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Effect of Some Medicinal Plant Seeds on CCl4 -Induced Hepatotoxicity in Experimental Rats

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Abstract

There are many plants which are used as medicinal plants by many people such as purslane, chia and garden cress .The present study was carried out to investigate the effect of purslane, chia and garden cress seed powders on CCl_4-induced hepatotoxicity in experimental rats. Rats were randomly assigned to 2 main groups including normal or negative control group (6 rats) which fed on basal diet only for 6 weeks, and injected group (36 rats) which injected subcutaneously with Ccl_4 in paraffin oil(50% v/v, 2ml/kg body weight) twice a week for two weeks to induce chronic damage in liver. After induction, rats were divided into 5 equal groups including positive control group which fed on basal diet only besides 4 herbs -treated groups which fed on basal diet supplemented with 5% of either dry purslane, chia,garden cress seed powders or their mixture,respectively.The curative periodcontinued for 4 weeks. By its end, body weight gain and relative weights of some internal organs were calculated. In addition, serum and liver tissue homogenates were biochemically analyzed. The obtained results revealed that Ccl_4 exposure led to liver and kidney dysfunction and induced hyper lipidemia due to its oxidative effect. As a result of their antioxidant and phenolic compound contents, using purslane, chia and garden cress seed powders singly or as a mixture improved liver and kidney functions and induced hypolipidemic effect.So, patients who suffer from hepatotoxicity as result of CCl_4 exposure can use these plant seeds to test their possible efficiency for their condition.

Key words: Hepatotoxicity, CCl_4, purslane seeds, chia seeds, garden cressseeds, phenolic compounds, rats

Introduction

Liver is the largest organ of the human body weighing approximately 1500 g, and is located in the upper right corner of the abdomen on top of the stomach, right kidney and intestines and beneath the diaphragm. The liver performs more than 500 vital metabolic functions ***(Naruseet al.,2007).*** including the synthesis of glycogen, plasma proteins, clotting factors bile, urea, etc. ***(Saukkonenetal., 2006).***

The liver disorders are one of the serious health problems,throughout the world. More than 350 million people were affected with chronic hepatic infections worldwide ***(Salhab and Canelo, 2011).***Hepatotoxicity refers to liver dysfunction or liver damage that is associated with an overload of drugs or xenobiotics ***(Navarro and Senior2006).***

Carbon tetrachloride (Ccl_4) is widely used for experimental induction of liver injury. The injury produced depends on Ccl_4 metabolism to a highly reactive of free radicals which initiate lipid peroxidation.

Antioxidant agents of natural origin have attracted special interest because they can protect from free radical. Numerous medicinal plants and their formulation are used for liver disorders in ethnomedical practices as well as intraditional medicine***.(Parolaet al.,1992)***

Portulaca oleracea L. (POL), commonly known as purslane, is listed in the World Health Organization as one of the most used medicinal plants and it has been given the term 'Global Panacea' ***(Isinet al., 2007).*** POL, as “vegetable for long life” in Chinese folklore, has a cosmopolitan distribution and widely used in many countries ***(Jinet al., 2013).*** Modern studies have shown that POL was a rich source of linolenic acid (LNA) and α-tocopherol (α-TCP) ***(Teixeira et al., 2010).*** POL exhibited a wide range of pharmacological effects such as anti-inflammatory **(Chan *et al*., 2000)**, antibacterial ***(Zhang et al., 2002)***, skeletal muscle relaxant ***(Parry et al., 1993),*** stomach and mouth ulcers ***(Karimi et al., 2004)***,diabetic complications ***(Lee et al., 2012)*** and liver injuries ***(Liu et al., 2015).***

Chia (*Salvia hispanica*L.) is an annual herbaceous plant which is native to southern Mexico and northern Guatemala ***(Ayerza and Coates, 2011; Capitaniet al., 2012).*** In recent years, chia seeds have been included in the human diet due to the health benefits associated with their composition ***Ixtainaet al., (2011).***According to ***Marineliet al. (2014),*** chia has been investigated and recommended for use due to its high nutritional value. It also contains a high number of antioxidants. Moreover, heavy metal analysis showed that chia seed contains them at safe levels, not exceeding the maximum metal levels for food safety, and the seed is also free from mycotoxins ***(Tetens, 2009).*** However, high percentage of fatty acids which are beneficial to health (mainly ω-3 PUFAs, especially α-linolenic acid) is the major cause behind the deep recommendations for use of chia seeds in supplementing commercial human diets ***(Cooreyet al. 2012).***

