Effect of alcoholic extract of black currant (*Vitis vinifera L.*) on hepatic function and damage induced by hydrogen peroxide and methionine overload in rats

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Abstract

This study was designed to investigate the prophylactic effect of alcoholic extract of black currant on some physiological parameters related with liver disease in male rats treated with H_2O_2 and methionine overload. Fifty adult male rats were divided randomly into five equal groups and were treated as following for 42 days: Rats in the first group (C) received normal tap water and considered as a control group; the second group (T 1) received 0.5% H_2O_2 in drinking water, while rats of the third group (T 2) were intubated daily with 100 mg/kg B.W. of methionine; animals in the fourth group (T3) received orally 60mg/kg B.W. of alcoholic extract of black currant plus 0.5% H_2O_2 in drinking water and rats in the fifth group (T 4) intubated daily with methionine plus alcoholic extract of black currant orally. Fasting blood samples were collected at 0, 21, and 42 days of experiment to study the following parameters: serum concentrations of alanine aminotransferase (ALT), alkaline phosphatase (ALP), aspartate amino transferase (AST), total cholesterol (TC) and total serum protein (TSP). Furthermore sections of liver were assessed for histological studies. The results revealed that administration of 0.5%H_2O_2 in drinking water (T_1) and oral intubation of methionine(T 2) for 42 days caused significant increase ($P< 0.05$) in serum ALT, AST, ALP and TC with significant decrease ($P< 0.05$) in TSP concentration as compared to other groups, on the other hand the animals treated with 0.5%H_2O_2 plus 60mg/kg alcoholic extract of black currant (T_3) showed significant decline in level of ALT, AST, ALP and TC concentrations with significant elevation in TSP concentration comparing to (T 1) and control group. The results also showed that oral intubation of alcoholic extract of black currant plus methionine (T4) significantly decrease ($P<0.05$) the serum concentrations of ALT, AST, ALP and TC with significant elevation of TSP concentration comparing to methionine group (T 2) and control group. Histological studies revealed the treatment of animals with H_2O_2 or methionine initiated hepatic damage. While alcoholic extract of black currant showed mild regression of lesion. It seems that alcoholic extract of black currant exert protective actions against H_2O_2 and methionine overload induced oxidative stress and change in some biological markers related to liver disease.

تأثير المستخلص الكحولي للزبيب الأسود على وظيفة الكبد في الجرذان المعاملة بفرط المثيونين وبيروكسيد الهيدروجين

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الخلاصة

أجريت هذه الدراسة لغرض معرفة التأثير الوقائي للمستخلص الكحولي للزبيب الأسود في بعض المعايير الحيوية المتعلقة بوظيفة الكبد في ذكور الجرذان المعاملة ببيروكسيد الهيدروجين وفرط المثيونين. تم استخدام 50 من ذكور الجرذان البالغة قسمت عشوائيا إلى خمسة مجاميع متساوية (عشر حيوانات/ مجموعة) وعوملت كالتالي لمدة 42 يوم: أعطيت المجموعة الأولى (C) الماء العادي وجرعت محلول دارئ الفوسفات (1مليليتر/حيوان) وعدت كمجموعة سيطرة؛ وأعطيت المجموعة الثانية (T_1) الماء الاعتيادي مضافاً إليه بيروكسيد الهيدروجين بتركيز (0.5%)؛ أما المجموعة الثالثة (T_2) فقد جرعت بالمثيونين (100ملغم/كغم من وزن الجسم) مذاباً بمحلول دارئ الفوسفات؛ أما المجموعة الرابعة (T_3) فقد جرعت فموياً المستخلص الكحولي للزبيب الأسود (60 ملغم/كغم من وزن الجسم) بالإضافة إلى بيروكسيد الهيدروجين وجرعت المجموعة الخامسة (T_4) المثيونين بتركيز (100ملغم/كغم من وزن الجسم) مذاباً بمحلول دارئ الفوسفات بالإضافة إلى تجريعها المستخلص الكحولي للزبيب الأسود بنفس التركيز أعلاه. تم جمع عينات الدم في الأيام 0، 21، 42 من التجربة لغرض دراسة المعايير التالية: فعالية الأنزيمات الناقلة للأمين ALT وAST وفعالية إنزيم الفوسفاتيز القاعدي (ALP)، تركيز الكولستيرول الكلي TC، والبروتين الكلي بالمصل(TSP). فضلاً عن اخذ مقاطع نسيجية من الكبد لغرض دراسة التغيرات النسيجية المرضية. أظهرت النتائج حدوث زيادة معنوية ($P<0.05$) في مستوى الأنزيمات الناقلة للأمين ALT,AST وفعالية إنزيم الفوسفاتيز القاعدي، تركيز الكولستيرول الكلي في مصل الدم في المجموعتين المعاملتين T_1 وT_2، إضافة إلى حدوث انخفاض معنوي($P<0.05$) في تركيز البروتين الكلي في مصل الدم مقارنه مع المجاميع الأخرى. كما أدت المعاملة ببيروكسيد الهيدروجين والمستخلص الكحولي للزبيب الأسود (T_3) وجود انخفاض معنوي ($P<0.05$) في فعالية كل من TC,ALP,AST,ALT في مصل الدم وارتفاعا معنويا ($P<0.05$) في تركيز TSP مقارنه مع المجموعة المعاملة بالمثيونين (T2) ومجموعة السيطرة. بينت نتائج الفحص النسيجي لكبد الجرذان المعاملة ببيروكسيد الهيدروجين أو الميثيونين حدوث التلف الكبدي في حين معالجة الحيوانات المستخلص الكحولي للزبيب الأسود تسبب في انكفاء بسيط في التلف النسيجي يستنتج من هذه الدراسة ان المستخلص الكحولي للزبيب الأسود ذو تأثير وقائي ضد الإجهاد التأكسدي المستحدث ببيروكسيد الهيدروجين وفرط المثيونين في بعض المعايير الحيوية التي تعد مؤشراً لوظيفة الكبد.

