The Effect of Saliva Officinalis L (Sage Tea) on Biochemical and Pathological Changes Improvment in Adult Male Rats Induced by a High Fat Diet

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Abstract

In order to investigate the physiological-protective effect of sage tea (Salvia officinalis L.) through its role in lipid profile regulation in male laboratory rats, current research has been carried out. In this study, sixty albino male laboratory rats (100-160 g) and older rats (4-7 weeks) were used. Based on the experimental nature of the study, animals were randomly divided into three main groups (six rats per group), a control group was considered to be the first group to be fed on a standard diet, and a 28-day atherogenic diet group was considered to be the second group to be fed on a standard diet (A). And the other group (B) (including subgroups) were previously fed 28 days on an atherogenic diet; oral administration was conducted as follows: the third group (B) included subgroups (B1) and (B2) administered 14 and 28 days of sage tea (S. officinalis) (0.086 mg/kg body weight) respectively. The measurement of changes in body weight and liver function enzymes (ALT, AST and ALP) and liver organ histopathology trials was done.In the results of the study, a significant increase ($p \leq 0.05$) in the body weight of rats fed a high-fat diet (HFD) (group A) was seen compared to the control group fed a standard diet. Although body weights in The other groups were reduced in the sage tea treated group (group B), the findings of the test of liver function enzymes in animals fed on an atherogenic diet (group A) revealed a substantial increase ($p \leq 0.05$) in the level of the ALT enzyme associated with the non-changeable rate of the enzymes (AST) and (ALP), although they revealed a mild elevation relative to the control group. a slight decrease in all serum liver enzyme levels without significant difference in all experimental treatments (groups B) for both periods of 14 and 28 days. In relation to group (A), the increase and stabilization of liver enzyme levels at normal levels relative to control group values was reported, especially in the long term (28 days). In addition, histopathological examinations in the present sample showed histological changes in the liver organ compared with the control group due to feeding on a high fat diet (group A). These changes include blood vessels congestion, fat accumulation of liver connective tissue. In animals treated with sage tea (group A), a microscopic analysis of the liver showed typical histological characteristics with less fat deposition and minimal changes in histo-structural characteristics relative to the atherogenic diet group of animals. This indicates that improvement has been associated with long-term therapy (28 days). In conclusion, in reducing the functional performance and normal histological characteristics of long-term treatment-related liver and kidney organs, sage tea administration has an important synergistic protective role (28 days).

Keyword: *Saliva officinalis L (sage tea); biochemical; pathological changes; fat diet*

Introduction

Salvia officinalis is a family plant that consisted of over 900 species around the world. It is native to the Mediterranean and Middle East areas, but has now become internationally naturalized [1]. In common medicine, S.officinalis has been used to treat different types of diseases, such as epilepsy, ulcers, gout, rheumatic inflammation, dizziness, tremor, paralysis, diarrhea, hypercholesterolemia and hyperglycemia [2]. It has been shown that the administration of S.officinalis extract stimulates memory in rats and has an important effect on the treatment of Alzheimer's disease in relation to both primary and secondary cardiovascular disease prevention [3]. The beneficial effect of S.officinalis may be correlated with the presence of flavonoids in the herb for dyslipidemia. The current study shows that such biochemical studies are conducted, such as parameters of liver function, include: Alanine aminotransferase (ALT) is referred to as Glutamate-Pyruvate Transaminase because transaminase occurs at relatively high levels in the heart and liver tissues, the damage to these organs leads to transaminase leakage into the blood serum, and the measurement of the concentration of various transaminases in the blood serum is used to measure the degree of damage to the heart and liver [5].

