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Evaluation of some hepatoprotective preparations in experimentally induced hepatopathy in Baladi goats

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ABSTRACT

This work aimed to evaluate the hepatoprotective effect of garlic oil extract and artichoke extract with regarding to clinical, hematobiochemical alteration and oxidative stress status of induced acute hepatopathy in Baladi goats. Fifteen Baladi goats were kept for experimental induction of hepatopathy that treated orally with 0.3 ml /kg of carbon tetrachloride (CCl4) once and divided randomly into 3 groups each of five. Group A was kept as control positive. Group B and Group C were treated by garlic oil extract in dose 0.8mg/kg and artichoke extract in dose 10mg/kg for 15 days for hepatic protection before induction. Clinical and hematobiochemical examination were carried out at 1st, 3rd and 7th day after induction. Clinical examinations of CCl4 treated group at first day showed dullness, inappetence, pale mucous membranes, elevated body temperature and pulse rate and nervous manifestations. While garlic and artichoke extracts treated groups showed less severe clinical signs that began to disappear at 3rd day after induction. With the Hematobiochemical examination, the induced acute hepatopathy group showed significant (P<0.05) decrease in RBCs, Hb, PCV, GPX and SOD and significant (P<0.05) increase in WBCs, ALT, AST, GGT, total and direct bilirubin, blood urea nitrogen, creatinine and MDA. While garlic and artichoke extracts treated groups showed significant (P<0.05) increase in RBCs, Hb, PCV and antioxidant status with significant (P<0.05) decrease in liver damage indices of treated animals. Therefore, we concluded that garlic oil extract and artichoke extract could be used as hepatoprotective agent in Baladi goats.

1. INTRODUCTION

Liver diseases have an economic impact in countries where livestock industry is an important segment of agriculture (Berhe 2009).There are many causes of liver diseases and hepatobiliary diseases in ruminants as hepatic lipidosis, hepatic abscesses, bacterial hepatitis and ingestion of toxic substances (Davoudi et al., 2013). Negative energy balance in case of ovine pregnancy toxemia is the main cause of hepatic fatty degeneration that resulted from increased fat mobilization to liver more than oxidation and secretion and increase deposition of fat in liver lead to fatty liver (Bobe et al., 2004).

Fatty degeneration of liver and centrilobular necrosis can be produced in rat by administration of single dose of Carbon tetrachloride (Slater *et al.*, 1985). CCl4 administration results in fatty liver and hepatocyte necrosis, in addition, induces accumulation of triglycerides, decrease of reduced glutathione level, membrane damage and loss of enzyme activity (Recknagel *et al.*,1989). Hepatotoxic effects of CCl4 depends on its activation by cytochrome P4502E1, CYP2B1 or CYP2B2 and possibly by CYP3A to form the trichloroethyl radical (CCL3). This toxic free radical reacts with various biologically important substance such as amino acids, nucleotides, fatty acids as well as proteins nucleic acids and lipids and impairment of lipid metabolism that result in fatty liver (Weber *et al.*, 2003). Herbal medicine has been proven to be effective as hepatoprotective agents (Kashaw *et al*., 2010). Garlic oil contains numerous organosulfur compounds that have potential hepatoprotective effect (Sheen *et al*., 1999) and decrease the activation of cytochrome P450 2E1; which is important for the bioactivation of a wide variety of hepatotoxic substances and for generation of toxic free radicals (Kwak *et al.*, 1995). Additionally, organosulfur compounds in garlic oil increase the activity of antioxidant enzymes as glutathione peroxidase and superoxide dismutase (Banerjee *et al.*, 2001) and inhibit lipid peroxidation (El-Khayat *et al*., 2013).

It was reported that treatment using the preparation called HEPARENOL which includes methionine, lysine, betaine, extract of artichoke and choline in its composition possibility preventing of fatty liver in cow during the periparturient period (Šamanc *et al.*, 2008). Sulfur containing amino acids, such as methionine and lysine are essential in the maintenance of normal cellular functions therefore, they have powerful role in antioxidant system of the cell (Colovic *et al.*, 2018). Artichoke is important in protection the normal liver function, preserved the hepatic redox status by significant increase in antioxidant enzyme activities by inhibition of lipid peroxidation in the liver (Ali *et al*., 2012).

Therefore, the present work was designed for evaluation of the hepatoprotective effect of garlic oil extract and artichoke extract with regarding clinical,

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hematobiochemical alteration and oxidative stress status of acute induced hepatopathy in Baladi goats.

2. MATERIAL AND METHODS

2.1. Experimental animals

This study was carried out on fifteen Baladi goats with average body weight (15-20) kg. The experiment was conducted at faculty veterinary medicine, Benha University. Goats were collected from local market and kept for one week before the onset of experiment to allow time of acclimatization. They were fed on wheat straw bedding under condition of natural light and ambient temperature and with free access to water and feed were allowed ad libtium. They were fed daily on commercial concentrate mixture consist of (30% crushed maize, 35 % wheat bran and 32% ground beans) and supplement with 1% common salts to provide balanced ration (NRC, 1985). Rations were formulated to be iso-nitrogenous and iso-energic.