Introduction

Methionine is an essential amino acid found in both animal and plant proteins converted via enzymatic transmethylation to homocysteine(Hcy) (1, 2). Methionine is a lipotropic and protective factor against various types of liver damage, but excessive dietary methionine is hepatotoxic (3). When the metabolic pathways of methionine are interrupted due to malnutrition or inherited gene error, homocysteine level in the circulation will be

elevated (4). Hyperhomocysteinemia(hHcy) may result from genetic defects in the enzymes involved in the metabolism of homocysteine or from deficiencies of enzyme cofactors or cosubstrat {i.e. folic acid, vitamin B_6 (pyridoxine), or vitamin B_{12} (cyanocobalmine)}, or some chronic medical conditions and drugs (5, 6). Hcy level tend to increase with older age in smoker (7), renal dysfunction, Hypothyroidism and solid organ transplantation are associated with hHcy (8). Finally, several commonly used medication, including methotrexate, nitrous oxide (No), phenytion, carbamazepine, nicotinic acid and thiazide diuretics, increased total Hcy level (9,10). Extensive evidences shows that elevated plasma Hcy concentration, a reflection of impaired cellular metabolism of methionine, can be considered as an independent risk factor for atherothrombotic vascular disease (11). Hcy has been shown to affect lipid metabolism, which in turn contributes to the development of atherosclerosis (12). Hyperhomocysteinemia could increase bone resorption by stimulation of osteoclast formation and activity (13) and Hcy enhanced apoptosis (14). Free radicals generation during the oxidation of homocysteine was documented as a mechanism of homocysteine toxicity (15), so it contributes to the development of cancer and brain aging such as in Alzheimer's and Parkinson's disease (16,17). The liver is the main detoxifying organ in the body, found to be subjected to many insults potentially causative of oxidative stress. The liver plays a central role in the synthesis and metabolism of Hcy, given the fact that the majority of dietary methionine is metabolized in this organ (18). Grape seeds polyphenols (proanthocyanidins) were found to be highly bioavailable antioxidant providing significantly greater protection against free radical-induced lipid peroxidation and DNA damage, than that observed with vitamins C, E and β-carotene, (19,20). Because micronutrient from grape seeds may have beneficial hepatoprotective effect, the hypothesis that alcoholic extract of black currant (*Vitis Vinifera. L*) might affect several measures of liver health were tested in rats exposed experimentally to oxidative stress by oral intubation of 0.5 % H_2O_2 and 100 mg/kg of methionine.

Materials and Methods

Black currant was obtained from commercial sources and the vouchers specimen of the plant was deposited to be identified and authenticated at the National Herbarium of Iraq Botany Diretorate in Abu-chraib, under scientific name *Vitis Vinifera L* belongs to the Family vitaceae. Seventy percent of alcoholic extract of black current was prepared according to the procedure of (21). Fifty (50) male rats (175-250 gm) were used in this investigation. Their ages were ranged between (2.5-3.0) months. Animals were housed in plastic cages in conditioned room (22-25 Ċ) and divided into equally five groups (each of ten) and were treated as follows for 42 days:- Group C: Animals in this group treated with phosphate buffer (0.1 M) PH 7daily using cavage needle and served as control group. Group T_1:- Animals in this group were subjected to *ad libitum* supply of drinking water containing 0.5% H_2O_2. Group T_2:- Animals in this group were administered daily with methionine 100 mg /kg B.W (22) diluted with buffer (0.1 M) PH 7 using gavage needle. Group T_3:- In addition to (0.5%) H_2O_2 in drinking water, animals were administered daily with 60 mg/kg B.W of alcoholic extract of black currant (23). Group T_4:- Animals in this group were administered orally with methionine (100mg/kg B.W) diluting in buffer (0.1 M) PH 7 plus crude alcoholic extract of black currant (60mg/kg B.W). Fasting blood samples were collected at different intervals Zero, 21, 42 days of the experiment. Blood were drawn via cardiac puncture technique from anesthetized rats, and serum was collected by centrifugation (2000rpm) for 15 minute, a liquated and frozen at -20C until analysis.

