

## EFFECT OF LOW-FAT DIET IN THE PRESENCE OF ARTICHOKE LEAVES ON OBESE RATS SUFFERING FROM DAMAGE IN THE LIVER

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### Abstract

This study was performed to examine the impact of three levels of artichoke leaves on obese rats suffering from liver damage triggered by carbon tetrachloride (CCl<sub>4</sub>). This study was designed as follows: Forty-eight male albino rats weighting (200±10g) were utilized in this research. The rats were categorized into two main groups; Group 1 (the control negative group), included six rats that received a basal diet; Group 2 included 42 rats that received a high-fat diet (HFD) for six weeks to induce obesity. Subsequently, animals in Group 2 were treated with CCl<sub>4</sub> subcutaneous injection (for 14 days) to induce liver damage. Alanine amino transaminase (ALT), weight gain, aspartate amino transaminase (AST), as well as lipid profile were assessed in both groups after this period to ensure obesity as well as liver damage induction. The animals in Group 2 were subdivided into seven subgroups: Subgroup (1) received HFD and was utilized as positive controls. Subgroups (2, 3, and 4) received HFD containing (25g, 50g, and 100g dried Artichoke leaves/kg diet), respectively. Subgroups (5, 6, and 7) received a low-fat diet LFD containing (25g, 50g, and 100g dried Artichoke leaves/kg diet), respectively. By the end of the trial, feed intake and the proportion of gaining bodyweight were estimated. In addition, serum glucose, lipid profile, liver enzymes, and kidney functions were determined in all groups. The obtained results revealed that all groups treated demonstrated substantial improvement in these

indices. Treatment of obese groups suffering from damage in the liver with a low-fat diet containing the three levels from artichoke leaves, induced a substantial improvement in these indices compared to the obese groups, which were suffering from liver damage and treated with an HFD containing the same levels from the artichoke. Based on these outcomes, we may infer that Artichoke leaves may improve the adverse effects of obesity and liver disease.

**Keywords:** Artichoke Leaves, CCL4, liver damage, obesity.

## INTRODUCTION

Overweight and obesity induced by HFD is a multifactorial illness, including increased adipose tissue mass, which can contribute to hypertension (**Klop *et al.*, 2013**) and cardiovascular diseases (**London *et al.*, 2007** and **Fantuzzi, 2005**). In addition, obesity has a negative impact on antioxidant enzymes as well as the liver. Several studies have revealed that HFD as well as fat accumulation are correlated with elevated intracellular reactive oxygen species, thus inducing oxidative stress (**Bakos *et al.*, 2011** and **Roushandeh *et al.*, 2015**).

The term "liver disease" refers to any liver damage that impairs its function. This broad word encompasses all potential issues that may cause the liver to fail to fulfill its functions (**Guan and He, 2013**). Liver disease is pervasive across the globe and varies from mild steatosis to severe hepatitis, cirrhosis, fibrosis, as well as hepatocellular carcinoma (HCC) (**Li *et al.*, 2016**). In general, developing countries have a higher burden of liver diseases (**Elizabeth, 2008**). Egypt's burden of liver diseases is particularly high, with the highest frequency of hepatitis C virus in the world and growing rates of hepatocellular carcinoma (**Strickland, 2006**).

Many investigations using CC14 have triggered oxidative stress as well as liver damage in rats since CC14 is a hazardous chemical utilized for inducing liver damage in laboratory animals (Plaa and Charbonneau, 1989 **Recknagel *et al.*, 1989**). The Cytochrome P450 enzyme in the liver endoplasmic reticulum

converts CC14 to the highly reactive trichloromethyl free radical (**Brent and Rumack, 1993**). Many species' livers and kidneys are highly vulnerable to CC14 damage (**Srivastava and Shivanandappa, 2011**).

*Cynara scolymus* L. (Asteraceae), referred to as artichoke, is characterized by several pharmacological actions. It has been demonstrated to have antitoxic activity (**Heidarian et al., 2013**) as well as antiulcerogenic properties (**Nassar et al., 2013**). One such macronutrient is artichoke leaves extract (ALE), often ingested as part of a typical Mediterranean diet (**Rondanelli et al., 2016**). In pre-clinical as well as clinical trials, ALE has demonstrated potential as a hepatoprotective and lipid-lowering agent (**Rondanelli et al., 2013**). In STZ-treated rats, the findings indicate that ALE has a favorable lowering impact on triglycerides, serum cholesterol, low-density lipoprotein-cholesterol, glucose levels, and low-density lipoprotein-cholesterol, and plasma malondialdehyde MDA levels in STZ-treated rats (**Heidarian and Soofiniya, 2011**).

Artichoke leaves are known in herbal medicine, in which foliage leaves are used to produce commercial extracts utilized as choleric and hepatoprotective in food supplements (**Gebhardt, 2005**). These significant activities are attributed to numerous metabolites including polyphenols such as caffeoylquinic, cynarin, chlorogenic acid, flavonoids like glycosides, or luteolin (**Lattanzio et al., 2009 and El Senousy et al., 2014**). Consequently, this study examined the impact of three levels of artichoke leaves on obese rats with liver damage.

## MATERIALS AND METHODS

### Materials:

- Artichoke leaves were purchased from Agricultural Research Center, Giza, Egypt.
- Minerals, vitamins, casein, cellulose, choline chloride, and CC14 were purchased from El-Gomhoria Company, Cairo, Egypt.

- Corn starch, saturated fat, and soybean oil were obtained from Cairo, Egypt's local market.
- Normal 48 male albino rats Sprague - Dawley Strain (200±10) were purchased from the National Research Centre, Cairo, Egypt.

### Methods:

#### Dried Artichoke leaves:

The artichoke was dried in an air-drying oven set to 60°C. The dry components were ground to powder and stored at room temperature in sealed bags (**Xianfeng et al.,2004**).

#### Chemical composition of Artichoke leaves:

- Fiber, ash, moisture, and protein were evaluated following the **A.O.A.C.** technique (**2005**). Total lipid was evaluated following the **A.O.A.C.** (**2000**), whereas total carbohydrates were evaluated by difference.
- HPLC was used to identify phenolic components in Artichoke leaves: Phenolic chemicals in plant samples were extracted using the technique specified by (**Ben-Hammouda et al., 1995**).

