly eliminated by the kidney[7]. On the other hand, a small percentage of APAP is metabolized by CYP2E1, a member of the CYP family, through oxidation reaction phase I process to a highly toxic metabolite namely N-acetyl-p-benzoquinoneimine (NAPQI), which was then detoxified by glutathione [8]. However, at higher doses the cytochrome P450 system and glutathione become saturated, resulting in NAPQI accumulation and subsequent interaction with the cellular proteins to form reactive oxygen species (ROS) depleting GSH in the process of oxidative stress. ROS, such as superoxide radicals, hydrogen radicals and hydroxyl radicals induce oxidative stress, which can attack biological molecules such as DNA, protein, and phospholipids. Thus, this results in lipid peroxidation indicated by increasing production of malondialdehyde (MDA) and depletion of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase , mitochondrial malfunction, disruption of calcium and nitric oxide homeostasis, and ultimately cell death via necrosis and apoptosis [9]. MDA is a reactive aldehyde that is produced as a byproduct of polyunsaturated fatty acid peroxidation in cells. As such, it raises the generation of free radicals, which in turn increases MDA synthesis. MDA is a marker of oxidative stress[10].

The best antidote against acetaminophen poisoning is widely recognized to be N-acetylcysteine (NAC). Is available in intravenous solution and oral forms for the treatment of acetaminophen overdose ,yet using it carries some risks [11]. This medication can cause a number of undesirable side effects, including bronchospasm, angioedema, allergy, and anaphylaxis. Moreover, it has been reported that documented adverse drug reactions showed a high incidence of more than 60% of individuals receiving NAC [12] .

The aim of this study was to find out a potentially less toxic alternative to NAC for treatment of APAP induced liver injury in rats. Based on these facts, antioxidant therapy appears to be the most appropriate strategy for treating a range of liver diseases, either on its own or in conjunction with other pharmaceuticals [13]. Antioxidants can influence biological systems through a variety of processes, such as co-antioxidant activity, electron donation, metal ion chelation, modulation of gene expression, and others[14][15][16]

Antioxidants like vitamin C and vitamin B12 can either restore the normal level of liver enzyme, albumin and lipid profile that paracetamol has disrupted, or they can lessen the damaging effects of free radicals by inhibiting the oxidation of polyunsaturated fatty acid in the cell membrane. In various liver injury models, antioxidants such as vitamin C and vitamin B12 have been shown to have hepatoprotective effect as reported in previous studies [17], [18].

Vitamin C is a strong, naturally occurring, water-soluble antioxidant[19] that can be administered orally or intravenously[20]. Reported researches showed that vitamin C has hepatoprotective property, which linked to its antioxidative property. It has been observed that vitamin C, particularly in animals, may reduce the liver damage caused by some chemical agents. The research of Bashandy and Alwasel et al supported this fact. They found that vitamin C restored normal levels of alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, and malondialdehyde after given carbon tetrachloride to induce liver injury[21]. Additionally, vitamin C can greatly lessen the liver-damaging effects of both mercury and cadmium in rabbits[22].

Albumin is synthesized in the liver and then immediately secreted into the portal circulation. Vitamin C had the best level of defense against APAP-induced albumin depletion. This may be due to its remarkable capacity to protect injured hepatocytes, reserving its function in modulating albumin levels [23].

The water-soluble micronutrient cobalamin, often known as vitamin B12, is critical for immunity and cell homeostasis. Myelin, DNA, erythrocyte production, and cell development are all impacted by vitamin B12 [18].The liver serves as vitamin B12 the storage, and transportation site [24]. It is conceivable that alterations in the intrinsic concentration of vitamin B12 could potentially be linked to liver pathology. Evidence already exists to suggest that vitamin B12 may mitigate liver disorders by maintaining both the integrity of lobular architecture and the proper metabolic stat. There have been reports of cobalamins' possible antioxidative properties [16] .Therefore, we focused also on the role of vitamin B12 in APAP-induced liver toxicity in rats. The aim of the current study is to investigate the effect of vitamin C and vitamin B12 on acetaminophen induced liver injury in rats.

2. Materials & Methods

2.1 Study area and duration

The study was carried out in pharmacology (animal house) laboratory at Faculty of Pharmacy, Aden University. In the period from July to September 2023.

2.2 Study design

The type of design was an experimental study investigating quantitative and qualitative variables.

2.3. Sample size

Twenty-five healthy adult female albino rats weighing (180-250 gm) were used in this study.

Sample size was calculated by:

E = Total number of animals – Total number of groups

E= 25-5, E=20, so E lies within 10 to 20 for optimum sample size [25]. Therefore, 25 animals were in this experiment.