Alanin aminotransferase and Aspartate aminotransferase (ALT,AST) activities were enzymatically measured based to using standard assay Kits (BiolaB SA, Company–France) (24). Serum alkaline phosphatase activity was measured enzymatically using standard assay Alkaline phosphatase kit (BiolaB SA, Company–France) (25). Serum total cholesterol concentration(TC) was enzymatically measured using standard assay (cholesterol kit–Biocon chemicals), (26).Total serum protein was measured using standard assay (Total protein kit) product of spinreact SA, company Spain. For histological studies, rats were killed the liver was excised, and preserved in 10% neutral formalin buffer solution. Tissues section was prepared, stained with hematoxylin–Eosin (H&E) stains (27). Statistical analysis of data was performed on the basis of Two-Way Analysis of Variance (ANOVA) using significant level of ($P< 0.05$). Specific group differences were determined using least significant differences (LSD) (28).

Results

A significant increase ($P<0.05$) in ALT activity was found in groups T_1, T_2, T_3 and T_4 in comparison with the control group after 21 day of treatment with methionine, H202 alone or in combination with black current. Further significant increase ($P<0.05$) was observed after exposure to H_2O_2 and methionine alone in day 42 of experiment comparing to control, T_3 and T_4 groups. It's appearing that alcoholic extract of black currant reduced elevated ALT activity caused by H_2O_2 and methionine exposure at the end of the experiment. Non Significant differences in ALT activity were observed in T_3 after 42 days of treatment in comparison with the pretreatment period (Table 1). Serum ALP activity was significantly elevated ($P<0.05$) after 21 days of treatment in group T_1 and T_3 in comparison with control, T_2 and T_4 groups (Table2). Intubations of animals with alcoholic extract of black currant (T_4) showed a marked reduction in serum ALP activity after 42 days of treatment in comparison with T_1, T_2 and T_3.Within the time, the data also showed non significant differences in ALP activity in rats treated with methionine plus alcoholic extract of black currant (T_4) and in group (T_3) treated with H_2O_2 plus alcoholic extract of black currant relative to pretreatment period. Besides, the results showed that oral intubation of rats with 0.5% H_2O_2 and methionine (T_1 and T_2) caused significant elevation in serum AST activity at the end of the experiment comparing to the control and black currant treated groups (Table3). From the data observed in the table, showed that alcoholic extract of black currant suppressed the elevation serum AST activity at group $T_3$and T_4 group comparing to methionine and H_2O_2 treated groups at day 42 of the experiment. Analysis of data in table-4 revealed that the mean value of TC concentration increased significantly ($P<0.05$) in T_1 and T_2 treated groups at the day 21 and 42 of treatment comparing to control and other two treated groups T_3 and T_4. It should be mentioned that treatment of rats with alcoholic extract of black currant concurrently with methionine (T_4) cause a significantly reduction ($P<0.05$) in TC concentration at day 42 compared to the pretreatment period. There was a clear reduction ($P<0.05$) in TSP concentration after 21 days of treatment in all treated groups compared with the control group. Moreover, TSP concentration in rats treated with black currantT3 and T4 showed a significantly increased concentration ($P<0.05$) in day 42 as compared to T_1 and T_2. While alcoholic extract of black currant T_3 and T_4 concurrently with H_2O_2 or methionine, significantly corrected most of TSP values and succeeded to normalize them nearly to control value. (Table5) Within the time significant reduction ($P<0.05$) in mean value of TSP were observed in T_1 and T_2 treated groups comparing to the pretreated period.

The histological examination of liver sections in H_2O_2 treated group (T_1) showed a cellular vacoulation with necrotic changes in hepatocyte characterized by pyknosis or disappearance of nuclei of the cell and apoptosis is observed in hepatocyte figure (2), and the histological sections also show multifocal granulomatous lesions characterized by aggregation of lymphocytes and macrophages with degenerative changes in the hepatocytes figure (3) as compared to control group figure (1). While oral intubation of rats with methionine (T2) produce multifocal granulomatous lesion characterized by mononuclear aggregations in liver parenchyma and also around the blood vessel figure (4). Perivasicular aggregations of the lymphocytes and mononuclear cells in the portal area were observed in figure (5), related to section in liver of H_2O_2 plus alcoholic extract of black currant in (T_3) treated rats. Moreover oral intubation of alcoholic extract of black currant concurrently with methionine caused regression of pathological lesion and black currant preserved the histological structure of liver, with proliferation of kupffer cells and regeneration of liver tissue figure (6) as compared to control figure (1).

Table (1) Effect of hydrogen peroxide, methionine and alcoholic extract of black currant on serum alanine aminotransferase (IU/L) in male rats

Groups / Time (Days)	Control Group(C)	H2O2 O.O5% Group(T_1)	Methionine Group (T_2)	H2O2+Extract Group(T_3)	Methionine +Extract Group (T_4)
Zero	10.60 ± 0.75 A a	10.80 ± 0.86 A a	10.0 ± 0.54 A a	10.8 ± 1.07 A a	10.0 ± 0.81 A a
21	10.0 ± 1.14 A a	13.80 ± 1.02 B b	13.20 ± 0.44 B b	13.0 ±1.18 B a	12.6 ± 1.21 B b
42	10.20 ± 0.44 A a	17.1± 1.50 B c	15.20 ± 1.39 B c	12.6 ± 1.2 A a	12.2 ± 0.91 A ab

Values were expressed as Mean± SE, n=10/group
Capital letters denote between groups differences, P<0.05. vs. control
Small letters denote within group differences, P<0.05.

