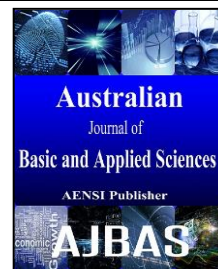




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### Biological effect of *Cynara cardunculus* on liver and heart status for hypercholesterolemic rats

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#### ABSTRACT

**Background:** Hypercholesterolemia and lipid peroxidation play complementary roles in atherosclerosis, liver dysfunction. Artichoke (*Cynara cardunculus*) leaf and pulp extracts) are rich in antioxidants, have cholesterol-reducing. **Objectives:** effect to study the biological effect of cynara cardunculus on liver and heart status for hypercholesterolemic rats. **Materials & Methods:** We investigated the effects of CCL and CCP on serum and hepatic lipid levels and pro-oxidant-antioxidant balance in the liver and heart of hypercholesterolemic rats. All rats were fed on basal diet for one week before starting the experiment for acclimatization. After one-week period, the rats were divided into two main groups. The first group (n =10 rats) was fed on the basal diet only, as a control negative (healthy rats) (G I). The second main group (n = 50 rats) was fed for two weeks on the basal diet plus cholesterol 2% to induce hypercholesterolemia before starting the experiment. After two weeks feeding only on standard basal diet and served as positive control group (G II). The remnant second main group of rats was divided into 4 subgroups. **Result:** The results showed that *Cynara cardunculus* in leaf and pulp form had a significant effect in reducing the BWG and FER of hypercholesterolemic rats. Cholesterol levels showed a decreased with the uptake of *Cynara cardunculus* in the two forms, and the decrease was more significant with the higher dosage. On evaluation of the effect of *Cynara cardunculus* on hepatic functions (AST, ALT and ALP) for hypercholesterolemic rats. **Conclusion:** It was found that both CCL and CCP decrease the concentration of the respective enzymes (An increase in levels of AST, ALT,ALP, are indicator of liver dysfunction),hence serving a hepatoprotective and regenerating effects.

#### INTRODUCTION

Hypercholesterolemia has become a significant health concern in recent years. Hypercholesterolemia is a high risk value for the development of cardiovascular diseases including atherosclerosis, myocardial infarction, liver dysfunction, and cerebral paralysis (Avci, *et al.*, 2006).

Curing hypercholesterolemia without any side effects remains a challenge for modern medicine. Plant-derived products are frequently considered to be less toxic, with few or no side effects, than their synthetic equivalents. Plants play a major role in the introduction of new therapeutic agents, and have received much attention as sources of biologically active substances. Artichokes (*Cynara scolymus* L., *Asteraceae*) is one such example.

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Artichokes (*Cynara scolymus* L., *Asteraceae*) are an ancient crop and medicinal plant, (Lattanzio *et al.*, 2009). The globe artichoke, or *Cynara scolymus*, is the immature flowers of a thistle plant, a vegetable native to the Mediterranean region including North Africa and Southern Europe. However, it is also now extensively grown in South America, United States and China. It contains caffeoylquinic acid derivatives (cynarin and chlorogenic acid) and flavonoids (luteolin and apigenin) (Pandino *et al.*, 2013; Wang *et al.*, 2003) Globe artichoke is considered a healthy food, due to its nutritional and phytochemical composition. It contains proteins, minerals, a low amount of lipids, dietary fiber and a high proportion of phenolics. (Avci, *et al.*, 2006; Pandino *et al.*, 2013; Wang *et al.*, 2003) The phenolics include cynarin (1,3-di-O- caffeoylquinic acid), luteolin, cynaroside (luteolin-7-o-glucoside), scolmoside (luteolin-7-o-rutinoside); phenolic acids such as caffeic, coumaric, hydroxycinnamic, ferulic, caffeoylquinic acid derivatives; mono- and dicaffeoylquinic acids, including chlorogenic acid; acid alcohols; flavonoid glucosides, among others. (Fратиanni, *et al.*, 2007; Sanchez-Rabaneda *et al.*, 2003). The extract obtained from the leaves has been shown to be hepatoprotective,<sup>6</sup> (Mehmetçik *et al.*, 2008) and improve liver regeneration after partial hepatectomy (Adzet *et al.*, 1987; Kirchhoff *et al.*, 1994; Kraft, 1997; Speroni *et al.*, 2003). These extracts also have antioxidative and protective properties against hydroperoxide-induced oxidative stress in cultured rat hepatocytes (Gebhardt and Fausel, 1997; Miccadei *et al.*, 2004). In addition, ALE has been found to decrease the production of reactive oxygen species, the oxidation of low density lipoproteins (LDL), and lipid peroxidation. (Juzyszyn, *et al.*, 2008) (Speroni *et al.*, 2003). Total LE extracts or their constituents reportedly have a beneficial effect in hepato-biliary diseases.