#### Experimental animals:

Forty-eight male albino rats (200±10g) were kept in cages under sanitary conditions. This research was conducted in full accordance with the Animals Health Research Institute of Egypt's Guidelines for the Care and Use of Laboratory Animals. For adaptation, rats were given a basal diet for one week. The baseline diet was prepared according to **Reeves et al. (1993)**. The vitamin mixture was prepared in accordance with **A.O.A.C. (1975)**. After this period, animals were assigned into two main groups: Group 1, which included six rats and received a basal diet, was assigned as the negative control group. Group 2 included 42 rats and received HFD that included (soybean oil 1% to provide essential fatty acids, saturated fat 19%, casein 20%, sucrose 10%, cellulose 5%, salt

mixture 3.5%, vitamin mixture 1%, choline chloride 0.25% and the remainder is corn starch) six weeks to induce obesity in rats (**Min et al., 2004**). Subsequently, blood samples were collected from the eye of both groups to determine triglycerides and cholesterol levels, and the bodyweight in both groups was evaluated to ensure the induction of obesity. Animals in Group 2 were subcutaneously injected with CC14 in paraffin oil (50% v/v 2ml/kg) to induce liver damage (**Jayasekhar et al., 1997**). ALT and AST were assessed after this period to ensure the induction. Animals in Group 2 were subsequently categorized into seven subgroups (n = 6) as follows: **Subgroup (1)**: received HFD as the positive controls. **Subgroups (2, 3 and 4)**: received HFD that includes 25g, 50g, and 100g dried artichoke leaves/kg diet, respectively. **Subgroups (5, 6 and 7)**: received a low-fat diet that contained 5% oil, as well as 25g and 50g, and 100g dried artichoke leaves/kg diet, respectively.

Diets and body weights were assessed twice weekly throughout the trial period. The animals fasted overnight by the end of the experiment and then anaesthetized and sacrificed. All rats were subjected to blood sampling from the aorta. The blood samples were centrifuged, and serum was separated to determine some biochemical indices such as serum glucose **Trinder, (1969)**, cholesterol (**Allain et al., 1974**), triglycerides **Fossati and Principe (1982)**., high-density lipoprotein HDL-c (**kostener, 1977**), low-density lipoprotein LDL-c and VLDL-c (**Friedwald et al., 1972**), uric acid (**Fossati et al., 1980**), urea nitrogen (**Patton and Crouch, 1977**) creatinine (**Bohmer, 1971**), AST and ALT (**Reitman and Frankel 1957**), Alkaline Phosphatase (ALP) (**Belfield and Goldberg 1971**).

#### **Histopathological examination:**

Specimens from liver tissue was taken immediately after sacrificing animals, and fixed in 10% buffered neutral formalin solution. The fixed specimens were then trimmed, washed and dehydrated imbedded in paraffin, cut in sections of 46 microns' thickness and stained with haematoxylin and eosin stain, according to **Sheehan and Hrapchak, (1980)**.

### Statistical analysis:

The results of each group's biological assessment were statistically assessed (one-way ANOVA test as well as mean  $\pm$  standard deviation) utilizing the SAS package and were compared utilizing the appropriate test, The level of significance was determined at  $P < 0.05$  (SAS, 1996).

## RESULTS AND DISCUSSION

### Chemical composition of dried Artichokes Leaves

Table (1) depicts values of moisture, protein, crude fiber, lipid, ash, and carbohydrate values, as well as the amount of moisture in fresh Artichokes leaves (84.23%). This amount decreased by drying to 3%. Dried Artichokes leaves increased protein, crude fiber, ash, and carbohydrate levels; these nutrients were (17.97, 33.83, 8.19, and 35.12%), respectively.

**Table (1) Chemical composition of dried Artichokes Leaves**

Samples	Initial Moisture	Moisture After Drying	Protein	Crude Fiber	Total Lipid	Ash	Carbohydrates
Artichoke leaves	84.23	3.00	17.97	33.83	1.89	8.19	35.12

In this respect, **El Sohaimy, (2013)** reported that the amount of moisture in fresh Artichokes leaves was 75.8%. In contrast, **Ben Salem et al., (2017)** found that protein content in artichoke leaves 16.64 g/100g. However, the results of protein were less than that of **Wan-Chang et al., (2014)**, who illustrated that the artichoke protein content was 13.1 g/100g.

These findings align with **Hosseinzadeh et al., (2013)**, who demonstrated that artichoke leaves' fat content varies from 1.6 to 2.3% on dry wt. basis. Likewise, **Jimenez-Escrig et al., (2003)** reported that artichoke heads' fat content was only 1.69%. On the contrary, **Al-Subhi, (2017)** reported that artichoke leaves contain

(32.41% fiber), and the amount of fiber decreased in the heads of artichoke (29.61%).

Data in Table (2) displays the content of polyphenols extracted from artichoke leaves. The data in this table revealed that the methanolic extract in these leaves resulted in 14 phenolic compounds.

**Table (2) HPLC analysis of polyphenols extracted from Artichoke Leaves**

Phenolic Compounds	Amount (ppm)
pyrogallol	2.56
Gallic	0.11
3-OH Tyrosol	0.86
Catechol	1.53
4-Aminobenzioc	0.23
Catechein	4.91
Chlorogenic acid	5.14
Benzoic	1.52
Caffeic acid	154
Vanillic	2.90
Ferulic	1.91
Ellagic	3.93
Coumarin	1.11

Caffeic acid, chlorogenic acid, catechin, and ellagic acid had the most significant concentrations of total phenolic content in Artichoke leaves, at 154, 5.14, 4.91, and 3.93 ppm, respectively. In contrast, the lowest concentration was recorded in gallic and 4-Aminobenzioc, respectively. Similarly, **Hosseini et al., (2014)** revealed that chlorogenic acid might enhance glucose uptake in peripheral tissues (insulin-like activity), minimize the absorption of intestinal glucose by blocking digestive enzymes, heal injured cells, and promote the  $\beta$  cell to insulin secretion. In contrast, **Biel et al., (2020)** reported that artichoke extract is a rich source of antioxidants as well as minerals that may have uses in the treatment of chronic noncommunicable illnesses induced by

oxidative damage. According to **Perez- Garcia *et al.*, (2000)**, the pharmaceutical as well as nutritional characteristics of the leaves of the artichoke are attributed to their particular chemical composition, including elevated inulin as well as polyphenolic levels, which have potent antioxidant activity. **Lattanzio *et al.*, (2009)** found that the artichoke by-product is high in phenolic compounds and thus may be considered a functional food.

### **Effect of low-fat diet in the presence of Artichoke Leaves on feed intake and body weight gain% of obese rats suffering from damage in the liver**

The effect of LFD in the presence of artichoke leaves on obese rats' bodyweight gain% as well as feed intake suffering from damage in the liver are depicted in Table (3). Data in the table indicate that the mean value  $\pm$  SD of feed intake of the negative control group (healthy rats) was  $18.105 \pm 0.716$  g/day/each rat, while it was  $17.860 \pm 0.256$  g/day/each rat for the positive control group (obese rats suffering from damage in the liver). The table depicts the non-significant changes in feed intake of all treated groups compared to the positive controls.