Table (2) Effect of hydrogen peroxide, methionine and alcoholic extract of black currant on serum alkaline phosphatase (IU/L) in male rats

Groups / Time (Days)	Control Group(C)	H2O2 O.O5% Group(T_1)	Methionone Group (T_2)	H2O2+Extract Group(T_3)	Methionone +Extract Group (T_4)
Zero	110.8 ± 3.4 A a	107.0 ± 2.57 A a	109.2 ± 3.27 A a	112.0 ± 5.84 A a	108.2 ± 4.04 A a
21	110.0 ±1.67 A a	158.0 ± 8.6 B b	122.6 ± 6.8 A a	141.0 ±9.8 C b	126.0 ± 8.74 A b
42	110.4 ± 3.55 A a	194.5± 12.85 B c	179.0 ±13.49 B b	126.2 ± 5.7 C a	119.0 ± 3.15 AC a

Values were expressed as Mean± SE, n=10/group
Capital letters denote between groups differences, P<0.05. vs. control
Small letters denote within group differences, P<0.05.

Table (3) Effect of hydrogen peroxide, methionine and alcoholic extract of black currant on serum aspartate aminotransferase (IU/L) in male rats

Groups / Time (Days)	Control Group (C)	H2O2 O.O5% Group(T_1)	Methionone Group (T_2)	H2O2+Extract Group (T_3)	Methionone +Extract Group (T_4)
Zero	10.8 ± 0.58 A a	11.2 ± 0.86 A a	11.8 ± 0.66 A a	11.0 ± 0.54 A a	11.2 ± 0.54 A a
21	10.2 ±0.71 A a	12.4 ± 0.75 A a	11.9 ± 1.07 A a	12.0 ± 0.89 A a	11.8 ± 1.02 A a
42	10.4 ± 0.68 A a	15.2 ± 1.24 BC b	13.4 ± 0.87 C a	11.6 ± 1.03 AC a	11.0 ± 0.89 AC a

Values were expressed as Mean± SE, n=10/group
Capital letters denote between groups differences, P<0.05. vs. control
Small letters denote within group differences, P<0.05.

Table (4) Effect of hydrogen peroxide, methionine and alcoholic extract of black currant on serum total serum cholesterol (mg/dl) in male rats

Groups / Time (Days)	Control Group(C)	H2O2 O.O5% Group(T_1)	Methionone Group (T_2)	H2O2+Extract Group (T_3)	Methionone +Extract Group (T_4)
Zero	91.1± 4.74 A a	90.2 ± 2.47 A a	91.2 ± 4.17 A a	91.2 ± 3.8 A a	90.4 ± 2.09 A a
21	90.2 ±3.75 A a	118.2 ± 8.15 B b	116.8 ± 3.3 B b	85.2 ± 2.7 A a	85.4 ± 2.3 A a
42	90.6 ± 1.95 A a	134.1± 7.74 B c	135.4 ±5.06 B c	83.5 ± 2.54 AC a	75.7 ± 2.7 C a

Values were expressed as Mean± SE, n=10/group
Capital letters denote between groups differences, P<0.05. vs. control
Small letters denote within group differences, P<0.05.

Table (5) Effect of hydrogen peroxide, methionine and alcoholic extract of black currant on total serum protein (gm/dl) in male rats

Groups / Time (Days)	Control Group (C)	H2O2 O.O5% Group(T_1)	Methionone Group (T_2)	H2O2+Extract Group(T_3)	Methionone +Extract Group (T_4)
Zero	4.31± 0.08 A a	4.40 ± 0.11 A a	4.32 ± 0.13 A a	4.30 ± 0.10 A a	4.38 ± 0.10 A a
21	4.36 ± 0.08 A a	3.90 ±0.16 B b	3.88± 0.12 B b	4.06 ± 0.10 B b	3.92 ± 0.16 B b
42	4.46 ± 0.08 A a	3.8 ± 0.14 B b	3.84 ± 0.12 B b	4.20 ± 0.13 A ab	4.30 ± 0.11 A ac

Values were expressed as Mean± SE, n=10/group
Capital letters denote between groups differences, P<0.05. vs. control
Small letters denote within group differences, P<0.05.