Glutamate Transaminase oxaloacetate, also referred to as aspartate aminotransferase (AST), is predominantly found in the liver but is also present in red blood cells, heart cells, muscle tissue, and other tissues, such as the pancreas and kidneys [6]. In drinking sage tea, the liver enzymes ALT and AST are hepatocellular markers that do not cause hepatotoxicity and do not induce other adverse effects [7]. Herbs are capable of reducing serum transaminase levels, affecting hepatic histopathology and curing any chronic liver disease. Bifidobacterium Probiotic is also used to increase enzymes in the liver and to avoid liver cirrhosis [9]. An active enzyme, alkaline phosphatase (ALP), is useful for diagnosis and clinical evaluation and also is determined in both healthy individuals and patients. Alkaline phosphatase is available in most human tissues, including the bone, stomach, kidney, liver, placenta and white blood cells [10]. Damage to these tissues contributes to the release of ALP into the bloodstream, blood testing may detect elevated levels, and certain medical conditions are associated with elevated alkaline phosphate [11]. In the case of those with obesity and cardiovascular disease (CVD), elevated alkaline phosphatase enzyme levels have been found, a study has recorded that higher serum alkaline phosphatase levels have been reported in obese than in non-obese patients, and the link between alkaline phosphatase and obesity is still being tested [12]. Kidney disease has been associated with high ALP levels [13].

Material and Methods

Design of experimental study

Sixty healthy male albino rats were randomly divided into the following three groups:

- First group: a control group fed for 28 days on a standard diet.

- Second group (A): an atherogenic group fed for 28 days on an atherogenic diet.

-Third group (B): fed for 28 days on an atherogenic diet and then split into two subgroups:

- Treatment category (B1): Treated with a single oral dose (0.086 gm / kg B.W.) of sage tea consumed every day at an equivalent volume (1 ml)

For 14 days, depending on the body weight of the rats.

-Treatment group (B2): Treated a single oral dose of sage tea (0.086 gm / kg B.W.) with an equivalent volume (1 ml) every day for 28 days based on the body weight of rats.

Animals

In the current research, healthy adult male Wistar strain albino (Rattus norvegicus) (2-4months old) ranging between 120 and 160 gm was used. Rats obtained from the Department of Biology, College of Science / University of Baghdad, Iraq, animal house. Clean cages and wood shavings were placed on and sterilized by 70 percent ethanol with perfusion cleaning bottles on a routine basis. The animals were adapted for one week before the starting of the experiments to their new living environment. The rats were housed in a temperature-controlled room with a 12-hr light / dark schedule at 20 ± 2 ° C during this duration and all the experimental time. Then they were given tap water and libitum was added to a standard diet.

Standard and atherogenic diet

In this analysis, the standard and atherogenic diets used as feed for male laboratory rats were prepared according to the method [14] with standard composition.

Blood samples

Blood was collected by heart puncture using a disposable syringe(5ml) and then left for coagulation at room temperature, after that the clotted blood was centrifuged at 3000 RPM for 10 minutes, then the serum was collected and stored at (-20 C) until serum biochemical analysis and obesity biomarkers were used for measurement [15].

Methods:

1-Preparation of sage tea drinking (S. officinalis L.) with traditional dose

In Babil Province, Iraq, dry sage Salvia officinalis L. was purchased from a common market. Traditional sage tea preparation includes boiling 4 gm of dry sage aerial parts in 300 ml of distilled water and left for boiling and then allowed to cool for a period of (5-10) minutes at room temperature, then filtered with gauze as described [16]. The sage tea was made as a drink by boiling 6 gm in it above manner in the present study . In each experiment, filtered sage tea drinking was delivered orally to rats based on the acceptable body weight of rats by using a stomach tube of equivalent volume (1 ml) at a dosage of sage tea (0 .086 gm / kg B. W.)

2-Body weight

The total body weight of male rats for both groups were reported daily until it was obtained by electrical balance during the 14 and 28 day periods of each experiment.

3- Test for enzymatic liver function

Assay of -Aspartate aminotransferase (AST)

In this analysis (AST), the kit supplied by Cobas111(USA) was determined.

Assay -Alanine aminotransferase (ALT)

(ALT) determined by the Cobas111(USA) supplied kit.

- Assay for alkaline phosphatase (ALP)

(ALP) determined by the Cobas111(USA) supplied kit.

4- Study in Histopathology

Histopathological studies on the liver of rats were performed in accordance with measures that identified by [17].