2.2. Experimental design:

Goats were randomly allotted into three groups each of 5 goats. Group A was subjected to CCl4 treatment only for induction of hepatopathy, group B was subjected to garlic oil extract 15 day then induction of hepatopathy by with CCl4 and group C was subjected to artichoke extract in Heparenol® (COOPHAVET COMP., France, imported by Tradimpex Company, Egypt) which composed of (cysteine, choline, betaine and artichoke extract), 15 days for hepatic protection then induction of hepatopathy by treatment them with CCl4.

2.3. Experimental induction of hepatopathy

Hepatopathy was induced in all animal groups by CCL4 (99.9 % made in Germany obtained from El-Almeen company, Egypt) at dose of 3 ml/10 kg body weight diluted with liquid paraffin in 1:1 ratio via stomach tube directly into the rumen (vajdovich *et al*., 1995).

2.4. Clinical examination of the animals:

Body temperature, respiratory rates, pulse rates and mucous membranes of the goats were examined and recorded as previously described by Kelly (1974).

2.5.Sampling:

Blood samples were collected four times at zero day before the induction, 1st, 3rd and finally in the 7th day at morning from jugular vein according to (Pugh and Baird (2012). Two blood samples obtained from each goat, the first set of samples were collected on labeled test tubes containing 5 mg k_2EDTA in concentration of 1 mg/1ml blood (Coles, 1986) as an anticoagulant for hematological examination. The second set of samples were collected without anticoagulant to obtain clear sera that were transferred into clear dry labeled Eppendorf tubes and stored at -20◦C till the biochemical analysis.

2.6. Hematological analysis:

The total erythrocytic count, total leukocytic count, PCV%, Hb concentration (g/dl) and differential leukocytic count (lymphocytes, monocytes and granulocytes) was determined using hematology analyzer (FX9080) according to the methods described by Jain (1993).

2.6.1. Serum biochemical analysis:

The Serum γ-glutamyl transferase (GGT), alanin aminotransferase (ALT), aspartate aminotransferase (AST) , alkaline phosphatase Serum total protein, Albumin, total bilirubin, direct bilirubin cholesterol and triglycerides were determined spectrophotometrically by using of the special kits as described by Reitman and Frankels (1957), Thefeld (1974), Ritman and Frankel (1957), Roy(1970), Henary *et al*., (1974), Doumas *et al*., (1971), kataki et al., (2012) and Allain et al. (1974), respectively. Serum creatinine and blood urea nitrogen were estimated according to Houot (1985) and patton and crouch (1977), respectively. GSH-PX enzyme was determined spectrophotometrically by Beutler *et al.* (1963), Superoxide dismutase concentration (SOD) and Serum L- malondialdehyde were determined calorimetrically by Nishikimi *et al.* (1972) Satoh (1978) and Ohkawa *et al.* (1979) respectively.

2.7. Statistical analysis:

Statistical analysis was achieved using SPSS (Chicago, USA) statistics version 25. The data was statistically analyzed using mixed two-way analysis of variation (ANOVA) with Duncan as post hoc test as previously described (Duncan ,1955). Values was represented as mean ± standard error (SE). All differences were considered statistically significant when $P< 0.05$.

3. RESULTS

3.1. Clinical findings:

In the 1st day after CCl4 treatment, all goats showed inactivity, lethargy, inappetence, dullness, dropping of ear, accelerated respiratory rate, signs of pain (grinding on teeth, pawing in ground, fighting with each other) and slight increase in body temperature with shivering in some animal. In the 3rd day CCl4 treated group still showed inappetence, dullness, slight increase in body temperature and pale mucous membranes. While with garlic and artichoke extract treated groups, goats return to normal state except paleness in mucous membranes. Data presented in table (1) showed that body temperature, respiratory rate and heart rate were significantly increase ($P< 0.05$) in the first day after induction in all animal groups and returned to normal level in the 3rd day and 7th day in garlic and artichoke extract treated groups but the CCl4 treated group had sustained slightly elevated body temperature.

3.2. Hematological findings

As presented in table 2, the values of RBCs count, HB and PCV significantly ($P< 0.05$) increased in the control group compared to the other experimental groups, while significantly ($P< 0.05$) decreased with CCl4 treated group compared to garlic and artichoke extract treated groups. In contrast, CCl4 group showed a significant increase ($P< 0.05$) in WBCS, neutrophil, monocyte and significant decrease in lymphocyte all over the time of experiment while garlic extract and artichoke extract group showed a significant increase ($P< 0.05$) in neutrophil and monocyte and significant decrease in lymphocyte compare to control group (table 2).

3.3. Biochemical parameters

Table (3) showed significant increase ($P< 0.05$) in serum ALT, AST, ALP and GGT level in CCl4 group all over the time of experiment compared to the other experimental groups. While, garlic extract and artichoke extract treated groups showed significant increase ($P< 0.05$) in ALT, AST and ALP levels in the 1st day and 3rd days of examination.

Table 1 Body temperature, respiratory rate and pulse rate in CCl4, garlic and heparenol treated groups at 1st, 3rd and 7th day of experimental induction of hepatopathy.