No significant difference in feed intake has been observed between obese rats suffering from damage in the liver and fed on HFD containing 25g, 50g, and 100g dried artichoke leaves/kg diet and the negative control group. In contrast, the mean value of feed intake in obese rat groups suffering from damage to the liver and fed on a low-fat diet containing the three levels of artichoke demonstrated a substantial decline of  $p \leq 0.05$  compared to negative controls. Therefore, these treatments showed the lowest mean values in feed intake.

**Table (3): Effect of low-fat diet in the presence of Artichoke Leaves on feed intake and body weight gain% of obese rats suffering from damage in the liver**

Groups		Treatments	Feed Intake (g/day/each rat)	Body Weight Gain%
Control negative group			18.105 <sup>a</sup> ± 0.716	9.896 <sup>d e</sup> ± 0.941
Control positive group			17.860 <sup>a b</sup> ± 0.256	25.649 <sup>a</sup> ± 2.940
Obese rats suffer from liver damage and fed on HFD containing	25g dried artichoke leaves/kg diet		17.861 <sup>a b</sup> ± 0.199	19.737 <sup>b</sup> ± 1.685
	50 g dried Artichoke leaves / kg diet		17.865 <sup>a b</sup> ± 0.053	15.940 <sup>c</sup> ± 0.829
	100g dried Artichoke leaves / kg diet		17.880 <sup>a b</sup> ± 0.112	11.313 <sup>d</sup> ± 0.552
Obese rats suffer from liver damage and fed on	25g dried artichoke leaves/kg diet		17.355 <sup>b</sup> ± 0.287	16.538 <sup>c</sup> ± 0.832
	50 g dried Artichoke leaves / kg diet		17.352 <sup>b</sup> ± 0.249	14.618 <sup>c</sup> ± 0.472
	100g dried Artichoke leaves / kg diet		17.367 <sup>b</sup> ± 0.274	8.330 <sup>e</sup> ± 1.131

HFD: High Fat Diet

LFD: Low Fat Diet

Mean values in each column with the same letters are not significantly different.

LSD: Least significant differences ( $P < 0.05$ ).

The mean value of bodyweight gain% (BWG%) in positive controls substantially increased ( $p \leq 0.05$ ) compared to negative controls (25.694±2.940) vs. (9.896±0.941), respectively. The previous table demonstrates that the bodyweight gain% of all treated groups substantially diminished ( $P < 0.05$ ) compared to the positive controls. The most significant decline in body weight gain% was recorded for the group that received LFD containing 100g dried Artichoke leaves/kg diet, followed by the group fed on a containing

100g HFDg dried artichoke leaves/kg diet, respectively. In contrast, the obese group of rats suffering from damage in the liver and fed on LFD containing 100g dried artichoke leaves/kg diet demonstrated a non-substantial change in BWG% compared to the negative controls.

The finding was similar to that recorded by (Maha, 2014) who found that treating rats suffering from hepatotoxicity with (200mg and 400 mg/kg of artichoke leaves and pulp extracts) improved body weight gain compared to the positive control group. On the contrary, Kusku-Kiraz *et al.*, (2010) illustrated that an HFD induced obesity following HFD. The increased body weight was counteracted in groups that received artichoke water extract utilizing high or low dosage. In this respect, Abdulkhaleq *et al.*, (2018) illustrated that rats that received HFD as well as treated with low and high doses of artichoke water extract (600 and 1500 mg/kg b.w./day) experienced a substantial decline in body weight gain compared to the HFD group. Also, Ismail, (2019) found that rats with oxidative stress, when orally given ALE alone, gained more weight as compared with positive controls.

#### **Effect of low-fat diet in the presence of Artichoke Leaves on liver and kidney weight / body weight % of obese rats suffering from damage in the liver**

The effect of LFD in the presence of artichoke leaves on some organs weight/body weight % of obese rats with liver damage is displayed in Table (4), which demonstrates that the mean values of liver and kidney weights/body weight% are substantially elevated in the positive controls compared to the negative controls (3.800±0.057 and 0.930±0.043) vs. (2.547±0.109 and 0.649±0.011), respectively. Liver weight/body weight% of obese groups with liver damage and fed on an LFD containing (25g, 50g, and 100g Artichoke/kg diet) markedly diminished ( $p \leq 0.05$ ) compared to similar groups that were fed an HFD, which contained the same levels from the artichoke. In contrast, kidney weight/body weight% of obese groups suffering from damage in the liver and fed on an LFD containing the three levels from artichoke revealed non-

significant changes compared to similar groups fed an HFD, which contained the same levels from the artichoke.

The best results in the percentage of liver and kidney weight/body weight were recorded for the obese group, which was suffering from damage in the liver and fed on an LFD containing 100 g Artichoke/ kg diet, followed by the obese group suffering from damage in the liver which was fed on an LFD containing 50 g Artichoke/ kg diet. The obese group with liver damage fed on (HFD) contained a 100g Artichoke/ kg diet. The data in this table revealed that feeding the obese group, which suffered from damage in the liver on LFD containing 100g Artichoke/kg diet led to insignificant changes in liver and kidney weights/body weight% compared to negative controls, which demonstrated the best result in organ weight.

The obtained results are consistent with those obtained by **Abdulkhaleq *et al.*, (2018)**, who confirmed that feeding rats on an HFD and treated with low and high doses of LED led to a significant decrease in liver and kidney weight compared to the rats fed on an HFD only.

**Table (4):Effect of low-fat diet in the presence of Artichoke Leaves on liver and kidney weight / body weight % of obese rats suffering from damage in the liver**

Groups		Treatments	Organs weight/body weight%	
			Liver	Kidney
Control negative group			2.547 <sup>f</sup> ± 0.109	0.649 <sup>e</sup> ± 0.011
Control positive group			3.800 <sup>a</sup> ± 0.057	0.930 <sup>a</sup> ± 0.043
Obese rats suffer from liver damage	25g dried artichoke leaves/kg diet		3.450 <sup>b</sup> ± 0.118	0.800 <sup>b</sup> ± 0.016
	50 g dried Artichoke		3.000 <sup>d</sup>	0.742 <sup>c d</sup>

	leaves / kg diet	± 0.141	± 0.038
	100g dried Artichoke leaves / kg diet	2.850 <sup>e</sup> ± 0.057	0.702 <sup>d e</sup> ± 0.057
Obese rats suffer from liver damage and fed on LFD containing	25g dried artichoke leaves/kg diet	3.240 <sup>c</sup> ± 0.106	0.782 <sup>b c</sup> ± 0.042
	50 g dried Artichoke leaves / kg diet	2.800 <sup>e</sup> ± 0.029	0.701 <sup>d e</sup> ± 0.017
	100g dried Artichoke leaves / kg diet	2.607 <sup>f</sup> ± 0.115	0.662 <sup>e</sup> ± 0.008

HFD: High Fat Diet

LFD: Low Fat Diet

Mean values in each column with the same letters are not significantly different.