2.4 Experimental design:

A total of 25 healthy adult female albino rats were randomly divided into five groups (for each n=5 rats) their dosing and route of administration provided in Table 1.

Table 1: Experimental study groups.

Group	Treatment	Dosage
I	NS	10ml/kg po
II	APAP	APAP 2000mg/kg po
III	Vit C+ APAP	Vit c(500mg/kg po)+ (APAP 2000mg/kg po)
IV	Vit B12+ APAP	Vit B12(10mg/kg po) + (APAP 2000mg/kg po)
V	NAC+ APAP	NAC(150mg/kg po)+ (APAP 2000mg/kg po)

Po= means by mouth; NS=Normal saline 0.9% solution

2.5 Materials

2.5.1 Drugs

The drugs for the experiment were normal saline 0.9% solution (Amanta Healthcare Limited-India), Vitamin C 99% pure powder, Vitamin B12 99% pure powder. N-acetylcysteine and acetaminophen 99% pure powder (were received as kind gifts from the Yemenia-Egyptian Pharmaceutical Manufacturing Company and Modern Drug Company) as well as Ketamine (Rotixmedica-Germany).

2.5.2 Chemicals

The chemicals for the experiment were 10% formalin (Isochem-labratories-India), paraffin (Numaligarh Refinery Limited India), Haematoxylin and Eosin Kit (Benzmicroscopic optic- Ireland).

2.6 Instruments and Equipment

The Instruments used were Electronic Balance (Spanish-LABORCOM), Sensitive Electronic Balance (Spanish- P SELECTA), Centrifuge (Spanish- P SELECTA) Screen master Plus-Biochemical system international Srl (Italy-IVD), Elisa (USA-Star Fax 4700).

2.7 Treatment of animals

Twenty-five adult none pregnant female albino rats weighing between (180-250 gm) were included in this study. All animals were healthy and of the same species and gender with normal behaviors, housed at the Animal House Unit of the Faculty of Pharmacy Aden University. Rats were allowed free access to food and water, kept in air-conditioned environment under controlled temperatures, humidity, and photoperiod cycles (12-h light/dark cycle; 25 ± 3°C; 55–60 % humidity), acclimatized for 10 days before experimenting to alleviate the stress caused by the change in their environment. Before the acclimation period, animals were randomly divided into five groups of 5 rats per cages.

2.8 Methods

2.8.1 Preparation of solutions

All preparations were made freshly before use. VitC and VB12 are water-soluble vitamins, acetaminophen was dissolved in distilled water and became suspension.

2.8.1.1 Preparation of Acetaminophen solution

Acetaminophen (2000 mg/kg) was weighed on a sensitive balance. The solution was freshly prepared before use by weighing the rat body weight based amount of the drug and suspended in 10 ml distilled water, nearly 2 ml of the suspension was given for each rat by oral gavage using disposable syringe. The dose was selected based on previous studies [26].

2.8.1.2 Preparation of Vitamin C solution

Vitamin C (500 mg/kg) was weighed on sensitive balance. Vit C was freshly prepared before use by weighing rat body weight based amount of the drug and dissolved in 10 ml distilled water , nearly 2 ml of Vit C solution was given for each rat by oral gavage using disposable syringe. The dose was selected based on previous studies [23].

2.8.1.3 Preparation of Vitamin B12 solution

Vitamin B12 (10 mg/kg) was weighed on sensitive balance . Vit B12 was freshly prepared before use by weighing rat body weight based amount of the drug and dissolved in 10 ml distilled water, nearly 2 ml of Vit B12 solution was given for each rat by oral gavage using disposable syringe. The dose was selected based on previous studies [23].

2.8.1.4 Preparation of NAC solution

NAC (150 mg/kg) was weighed on sensitive balance. NAC solution was freshly prepared before use by weighing rat body weight based amount of the drug and dissolved in 10 ml distilled water, nearly 2 ml of c solution was given for each rat by oral gavage using disposable syringe. The dose was selected based on previous studies [27].