Parameter	Duration of Experiment	Experimental Groups			
		Control Group (N=15)	CCl_4 Group (N=5)	Garlic Group (N=5)	Heparenol Group (N=5)
Body temperature (C)	1st Day	38.1± 0.01 Ca	40.00 ± 0.06 Aa	39.67 ± 0.09 Ba	39.77 ± 0.09 A,Ba
	3rd Day	38±0.01 Cb	39.80 ± 0.06 Aa	39.43 ± 0.23 Aa	39.43 ± 0.23 Aa
	7th Day	38.2 ±0.01 Ba	38.87 ± 0.09 Ab	38.33 ± 0.09 Bb	38.20 ± 0.12 Bb
Heart rate (pulse wave/min)	1st Day	73.33 ± 1.86 Ca	90.33 ± 0.88 Aa	83.33 ± 0.88 Ba	84.67 ± 2.19 Ba
	3rd Day	73.33 ± 0.88 Ca	86.67 ± 1.86 Aa	78.00 ± 1.53 Bb	78.67 ± 0.88 Bb
	7th Day	74.00 ± 1.53 Ba	78.67 ± 0.67 Ab	72.00 ± 1.15 Bc	72.67 ± 0.33 Bc
Respiratory rate (cycle /min)	1st Day	17.67 ± 1.45 Ca	31.33 ± 1.20 Aa	26.00 ± 1.00 Ba	29.67 ± 1.20 A,Ba
	3rd Day	17.67 ± 0.33 Ca	30.00 ± 0.58 Aa,b	23.33 ± 0.33 Cb	26.33 ± 1.33 Ba
	7th Day	19.00 ± 0.58 Ba	27.00 ± 1.00 Ab	18.67 ± 0.67 Bc	17.67 ± 1.45 Bb

Data are presented as (Mean ± S.E). S.E = Standard error. Mean values in the same column with different superscript Capital letters are significantly different at (P<0.05) between different groups at the same time. While, mean values in the same raw with different superscript. Small letters are significantly different at (P<0.05) in different times within the same group

Table 2 Hematological parameters in CCl4, garlic and heparenol treated groups at 1st, 3rd and 7th day of experimental induction of hepatopathy

parameter	Duration of Experiment	Experimental Groups			
		Control Group (N=15)	CCl_4 Group (N=5)	Garlic Group (N=5)	Heparenol Group (N=5)
RBCs ($10^6/\mu L$)	1st Day	2.57 ± 0.13 Aa	0.61 ± 0.05 Ca	1.21 ± 0.15 Bb	1.52 ± 0.06 Ba
	3rd Day	2.50 ± 0.31 Aa	0.38 ± 0.08 Cb	1.80 ± 0.06 Ba	1.60 ± 0.06 Ba
	7th Day	2.53 ± 0.30 Aa	0.63 ± 0.06 Ca	1.84 ± 0.01 Ba	1.83 ± 0.23 Ba
HB (g/dL)	1st Day	9.57 ± 0.35 Aa	5.33 ± 0.15 Ca	7.20 ± 0.57 Ba	6.27 ± 0.28 B,Cb
	3rd Day	10.13 ± 0.13 Aa	4.43 ± 0.66 Ca	7.57 ± 0.78 Ba	8.33 ± 0.38 Ba
	7th Day	9.93 ± 0.30 Aa	5.70 ± 0.21 Ca	8.80 ± 0.31 A,Ba	8.30 ± 0.60 Ba
PCV%	1st Day	3.46 ± 0.06 Aa	1.63 ± 0.18 Ca	2.47 ± 0.20 Ba	2.80 ± 0.06 Ba
	3rd Day	3.53 ± 0.03 Aa	1.20 ± 0.25 Ca	2.87 ± 0.18 Ba	2.67 ± 0.03 Ba
	7th Day	3.33 ± 0.28 Aa	1.43 ± 0.15 Ca	2.87 ± 0.12 A,Ba	2.47 ± 0.07 Bb
WBCs ($10^9/L$)	1st Day	10.93 ± 0.27 Ba	65.50 ± 14.15 Aa	20.10 ± 1.04 Ba	28.43 ± 3.15 Ba
	3rd Day	10.57 ± 0.54 Ba	52.03 ± 8.70 Aa	21.97 ± 3.43 Ba	20.10 ± 3.10 Ba
	7th Day	10.67 ± 0.44 Ba	38.53 ± 5.49 Aa	18.57 ± 2.46 Ba	18.70 ± 3.64 Ba
Neutrophil ($10^9/L$)	1st Day	33.67 ± 1.67 Aa	54.33 ± 8.33 Aa	64.00 ± 13.53 Aa	59.67 ± 10.65 Aa
	3rd Day	33.33 ± 3.18 Ba	70.33 ± 5.36 Aa	56.00 ± 4.16 Aa	57.33 ± 5.78 Aa
	7th Day	27.67 ± 4.10 Ca	71.33 ± 3.18 Aa	48.67 ± 2.40 Ba	55.33 ± 3.53 Ba
lymphocyte ($10^9/L$)	1st Day	63.33 ± 1.67 Aa	17.00 ± 2.08 Ca	63.67 ± 10.49 Aa	44.00 ± 2.65 Ba,b
	3rd Day	64.00 ± 2.00 Aa	23.67 ± 4.70 Ca	54.67 ± 0.88 Ba	48.00 ± 0.58 Ba
	7th Day	66.00 ± 2.08 Aa	23.67 ± 1.86 Ca	44.00 ± 3.06 Ba	37.67 ± 3.76 Bb
Eosinophil ($10^9/L$)	1st Day	1.00 ± 0.58 Ba	3.33 ± 0.67 Aa	1.33 ± 0.67 Ba	1.67 ± 0.33 A,Ba
	3rd Day	1.00 ± 0.58 Aa	2.67 ± 0.33 Aa	2.33 ± 0.33 Aa	2.33 ± 0.67 Aa
	7th Day	1.00 ± 0.58 Aa	3.00 ± 1.00 Aa	2.33 ± 0.33 Aa	2.67 ± 0.33 Aa
Monocyte ($10^9/L$)	1st Day	0.33 ± 0.33 Ba	3.00 ± 1.00 Aa	2.00 ± 0.58 A,Ba	1.67 ± 0.33 A,Ba
	3rd Day	0.33 ± 0.33 Ca	4.33 ± 0.33 Aa	2.33 ± 0.33 Ba	2.67 ± 0.33 Ba
	7th Day	0.33 ± 0.33 Ba	3.33 ± 0.67 Aa	1.67 ± 0.33 A,Ba	2.00 ± 0.58 A,Ba