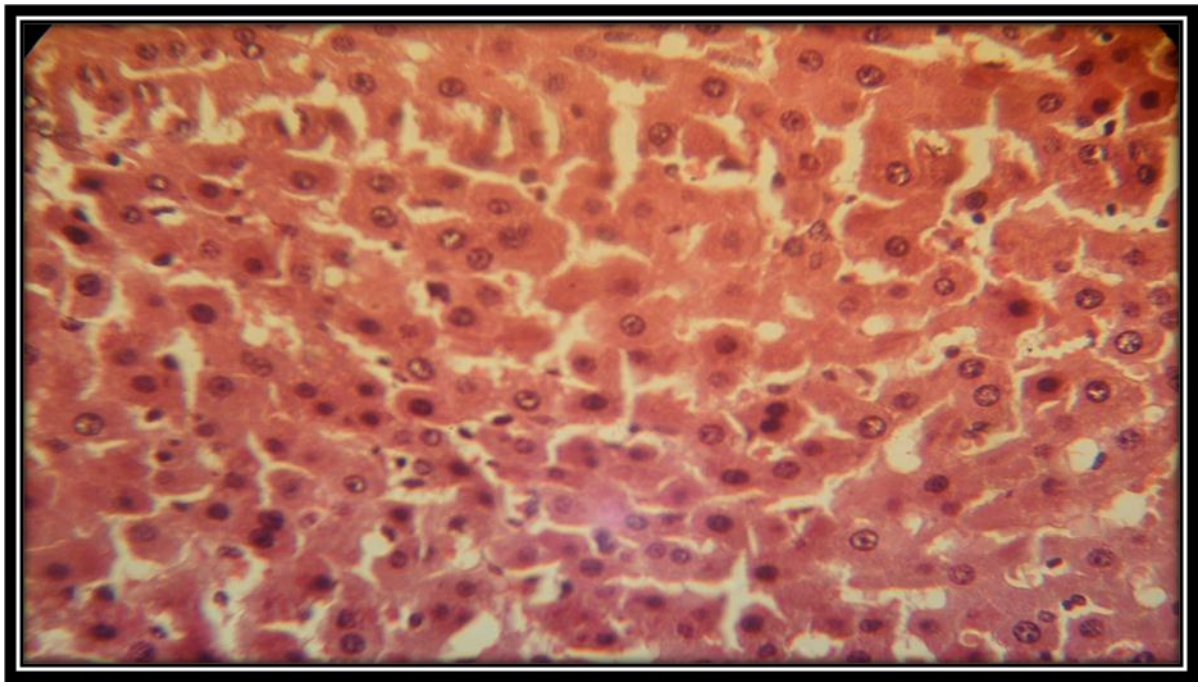

Fig. (1) Histological section in liver of control group. Show normal histology of liver section (H & E 40X)

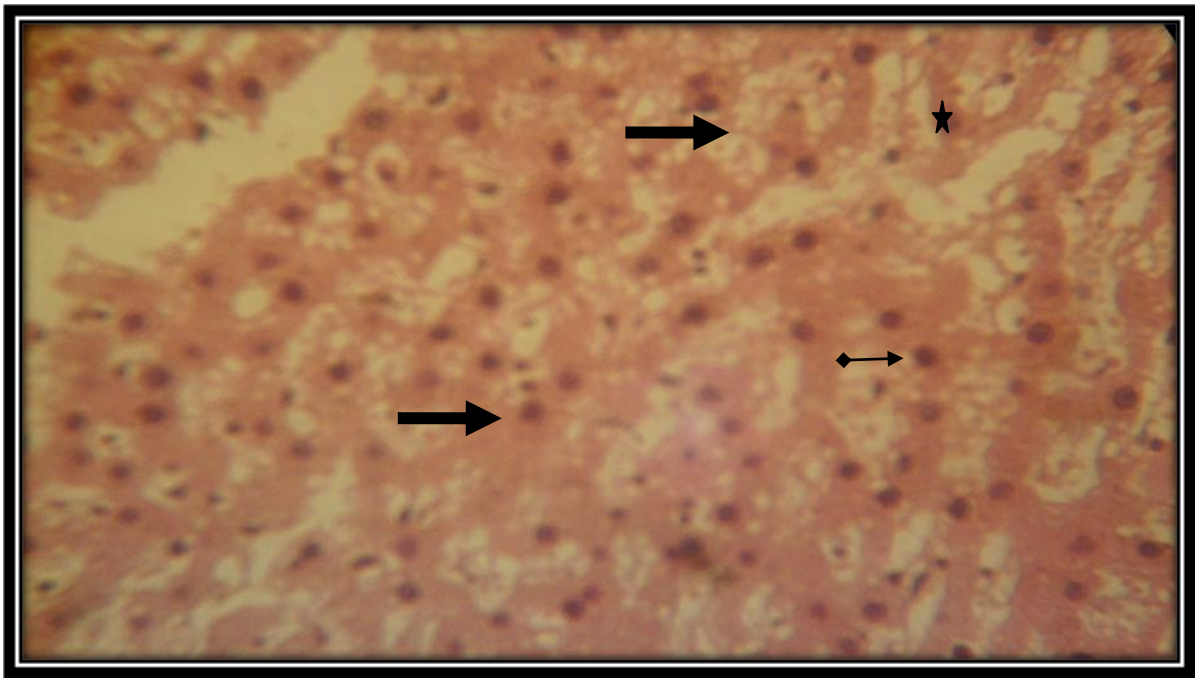

Fig. (2) Histological section in liver of H_2O_2 treated rats .Note degenerative changes in the hepatocyte (★) characterized by pyknosis of nuclei (⟷) &necrotic change in some hepatocyte (➡) (H & E 40 X)