Result and Discussion

The effect on body weight

The current study has shown that body weight improvements in the control, atherogenic and other treatment groups are shown in figures (1 to 3).

Figure (1) shows improvements in the control body weight (gm) and atherogenic (A) groups after feeding for 28 days on standard and atherogenic (high-fat) diets, respectively. The atherogenic group's rat body weight was slightly improved ($p \leq 0.05$) compared with the control group. This finding is also in line with the findings of [18], [19],[20], [21], which demonstrated a significant increase in body weight after high-fat diet rats were fed. A positive association was observed between the level of dietary fat and body weight / fat gained in both rats [22] and mice [23]. This result may will be attributed to the intake of a diet rich in fat that contributes to increase fatty tissue and hyperplasia of body mass. Because of the unique functions of certain fatty acids that have different metabolic activities, dietary fat composition can interfere in the development of obesity, which can alter both fat oxidation and deposition rates, resulting in changes in body weight and/or composition [24]. Alteration in both fat oxidation and deposition rates, resulting in changes in body weight and/or composition [24].The mean body weights of both sage tea groups (B1 and B2) treated with a single oral dose of sage tea (S. officinalis L.) for 14 and 28 days, respectively, as shown in figures (1) The body weight of the rat groups (B1 and B2) after 28 days of atherogenic diet was specifically decreased with non-significant variations ($p \geq 0.05$) after 14 days of treatment with sage tea (Figure 3-2) and 28 days (Figure 3) compared to the day of pre-treatment (Figure 3). Our reports were equally consistent with the results [25],[26] .

This decreased body weight may be explained by the fact that drinking sage tea is the easiest herb tea and the safest way to keep the body healthy and may demonstrate improvement in the nutritional status of the animal by decreasing body weight. Sage tea (S. officinalis) has therefore been used to regulate fat absorption and has been described as an efficient way to minimize body weight and obesity [27] . As anti-obese ingredients, the inhibitory effects of S.officinalis and its isolated active ingredients such as carnosic acid and carnosol (diterpenes) on pancreatic lipase function and lipid digestion have been investigated by suppressing serum triglyceride (TG) elevation, reducing body weight gain and obesity[28] .

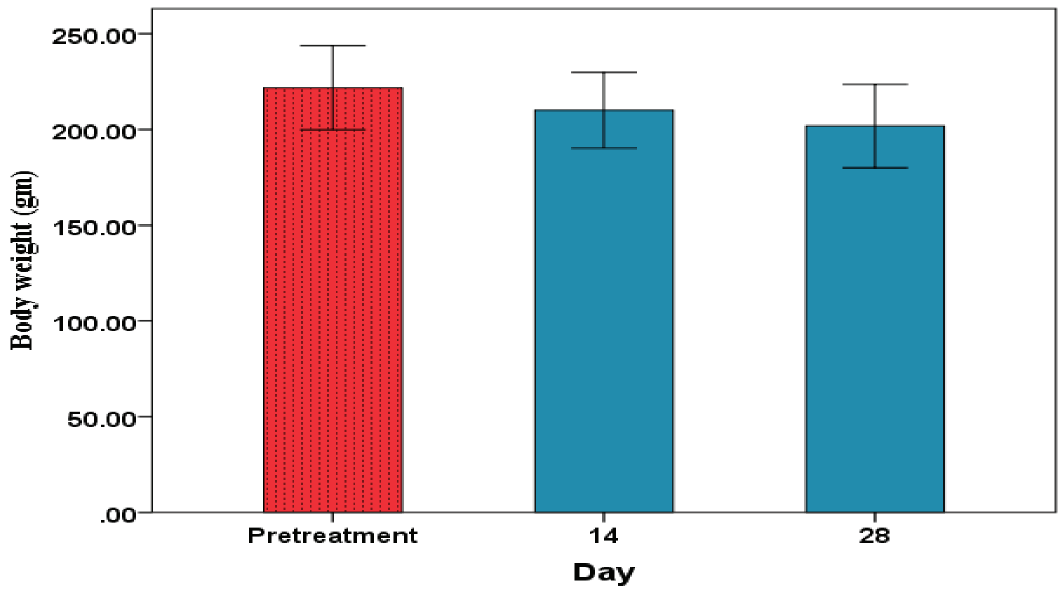

Figure (1): Body weight (gm) of group (B2) after treated with a single orally dose of sage tea (*S. officinalis* L.) for 28 days.