Data are presented as (Mean ± S.E). S.E = Standard error. Mean values in the same column with different superscript Capital letters are significantly different at (P<0.05) between different groups at the same time. While, mean values in the same raw with different superscript Small letters are significantly different at (P<0.05) in different times within the same group

Table 3 Liver enzymes in CCl4, garlic and heparenol treated groups at 1st, 3rd and 7th day of experimental induction of hepatopathy.

Parameter	Duration of Experiment	Experimental Groups			
		Control Group (N=15)	CCl_4 Group (N=5)	Garlic Group (N=5)	Heparenol Group (N=5)
ALT (U/L)	1st Day	18.40 ± 2.08 Ca	393.00 ± 44.84 Aa	46.67 ± 9.06 B,Cb	121.67 ± 24.69 Ba
	3rd Day	18.27 ± 0.56 Ca	322.67 ± 22.24 Aa	107.33 ± 7.84 Ba	138.00 ± 18.19 Ba
	7th Day	20.47 ± 0.65 Ba	113.4 ± 1.46 Ab	18.73 ± 2.11 Bc	16.00 ± 1.15 Bb
AST(U/L)	1st Day	48.90 ± 4.45 Ba	563.00 ± 71.67 Aa	93.00 ± 2.31 Bb	125.00 ± 4.16 Ba
	3rd Day	51.53 ± 8.59 Ca	478.33 ± 34.19 Aa	136.00 ± 10.69 Ba	130.67 ± 2.03 Ba
	7th Day	56.03 ± 1.55 Ba	152.33 ± 18.94 Ab	87.33 ± 2.85 Bb	124.67 ± 1.67 Aa
ALP(U/L)	1st Day	120.67 ± 3.53 Ba	458.97 ± 51.52 Ab	74.00 ± 0.67 Bc	106.33 ± 5.83 Bc
	3rd Day	119.67 ± 2.91 Da	941.83 ± 1.01 Aa	153.00 ± 1.53 Ca	234.97 ± 0.90 Ba
	7th Day	133.33 ± 12.02 Ba	186.27 ± 0.82 Ab	115.33 ± 1.45 Bb	123.67 ± 1.86 Bb
GGT(U/L)	1st Day	25.00 ± 6.03 Ba	70.33 ± 0.88 Aa	33.33 ± 1.86 Ba	64.33 ± 12.39 Aa
	3rd Day	18.33 ± 1.20 Ba	70.67 ± 3.67 Aa	32.67 ± 2.33 Ba	62.33 ± 11.05 Aa
	7th Day	31.33 ± 1.86 Aa	61.67 ± 9.28 Aa	38.00 ± 12.58 Aa	39.33 ± 9.84 Aa

Data are presented as (Mean ± S.E). S.E = Standard error.Mean values in the same column with different superscript Capital letters are significantly different at (P<0.05) between different groups at the same time. While, mean values in the same raw with different superscript Small letters are significantly different at (P<0.05) in different times within the same group

Data presented in Table (4) showed that CCl4 treated group had significant increase (P< 0.05) in total bilirubin, direct bilirubin, cholesterol, triglycerides, urea and creatinine and significant decrease (P< 0.05) in total plasma protein,

albumin and glucose all over time of experiment compared to the other experimental groups. The garlic and artichoke extract treated groups showed significant increase($P< 0.05$) in total bilirubin, direct bilirubin and urea significant increase compared to control group.

The level of Serum GPX and SOD significantly decreased ($P< 0.05$) in CCl4 treated group with increased serum MDA compared to other experimental groups at all periods of the experiment. While garlic and artichoke extract treated groups showed a significant increase ($P< 0.05$) in serum GPX and SOD and decrease in serum MDA level compared to CCl4 treated group.

Table 4 Biochemical analysis in CCl4, garlic and heparenol treated groups at 1st, 3rd and 7th day of experimental induction of hepatopathy.