As food, artichoke has a high nutritional value. It is rich in dietary fiber, proteins and micronutrients such as B vitamins, vitamin C, iron, calcium, magnesium, potassium, manganese and zinc. While the leaves are used in the preparation of food, artichoke flower is used to make a medicinal tea or tisane. This tisane is used in traditional medicine to cleanse the liver and as a diuretic.

Thus, the objective of this work was to study the biological effect of *cynara cardunculus* on liver and heart status for hypercholesterolemic rats.

## MATERIALS AND METHODS

### **Plants:**

Artichoke (*Cynara cardunculus* var. *scolymus*) was purchased from local market of Makkah, Saudi Arabia.

### **Rats:**

Sixty (n=60) adult male albino rats (190±10g B.Wt.each) of Sprague Dawley Strain were obtained from Laboratory Animal Centre, Department of Biochemistry, Faculty of Medicine, Umm Al-Qura University, Makkah, KSA.

### **Cholesterol:**

Cholesterol was obtained as a pure white crystalline powder from Elgomhoriya, Company for Med. Preparations, Chemical & Medical Equipment's, Cairo, Egypt.

### **Preparation of aqueous extracts:**

Artichoke (*Cynara cardunculus* var. *scolymus*) was ground using porcelain grinder to pass through sieve-mesh pores of 1mm diameter. The extract of plant was prepared by mixing 1gm powdered leaves with 100 ml distilled water. The mixture was boiled for 10 minutes and left to cool for 15 minutes. The aqueous extract was filtered using filter paper to remove the particulate matter (0.2mm) then the filtrate was freely dried (Lyophilized) and reconstituted in 1.5 ml of distilled water (100 mg/kg body weight) (Sofrata *et al.*, 2007).

### **Basal diet:**

Rates were fed standard basal diet (12% casein, 10% corn oil, 0.2% choline chloride, 1% vitamin mixture, 5% cellulose, 4% salt mixture, and up to 100% corn starch) according to N.R.C., 1995 and water *ad libitum*. The animals were acclimatized to laboratory conditions for one week prior to the experiment.

### **Experimental animals:**

Adult male albino rats weighing (190±10 gm) were used in the present study. Animals were obtained from Laboratory Animal Centre, Department of Biochemistry, Faculty of Medicine, Umm Al-Qura University, Makkah, KSA. Biological investigation has been carried out in the animal house facility of the faculty of Applied Medical Sciences, Umm Al-Qura University, where animals were housed in a clean polypropylene cages with not more than four animals *per* cage and maintained under standard laboratory conditions (temperature 25 ± 2 °C with 12/12 h dark/light cycle). All procedures described were reviewed and approved by the Animal care and use Bioethical Committee of Medical Sciences, Umm Al-Qura University, KSA.

**Induction of hypercholesterolemic rate and experimental design:**

All rats were fed on basal diet for one week before starting the experiment for acclimatization. After one-week period, the rats were divided into two main groups. The first group (n = 10 rats) was fed on the basal diet only, as a control negative (healthy rats) (G I). The second main group (n = 50 rats) was fed for two weeks on the basal diet plus cholesterol 2% to induce hypercholesterolemia before starting the experiment. After two weeks feeding only on standard basal diet and served as positive control group (G II). The remnant second main group of rats was divided into 4 subgroups as follows:

G III was fed on basal diet + *Cynara cardunculus* leaves CCL at doses 200 mg/kg.

G IV was fed on basal diet + *Cynara cardunculus* leaves CCL at doses 400 mg/kg.

G V was fed on basal diet + *Cynara cardunculus* pulp CCP at doses 200 mg/kg.

G VI was fed on basal diet + *Cynara cardunculus* pulp CCP at doses 400 mg/kg.

At the end of the experiment, biological evaluation of the different diets was carried out by determination of body weight gain% (BWG%) and food efficiency ratio (FER) according to Chapman *et al.*, (1950). All rats were weighted once weekly.

**Blood and organs sampling:**

After 24 hours of the last feeding, blood samples were collected by sacrificing each hypercholesterolemic and control rats. The animals were anesthetized in a chamber containing diethyl ether. Two blood samples were collected from each animal into a heparin containing tube and plane tube, respectively. For serum production, collected blood samples in plane tubes were centrifuged at 3000 rpm for 10 minutes. The produced serum was collected and stored at -20°C until further analysis.