The effect of atherogenic diet on liver enzymes

Animals feeding on an atherogenic diet for 28 days reported a significant elevation ($p<0.05$) in alanine aminotransferase (ALT) activity in serum liver function enzymes relative to control animals feeding on a standard diet. Although serum levels of aspirate aminotransferase (AST) and alkaline phosphatase (ALP) were not significantly altered ($p \geq 0.05$), the liver enzyme activity was marginally higher than those of control animals (table 1).

In current work, the serum elevation of the activity of hepatic enzymes was consistent with a study [29] which observed elevated levels of high fat diet among experimental groups. In experiments that were carried out , a similar elevation of hepatic enzymes was observed [30] . The same elevation as studied in human adults in the United States [31There is also a poorly understood pathway contributing to the formation of hepatic steatosis, often characterized by excess lipid deposition, hepatic damage, and dyslipidemia. Studies also shown that the liver is susceptible to secondary insults, such as those induced by oxidative stress, which will accelerate the development of hepatic steatosis to NAFLD [29], a more debilitating and advanced level of non-alcoholic liver fat disorder. NAFLD can result from the consistent consumption of a diet rich in saturated fats over a long period of time. Non-alcoholic fatty liver disease is a general concept that encompasses a variety of liver diseases from fatty liver and steatosis to non-alcoholic steatohepatitis (NASH), a disorder that may lead to liver disease at the end of the stage. The most prevalent cause of chronic liver disease (CLD) is non-alcoholic fatty liver disease, and its prevalence is growing globally [32].

The effect of sage tea on: Serum alanine aminotransferase (ALT) level

Tables (1 and 2) showed the values of ALT hepatic enzyme activity anticipated after 14 and 28 days of sage tea treatment. In the control group (B1: 82.00±3.08), the hepatic enzyme ALT showed a negligible decrease in non-significant (p ≥ 0.05) control periods of 14 days and 28 days (B2: 78.33±2.79) relative to group (A) (87.00±2.89 U / I). As a consequence, this reduces the activity of ALT within the standard serum range.

-Serum aspirate aminotransferase (AST) level

As shown in Table (1 and 2), the serum activity of the liver enzymes ASL and ALP showed a statistically non-significant difference (p ≥0.05) on days 14 and 28, but also not significantly lower than the atherogenic group (A) of all treatment groups for sage tea.

-Serum alkaline phosphatase (ALP) level

Similarly, ALP hepatic enzyme serum showed a statistically non-significant difference (p ≥ 0.05) between both the 14th and 28th days in all sage tea treatment groups, but also not significantly lower than the atherogenic group (A).

In the current research, the consistent decrease in serum hepatic enzyme levels (ALT, AST and ALP) in all treated rats attributed to herbal sage can probably be due to the presence of polyphenols. For instance, the two most representative phytochemicals present in S are rosmarinic acid and luteolin-7-glucoside. Extract of officinalis (tea sage) as described in [16]. The protective effect of *S. officinalis* decrease the release of enzymes ALT, AST and ALP from hepatocytes and then reduce their levels in blood [16],. It has been noticed that drinking S. Officinalis tea enhanced the antioxidant status of the liver in mice and rats, where, among other things, increased activity of liver enzymes was observed, protective effects of drinking sage tea against free radical formation, as well as the function of S. Officinalis can enhance biochemical parameters due to the activity of antioxidants[33], who found that the aqueous extract of *S. officinalis* inhibit the product of lipid peroxidation Malondialdehyde (MDA) in brain and liver of rats, besides the extract caused significant increase in glutathione -S- transferase and glutathione reductase in rat liver. However,[34] it was suggested that the methanol extract of sage showed complete safety for liver and kidney functions. Thus, the current findings revealed that normal serum hepatic enzymatic efficacy was approved for marked safety administration of sage tea.