LSD: Least significant differences ( $P < 0.05$ )

### Effect of low-fat diet in the presence of Artichoke Leaves on serum glucose of obese rats suffering from damage in the liver

The results in this table demonstrates that serum glucose mean values were substantially elevated ( $p \leq 0.05$ ) in positive controls compared to the negative controls. Serum glucose of all treated groups decreased significantly ( $P < 0.05$ ) compared to the positive control group. The results in this table revealed that insignificant differences in serum glucose mean values were observed between obese rats groups that were suffering from damage in the liver and fed on an LFD containing (25, 50, and 100g artichoke leaves/kg diet group). In contrast, serum glucose mean values decreased gradually with increasing the levels of artichoke leaves when the obese rats with liver damage and fed on HFD.

The most significant decline in serum glucose was recorded for the LFD group, followed by the groups fed on a basal diet containing 50g and 25g dried artichoke leaves/kg diet, respectively. In this respect, **Al-Subhi, (2017)** showed that the artichoke head and leaves significantly lowered lipid parameters and serum glucose in hypercholesterolemia and diabetic rats; these effects might be due to the presence of elevated amounts of natural antioxidants and fiber in the artichoke head and leaves. The fiber in artichokes, according to the author, causes glucose to be absorbed more slowly in the blood,

and since fiber is a component that can be digested and does not need insulin, fiber does not count towards the quantity of digested carbs or glucose. Therefore, the author recommended that the fed with different parts of the artichoke is beneficial, healthy food to improve the nutritional status of diabetics and hyperlipidemia. A nether study by **Entaz et al., (2017)** reported that ethanol extracts oral administration from leaves of *C. scolymus* at dosages of 200 mg/kg and 400 mg/kg on streptozotocin (STZ) led to decreased blood glucose in diabetic rats. In this respect, **Vessal et al., (2003)** reported that some flavonoid compounds were detected in ethanol extract from *C. scolymus* leaves by HPLC, e.g., Quercetin has been proven to lower the fasting blood glucose, in addition to enhancing glucose tolerance.

**Table (5): Effect of low-fat diet in the presence of Artichoke Leaves on serum glucose of obese rats suffering from damage in the liver**

Groups		Treatments	Serum glucose mg/dl
Control negative group			65.415 <sup>f</sup> ± 0.645
Control positive group			169.300 <sup>a</sup> ± 4190
Obese rats with liver damage and fed on HFD containing	25g dried artichoke leaves/kg diet		108.967 <sup>b</sup> ± 3.286
	50 g dried artichoke leaves/kg diet		102.717 <sup>c</sup> ± 7.434
	100g dried artichoke leaves/kg diet		86.492 <sup>d</sup> ± 1.773
Obese rats with liver damage fed on LFD containing	25g dried artichoke leaves/kg diet		81.092 <sup>e</sup> ± 2.670
	50 g dried artichoke leaves/kg diet		80.275 <sup>e</sup> ± 2.280
	100g dried artichoke leaves/kg diet		76.092 <sup>e</sup> ± 2.128

HFD: High Fat Diet

LFD: Low Fat Diet

*Mean values in each column with the same letters are not significantly different.**LSD: Least significant differences ( $P < 0.05$ )***Effect of low-fat diet in the presence of Artichoke Leaves on lipid profile of obese rats suffering from damage in the liver**

LFD and HFD effect in the presence of artichoke leaves on very-low-density lipoprotein VLDL-c (mg/dl), low-density lipoprotein LDL-c, high-density lipoprotein HDL-c, triglycerides TG, as well as serum cholesterol in obese rats with liver damage are presented in Table (6). Data illustrated that serum cholesterol, TG, LDL-c, as well as VLDL-c, markedly increased in the positive control group  $p \leq 0.05$ , while HDL-c is substantially diminished compared to the negative controls.

Treatment of obese rats with liver damage and fed with HFDs or LFDs containing 25, 50, and 100g artichoke leaves/kg diet resulted in a substantial decline  $p \leq 0.05$  in all lipid profiles, except HDL-c, as compared to positive controls (obese rats suffering from damage in the liver). Most lipid fractions, except HDL-c, decreased gradually with increasing artichoke leaves' levels in preparing diets. HDL-c increased in all treatments with different levels of artichoke leaves. The data in this table showed that treating obese rats with LFDs that contain the three levels of artichoke leaves achieved more improvement than that obese rats treated with HFDs containing the same levels of artichoke leaves. The LED group (100g artichoke leave/kg diet) demonstrated the most significantly improved lipid profile.

Dyslipidemia is described as aberrant lipoprotein metabolism, which includes elevated reduced high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), and total cholesterol (TC) (Haney *et al.*, 2007). In contrast, Bhattacharya *et al.*, (2016) reported that LDL, triglycerides, as well as serum cholesterol, were markedly elevated, and HDL was substantially diminished in hepatitis with complications compared to uncomplicated hepatitis ( $p < 0.01$ ).

**Okada et al., (2017)** indicate that artichoke is characterized by anti-fatty liver effects based on improved hepatic lipid profile as well as glucose tolerance. Additionally, **Santos et al., (2018)** reported that cooked artichoke (*Cynara scolymus*) hearts or ALE are believed to be helpful in the treatment of dyslipidaemia, because the artichoke provides soluble fibres, particularly inulin, which improves lipid profile. On the contrary, **Antuono et al., (2015)** reported that the polyphenolic compounds and phytosterols found in artichoke had been proven to be the main promoters of improving the lipid profile.

Besides lowering TG and TC concentrations, artichoke may have a preventative impact owing to its capacity to reduce oxidative stress and suppress inflammatory pathways (**Tang et al., 2017**). ALE inhibits lipid peroxidation via atunating the levels of malondialdehyde (MDA) and increasing the concentrations of superoxide dismutase (SOD) and glutathione (GSH) in liver disease rodent models (**Heidarian et al., 2013**).