**Biochemical analysis:**

Total triglycerides, total cholesterol, cholesterol- HDL, AST (Human, Diagnostic Co. Germany), The VLDL- and LDL-cholesterol concentrations were calculated from the Reitman and Frankel (1957) equation: LDL-Cholesterol = Total cholesterol - (HDL- cholesterol + VLDL-cholesterol), and VLDL-cholesterol = Triglycerides/5. As well as ALT and ALP (Crescent Diagnostic Co. KSA) were estimated spectrophotometric according to enclosed pamphlet.

**Tissue specimens:**

Specimens from liver and heart were collected from rats of all experimental groups at the end of the experimental period.

**Histopathological Examination:**

Small tissue specimens from liver and heart of rats in different groups were collected and immediately fixed in 10% formalin. After proper fixation, the specimens were dehydrated in ethyl alcohol, cleared in xylol, embedded and casted in paraffin. Thin paraffin sections were prepared and stained with hematoxylin and eosin stain according to Bancroft *et al.*, (1990). The histological examination was done in pathology lab faculty of medicine Umm Alqura university, Saudi Arabia.

**Statistical Analysis:**

Serum biochemical parameters were analyzed by analysis of variance using SPSS. 20 for window. The mean and standard deviation were calculated for each variable. Data are expressed as Mean±SD of eight experiments. Paired-sample t-test was used to compare the parameters between controls positive group and hypercholesterolemic rats groups. A P-value less than 0.05 was considered statistically significant. Parameters of G II were compared to that of G I, and parameters of G III, G IV, G V and G VI were compared to that of G II. \*(P≤ 0.05) significant change; \*\*(P≤ 0.01) high significant change and \*\*\*(P<0.001) very high significant change.

**Results:**

Table 1. Showed that biological effect of *Cynara cardunculus* on BWG and FER of hypercholesterolemic rats after 6 weeks of feeding. Concerning BWG for rates in G III, G IV& G VI, it was found that significant decreased (P<0.05) compared with control +ve. The mean values were (60.23±5.62, 51.3±4.94, 57.67±5.21 and 72.47±6.58 respectively). It is evident that lowest value of BWG was found for G IV fed on CCL 400 mg/kg B.Wt. The same trend was observed for FER, there was significant difference(P<0.05) in G IV compared to cholesterol diet treatment (0.035±0.0026 and 0.045±0.00073). In both treatments groups FER were higher than that of the Control -ve.

**Table 1:** Biological effect of *Cynara cardunculus* on BWG<sup>1</sup> and FER<sup>2</sup> of hypercholesterolemic rats after 6 weeks of feeding.

Groups		Extracts	Doses (mg/kg B.Wt.)	BWG	FER
Control -ve	G I	-	-	45.28±4.05**	0.024±0.0017**
Control +ve	G II	-	-	72.47±6.58	0.045±0.00073
Treated Groups	G III	CCL	200	60.23±5.62*	0.038±0.0009
	G IV	CCL	400	51.3±4.94*	0.035±0.0026*
	G V	CCP	200	67.39±7.83	0.041±0.0026
	G VI	CCP	400	57.67±5.21*	0.043±0.0022

<sup>1</sup>BWG: body weight gain <sup>2</sup>FER: food efficiency ratio. Data are expressed as Mean±SD of eight experiments. A P-value less than 0.05 was considered statistically significant. Parameters of G II were compared to that of G I, and parameters of G III, G IV, G V and G VI were compared to that of G II. \*(P≤ 0.05) significant change; \*\*(P≤ 0.01) high significant change and \*\*\*(P<0.001) very high significant change.

Table 2. Showed that *Cynara cardunculus* in leaf form as well as pulp form has a significant decrease on heart and liver to body weight ratio of hypercholesterolemic rats < in G III, G IV & G VI>. The mean values were 3.37±0.46\*, 3.11±0.19\*\*, 3.51±0.16\* for liver, and for heart significant decrease was seen w.r.t G IV and G VI i.e as the dosage was increased the body weight decreased. The mean values were 0.33±0.011\*\*, 0.33±0.011\*\*

**Table 2:** Biological effect of *Cynara cardunculus* on liver and heart to body weight ratio of hypercholesterolemic rats.

Groups		Extracts	Doses (mg/kg B.Wt.)	Liver (g./100g b.wt.)	Heart (g./100g b.wt.)
Control -ve	G I	-	-	3.42±0.31*	0.31±0.06**
Control +ve	G II	-	-	4.48±0.19	0.38±0.04
Treated groups	G III	CCL	200	3.37±0.46*	0.36±0.004
	G IV	CCL	400	3.11±0.19**	0.33±0.011**
	G V	CCP	200	3.76±0.17	0.36±0.018
	G VI	CCP	400	3.51±0.16*	0.33±0.011**

Data are expressed as Mean±SD of eight experiments. A P-value less than 0.05 was considered statistically significant. Parameters of G II were compared to that of G I, and parameters of G III, G IV, G V and G VI were compared to that of G II. \*(P≤ 0.05) significant change; \*\*(P≤ 0.01) high significant change and \*\*\*(P<0.001) very high significant change.