2.8.2 Experimentation

The rats were randomly placed into 5 groups of (n = 5 rats per group). The experimental animals were weighed and then orally treated for 6 days (Groups III ,IV and V) were treated with 500, 10, and 150 mg/kg/d of VIT C, VIT B12, and NAC, respectively. Then, all the animals except the control group (Group I) was orally treated by APAP 2000 mg/kg on day 7 and then was observed for 24 hours for blood sample collection before they were

sacrificed. At day 8, the animals were subjected for intraperitoneal anesthesia with ketamine (50mg/kg). Then, venous blood (3ml) was drawn via a capillary tube from the orbital-sinus capillary vein. The blood was left at room temperature for 15 minutes allowing clotting. Then, it was centrifuged (4000 rpm for 20 minutes) to obtain serum, stored at -20°C until requested for analysis of the liver function biochemical parameters (ALT, AST, ALP, LDH and albumin). The tests were done at Al-Markazia Lab by using Screen Master Plus-Biochemical System International Srl (Italy-IVD). The oxidative stress biomarker (MAD) was tested using ELISA kits according to the manufacturer procedures and instructions.

2.8.2.1 Experimental methods

2.8.2.1.1 Spectrophotometer Test

2.8.2.1.1.1 Serum Enzymatic activity

Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), lactate dehydrogenase (LDH) and albumin were measured following the steps of the instruction manual supplied by Screen Master Plus-Biochemical System International Srl(Italy-IVD) supplied by AGAPPE Lab by using a spectrophotometer. The unit of measurement for enzyme activity is the international unit per liter (IU/L).

2.8.2.1.2 Eliza Test

2.8.2.1.2.1 Determination of oxidative stress markers in the serum of rats.

Serum malondialdehyde (MDA) was measured following the steps of the instruction manual supplied by BT-LAB ELISA kit.

2.9 Statistical Analysis

Data were checked, then entered the Statistical Package for Social Sciences (SPSS) software version 25 (IBM SPSS Inc.). All results were presented as the mean ± SD. Treatment group means were compared by one-way ANOVA followed by post hoc Tukey's test for pair-wise comparisons. $P \leq .05$ was considered statistically significant for all tests.

2.10 Ethical Consideration

The study was approved by the Research Council at the Faculty of Medicine and Health Sciences, Aden University (REC- 157-2023). It was conducted in accordance with Institutional Guidelines on Animal Use, which adopts the guidelines of 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 bodies were buried.

3. Results

3.1 Vit C, Vit B12 and NAC decrease oxidative stress

Treatment of albino rats with APAP (2000 mg/kg) showed a high significant increase in MDA compared to the control group by 3.7nmol/ml vs 0.7 nmol/ml CG, respectively, P =0.000. Pretreatment of rats with VIT C (500 mg/kg), VIT B12 (10 mg/kg), NAC (150 mg/kg) reduced the increase in MDA levels to 1.47, 1.38, 1.12 nmol/ml, respectively as compared to APAP group (3.7 nmol/ml), P=0.000. However, the mean of MDA level of NAC group was the lowest comparable to VIT C and VIT B12 groups, Table 2.

Table 2: Serum levels (mean ± SD) of liver oxidative stress biomarker (MDA) among the groups (n=5).

Group	Treatment	MDA(nmol/ml)
I	CG	0.7± .28
II	APAP	3.7± .56***
III	Vit C+ APAP	1.47± .12###
IV	Vit B12+ APAP	1.38±. .08###
V	NAC+ APAP	1.12± .16###

CG=control group, APAP= Acetaminophen, VIT C=Vitamin C,VIT B12= Vitamin B12.Each data bar represents the Mean ± SD(n=5/group) ***p<0.001 vs CG, ###p<0.001 vs APAP. One-way Analysis of variance (ANOVA) test.

3.2 Vit C, Vit B12 and NAC decrease liver function biomarker

Administration of APAP at a dose of 2000 mg/kg to rats increased serum levels of AST (197.2 U/L) , ALT(118.2 U/L), ALP (356.8 U/L) and LDH (1977.8 U/L) as compared to the control group. The difference was statistically significant with P=0.000 for AST, ALT, ALP while P=0.004 for LDH. On the other hand, treatment with APAP reduced albumin compared to the control, but it was insignificant whit P=0.5. Table 3.

Prior to APAP administration, rats were treatment with VIT C, VIT B12, NAC which reduced APAP induced increment in biomarkers of liver function such as AST , ALT, ALP and LDH as compared with APAP values, the difference was statistically significant with p<0.05. In contrary, the vitamins and NAC slightly increase the level of albumin that was depressed by APAP. The difference was statistically insignificant with P=0.09 for VIT B12 and 0.4 for NAC while VIT C significantly increase APAP-reduced albumin with P<0.01. Table 3

Table 3: Serum levels (mean ± SD) of liver function biomarkers among the groups (n=5).