**Table (6): Effect of low-fat diet in the presence of Artichoke Leaves on lipid profile of obese rats suffering from damage in the liver**

Groups		Treatments	Cholesterol	Triglycerides	HDL-c	LDL-c	VLDL-c
		mg/dl					
Control negative group			68.835 <sup>d</sup> ± 1.553	41.250 <sup>b</sup> ± 2.817	45.997 <sup>a</sup> ± 0.383	14.587 <sup>a</sup> ± 1.373	8.250 <sup>b</sup> ± 0.563
Control positive group			171.912 <sup>a</sup> ± 5.484	55.552 <sup>a</sup> ± 3.323	24.464 <sup>f</sup> ± 3.434	136.337 <sup>a</sup> ± 1.526	11.110 <sup>a</sup> ± 0.664
Obese rats with liver damage on HFD containing	25g dried artichoke leaves/kg diet		107.582 <sup>b</sup> ± 4.271	46.492 <sup>b</sup> ± 3.264	30.634 <sup>e</sup> ± 2.416	67.650 <sup>b</sup> ± 2.010	9.298 <sup>b</sup> ± 0.652
	50 g dried Artichoke leaves / kg diet		103.670 <sup>b</sup> ± 4.237	44.285 <sup>b</sup> ± 4.839	33.498 <sup>de</sup> ± 2.101	61.314 <sup>c</sup> ± 2.020	8.857 <sup>b</sup> ± 0.967
	100g dried Artichoke leaves / kg diet		79.045 <sup>c</sup> ± 6.629	41.720 <sup>b</sup> ± 4.174	36.426 <sup>cd</sup> ± 2.614	34.275 <sup>e</sup> ± 3.502	8.344 <sup>b</sup> ± 0.834

Obese rats with liver damage on LFD containing	25g dried artichoke leaves / kg diet	102.420 <sup>b</sup> ± 2.794	44.017 <sup>b</sup> ± 2.495	32.494 <sup>e</sup> ± 3.025	61.122 <sup>c</sup> ± 1.115	8.803 <sup>b</sup> ± 0.499
	50 g dried Artichoke leaves / kg diet	83.965 <sup>c</sup> ± 3.394	42.452 <sup>b</sup> ± 2.423	37.275 <sup>bc</sup> ± 2.129	38.199 <sup>d</sup> ± 1.036	8.490 <sup>b</sup> ± 0.484
	100g dried Artichoke leaves / kg diet	78.837 <sup>c</sup> ± 3.598	41.702 <sup>b</sup> ± 1.739	40.704 <sup>b</sup> ± 1.235	29.792 <sup>f</sup> ± 2.391	8.340 <sup>b</sup> ± 0.347

HFD: High Fat Diet

LFD: Low Fat Diet

Mean values in each column with the same letters are not significantly different.

LSD: Least significant differences ( $P < 0.05$ )

**Effect of low-fat diet in the presence of Artichoke Leaves on liver enzymes of obese rats suffering from damage in the liver**

Table (7) displays the impact of HFD as well as LFD in the presence of artichoke leaves with three levels on liver enzymes, including (Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), and Alkaline Phosphates (ALP)) of obese rats suffering from damage in the liver. The results demonstrated that feeding obese rats with liver damage on HFD led to a substantial elevation  $p \leq 0.05$  in LP, ALT, as well as compared to negative controls fed on a basal diet. All treated groups with HDFs or LFDs compromising the three levels of artichoke demonstrated a significant decrease in these parameters compared to positive controls. Furthermore, the treated obese rats with liver damage and fed on LFD that contains 25 g, 50g, and 100g/kg diet was proven more effective in alleviating ALP, ALT, and AST, ALT than the obese group with liver damage fed on HFD containing the same levels from the artichoke.

**Table (7): Effect of low-fat diet in the presence of Artichoke Leaves on liver enzymes of obese rats suffering from damage in the liver**

Groups		Treatments	AST	ALT	ALP
			U/l		
Control negative group			49.917 <sup>g</sup> ± 2.520	23.520 <sup>e</sup> ± 2.002	71.402 <sup>e</sup> ± 13.580
Control positive group			139.447 <sup>a</sup> ± 8.162	103.417 <sup>a</sup> ± 13.049	868.250 <sup>a</sup> ± 61.862
Obese rats liver damage and fed on HFD containing	25g dried artichoke leaves/kg diet		107.460 <sup>b</sup> ± 5.909	55.317 <sup>b</sup> ± 3.975	524.750 <sup>b</sup> ± 46.241
	50 g dried artichoke leaves/kg diet		95.667 <sup>c</sup> ± 1.538	47.665 <sup>c</sup> ± 3.382	210.250 <sup>c</sup> ± 17.346

	100g dried artichoke leaves/kg diet	90.172 <sup>cd</sup> ± 1.406	40.252 <sup>cd</sup> ± 3.091	137.000 <sup>d</sup> ± 4.830
Obese rats suffer from liver damage and on LFD containing	25g dried artichoke leaves/kg diet	85.787 <sup>d</sup> ± 1.347	34.372 <sup>d</sup> ± 0.847	111.750 <sup>de</sup> ± 3.403
	50 g dried artichoke leaves/kg diet	76.777 <sup>e</sup> ± 2.738	31.560 <sup>d</sup> ± 0.730	98.500 <sup>de</sup> ± 1.732
	100g dried artichoke leaves/kg diet	69.480 <sup>f</sup> ± 3.325	27.897 <sup>de</sup> ± 1.966	92.132 <sup>de</sup> ± 1.424

HFD: High Fat Diet

LFD: Low Fat Diet

Mean values in each column with the same letters are not significantly different.

LSD: Least significant differences ( $P < 0.05$ )

The highest decrease in ALP, ALT, and AST was recorded for the group of rats treated with LFD containing 100g artichoke /kg diet, followed by the group of rats treated with LFD containing 50g artichoke /kg diet, respectively. **Abd El-salam et al., (2022)** reported that subcutaneous injection of CCl<sub>4</sub> caused hepatic pathological damage and substantially elevated serum ALP, ALT, AST, and hepatic levels of hydroxyproline and malondialdehyde. In addition, it diminished glutathione as well as superoxide dismutase activities. Also, **Asif et al., (2010)** reported that, with CCL<sub>4</sub>, the AST and ALT activities were markedly raised. **Dandona et al., (2001)** reported that obesity is related to oxidative stress due to prolonged postprandial hyperlipidemia, and obese people are characterized by elevated oxidative stress levels, alleviated by eight loss as well as diet restriction. On the contrary, **Anyanwu et al., (2014)** illustrated that obesity could lead to liver problems, as can drug and alcohol abuse.

Artichoke (*Cynara scolymus*) is a Mediterranean plant that is high in natural antioxidants and consequently utilized as herbal medication (**Mulinacci et al., 2004**). Artichoke is a plant that has

hepatoprotective properties (Kulza *et al.*, 2010). According to current scientific and clinical research, artichoke leaf extract may be utilized for hepatoprotection (Speroni *et al.*, 2003). For generations, artichoke has been utilized as a specialized liver and gallbladder cure for traditional medicine. Cynarin, the active element in artichoke, is found in the most significant amounts in the leaves. Cynarin, like silymarin, has shown strong liver-protecting and regenerative properties (Özlem and Başar, 2014). Similarly, Kumar and Khanna, (2018) observed that silymarin has been utilized to treat toxin-induced liver diseases, alcoholic liver disease, as well as chronic and acute viral hepatitis. In contrast, El-Mesallamy *et al.*, (2020) illustrated that artichoke administration effectively decreased the elevated oxidative stress as well as liver enzymes in rats.