Table 3. Showed that *Cynara cardunculus* in leaf form as well as pulp form has a significant decrease on serum HDL, cholesterol, LDL, triglycerides and VLDL Levels (mg/dl) of hypercholesterolemic rats. The decrease in the cholesterol level was highly significant with the increase in the dose < G IV & G VI>. The mean values were 156.58±17.3\*\* and 162.25±14.3\*, 62.41±9.3\*, 62.41±9.3\* and 57.24±2.4\*, 62.41±9.3\* and 32.45±5.6\*, 77.76±5.4\*\* and 113.04±5.3\* respectively. The HDL levels < good cholesterol> increased with higher dosage levels, whereas the levels of LDL < bad cholesterol> decreased with increase in dose.

**Table 3:** Effect of *Cynara cardunculus* on serum HDL, cholesterol, LDL, triglycerides and VLDL Levels (mg/dl) of hypercholesterolemic rats.

Groups		Extracts	Doses (mg/kg B.Wt.)	Cholesterol	Triglyceride	HDL	VLDL	LDL
Control -ve	G I	-	-	159.08±11.9**	112.58±10.9**	73.23±9.6**	22.52±3.7**	63.33±6.8**
Control +ve	G II	-	-	241.7±18.3	224.39±15.3	41.51±5.7	44.88±4.2	155.29±9.2
Treated Groups	G III	CCL	200	210.1±14.5	169.47±14.9*	67.69±8.3**	33.89±2.9	108.55±7.6*
	G IV	CCL	400	171.5±9.3**	156.58±17.3**	62.41±9.3*	31.32±4.3*	77.76±5.4**
	G V	CCP	200	228.7±12.8	171.47±12.1	51.25±5.3	34.29±4.1	143.12±4.9
	G VI	CCP	400	202.7±13.2*	162.25±14.3*	57.24±2.4*	32.45±5.6*	113.04±5.3*

Data are expressed as Mean±SD of eight experiments. A P-value less than 0.05 was considered statistically significant. Parameters of G II were compared to that of G I, and parameters of G III, G IV, G V and G VI were compared to that of G II. \*(P≤ 0.05) significant change; \*\*(P≤ 0.01) high significant change and \*\*\*(P<0.001) very high significant change.

Table 4. Showed the atherogenic index of *Cynara cardunculus* for hypercholesterolemic rats in GIII, GIV, GV and GVI. The LDL/HDL Ratio, T.C/LDL Ratio, T.C/HDL Ratio showed as highly significant decrease with the increase in dosage level of CCL. The mean values were 1.25±0.004\*\*, 2.21±0.012\*\*, 2.75±0.007\*\* respectively. The LDL/HDL Ratio, T.C/LDL Ratio, T.C/HDL Ratio showed significant decrease with the increase in dosage level of CCP. The mean values were 1.97±0.009\*, 1.79±0.005\*, 3.54±0.009\* respectively.

The results were more significant with CCL at a dose of 400 (mg/kg B.Wt.) in comparison to CCP at 400 (mg/kg B.Wt.)

**Table 4:** Atherogenic index of *Cynara cardunculus* for hypercholesterolemic rats.

Groups		Extracts	Doses (mg/kg B.Wt.)	LDL/HDL Ratio	T.C/LDL Ratio	T.C/HDL Ratio
Control -ve	G I	-	-	0.86±0.006**	2.51±0.07**	2.17±0.016**
Control +ve	G II	-	-	3.74±0.02	1.56±0.009	5.82±0.03
Treated Groups	G III	CCL	200	1.60±0.011*	1.94±0.007	3.10±0.004*
	G IV	CCL	400	1.25±0.004**	2.21±0.012**	2.75±0.007**
	G V	CCP	200	2.79±0.02	1.60±0.014	4.46±0.005
	G VI	CCP	400	1.97±0.009*	1.79±0.005*	3.54±0.009*

Data are expressed as Mean±SD of eight experiments. A P-value less than 0.05 was considered statistically significant. Parameters of G II were compared to that of G I, and parameters of G III, G IV, G V and G VI were compared to that of G II. \*(P≤ 0.05) significant change; \*\*(P≤ 0.01) high significant change and \*\*\* (P<0.001) very high significant change.