Parameter	Duration of Experiment	Experimental Groups			
		Control Group (N=15)	CCl_4 Group (N=5)	Garlic Group (N=5)	Heparenol Group (N=5)
Total bilirubin ((mg/dL)	1st Day	0.37 ± 0.01 ^{Ca}	0.56 ± 0.00 ^{Ac}	0.46 ± 0.03 ^{Ba}	0.45 ± 0.00 ^{Ba}
	3rd Day	0.40 ± 0.02 ^{Ba}	0.63 ± 0.00 ^{Aa}	0.42 ± 0.02 ^{Ba}	0.41 ± 0.00 ^{Bb}
	7th Day	0.37 ± 0.01 ^{Ca}	0.58 ± 0.00 ^{Ab}	0.40 ± 0.01 ^{Ba}	0.39 ± 0.01 ^{Bc}
Direct bilirubin (mg/dL)	1st Day	0.16 ± 0.02 ^{Ca}	0.28 ± 0.00 ^{Aa}	0.21 ± 0.00 ^{Ba}	0.21 ± 0.00 ^{Ba}
	3rd Day	0.17 ± 0.01 ^{Ca}	0.25 ± 0.00 ^{Ab}	0.19 ± 0.00 ^{Ba}	0.19 ± 0.00 ^{Bb}
	7th Day	0.15 ± 0.01 ^{Ba}	0.22 ± 0.00 ^{Ac}	0.16 ± 0.01 ^{Bb}	0.17 ± 0.00 ^{Bc}
Total plasma protein (g/dL)	1st Day	7.24 ± 0.08 ^{Aa}	3.13 ± 0.52 ^{Ba}	4.33 ± 0.52 ^{Bb}	4.23 ± 0.13 ^{Bb}
	3rd Day	7.14 ± 0.32 ^{Aa}	3.73 ± 0.37 ^{Ca}	5.67 ± 0.60 ^{Ba,b}	5.10 ± 0.10 $^{Ba.b}$
	7th Day	7.33 ± 0.23 ^{Aa}	4.33 ± 0.35 ^{Ca}	6.03 ± 0.15 ^{Ba}	6.23 ± 0.62 ^{Ba}
Albumin (g/dL)	1st Day	3.59 ± 0.25 ^{Aa}	2.80 ± 0.21 ^{Ba}	2.93 ± 0.23 ^{Ba}	3.13 ± 0.39 ^{Ba}
	3rd Day	3.49 ± 0.14 ^{Aa}	2.57 ± 0.12 ^{Ba}	2.33 ± 0.27 ^{Ba}	2.80 ± 0.15 ^{Ba}
	7th Day	3.65 ± 0.21 ^{Aa}	2.43 ± 0.23 ^{Ba}	3.57 ± 0.50 ^{A,Ba}	3.27 ± 0.38 ^{A,Ba}
Cholesterol (mg/dL)	1st Day	65.67 ± 6.69 ^{Ba}	99.93 ± 1.73 ^{Aa}	80.73 ± 7.26 ^{Ba}	81.90 ± 3.23 ^{Ba}
	3rd Day	63.00 ± 6.56 ^{B,Ca}	108.57 ± 5.06 ^{Aa}	81.23 ± 6.82 ^{Ba}	56.00 ± 8.19 ^{Cb}
	7th Day	53.67 ± 1.86 ^{Ba}	84.33 ± 3.71 ^{Ab}	56.00 ± 3.61 ^{Bb}	54.00 ± 1.15 ^{Bb}
Triglycerides (mg/dL)	1st Day	18.69 ± 2.17 ^{Ba}	31.60 ± 0.95 ^{Ab}	23.83 ± 1.64 ^{Ba}	23.27 ± 0.93 ^{Ba}
	3rd Day	15.65 ± 0.34 ^{Ba}	35.67 ± 0.88 ^{Aa}	17.63 ± 1.23 ^{Bb}	18.17 ± 0.78 ^{Bb}
	7th Day	18.10 ± 1.75 ^{Ba}	32.67 ± 0.33 ^{Ab}	13.67 ± 0.88 ^{Cb}	15.33 ± 1.20 ^{B,Cb}
Glucose (mg/dL)	1st Day	62.00 ± 7.81 ^{Aa}	44.00 ± 3.06 ^{Ba}	60.00 ± 2.65 ^{Aa}	64.33 ± 2.73 ^{Aa}
	3rd Day	64.67 ± 3.71 ^{Aa}	47.67 ± 1.45 ^{Ba}	66.00 ± 2.08 ^{Aa}	66.33 ± 8.11 ^{Aa}
	7th Day	63.67 ± 4.10 ^{Aa}	48.67 ± 1.76 ^{Ba}	63.00 ± 4.36 ^{Aa}	66.00 ± 3.61 ^{Aa}
Blood urea nitrogen (mg/dL)	1st Day	11.93 ± 0.23 ^{Ca}	60.67 ± 2.33 ^{Aa}	49.67 ± 2.73 ^{Ba}	48.33 ± 4.33 ^{Ba}
	3rd Day	12.43 ± 1.39 ^{Ca}	36.67 ± 3.18 ^{Ab}	28.00 ± 2.08 ^{Bb}	22.67 ± 2.60 ^{Bb}
	7th Day	11.07 ± 0.64 ^{Ca}	26.83 ± 1.42 ^{Ac}	11.73 ± 1.75 ^{Bc}	16.70 ± 2.15 ^{B,Cb}
creatinine(mg/dL)	1st Day	0.53 ± 0.07 ^{Ba}	0.94 ± 0.04 ^{Aa}	0.57 ± 0.03 ^{Ba}	0.57 ± 0.03 ^{Ba}
	3rd Day	0.47 ± 0.03 ^{Ba}	0.78 ± 0.04 ^{Ab}	0.50 ± 0.06 ^{Ba}	0.40 ± 0.06 ^{Ba}
	7th Day	0.47 ± 0.09 ^{Ba}	0.83 ± 0.03 ^{Aa,b}	0.47 ± 0.03 ^{Ba}	0.30 ± 0.12 ^{Ba}

Data are presented as (Mean ± S.E). S.E = Standard error.Mean values in the same column with different superscript Capital letters are significantly different at ($P<0.05$) between different groups at the same time. While, mean values in the same raw with different superscript Small letters are significantly different at ($P<0.05$) in different times within the same group.