### **Effect of low-fat diet in the presence of Artichoke Leaves on kidney functions of obese rats suffering from damage in the liver**

Results from the table (8) showed the effect of HFD as well as LFD in the presence of artichoke leaves (25, 50, and 100g artichoke leaves /kg diet) on the functions of the kidney (e.g., creatinine, urea nitrogen, and uric acid) of obese rats with liver damage. This table demonstrates that urea nitrogen, uric acid, uric acid, and serum mean values substantially elevated  $P \leq 0.05$  in the obese group suffering from liver damage compared to negative controls.

The results indicated that feeding obese groups which fed on HFDs or LFDs containing the three levels of artichoke leaves decreased the mean values of serum (creatinine, urea nitrogen, and uric acid) gradually with increasing the level of artichoke. In contrast, treating obese groups fed on HFD containing the three levels of artichoke leaves lowered the mean values of serum (creatinine, urea nitrogen, and uric acid) compared to positive controls. The same trend was observed in obese groups which suffer from hepatotoxicity and are fed on LFD containing the same levels as artichoke, LFDs containing (25, 50, and 100g artichoke leaves) induced more improvement in kidney functions in obese groups

suffering from hepatotoxicity, comparing with HFDs groups. Feeding the obese group, which suffer from hepatotoxicity with LFD containing 100g artichoke/ kg diet recorded the best results in decreasing the average value of serum (creatinine, urea nitrogen, and uric acid), followed by LFD containing 50g artichoke/ kg diet. **Kang and Kim, (2009)** reported that CCl<sub>4</sub>-induced nephrotoxicity was observed mainly in the renal glomeruli and elevated blood urea nitrogen, as well as the levels of serum creatinine. **Mohamed and Ashour, (2016)** reported that obesity is correlated with several metabolic disorders, including dyslipidemia, insulin resistance, decreased glucose tolerance, as well as structural and morphological renal alternations, resulting in Glomerulosclerosis (GS) chronic kidney disease.

A study assessed artichoke's effect on renal impairment in rats, and it was found that administrating 400 mg/kg b.wt. of artichoke head or leaf induced a substantial decline in urea levels or plasma creatinine (**Ahmed et al., 2008**). Artichoke's nephroprotective effect has also been tested in rats with gentamycin-induced renal dysfunction. Oral delivery of ALEs dramatically lowered urea levels, uric acid, and creatinine in the blood (**Khatab et al., 2016**). In addition, the administration of artichoke head at dosages of 200 and 400 mg/kg enhanced renal dysfunction in diabetic rats (**Ben Salem et al., 2017**). Conversely, (**Kollia et al., 2017**) reported that artichoke is rich in flavonoids and caffeoylquinic acids, providing potent antioxidant activity that has a principal role in numerous pharmacological properties of artichoke. **Najim et al., (2018)** demonstrated that artichoke methanol extract might be a beneficial modulator in alleviating 5-Fluorouracil-induced nephrotoxicity in albino rats. **Fadlalla and Galal, (2020)** illustrated that ALE treatment resulted in a potential decline in the liver and kidney against histological and biochemical alterations as well as oxidative stress caused by paracetamol.

**Table (8): Effect of low-fat diet in the presence of Artichoke Leaves on kidney functions of obese rats suffering from damage in the liver**

Groups		Treatments	Uric acid	Urea nitrogen	Creatinine
			mg/dl		
Control negative group			1.100 <sup>h</sup> ± 0.053	23.750 <sup>f</sup> ± 1.500	0.467 <sup>f</sup> ± 0.072
Control positive group			1.942 <sup>a</sup> ± 0.060	42.000 <sup>a</sup> ± 3.741	0.945 <sup>a</sup> ± 0.023
Obese rats with liver damage and fed on HFD containing	25g dried artichoke leaves/kg diet		1.755 <sup>b</sup> ± 0.085	35.250 <sup>b</sup> ± 1.500	0.775 <sup>b</sup> ± 0.040
	50 g dried Artichoke leaves / kg diet		1.545 <sup>c</sup> ± 0.100	32.500 <sup>b c</sup> ± 2.081	0.665 <sup>c d</sup> ± 0.069
	100g dried Artichoke leaves / kg diet		1.355 <sup>d</sup> ± 0.023	31.250 <sup>c d</sup> ± 1.707	0.625 <sup>d e</sup> ± 0.064
Obese rats with liver damage and fed on LFDcontaining	25g dried artichoke leaves/kg diet		1.307 <sup>d e</sup> ± 0.012	30.000 <sup>c d e</sup> ± 2.160	0.710 <sup>b c</sup> ± 0.046
	50 g dried Artichoke leaves / kg diet		1.250 <sup>f g</sup> ± 0.101	28.500 <sup>d e</sup> ± 1.914	0.600 <sup>d e</sup> ± 0.035
	100g dried Artichoke leaves / kg diet		1.185 <sup>g h</sup> ± 0.051	27.250 <sup>e</sup> ± 1.707	0.567 <sup>e</sup> ± 0.068

**LD:** Liver Damage    **HFD:** High Fat Diet

Mean values in each column with the same letters are not significantly different.

LSD: Least significant differences ( $P < 0.05$ )

**Histopathological examination results of the liver:**

Microscopically, the liver of rats from the control negative group revealed a normal histological structure of the hepatic lobule (Figs. 1 and 2). On the contrary, the liver of rats from the positive control group (the obese group with liver damage) showed hepatocellular steatosis (Figs. 3, 4, 5 and 6), necrosis, and apoptosis (Fig. 4) as well as hyperplasia of oval cells (Fig. 5), fibroplasia and Kupffer cells activation (Fig. 6). Meanwhile, the liver of the obese rats, with liver damage and fed on HFD containing 25g dried Artichoke leaves/kg diet, revealed focal hepatocellular steatosis and deposition of haemosiderin pigment (Figs. 7 and 8). However, the liver of obese rats with damaged liver and fed on HFD containing 50g dried artichoke leaves/kg diet demonstrated Kupffer cells activation (Figs. 9 and 10), few mononuclear cells infiltration (Fig. 9), and deposition of haemosiderin pigment (Fig. 10). Furthermore, liver-obese rats with liver damage fed on HFD containing 100g dried artichoke leaves/kg diet showed hepatocellular of some hepatocytes (Fig. 11), cytoplasmic vacuolization hepatocytes, and congestion of hepatic sinusoids (Fig. 12). Moreover, sections from the obese group with liver damage and fed on a basal diet containing 25g dried Artichoke leaves/kg diet exhibited focal hepatocellular steatosis and slight Kupffer cells activation (Figs. 13 & 14). The improved picture was noticed in the liver of rats from the obese group with liver damage and fed on a basal diet containing 50g dried Artichoke leaves/kg diet. Examined sections revealed slight Kupffer cells activation and slight deposition of haemosiderin pigment (Figs. 15 and 16). Moreover, marked improvement was noticed in sections of the obese group with liver damage fed on a basal diet containing 100g dried Artichoke leaves/kg diet, as it revealed slight vacuolation of some hepatocytes and slight deposition of haemosiderin pigment (Figs. 17 and 18).