Table 5. Showed the effect of *Cynara cardunculus* on hepatic functions (AST<sup>1</sup>, ALT<sup>2</sup> and ALP<sup>3</sup>) for hypercholesterolemic rats in GIII, GIV, GV and GVI. The AST (U/L), ALT (U/L), ALP (U/L) levels showed as highly significant decrease with the increase in dosage level of CCL. The mean values 41.12±1.98\*\*, 41.54±6.39\*\*, 141.38±12.5\*\* respectively. The AST (U/L), ALT (U/L), ALP (U/L) levels showed significant decrease with the increase in dosage level of CCP. The mean values were 59.5±3.02\*, 53.28± 3.34\*, 159.64±18.9\*\* respectively.

The results were more significant with CCL at a dose of 400 (mg/kg B.Wt.) in comparison to CCP at 400 (mg/kg B.Wt.)

**Table 5:** Effect of *Cynara cardunculus* on hepatic functions (AST<sup>1</sup>, ALT<sup>2</sup> and ALP<sup>3</sup>) for hypercholesterolemic rats.

Groups		Extracts	Doses (mg/kg B.Wt.)	AST (U/L)	ALT (U/L)	ALP (U/L)
Control -ve	G I	-	-	38.41±4.86**	33.59±4.13**	119.5±21.5**
Control +ve	G II	-	-	81.13±5.87	71.46±3.18	281.28±26.6
Treated Groups	G III	CCL	200	60.41±3.32*	51.35±2.24**	167.85±20.3**
	G IV	CCL	400	41.12±1.98**	41.54±6.39**	141.38±12.5**
	G V	CCP	200	64.94±6.15*	59.59±3.27*	179.5±28.6*
	G VI	CCP	400	59.5±3.02*	53.28± 3.34*	159.64 ±18.9**

<sup>1</sup>Aspartate Amino Transferase , <sup>2</sup>Alanine Amino Transferase , <sup>3</sup>Alkaline Phosphatase. Data are expressed as Mean±SD of eight experiments. A P-value less than 0.05 was considered statistically significant. Parameters of G II were compared to that of G I, and parameters of G III, G IV, G V and G VI were compared to that of G II. \*(P≤ 0.05) significant change; \*\*(P≤ 0.01) high significant change and \*\*\* (P<0.001) very high significant change.

### Histopathological Study:

#### Liver:

Normal hepatic architecture was observed in control negative rats (G I), which fed on basal diet only. Liver of normal control rats showing normal hepatocytes radiating in cords from the central vein (Fig. 1). While in rats fed on cholesterol at a concentration of 2% for two weeks (G II) liver showed hepatocytes fatty vacuolation with foamy cytoplasm, congested and dilated blood vessels, thickened in the wall b. (Fig. 2).

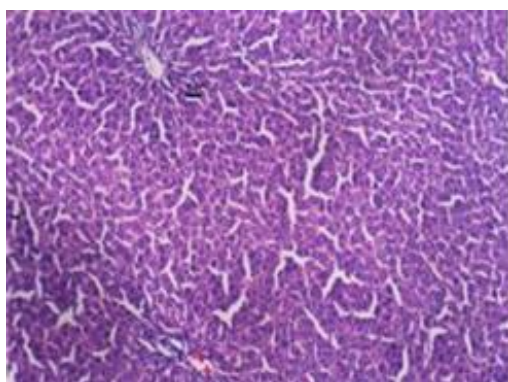
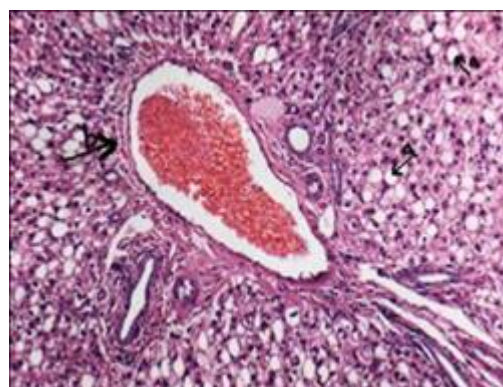
**Fig. 1:** (H & E 100).**Fig. 2:** (H&E 400).

Fig.3 show milled and dilated, congested blood vessels, necrosis of hepatocytes with accumulation of fat globules and disorganization of hepatic cords were observed in rat fed on CCL at doses 200 mg/kg B.W. (G III) . Rats in (G IV) which fed on CCL at doses 400 mg/kg B.W. give the same lesions observed in the previous group (Fig. 4).