Table (1): Liver function enzymes levels of control, atherogenic (A), and treated group (B1) for 14 days in laboratory rats.

Parameter U/I	Group			
	Control	A	B1	B2
ALT	78.50 ± 2.92 a	87.00 ± 2.89 b	82.00 ± 3.08 ab	78.33 ± 2.79 ab
AST	77.00 ± 2.57 a	84.00 ± 2.78 a	80.00 ± 2.28 a	77.83 ±2.51 a
ALP	195.67±10.89 a	100.67±2.64 a	95.00 ±1.29 a	92.50 ± 1.34 a

Data = Mean ± S.E.M. (n= 6 rats in each group) ; Control group: fed on standard diet for 28 days;Group (A): fed on atherogenic diet for 28 days ;Group B1: Received a single orally dose of sage tea (0.086 gm/kg B.W.) daily for 14 days ;Mean with different superscripts are different significantly (p <0.05) ;Group B2: Received a single orally dose of sage tea (0.086 gm/kg B.W.) daily for 28 days.

Histopathological study

Liver

A clear hepatocyte radically arranged as cords or sheaths around central veins inside the portal lobule sinusoids were very clear between the cords of hepatocytes composed of endothelial and kupffer cells (figure 2a and b) in the present histological analysis of hepatic tissue in the normal group fed with a normal diet. The histological light microscopic analysis in the atherogenic group (rats fed a high-fat diet for 28 days) which shows certain changes in the liver structure, including congestion of the blood vessels and deposition of fat in the connective tissue between the lobules (figure 3 a and b), This observation was consistent with many studies that indicated that atherogenic diet induced fatty liver and hepatotoxicity[35,36] that suggested that hepatic tissue modifications were induced by a high cholesterol diet. In addition, other studies [37] indicate that atherogenic diets in rats with obesity have developed fatty liver disease. High cholesterol diets also contribute to inflammatory infiltration [38]. In addition, several studies have shown that histopathological changes in the liver are caused by oxidative stress resulting from high-fat dietary intake [39].

Poor accumulation of fat in liver tissue in animals were previously fed with an atherogenic diet and treated with oral administration of sage tea for 28 days in rats. Hepatocytes, sinusoids and kupffer cells tended to have normal status (figure4). In a microscopic analysis of liver tissue after once daily oral administration of sage tea drinking at a traditional single dose (0.057 g / kg B.W.) for 28 days, appreciably normal liver section characterized by simple congestion of the central hepatic vein, with simple dissociation of the granules, increased liver inflammation using sage extract in obese animals was shown. Antioxidant activity and elimination of reactive oxygen species may be the therapeutic effect of sage extract; S.officinalis extract may effectively improve liver damage. Reduced lipid peroxidation and strengthened hepatocyte defences against reactive oxygen species could be due to the defensive properties of sage extract. Therefore, current work objectively supports the use of this herbal plant as an alternative treatment for liver diseases in conventional therapies. This will support research indicating that Salvia species may potentially offer novel natural therapies for the relief or cure of many serious and life-threatening diseases such as depression, dementia, obesity, diabetes, lupus, heart failure, and cancer, in addition to treating minor common diseases [28].