Group	Treatment	AST (IU/L) Mean ±SD	ALT (IU/L) Mean ±SD	ALP (IU/L) Mean ±SD	LDH (IU/L) Mean ±SD	Albumin (g/dL) Mean ±SD
I	CG	36.4±3.57	30.4± 4.5	103.2± 9.25	629.4±255.14	4.2±0.15
II	APAP	197.2±44.16***	118.2±29.6***	356.8±57.99***	1977.8±942.71**	3.8±0.08
III	Vit C+ APAP	85.8± 37.59###	58.2±22.02###	218.8± 39.7##	843.6±357.86#	4.8±0.4##
IV	Vit B12+ APAP	108 ± 41.3##	71.6±18.43##	211.8±67.19###	611.2±143.22##	4.5 ± 0.6
V	NAC+ APAP	49.8 ± 11.6###	49.6± 6.58###	197.2± 9.3###	841.2±491.31#	4.3 ±0.6

CG=control group, APAP= Acetaminophen, VIT C=Vitamin C,VIT B12= Vitamin B12.Each data bar represents the Mean ± SD(n=5/group)
***p<0.001,** p<0.01 vs CG, ###p<0.001, ##p<.0.01 vs APAP. One-way Analysis of variance (ANOVA) test.

4. Discussion

The antioxidant properties and the regulatory functions of vitamins have been documented to confer pharmacological protection against hepatotoxic effect of drugs and some chemical agents [23]. This study examined VIT C and VIT B12 for their hepatoprotective effect against APAP induced liver injury in comparison to NAC treated group. In animal models, it has been demonstrated that APAP can cause hepatic damage, which is typically shown as hepatocyte necrosis and apoptosis. In addition high doses of APAP reduced hepatocyte viability and survival[2]. The result of this study was in line with this report in term of APAP induced liver toxicity.

Acetaminophen-induced hepatotoxicity by increasing oxidative stress and increasing free radical formation reflected by MDA rise. Polyunsaturated fatty acids which are present in quite large concentrations in liver tissue, are very susceptible to peroxidative damage. MDA was employed as an easy-to-use measure to assess the severity of lipid peroxidation reactions in the liver[28],[15].

The present study revealed a significant increase in MDA after Acetaminophen administration, which was almost more than five times that found in control group. This result was in consistence with that of Mohammed et al from Iraq who reported significant elevation in MDA after 7 days of Acetaminophen dose administration[10]. Furthermore this finding agrees with abdulkhaleq et al from Jordan, who reported markedly increase in MDA levels by nearly 2-fold of the control level after Acetaminophen administration [23].

However, pre-treatment with Vitamin C (500 mg/kg) significantly decreased the APAP induced MDA elevation (p= 0.000). This agrees with a study done by Abdulkhaleq et al and Khan et al from Bangladesh, who reported a significant reduction in MDA levels in VIT C pre-treated group [23], [29].

Pre-treatment with vitamin B12 in a dose of 10 mg/kg significantly decreased APAP induced elevation in MDA levels (p= 0.000). This finding agrees with previous studies [10] [23]. Moreover, our finding agrees with a study done by Azza et al from Egypt who showed significant reduction in MDA levels in groups administered either vitamin C or vitamin B12 before UVC exposure[17].

In this study, acetaminophen treatment significantly increased the serum levels of the liver enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT), alkaline phosphatase (ALP), and lactate dehydrogenase (LDH), compared with the control group's values. These enzymes usually present in the cytosol and then released into the blood after liver damage or injury. This finding was in line with Mohammed et al and Moke et al from Nigeria, who reported significant elevation in serum levels of liver enzymes after administration of APAP[10], [30]. However, in the current study, pre-treatment with VIT C hold down the elevation in serum levels of AST, ALT, ALP and LDH significantly compared with APAP group. This results were consistent with the work of Mumtaz et al from Pakistan, who reported ameliorative effect in serum liver enzymes of vitamin C in metals-administered rabbits [22].

Likewise, pre-treatment with VIT B12 decreased the elevated serum levels of AST, ALT, ALP and LDH as compared with APAP group. These results were in line with the work of previous studies [23] and Ahmad et al from India[31]. But, in contrary to Abdulkhaleq et al, in which only ALT and ALP levels were significantly reduced, our findings were statistically significant to all enzyme levels. Since the tested vitamins appear to have membrane-stabilizing activity, the reduction in liver enzymes might be a sign of their capacity to restore membrane integrity and liver cell regeneration, which would minimize the amount of liver enzymes leaking into the blood[32].

Concerning the effectiveness of the tested vitamins, the study showed that vit C is more effective than B12 in terms of percentage reduction in AST, ALT values but ALP and LDH reduction was less than B12 as compared to APAP values. The results shown that VIT C reduced AST, ALT, ALP and LDH by 56.5%, 50.8%, 38.7%and

57.4% and VIT B12 by 45.2% ,39.4% ,40.6% and 69.1% respectively as compared to APAP group.