Table 5 Antioxidant and oxidative marker in CCl4, garlic and heparenol treated groups at 1st, 3rd and 7th day of experimental induction of hepatopathy.

Parameter	Duration of Experiment	Experimental Groups			
		Control Group (N=15)	CCl_4 Group (N=5)	Garlic Group (N=5)	Heparenol Group (N=5)
GPx (U/mL)	1st Day	98.00 ± 4.73 ^{Aa}	13.25 ± 1.52 ^{Cc}	27.62 ± 2.83 ^{Bc}	32.02 ± 2.73 ^{Bb}
	3rd Day	98.67 ± 6.39 ^{Aa}	26.01 ± 2.99 ^{Cb}	41.96 ± 4.15 ^{Bb}	39.03 ± 2.52 ^{B,Cb}
	7th Day	99.33 ± 7.22 ^{Aa}	38.33 ± 3.18 ^{Ca}	56.11 ± 2.47 ^{Ba}	57.67 ± 1.45 ^{Ba}
SOD (U/mL)	1st Day	25.37 ± 2.06 ^{Ba}	4.85 ± 0.28 ^{Ac}	8.51 ± 0.62 ^{Ba}	9.90 ± 0.30 ^{Bb}
	3rd Day	27.61 ± 3.08 ^{Ba}	6.45 ± 0.42 ^{Ab}	9.62 ± 0.68 ^{Ba}	11.13 ± 0.32 ^{Ba,b}
	7th Day	29.33 ± 4.24 ^{Ba}	8.27 ± 0.50 ^{Aa}	9.99 ± 0.02 ^{Ba}	11.96 ± 0.54 ^{Ba}
MDA (nmol/mL)	1st Day	23.47 ± 2.36 ^{Ca}	167.88 ± 6.54 ^{Aa}	117.67 ± 8.82 ^{Ba}	99.33 ± 12.14 ^{Ba}
	3rd Day	20.37 ± 0.33 ^{Ca}	97.00 ± 8.33 ^{Ab}	55.67 ± 3.18 ^{Bb}	52.11 ± 1.63 ^{Bb}
	7th Day	25.22 ± 3.79 ^{Ca}	61.60 ± 5.17 ^{Ac}	45.18 ± 3.95 ^{Bb}	41.51 ± 0.88 ^{Bb}

Data are presented as (Mean ± S.E). S.E = Standard error.Mean values in the same column with different superscript Capital letters are significantly different at ($P<0.05$) between different groups at the same time. While, mean values in the same raw with different superscript Small letters are significantly different at ($P<0.05$) in different times within the same group.

4. DISCUSSION

Liver diseases are remaining a worldwide problem that represents one of a major threat to public health (Asha and Pushpangadan, 1998). Goats with experimentally induced hepatopathy showed clinical signs that related to hepatotoxic effect of CCl4 that induce fatty liver injury in goats. These findings are matched with the result of Vajdovich et al. (1995); Weber et al. (2003); Sen et al. (2005) and constable et al. (2016). CCl4 intoxication was due to induction of oxidative stress through production of reactive oxygen species (ROS) and reduction in glutathione level (Nwidu *et al*., 2017). A large production of ROS could increase the lipid peroxidation of cellular membranes and the oxidation of protein and DNA causing hepatocyte damage (Chien *et al*., 2003).These clinical signs alterations

were similar to signs of ketosis in goats that include inactivity, dullness, lethargy and nervous manifestations, grinding on teeth, pawing in ground as mention by Hefnawy et al. (2010). Rapid fetal developments at the late stage of pregnancy lead to rapid movement of the fat stores to assure sufficient energy. The liver also increases gluconeogenesis to facilitate glucose ease of use to the fetus. However, in the negative energy balance, this increased mobilization may overpower the ability of the liver resulting in hepatic lipidosis (Hefnawy et al., 2010). Moreover, Nervous manifestation include grinding on teeth and pawing in the ground that appear on goats with experimental induced hepatopathy may be attributed to increase fatty degeneration and centrilobular necrosis of the liver (Recknagel et al., 1989) which results in fat deposition in liver which followed by reduction of hepatocellular function , glucose deficiency with intermittent hypoglycemia(Bouhrim et al., 2018) that results in decrease of glucose utilization by the brain leading to development of cerebral hypoglycemic encephalopathy and perhaps due to increase cortisol level in the blood (Radostits et al., 2007).

Goats in garlic extract treated groups returned to normal physical status in the 3rd day after induction. This result could be due to the anti-oxidative effect of garlic oil extract that contain organosulfur compounds (such as diallyle disulfide and diallyle sulfide), which have antioxidant and detoxifying properties as it protect liver cell from hepatic degeneration as garlic oil compound scavenging free radical (chung, 2006); Mirzaei-Aghsaghali et al., 2012 and Munday and Munday, 2004). Artichoke extract treated group began to retain normal appetite, body temperature, respiration and heart rate in the 3rd day after induction as heparenol contain artichoke and betaine which have hepatoprotective effect (Tsai *et al.*, 2015 and Gebhardt, 2002). Artichoke had a marked antioxidative potential that protects hepatocytes from an oxidative stress (Miccadeia *etal.*, 2008).