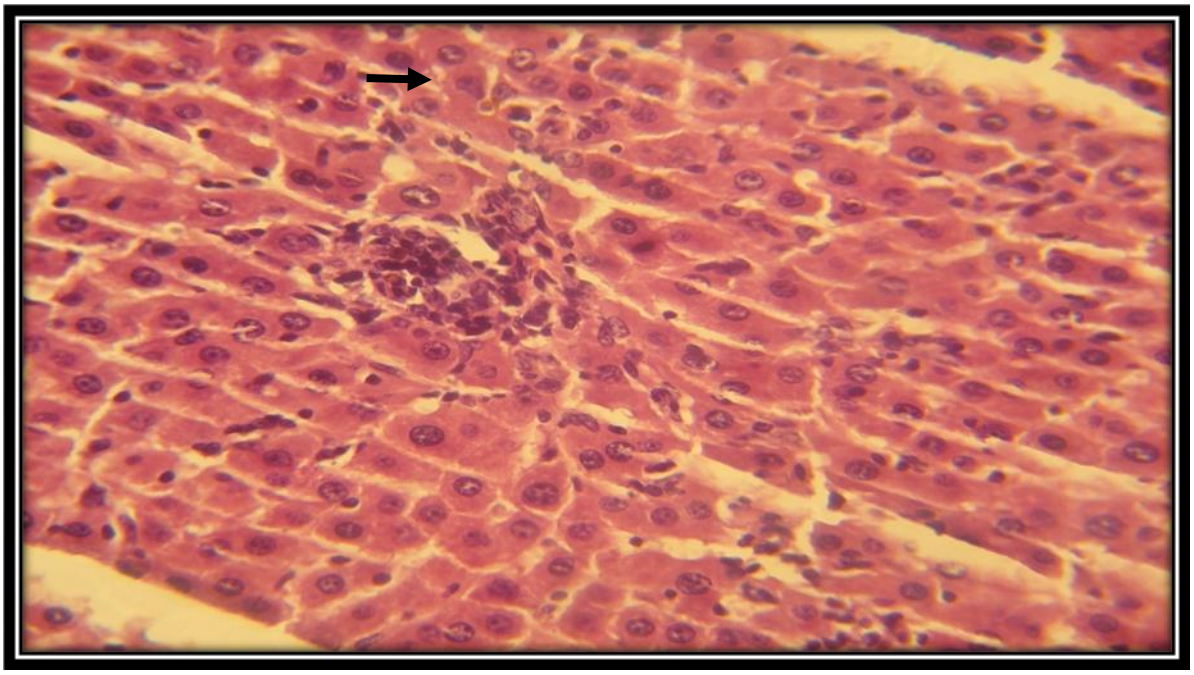

Fig.(3) Histological section in liver of H_2O_2 treated rats .Note multifocal granulomatous lesion (→) (H & E 40 X)

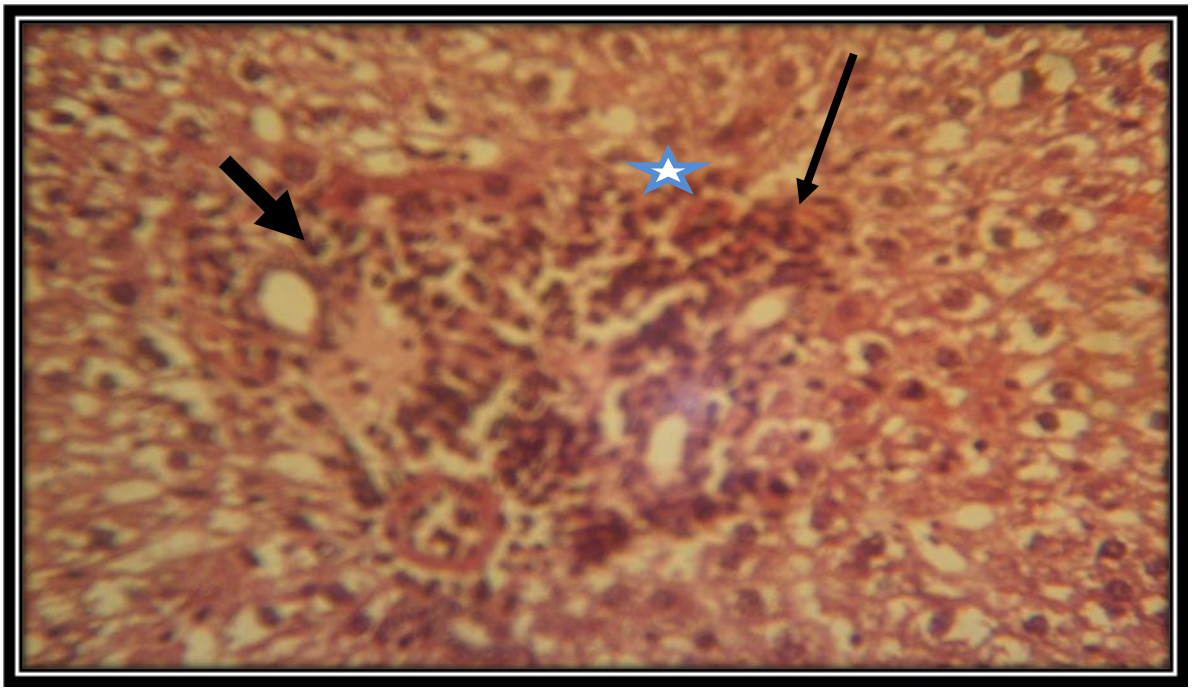

Fig.(4) Histological section in liver treated with methionine. Note multifocal granulation (→) characterized by mononuclear aggregation in liver parenchyma (☆) also around blood vessel (➡) (H &E 40X)