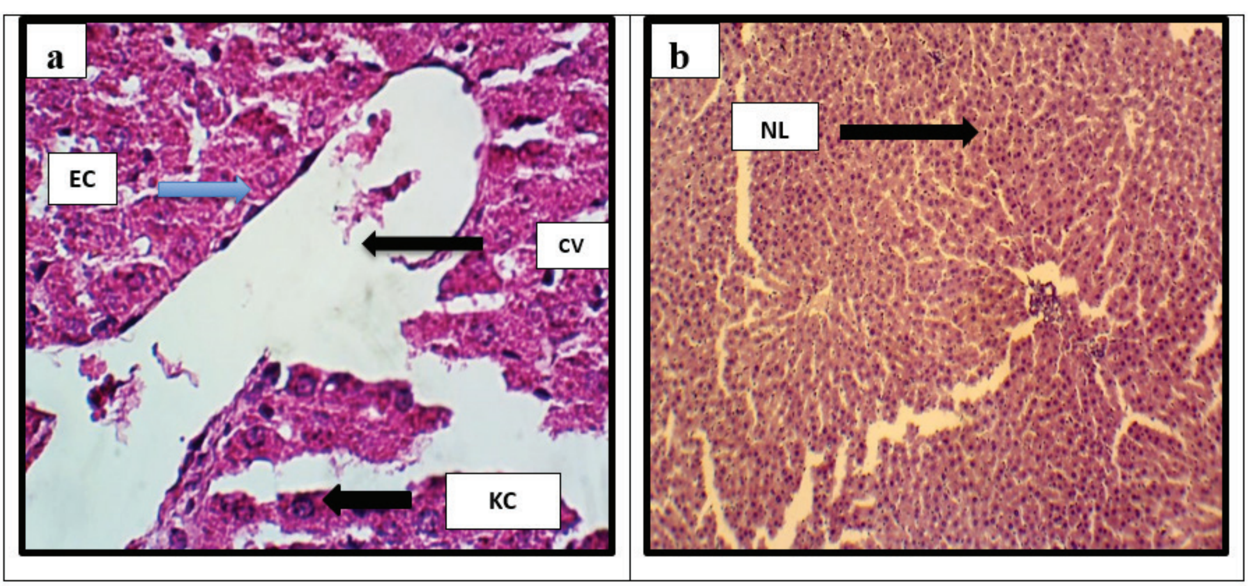

Figure (2): (a) Light microscopic image (cross-section) of central vein (CV) control group liver tissue; endothelial cells (EC) and hepatocyte(KC) kupffer cells (b) microscopic section of the liver tissue of control group which showing normal hepatic lobule (NL) and central vein (CV) (H and E 100x).

In addition, related findings have been reported [40], indicating that the beneficial effects of Rosmarinus *officinalis L.* on obesity and related dysfunction of lipids. Rosmarinus officinalis has been shown to suppress weight gain and obesity-induced steatosis of the liver during high-fat feeding. It also acts as a potential active ingredient for reducing weight gain and avoiding obesity-related hepatic lipid accumulation.