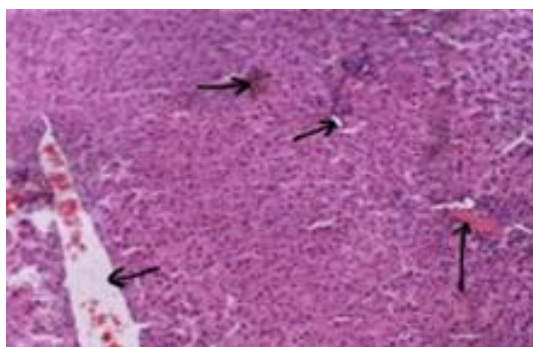


Fig. 3: (H &amp; E 100)

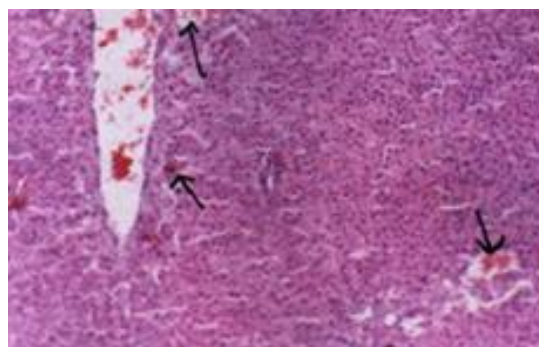


Fig. 4: (H &amp; E 100)

Liver tissue in (G V) for rats fed on *CCP* at doses 200 mg/kg B.W. showing more severe vacuolar degenerative changes in addition to scattered mitotic figures and binucleated hepatocytes (Fig. 5). Liver tissue in rats fed on *CCP* at doses 400 mg/kg B.W. (G VI) showing high vacuolar degenerative changes and binucleated hepatocytes (Fig. 6).

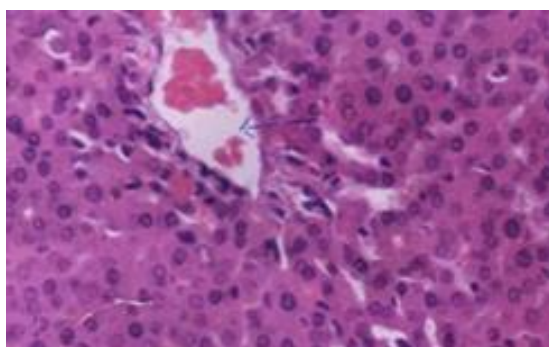


Fig. 5: (H &amp; E 400)

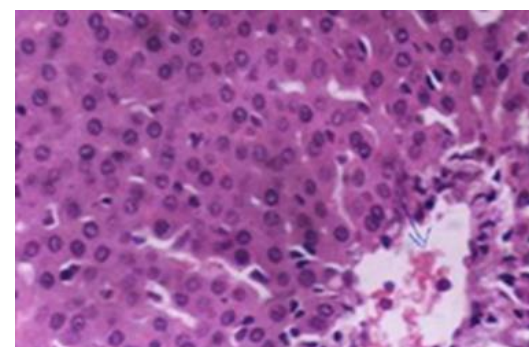


Fig. 6: (H &amp; E 400)

#### Heart:

Heart of control negative group showed normal histological structure in cardiac muscles (G I) (Fig. 7) in case of rats fed on cholesterol 2% for two weeks showed myxomatous degeneration of the heart valve, swelling of its endothelial lining and showing fatty deposits in the subbed helical layer (G II) (Fig. 8).

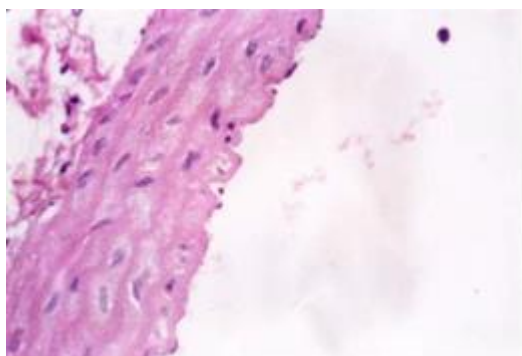


Fig. 7: (H &amp; E 400)

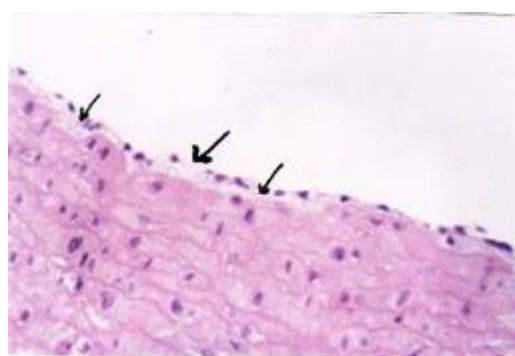


Fig. 8: (H &amp; E 400).

In (G III) which fed on *CCL* at doses 200 mg/kg B.W. showed a few extravagated RBC,S were seen scattering with in the connective tissue parenchyma and mild vascular degenerative changes with- in muscles fiber were also seen (Fig. 9) the same pathological lesions were recorded in rats fed on *CCL* at doses 400 mg/kg B.W. (GIV) (Fig. 10).