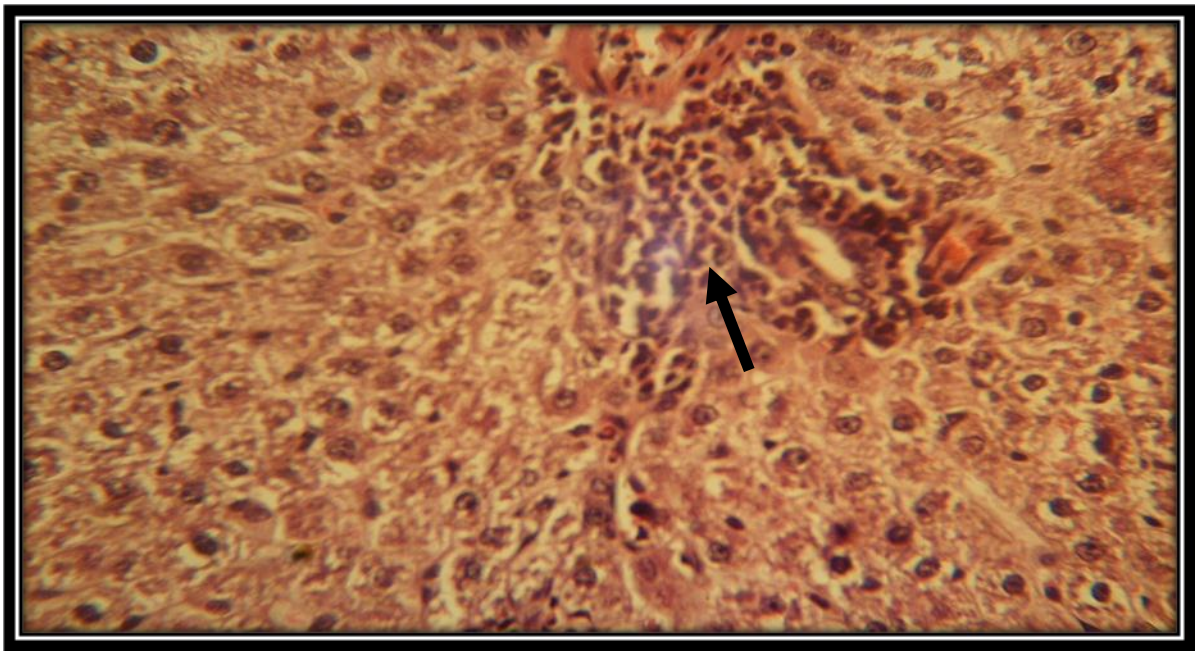

Fig. (5) Histological section in liver treated with H_2O_2 +alcoholic extract of black currant. Note aggregation of the lymphocyte around blood vessels in portal area (⟶) (H &E 40X)

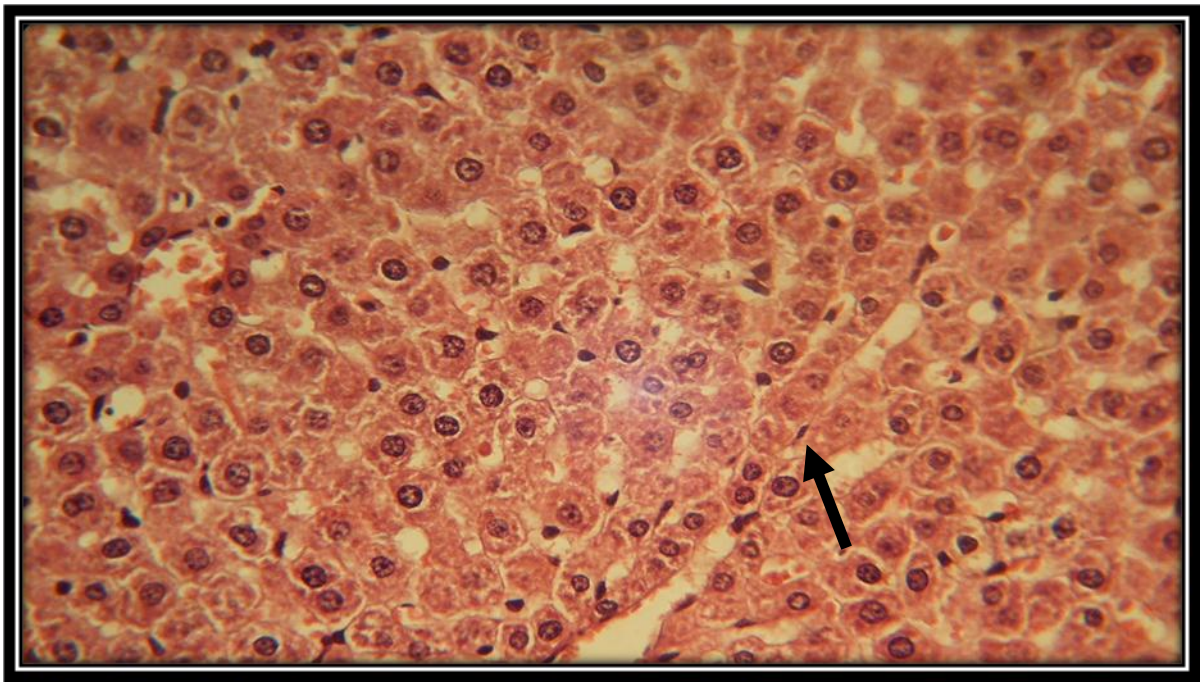

Fig. (6) Histological section of liver treated with methionine +alcoholic extract of black currant. Note proliferation of kupffer cell (⟶) (H & E 40X)