Lepidium sativum L. (*Brassicaceae*), a medicinal plant origin in Egypt and Middle East, is now cultivated in whole world and often referred to as garden cress. *Lepidium sativum* L. is used as remedy for inflammatory diseases, such as diabetes, arthritis, traumatic injuries, and hepatitis in traditional medicine ***(Bigoniya and Shukla, 2014).***The extract of*Lepidium sativum* L. is reported to have various in vitro biological effects including antioxidant, anti-inflammatory, antidiarrheal, antimicrobial, antispasmodic and hepatoprotective action against oxidative damage and have a great potential for use as herbal hepatoprotective or dietary supplements ***(Del Valle Mendozaet al., 2014; Al-Sheddiet al., 2016).***The present investigation was carried out to evaluate the effect of purslane, chia and garden cress seeds powder on hepatotoxicity induced by carbon tetra chloride($CCL_{4)}$ in experimental rats.

Materials and Methods

Materials*:*

Dry seeds of purslane (*Portulaca oleracea L.*), chia (*Salvia hispanica L.*) and garden cress (*Lepidium sativum L.)* were purchased from Arab company for Pharmaceutical and Medicinal plants, MEPACO, Egypt. A total of 42 adult male albino rats (*Sprague_ Dawley strain*) were obtained from the animal colony, Helwan farm, Vaccine and Immunity Organization, Ministry of Health, Cairo Governorate, Egypt All required chemicals were obtained from Elgomhouria Company for Trading Drugs, Chemicals and Medical Appliances, Cairo, Egypt.

Casein, Vitamins mixture and salt mixture: Were purchased from El-Gomhoria Company, Cairo, Egypt.

Methods:

Chemical analysis of seeds

Phenolic compounds in seed powders were identified and determined by HPLC according to ***Goupy et al., (1999).***

Experimental animal

Forty-two mature white Albino rats of an average body weight 150±10 g of *Sprague Dawley* Strain wasused... Rats were fed on basal ration supplying the essential vitamins and trace elements and water supply was given ad-libitum

Preparation of Experimental diet

Basal diet was prepared from fine ingredient per 100 g as follows:It had the following composition: Casein (≥ 80% protein) 14%, soybean oil 4%,cellulose 5%, mineral mixture 3.5%, vitamin mixture 1%, cholinechloride 0.25%, DL-methionine 0.3% and corn starch up to 100g **(*Reeves et al., 1993)***

Experimental design

Rats were divided into **2** main groups as follows:

The first main group (6 rats): normal rats were fed on basal diet only as a negative control group for six weeks.**The second main group (36rats):** normal rats were injected subcutaneously with CCl_4 in paraffin oil(50% v/v, 2 ml/kg body weight)twice a week for two weeks to induce chronic damage in the liver ***(Jayasekharet al., 1997).***Six rats were Slaughtered after injection (at the end of two weeks) to ensure of liver injury. AST and ALT were determined to ensure the induction, then the injected remaining rats divided into 5 equal groups as follows:**The second injected group(**6 rats):were fed on basal diet only for 4 weeks as a positive control group.**The third injected group(**6 rats):were fed on basal diet supplemented with 5% dry purslane seeds for 4 weeks.**The fourth injected group (**6 rats):were fed on basal diet supplemented with 5% dry chia seeds for 4 weeks.**The fifth injected group (**6 rats):were fed on basal diet supplemented with 5% dry garden cress seeds for 4 weeks.**The sixth injected group (**6 rats):were fed on basal diet supplemented with the three dry seeds as a mixture (5%)for 4 weeks which were taken (5%) from each seeds and the mixture taken (5%) Body weight and feed intake were checked once a week. At the end, animals were weighed, fasted overnight, and then sacrificed under very light ether anaesthesia.

Biological evaluation

At the end of the experiment, feed intake, body weight gain, relative organs weight and feed efficiency ratio were calculated according to ***Chapman et al., (1959)***

Biochemical analysis of serum:

After sacrifice of rats, Blood samples were collected from hepatic portal vein of each rat into dry clean centrifuge tubes. Serum was carefully separated by centrifugation of blood samples at 3500 round per minute (rpm)for 15 minutes at room temperature, transferred into dry clean ebendorf tubes, then kept frozen at - 20˚C for later determinations.