In this respect, **Okada *et al.*, (2017)** reported that histopathological analyses of liver sections of normal rats, HFD rats, and HFD rats treated with artichoke revealed that the accumulated glycogen and fat were detected in the liver of rats fed an HFD, but not in the liver of rats fed a normal diet. Fat and glycogen accumulation was found in the livers of HFD + artichoke animals; nonetheless, this increase was less significant compared to the HFD group. However, **Al-Ahdab, (2014)**

also reported that the examination of the liver of rats pretreated with a large dose of 400 mg/kg of Artichoke pulp extract (APE) demonstrated the presence of necrosis as well as moderate fatty changes compared to rats injected with CCl<sub>4</sub> which induced severe fatty degeneration with leukocyte inflammatory cells infiltration. **Fadlalla and Galal, (2020)** found that sections of livers in the control group demonstrated the normal histological structure of hepatic lobule. Meanwhile, liver sections of paracetamol-intoxicated rats showed apoptosis of hepatocytes, portal infiltration with mononuclear cells, proliferated oval cells, and fibroplasia in the portal triad liver tissue sections paracetamol-intoxicated rats treated with artichoke extract showed mild improvement in hepatic histopathology. In contrast, **(El-Mesallamy et al., (2020)** revealed that artichoke extract at a dose level 1.5g/kg day reduced liver tissue lesions when damaged by Thioacetamide and showed almost normal histological architecture of hepatic lobule.

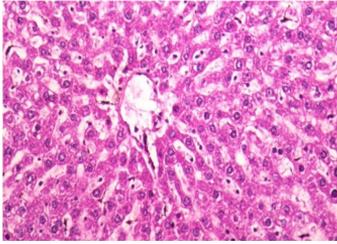


Fig. (1): Liver of rat from the control negative group showing the normal histological structure of hepatic lobule (H & E X 400).

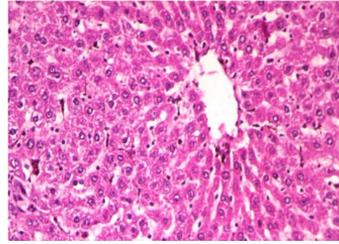


Fig. (2): Liver of rat from the control negative group showing the normal histological structure of hepatic lobule (H & E X 400).

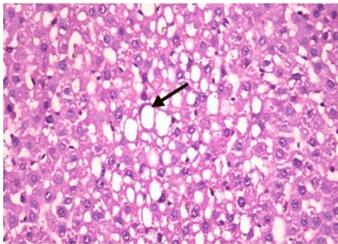


Fig. (3): Liver of rat from the positive control group (the obese group which was suffering from damage in the liver) showing hepatocellular steatosis (H & E X 400)

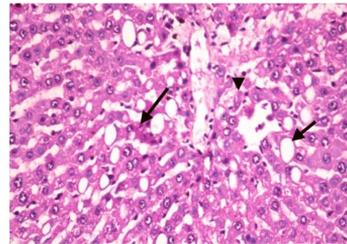


Fig. (4): Liver of rat from the positive control group showing hepatocellular steatosis, necrosis, and apoptosis (H & E X 400)

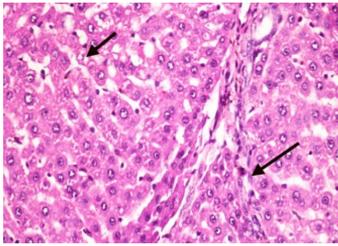


Fig. (5): Liver of rat from the positive control group showing hepatocellular steatosis and hyperplasia of oval cells (H & E X 400).

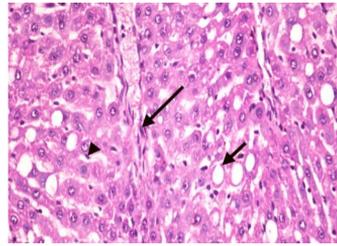


Fig. (6): Liver of rats from the positive control group showing hepatocellular steatosis, fibroplasia, and Kupffer cells ctivation (H & E X 400).

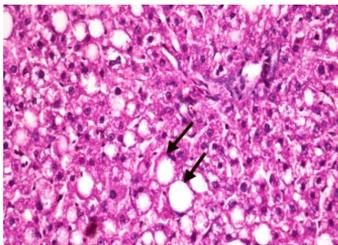


Fig. (7): The liver of obese rats which suffer from LD and fed on HFD containing 25g dried Artichoke leaves/kg diet showing focal hepatocellular steatosis (H & E X 400).

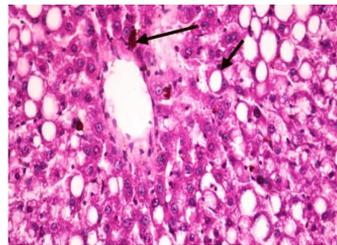


Fig. (8): Liver of obese rats which suffers from LD and fed on HFD containing 25g dried Artichoke leaves/kg diet showing focal hepatocellular steatosis and deposition of haemosidrin pigment (H & E X 400).

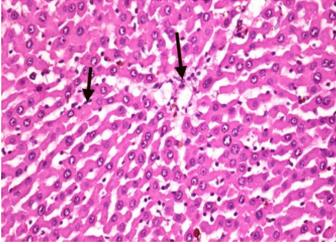


Fig. (9): The liver of obese rats which suffers from LD and fed on HFD containing 50g dried Artichoke leaves/kg diet showing Kupffer cells activation and few mononuclear cells infiltration (H & E X 400).

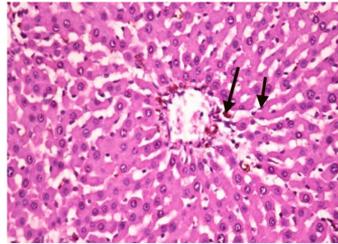


Fig. (10): Liver of obese rats which suffers from LD and fed on HFD containing 50g dried Artichoke leaves/kg diet showing Kupffer cells activation and deposition of haemosiderin pigment (H & E X 400).

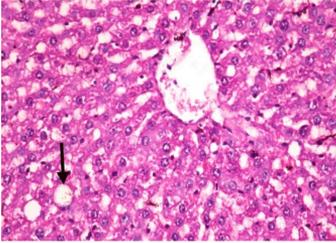


Fig. (11): Liver of obese rats which suffer from LD and fed on HFD containing 100g dried Artichoke leaves / kg diet showing hepatocellular steatosis of some hepatocytes (H & E X 400).