Discussion

Our result showed that daily oral intubation of methionine overload and H_2O_2 0.5% in drinking water for 42 days caused elevation of liver enzyme activities (Tables1,2,3), indicating the occurrence of liver injury. The liver produces a large amount of ALT, AST and ALP which are secreted to the circulation with injury or death, where leakage enzyme escapes from the cytosol leading to a rise in the serum level of these enzymes (29, 30).So elevated Hcy after methionine overload may cause liver damage and leakage of such enzymes. HHcy caused by folic acid deficiency may lead to increase in ALT and AST activities in serum (31). Increase in ALP level may be due to increase in lysosome activity that represent one of the important changes before cell death or may be disruption of bile flow either inside or outside hepatocyte this may lead to increase in ALP activity concentration in serum (32). Histological examination of the liver in this study supported this speculation in which hepatic damage were observed following methionine overload. An increase in ALP may be taken as an index of hepatic paranchymal damage and hepatocytic necrosis (33). Methionine supplementation leads to increase in the acidic condition of the body and may also elevate cortisol concentration leading to severe chronic bone loss and subsequently elevation of ALP levels (34). Such positive correlation between hHcy concentration and ALP activity was documented (35). The present study showed that the administration of alcoholic extract of black currant effectively improve liver function by lowering the activities of ALT, AST and ALP. Many investigators have demonstrated the efficacy of grape seed proanthocyanidins and grape juice as an inhibitor of lipid peroxidation and as a powerful free radical scavenger in vitro as well as in vivo (36,37). It is has been shown that, black currant content possesses an antioxidant activity through scavenging capacity of H_2O_2 and thus lowering lipid peroxidation (37). Thus suggesting that the alcoholic extract of black currant possessed compounds that protect the hepatocytes from liver damage and subsequent leakage of enzymes into the circulation, and may have a curative effect (decrease levels of enzyme markers).

The result of the present study revealed that methionine overload and oral intubation of 0.5% H_2O_2 in drinking water showed a significant ($P<0.05$) elevation in serum total cholesterol (Table 6). It has been suggested that Hcy caused an up-regulation 3-hydroxy-3-methylglutaryl-coA (HMG-COA) reductase synthesis at the transcription or translation level (38, 39). This result in an enhanced hepatic cholesterol biosynthesis will lead to elevation of cholesterol concentration in the plasma of hyperhomocysteinemic rat (40, 41). Elevations in TC may reflect the suppression of lipid metabolism due to H_2O_2 induced oxidative stress (42). However, the pathogenesis of hypercholesterolemia in H_2O_2 induced oxidative stress in rats has been elucidated (43).

The hypolipidemic effect of alcoholic extract of black currant was documented in this study (Table 6). The result of this study is in agreement with the result of other workers in which different currant species, and experimental duration (23, 44, 45).Several active ingredients in black currant (seed, skin, concentrate juice) may attributed to the hypolipidemic effect of the currant: 1-They are regarded as food source of phytochemicals such as catechin, epicatechin, which are the known hypolipidemic active ingredients of the currant (46), 2-Antioxidant compound present in black currant oligomeric proanthocyanidins (OPCs) might have ability to scavenge OH* directly protect low density lipoprotein(LDL) from oxidation and reduces serum cholesterol level, and improving lipoprotein profile through decrease the LDL-C concentration (47,48,49). 3-Another

investigator postulated that vitamin C content could be considered the major contributor to the antioxidant capacity and the corresponding hypolipidemic effect of black currant (50). Methionine overload markedly suppresses voluntary food intake and may cause micronutrient deficiency then lead to growth retardation (51,52), as there was a positive relation between body weight and total protein, so we can postulated that hHcy occurred after methionine overload may lead to decrease in TSP in this study. As mentioned earlier, Hcy generates reactive oxygen species, can be rapidly auto-oxidized in circulation in the presence of ceruloplasmin (the major copper binding protein in plasma) to form Hcy and hydrogen peroxide, thereby generating oxidative stress with subsequent decrease in serum protein concentration (53). The hepatoprotective activity of alcoholic extract of black currant may be through stimulation of protein synthesis, accelerates the regenerated process and the production of liver cells (54).

Dose dependent increase in serum ALT,alkaline phosphatase activities and total cholesterol concentration in T1 and T2 treated groups were observed ,indicating increased generation of reactive oxygen species (ROS) and depletion in the antioxidant activities concurrently with increasing time of exposuer as well as subsequent elevation in hepatic damage (55,56).

In conclusion, it is plausible to suggest that H_2O_2 and methionine may triggered the production of ROS. Coupled with impaired oxidant/antioxidant balance leading to hepatotoxicity, and the disturbance in the level of hepatic enzymes. The extract of black currant exhibited a beneficial effect as a natural hepatoprotectant and attenuates the liver cells apoptosis.

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