Serum AST and ALT were determined in the serum according to the method described by ***Reitman and Frankel (1957).*** Serum albumin was determined according to ***Drupt (1974).***Serum globulin was calculated according to the equation described by ***Chary and Sharma (2004).*** Malondialdehyde (MDA) was carried according to ***Sushmakumariet al., (1989)*** Lipid peroxidation was estimated according to the method of ***(Ohkawaet al., 1979).*** Nitric oxide was followed as the method reported by ***Green et al.,(1982).***Uric acid was determined in the serum according to the method described by ***Fossati et al., (1980).***Urea nitrogen was determined in the serum according to the method described by ***Patton et al.,(1977).***Creatinine forms colored complex when react with alkaline Picrate. This reaction described by ***Faulkner and King (1976).***

Total cholesterol was determined in the serum according to the method described by ***Allain et al., (1974).*** Triglycerides were determined in the serum according to the method described by ***Trinder and Ann (1969).*** HDL-C was determined in the serum according to the method described by ***Lopes-Virella et al., (1977).*** Serum VLDL-C was calculated by the following equation: VLDL-C= Triglyceride/5 according to ***Friedwaldet al., (1972).***Serum LDL-C was calculated by the following equation: LDL-C = Total cholesterol – (HDL-C + VLDL-C) according to ***Friedwaldet al., (1972).***

***Organ sampling*:**

Livers and kidneys were removed from rats by careful dissection, washed in saline solution (0.9%), dried using filter paper and independently weighed. A specimen from each organ was kept at (-80 0 C) for preparation of tissue homogenate for determination of antioxidant parameters. The homogenation was centrifuged at 1000 r.p.m for 10 minutes.

Statistical analysis:

Statistical analysis were carried out using one-way analysis of variance(ANOVA) test followed by Duncan test through the program of statistical packages for the social science (SPSS). Results were expressed as mean**±** SD. The differences among means at $p < 0.05$ were considered significant ***(Snedecor and Cochran, 1989)***

Results

Phenolic compounds of seeds (µg/100g) by HPLC analysis

Purslane, chia,and garden cress seeds analyzed for their phenolic Compounds. The obtained results showed in table (1): purslane seeds recorded higher content of Protocatechuic, and catechol than garden cress and chia seeds. Purslane seeds recorded lower content of Gallic, 4-Amino benzoic, Caffeine, P-OH benzoic, Caffeic, Ellagic, P-Coumaric,3,4,4-Methoxy-cinnnamic and Coumarin than garden cress and chia seeds.

While Chia seeds recorded higher content of Caffeic,Vanillic,Ferulic, Salicylic, 3,4,5-methoxy-cinnamic, Coumarin, and Cinnamic than purslane and garden cress seeds. and recorded lower content of Chlorogenic than purslane and garden cress seeds.
Garden cress recorded higher content of Gallic, Pyrogallol, 4-Aminobenzoic, Catechin, Chlorogenic, Caffeine, P-Coumaric,Ellagic, Benzoic than purslane and chia seeds. and recorded lower content of Protocatechuic,Catechol, Salicylic and Cinnamic than purslane and chia seed.

Table (1)

Phenolic compounds of chia, purslane and garden cress seeds (µg /100g)

Phenolic compounds	Test Methods	Phenolic compounds (µg/100g)		
		Chia Seeds	Purslane seeds	Garden Cress Seeds
Gallic acid	Journal Sci. & food Agric. (1999) 79:1625-1634	34.20	15.54	56.94
Pyrogallol		476.88	332.11	732.43
4-Aminobenzoic		10.71	5.42	11.40
Protocatchuic		64.45	69.36	38.22
Catechein		104.34	124.28	312.05
Chlorogenic		29.52	33.37	76.37
Catechol		36.36	66.43	33.04
Caffeine		49.62	38.82	81.19
p-OH-benzoic		55.88	19.95	55.44
Caffeic		12.11	4.37	7.22
Vanillin		42.52	24.72	24.12
p-coumaric		9.23	6.02	20.94
Ferulic		15.11	10.74	11.08
Iso- ferulic		60.0	-	22.71
Ellagic		117.56	106.36	122.06
Alpha-coumaric		1.35	0.97	1.33
Benzoic		94.77	70.23	211.88
salycillic		128.14	85.47	77.69
3,4,5-methoxy-cinnamic		46.25	5.28	28.66
Coumarin		24.20	13.81	15.60
cinnamic		18.85	3.61	4.94