On the other hand, the reduction values displayed by vitamins were less than that produced by the comparator NAC, in which the proportion of AST reduction was 74.8% and of ALT was 58.1% and ALP 44.7% and LDH 57.5%.

Albumin represent as the major protein production that is typically inhibited by liver impairment. Rats given large doses of APAP alone showed a decrease in albumin levels. This was supported by the disruption of hepatocyte integrity caused by APAP in histopathological examination , which either resulted in a reduction of the liver's ability to synthesis proteins or an increase in proteolysis and degradation activities [23].

Unlike other groups, which exhibited insignificant effects, VIT C only demonstrated the most protection against APAP-induced albumin deficiency. This might be because of its essential ability to protect hepatocytes from damage and to maintain their ability to regulate albumin levels. Our findings was in line with Abdulkhaleq et al research, who reported that only VITC group's albumin level was significantly elevated, in contrast to the other groups.

5. Conclusion

Acetaminophen induced liver hepatocellular impairment through elevation of oxidative stress marker MDA and elevation of the liver function markers in the experimental rats. Vitamin C and vitamin B12 seem to have protective mechanisms in hepatic toxicity that was comparable to those of N-acetylcysteine (NAC).

Recommendation

Additional investigation and exploration of the molecular mechanisms behind the protective effects of vitamin C and vitamin B12 in the liver are necessary.

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مقالة بحثية

تأثير فيتامين C وفيتامين B12 على إصابة الكبد الناجمة عن الأسيتامينوفين في الجرذان البيضاء

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المُلخّص

تم التعرف على العديد من الفيتامينات، بما في ذلك فيتامين سي وفيتامين ب12، كمضادات للأكسدة وأظهرت تأثيرات وقائية للكبد ضد إصابة الكبد الناجمة عن جرعة زائدة من عقار اسيتامينوفين (APAP). تهدف الدراسة الحالية إلى التحقيق في تأثير هذه الفيتامينات في حماية الكبد من السمية الكبدية الناجمة عن عقار APAP في الفئران. أجريت تجربة على إناث الفئران البيضاء. كانت هناك خمس مجموعات من الحيوانات: مجموعة ضابطة تلقت محلول ملحي عادي (10 مل / كجم) ومجموعة عولجت بأسيتامينوفين (2000 مجم / كجم) ومجموعة عولجت بفيتامين سي (500 مجم / كجم) ومجموعة عولجت بفيتامين ب 12 (10 مجم / كجم) ومجموعة عولجت بـ NAC (150 مجم / كجم). أعطيت جميع الحيوانات أدوية عن طريق الفم لمدة ستة أيام. في اليوم السابع، تم إخضاع جميع الحيوانات باستثناء مجموعة الضابطة لـ APAP عن طريق الفم ثم تم مراقبتها لمدة 24 ساعة لجمع عينات الدم قبل التضحية بها. أظهر علاج APAP ارتفاعًا كبيرًا في بيروكسيد الدهون، وهو ما أكدته نتائج مالونديالدهيد في أنسجة الكبد (MDA)، وارتفاع مستويات إنزيمات الكبد في المصل، أسبارتات أمينوترانسفيراز (AST) ألانين أمينوترانسفيراز (ALT)، والفوسفاتيز القلوية (ALP)، ولاكتات ديهيدروجينيز (LDH) $p<0.001$، وانخفاض مستويات الألبومين، والتي تشير جميعها إلى إصابة الكبد. يعمل فيتامين سي وفيتامين ب12 على خفض هذا الارتفاع بشكل ملحوظ $p<0.01$، ولكنهما يرفعان مستويات الألبومين بشكل طفيف. أظهرت الدراسة أن عقار اسيتامينوفين تسبب في ارتفاع مؤشر الإجهاد التأكسدي ومؤشرات وظائف الكبد الدالة على إصابة كبد الفئران بالعقار. يبدو أن فيتامين سي وفيتامين ب12 لهما تأثيرات وقائية للكبد ضد الإجهاد التأكسدي الناجم عن عقار اسيتامينوفين في الفئران والذي يشبه الى حد ما تأثير الأسيتيل سيستائين. هناك حاجة إلى مزيد من الدراسات لتحديد الآليات التي تقف وراء هذه الفعالية.

الكلمات المفتاحية: الكبد، أسيتامينوفين، فيتامين ج، فيتامين ب12.

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