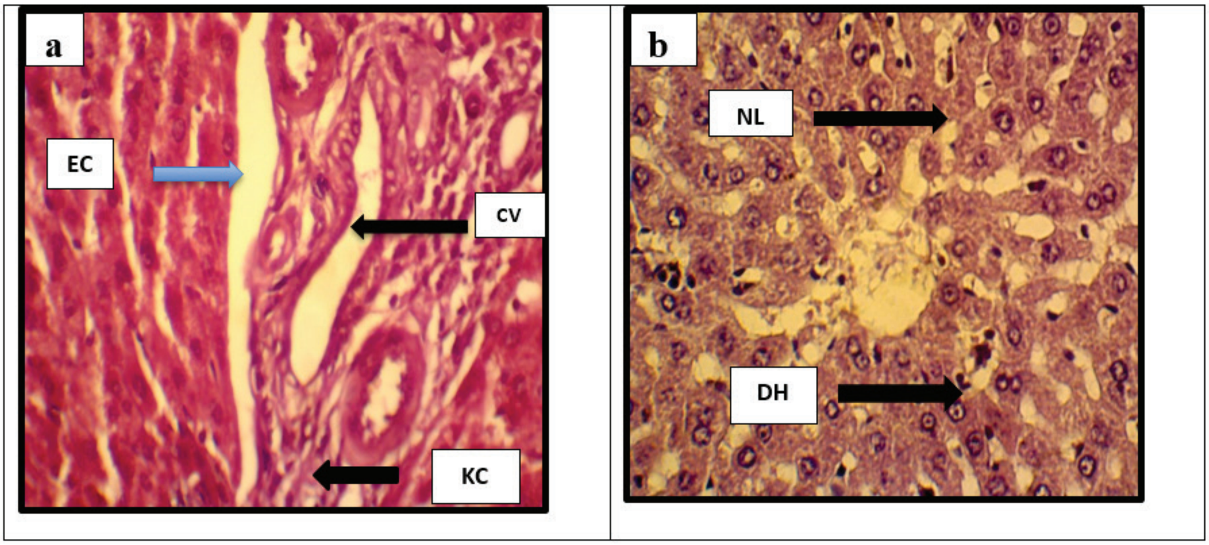

Figure (3): (a) Light microscopic image (cross-section) of the liver tissue of atherogenic group (A) which showing fats deposition in the arteriole tissue (FT); sinusoids (S); venule (V) ; arteriole (A) and hepatocyte (H);(b): Light microscopic image (cross-section) of the liver tissue of atherogenic group (A) which showing degenerative(fatty change) of hepatocyte fat tissues DH (H and E 400x).

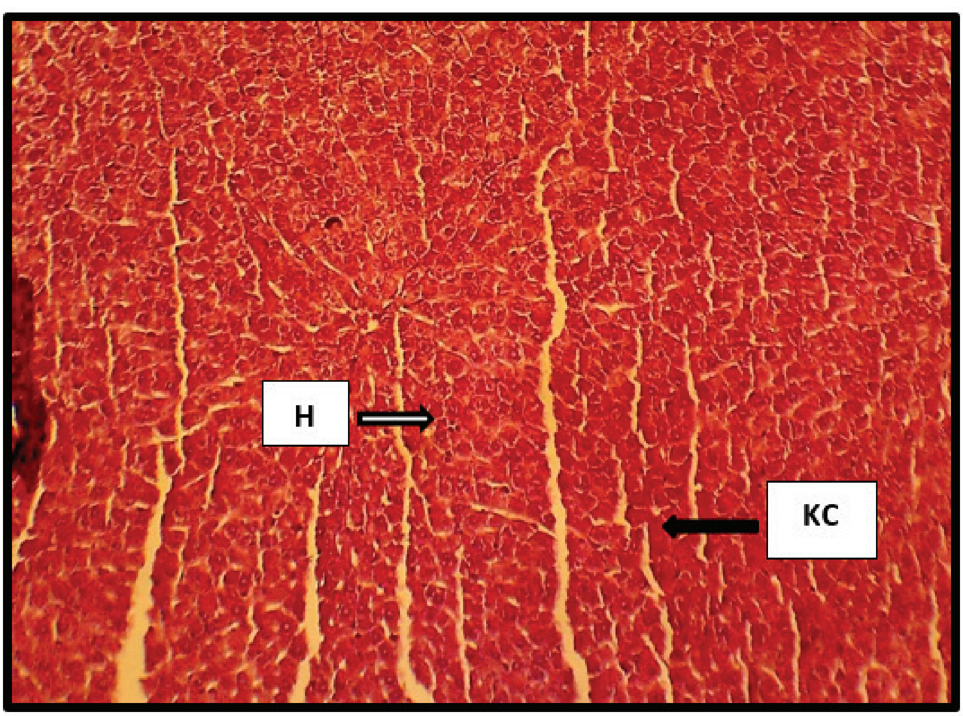

Figure (4): Light microscopic image (cross-section) of the liver tissue after treatment with sage tea for 28 days (group B2) which showing less fat tissue; hepatocyte (H) and kupffer cells (KC) (E and H 100x).

Conclusion

The administration of sage tea has an important synergistic protective role in reducing the functional efficiency and keeping normal histological characteristics of the liver organ associated with long-term therapy, concluded from current work (28 days).

Source of Funding: This research was funded by the AL-Qassim green university. The authors are grateful to dean of veterinary and department of pharmacy.

Ethical: This research has been approved by Ethics Commission of Veterinary Medicin according NO :533FD2.

Conflict of Interest: The authors confirm that there are no conflicts of interest to disclose.

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