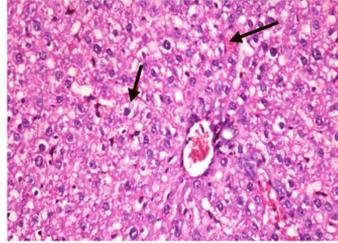


Fig. (12): Liver of obese rats suffer from LD and fed on HFD containing 100g dried Artichoke leaves / kg diet showing cytoplasmic vacuolization of hepatocytes and congestion of hepatic sinusoids (H & E X 400).

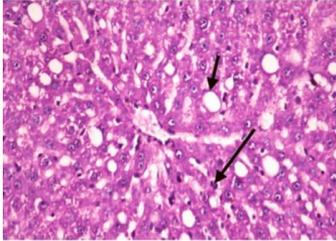


Fig. (13): Liver of obese rats which suffer from LD and fed on a basal diet containing 25g dried Artichoke leaves/kg diet showing focal hepatocellular steatosis and slight Kupffer cells activation (H & E X 400).

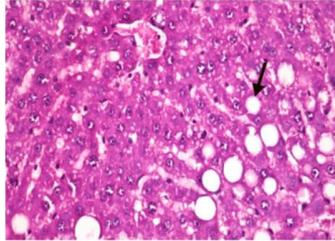


Fig. (14): Liver of obese rats which suffer from LD and fed on basal diet containing 25g dried Artichoke leaves / kg diet showing focal hepatocellular steatosis (H & E X 400).

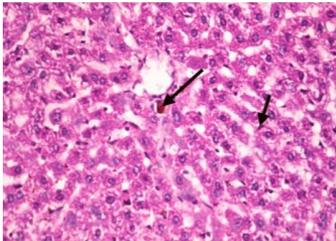


Fig. (15): The liver of obese rats which suffers from LD and fed on a basal diet containing 50g dried Artichoke leaves/kg diet showing slight Kupffer cells activation and slight deposition of haemosiderin pigment (H & E X 400).

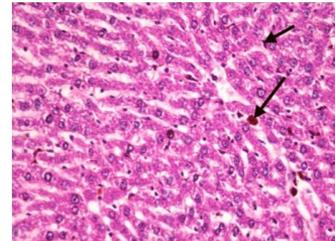


Fig. (16): The liver of obese rats which suffers from LD and are fed on a basal diet containing 50g dried Artichoke leaves/kg diet showing slight Kupffer cells activation and slight deposition of haemosiderin pigment (H & E X 400).

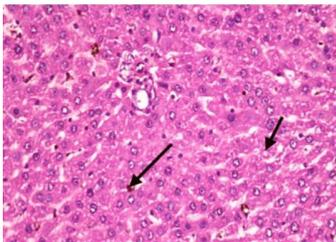


Fig. (17): The liver of obese rats which suffer from LD and fed on a basal diet containing 100g dried Artichoke leaves/kg diet showing slight vacuolation of some hepatocytes and slight deposition of haemosiderin pigment (H & E X 400).

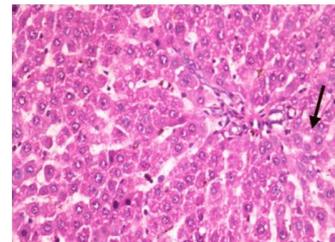


Fig. (18): The liver of obese rats which suffers from LD and fed on a basal diet containing 100g dried Artichoke leaves/kg diet showing slight vacuolation of some hepatocytes (H & E X 400).

## CONCLUSION

According to this findings of this study, groups which treated with a low-fat diet LFD containing 100g artichoke leaves /kg diet were more effective in improving the mean value of all parameters used in this study. The artichoke leaves with a diet improved the nutritional and biological status of obese rats suffering from damage to the liver.

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تأثير النظام الغذائي منخفض الدهون المحتوي على أوراق الخرشوف على  
الفئران البدينة المصابة بتحطم في الكبد

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الملخص

تهدف هذه الدراسة الي دراسة تأثير المستويات المختلفة من أوراق الخرشوف الجافة علي الفئران البدينة التي تعاني من تلف في الكبد الناتج عن التسمم بمادة رابع كلوريد الكربون . 48 فأر ذكر ألبينو ، تم تقسيمهم إلي مجموعتين رئيسيتين. المجموعة الرئيسية الاولي (6 فئران) تغذت علي الغذاء الأساسي واستخدمت كمجموعة ضابطة سالبة . والمجموعة الرئيسية الثانية (42 فأر) تغذت لمدة ستة أسابيع علي نظام غذائي عالي الدهن لإحداث السمنة في الفئران. بعد إنقضاء هذه المدة تم حقن الفئران في المجموعة الرئيسية الثانية بمادة رابع كلوريد الكربون مرة واحدة في الأسبوع بالحقن تحت الجلد (لمدة أسبوعين) لإحداث تحطم في الكبد. تم تقدير إنزيمات أسبرتات ناقل للأمين و وزن الجسم المكتسب والألانين ناقل للأمين وصورة الدهن في كل من المجموعتين للتأكد من إحداث الإصابة بالسمنة و تحطم الكبد. تم تقسيم فئران المجموعة الثانية الي سبع مجموعات فرعية كالتالي: المجموعة الفرعية الأولى: تم تغذيتها علي غذاء عالي الدهن ، واستخدمت كمجموعة ضابطة موجبة . المجموعات الفرعية الثانية والثالثة والرابعة تم تغذيتهم علي غذاء عالي الدهن المحتوي علي (25 جرام ، 50 جرام ، 100 جرام أوراق الخرشوف الجاف/ كيلوجرام)، علي التوالي. المجموعات الفرعية الخامسة و السادسة والسابعة تم تغذيتهم علي غذاء منخفض الدهن المحتوي علي (25 جرام ، 50 جرام ، 100 جرام أوراق الخرشوف الجاف/ كيلوجرام)، علي التوالي. في نهاية التجربة تم تقدير الطعام المأخوذ ووزن الجسم المكتسب بالإضافة إلى الجلوكوز و صورة الدهن و إنزيمات الكبد ووظائف الكلى لجميع المجموعات. أظهرت النتائج حدوث تحسن في هذه التقديرات. معالجة مجموعات الفئران التي تغذت علي غذاء عالي الدهن بنظام غذائي منخفض الدهن المحتوي على ثلاث مستويات من أوراق الخرشوف

ادت إلى تحسن ملحوظ في هذه التقديرات مقارنة بالمجموعات التي تغذت على غذاء عالي الدهون المحتوي على أوراق الخرشوف وتعاني من تحطم الكبد . بناءً على هذه النتائج نستنتج أن أوراق الخرشوف تحسن الآثار الضارة للسمنة وأمراض الكبد.

الكلمات المفتاحية : أوراق الخرشوف ، رابع كلوريد الكربون ، تحطم الكبد ، السمنة.