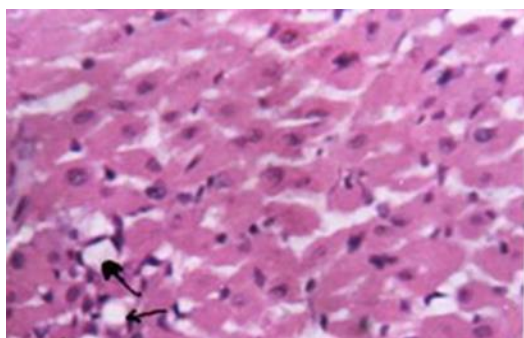


Fig. 9: (H &amp; E 400)

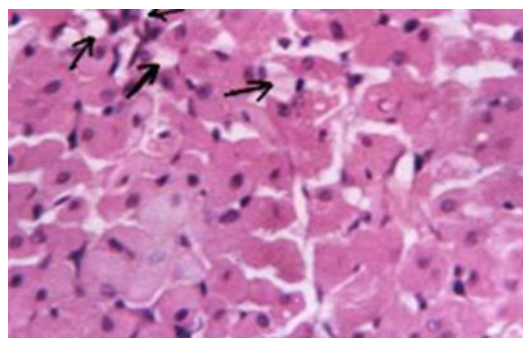


Fig. 10: (H &amp; E 400).

Thickening of the coronary blood vessels with necrotic changes of cardiac muscles were observed in the (G V) for rats fed on CCP at doses 200 mg/kg B.W. (Fig. 11, H & Ex 400). But in (G VI) which rats fed CCP at doses 400 mg/kg B.W. showing normal cardiac muscles (Fig. 12, H & Ex 400).

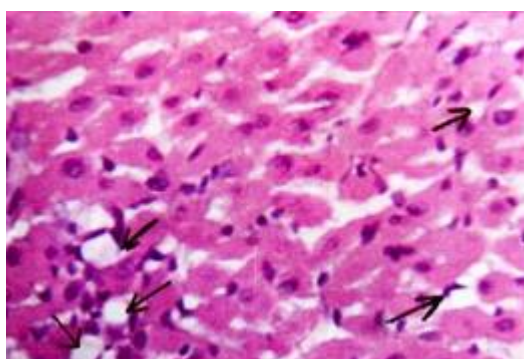


Fig. 11: (H &amp; E 400).

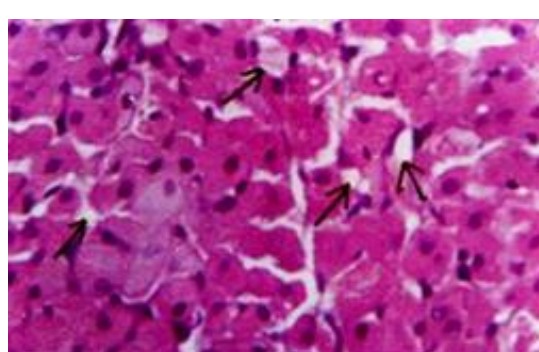


Fig. 12: (H &amp; E 400).

#### Discussion:

From the results it is clear that *Cynara cardunculus* in leaf and pulp form had a significant effect in reducing the BWG and FER of hypercholesterolemic rats. Cholesterol levels tends to decrease with the utake of *Cynara cardunculus* in leaf and pulp form as compared to the control negatives. Though, of the two forms of *Cynara cardunculus* leaf form was more effective in reducing the cholesterol levels as compared to the pulp form. Secondly, with the increase in dosage levels cholesterol showed a significant decrease. Table 1,3

On comparing the biological effect of *Cynara cardunculus* on liver and heart to body weight ratio of hypercholesterolemic rats (Table 2 it was seen that cholesterol levels showed a decreased with the uptake of *Cynara cardunculus* in the two forms ,and the decrease was more significant with the higher dosage. *Cynara cardunculus* showed a highly significant increase in HDL< good cholesterol>, cholesterol levels, and a decrease in LDL< bad cholesterol> levels of hypercholesterolemic rats. ( Table 3, 4.)

While artichokes may not be the easiest food to consume, the sheer volume of nutrients, minerals, and phytochemicals found in this extraordinary vegetable make eating them well worth it. Most people's favorite part of the artichoke is the heart, but the leaves are actually the source of a vast majority of its health benefits, as was seen in this study as well. In fact, artichoke leaf extract has proven to be an extremely beneficial food with a host of illness-fighting, age-extending properties. Our results were similar to the other works in this field. In 2004, the United States Department of Agriculture conducted its largest, most comprehensive study analyzing the antioxidant content of the most commonly consumed foods. (Available at: <http://www.oceanmist.com/health/antioxidant.aspx>. Accessed June 20, 2011.; Available at: [http://www.eurekalert.org/pub\\_releases/2004-06/aas-lus061504.php](http://www.eurekalert.org/pub_releases/2004-06/aas-lus061504.php). Accessed June 21, 2011).