CCl4 treated group only without any hepatoprotective agent showed significant decrease in hematological parameter while there was significant increase in WBCS count, neutrophils and monocytes with lymphocytopenia. This result was similar to that obtained by Mandal et al. (1998); Saba et al. (2010) Essawy et al. (2010) and Abdalla et al. (2013).This reduction in RBCs count and Hb content may be due to the effect ofCCl4 that disturbed hematopoiesis, erythrocytes destruction and decrease in the rate of their production or increase elimination from circulation (Tung *et al.*,1975). Additionally, CCl4administration produce macrocytic hypochromic anemia as CCl4 induce significant increase lipid peroxidation, destruction of membrane proteins, alterations of membrane-bound enzymes as well as erythrocyte osmotic fragility (Makni *et al.*, 2012). The free radicals resulting from CCl4 metabolism caused liver injury and a proportion of these free radicals liberated from the liver into the blood that lead to destruction of red blood cells (Sherlock and Dooley, 1993). In contrast, the significant increase in WBCs count could attribute to acute stress in animals that associated with increased leukocytic count occasioned by significant increase in the neutrophil count and the neutrophil/lymphocyte ratio (Huff *et al.*, 2005). Leukocytosis observed in animals under the influence of the stress hormone cortisol and catecholamine might not have been a result of increase production in WBC, but by the release of marginated neutrophils and other neutrophil pool into the circulation which produced the observed neutrophilia (Swenson, 1993). Significant increase in monocyte might be due to acute CCl4 induced liver injury lead to activation of hepatic non-parenchymal cells (including Kupffer cells and stellate cells). Kupffer cells in rapid response to tissue injury (macrophages in liver) produce TNF-α which indicated by Davis et al. (2010)

Significant increase in RBCs count and Hb concentration observed in garlic treated group compared to CCl4 group may be attributed to that garlic extract is an active oxygen scavenger and therefore it is possible that garlic ingredients challenge with Hb in the RBC for oxygen, resulting in hypoxia which then stimulates Hb synthesis and RBC production. In addition, garlic metabolism end-products in the body directly stimulate the kidney to produce and increase secretion of erythropoietin(Toghyani et al., 2011). Although non-significant changes in WBCs and lymphocyte and significant increase in neutrophils was observed at 3rd and 7th day this disagreed with Shokrollahi et al. (2016) that reported supplementation with garlic enhance WBC and lymphocyte concentrations but reduced that of neutrophils.

Artichoke extract treated group showed significant decrease in RBCs count , Hb, PCV, lymphocyte in contrast showed increase in neutrophils but total leukocytic count showed non-significant changes with control although significant increase than CCl4 treated group this attributed to treatment with artichoke which had a marked antioxidative potential that protects cells from an oxidative stress (Miccadeia *et al.*, 2008).

In this study there was significant increase in hepatic enzymes (ALT ,AST ,GGT ,ALP) in group A as enzymatic activation of CCl4 by CYP2E1, into trichloromethyl free radicals (CCl3) inside the endoplasmic reticulum membrane followed by progressive destruction of the unsaturated fatty acid ,chloromethylation and peroxidation of phospholipids of the endoplasmic reticulum membrane that responsible for functional and structural disruption of hepatocytes and resulted destruction of liver (Kotsanis and Metcalfe, 1991)and increase permeability of hepatocyte membranes was which lead to release enzymes into serum. These enzymes AST, ALT, ALP and their activities were considered as classical indicators of hepatocytes and liver injury (Recknagel et al., 1989). Significant increase in GGT level in experimental induction of hepatic degeneration support the occurrence of hepatic damage as serum concentration of GGT was considered as indicator for liver cell damage & bile duct malfunctions this result coincided with Ghanem and El-Deep(2010).

Administration of garlic extract to goats might stimulate the liver enzymes to return toward control level at end of experiment as the garlic extract can be considered as a potent drug for the treatment of liver disorders as discussed by Al-Tamimi*et al.* (2015). Garlic oil reduce damage of hepatocyte direct stimulation antioxidant defense system and inhibit lipid peroxidation by scavenge ROS and protect the integrity of the cell membrane in the liver (El-Khayat et al., 2013).artichoke extract reduced in the liver markers due to antioxidant effect of betaine as described by Zhang et al. (2016) as betaine protected hepatocytes mitochondria in both chronic and acute models of hepatotoxicity this protection alleviate oxidative stress in the liver as reported by Heidaria *et al.* (2018). In addition Fallah et al. (2011) who record significant reduction in the activities of ALT, AST, and ALP in pretreated rats with artichoke lead to

reduction of oxidative stress by decrease lipid peroxidation and increasing of the cellular antioxidant enzymes activity.

Increased bilirubin and total bilirubin in serum or tissue due to obstruction in the excretion of bile in case of hepatocellular damage(Naji *et al.*, 2017). In this study slight elevations of total and indirect bilirubin concentrations were noticed in the serum of CCl4 treated group that coincided with Sen *et al*. (2005) suggesting high serum direct bilirubin sensitive indicator of hepatic damage as partial and limited uptake of pigments due to hepatic damage reported by Saba et al. (2010). While no significant changes was observed in garlic treated group as garlic oil reduce hepatocellular damage (Abdel-Naim et al., 2002; Naji et al., 2017). In addition, artichoke extract treated group significant decrease than CCl4 this attributed to hepatoprotective and antioxidant effect of heparenol constitute as thy protect damage of hepatocyte(Abdalla, et al., 2011).