Gylling *et al.*, 2004. reported that, hypercholesterolemia are associated with abnormalities of lipoprotein levels in the blood, and streptozotocin increased the levels of LDL in the blood, and decreased the HDL level. They also added that, dyslipidemia is one of the major cardiovascular risk factors. In addition, our results are in accordance with the results of Heidarian and Soofiniya, 2011) reported that, the levels of serum total cholesterol and triglycerides in the streptozotocin-treated rats markedly increased, compared to normal control rats. However, the elevated serum triglyceride and total cholesterol levels significantly reduced by the oral administration of artichoke (200 and 400 mg/kg) in a dose-dependent manner. Artichoke leave extract (ALE) contains bioactive and flavonoid compounds such as caffeoylquinic acids and luteolin glucosides. As it is known, cynarin is a major dicaffeoylquinic acid and chlorogenic acid is the main monocaffeoylquinic acid, whereas luteolin-7-O glucoside is the major flavonoid. (Llorach, R. Espin, 2002; Wang, *et al.*, 2003; Sofrata, *et*

*al.*,2007). Their results indicated that ALE had a lipid lowering effect on the diabetic rats.(Llorach, R. Espin, 2002; Wang, *et al.*, 2003; Sofrata, *et al.*, 2007).

Our results are in accordance with the results of Kucukgergin *et al.*, 2010<sup>15</sup> who reported that, artichoke leaf extract treatment for hypercholesterolemic rats was useful for decreasing serum cholesterol and triglycerides levels of rats. Moreover, Esterbauer *et al.*,1992; Itabe 2003; Nakajima *et al.* reported that conditions leading to increased LDL oxidation have been considered to be a probable atherosclerotic risk factor.

Artichoke products have been reported to lower blood cholesterol and triglyceride levels in humans and animals. The net effect of Artichoke is claimed to be the result of both an inactivation of and an interference with cholesterol metabolism. Cynarin reportedly decreases the rate of cholesterol synthesis in the liver, enhances biliary excretion of cholesterol, and increases conversion towards the bile acids. (Chapman, 1950); N.R.C. (National Research Council), 1995; Reitman, (1957).

On evaluation of the effects of *Cynara cardunculus* on hepatic functions (AST, ALT and ALP) for hypercholesterolemic rats ,it was found that both CCL and CCP *decreases the concentration of the respective enzymes (AST, ALT,ALP, which are an indicator of liver dysfunction>,hence serving a hepatoprotective and regenerating effects*. The results of the study were also substantiated by the histopathological evaluation of heart muscles and liver muscles, which showed a more severe vacuolar degenerative changes in addition to scattered mitotic figures and binucleated hepatocytes with the uptake of artichoke, and, the degeneration was more with a higher dose,(Fig2,3,4,5,6) as compared to normal radiating pattern of hepatocytes in cords from as seen in control negatives.(Fig 1)

Artichoke had hepatoprotection after exposure of laboratory animals to the liver toxic substance tetrachloromethane. Hepatoprotective qualities of Artichoke seem to be linked to its antioxidant capacity and the Cynarin content, which is claimed to restore healthy growth and reproduction of liver cells. The antioxidant effect has been further supported by laboratory studies in both human and animal cells. Artichoke is also reported to have a stimulant activity on bile production in the liver; termed choleric action. Stimulating the flow of bile juices, Artichoke aids in breaking down hard to digest fats, thereby increasing digestion and the absorption of nutrients. Studies have reported that when patients with dyspeptic complaints take Artichoke as a supplement, symptoms rapidly disappear, reducing pain, nausea, retching and the sensation of fullness. The constituent Cynarin has been stated to be most active in this capacity (Available at: <http://www.foodforyourhealing.com/foods-for-liver-health/>. Accessed June 19, 2011).

Different studies have established that artichoke improves digestive and liver functions. It also improves gall bladder functions. In addition, available clinical evidence show that artichoke can raise HDL (high-density lipoprotein or “good”) cholesterol while lowering LDL (low-protein lipoprotein or “bad”) cholesterol. The hypocholesterolemic properties of artichoke involves the inhibition of the enzyme, HMG-CoA reductase. By lowering blood cholesterol levels and improving lipid profile, experts believe artichoke can reduce the risks of arteriosclerosis and coronary heart disease.

Thus, it was concluded that artichoke has a benefiting effect in cardiovascular and liver disease, though more studies are required to further substantiate the documented hypothesis.

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