Serum albumin levels were significantly reduced in CCl4 induced hepatic lipidosis was possibly related to the apparent destruction of albumin protein into smaller subunits (Folmar et al., 1993). Decrease hepatic capacity to synthesize protein might due to CCl4 reduce number of hepatocytes noted by Patrick-Iwuanyanwu *et al.* (2007). Garlic treated group serum total protein and albumin level return toward control level this attributed to antioxidant effect of garlic (Mirunalini *et al*., 2010).While, artichoke extract treated group showed decrease in total plasma protein and albumin return toward control level, this attributed to antioxidant effect of artichoke that significantly reduce effect of CCl4 onserum protein and albumin that coincided with Abd El-Aleem *et al.* (2009) and Abdalla *et al*. (2011).

Hyperlipidemia in CCl4 treated group in this experiment could be due to inhibiting hepatic lipoprotein lipase activity that leads to increase synthesis or decrease removal of lipoproteins (Zhang *et al.*, 2012) that matched with Abdel-Naim et al. (2002). Moreover, CCl4 treatment lead to alternation the activity of lipid metabolism enzymes in the liver resulted in limit the biosynthesis of bile acids, which is the only significant route for elimination of cholesterol from the body(Sun *et al.*, 2012; Zhang *et al.*, 2012). Thus, the balance between cholesterol biosynthesis and cholesterol catabolism by the liver is a critical determinant of serum cholesterol concentration (Ma *et al*., 2014). In this study garlic treated group showed no significant change with control group thus, garlic has a potential to inhibit hepatic fatty acid synthesis thus lead to reduction of lipid accumulation in the liver and triglycerides level in the plasma(Gofman *et al.*, 1966). Moreover, artichoke extract treated group showed non-significant changes in cholesterol and triglycerides level this could attributed to hepatoprotective effect of heparenol constituents (Tsai et al., 2015) reported that betaine provides hepatoprotective effects against several hepatotoxicants such as CCl4.

The liver is a key to glucose homeostasis. Liver disorders as structural integrity, or intracellular dynamics resulted disruption in glucose metabolism and may alter the liver's ability to maintain normal glucose homeostasis. When such disruption affects hepatic glucose output, hypoglycemia may resulted (Arky 1989).In CCl4 treated group significant decrease in glucose level was noticed thus agreed with Bouhrim et al., (2018) but disagree by Khan *et al., (*2015) who reported that glucose level increase in animal which treated with CCl4 as a result of decreasing the pancreatic secretion of insulin from β-cells of islets of Langerhans because of fatty changes in the cells of islet resulting from the toxicity of CCl4.

Garlic treated group showed no significant changes in serum glucose level with control group this attributed to hepatoprotective and antioxidant effect of garlic as reported by Borek, (2001) and Pirmohammadi et al., (2014) who recorded that garlic supplementation in pre-partum goats significantly improved serum glucose, which showed that may improve the efficiency of feed utilization. artichoke extract treated group showed no significant changes in glucose level compared to control group which could be attributed to potent hepatostimulating properties of artichoke and hepatoprotective against hepatic cell damage (Gebhardt, 2002).

The significant increase in blood urea nitrogen and creatinine level in CCl4 treated group could be attributed renal damage. Kidney originated cytochrome P450 enzymes activated CCl4 to form reactive toxic metabolites which can lead to the kidney damage in vivo which is associated with membrane lipid peroxidation and cell necrosis (Hismiogullari et al., 2015).

Garlic extract group showed non-significant changes with control group may due to antioxidant effect of garlic which protected cell from oxidation by scavining of free radicals (El-Khayat, et al. 2010). Moreover, pretreatment by betaine prevent glomerular and tubular alterations in the renal cortex that resulted after exposure to CCl4 in artichoke extract treated group that resulted no significant change with control reported by Ozturk et al., (2003)

Our study exhibit significant increase serum MDA inCCl4 treated group that revealing of increased oxidative damage and hepatocellular peroxidation in liverthat coincided with Vajdovich *et al.,* (1995). Biological systems have antioxidant mechanisms to control damage of cell has enzymatic and non-enzymatic natures that allow ROS to be inactivated. The endogenous antioxidants are enzymes, such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (Santos-Sánchez et al., 2019). Goats treated with garlic extract showed significant increase in SOD level, GPX than CCl4 treated group and decrease in MDA level this attributed to antioxidant effect of garlic this agreed with Abdel-Naim et al, (2002) that demonstrated the protective antioxidant properties of Garlic oil as contains certain compounds such as organosulpher compound, germanium and selenium (El-Khayat et al., 2010). These ingredients have been shown to possess antioxidant activity and to protect against experimentally induced liver damage (Wu et al., 2001).In addition, artichoke extract increase level of SOD, GPX and decrease MDA level suggested that artichoke have a role in hepatic cellular protection against oxidative stress-induced damage by free radicals as reported by Abd El-Aleem et al. (2009) and Abdallaet al. (2011).

5. CONCULSION

Based on the results of the present study we concluded that CCl4 could produce acute hepathopathy in goats with characteristic clinical signs and hematobiochemical alterations. Garlic oil extract and artichoke extract could be used as supplementation to protect goat from hepatic damage and lipidosis.

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