Biological evaluation:

Nutrition evaluation:

Data presented in Table (2) showed the effect of feeding Purslane,Chia, Garden Cress, and their Mixture on feed intake, body weight gain and feed efficiency ratio in CCl_4-intoxicated rats.It could be noticed that the(+ve) control group recorded a significant decrease in feed intake ,body weight gain and feed efficiency ratio compared with the (-ve)control group ($p<0.05$) . All seed- treated group recorded a significant increase compared with (+ve) control group , but they couldn't return three parameters toward its normal value recorded by (-ve)control group . Feeding mixed seeds improved the three parameters to value near the (-ve) control group .

Table (2)

Effect of feeding Purslane,Chia, Garden Cress seeds, and Seeds mixture on feed intake, body weight gain and feed efficiency ratio in rats

Groups \ Parameters		FI (g/28 day) rat	BWG %	FER %
(-ve) control		505±11.80^{a}	36.40±2.30^{a}	.0981±.004^{a}
Ccl_4 injected groups	(+ve) control	351.60±8.03^{c}	16±1.30^{d}	.070±.006^{c}
	Purslane Seeds (5%)	487.40±5.30^{b}	25.30±1.90^{c}	.081±.007^{b}
	Chia Seeds (5%)	487±5.20^{b}	26.40±1.70^{c}	.078 ± 015^{cb}
	Garden Cress Seeds (5%)	484.50±7.10^{b}	24.90±2.05^{c}	.081±.006^{b}
	Seed mixture	507.90±8.80^{a}	30.30±1.70^{b}	.094±.004^{a}

Values are expressed as mean ± S.D.

Significance differenceis expressed at $p<0.05$ using one-way ANOVA test and LSD test.

Values which have different letters in each column differ significantly, while thedifference among those with similar letters completely or partially not significant

Relative organs weight

Data presented in Table (3) showed the effect of feeding Purslane, Chia, Garden Cress, and Seeds Mixture on relative organs weight (liver and kidney) for hepatotoxicity rats.Relative liver and kidney weight values showed significant increase in control (+ve) group as compared with negative control group (P < 0.05). Supplemented diets with Purslane, Chia and Garden cress (5%) showed significant decrease (P<0.05) when compared with control positive. The best result was found in rats fed on seeds mixture (5%) that showed significant decrease as compared to the control positive rats.

Table (3)

Effect of feeding Purslane,Chia, Garden Cress seeds and Seeds Mixture on relative organs weight (liver and kidney)in rats.

Groups \ Parameters		Liver %	Kidney%
(-Ve) control		6.90±.24^{d}	1.30±.21^{b}
Ccl_4 injected groups	(+Ve) control	13.30±1.06^{a}	1.90±.14^{a}
	Purslane Seeds	8.10±.18^{b}	1.40±.23^{b}
	Chia Seeds	7.80±.75^{bc}	1.20±.23^{b}
	Garden Cress seeds	7.40±.39^{bcd}	1.50±.20^{b}
	Seed mixture	7.08±.52^{cd}	1.30±.22^{b}

Values are expressed as mean ± S.D.

Significancedifference is expressed at p<0.05 using one-way ANOVA test and LSD test.

Values which have different letters in each column differ significantly, while thedifference among those with similar letters completely or partially not significant.

Biochemical Evaluations:

Liver functions:

Data presented in Table (4) showed the effect of feeding Purslane, Chia , Garden cress and their Mixture on serum Aspartate amino transferase (AST) ,Alanine amino transferase (ALT) , Alkaline phosphatase(ALP) , and Total bilirubin (Bil) in CCl_4-intoxicated rats.The mean values of AST, ALT, ALP and Bilin the (+ve) control group showed significant increase as compared to the (-ve) group. The rats received purslane, chia and garden cress seeds as a powder (5%) showed significant decrease(P<0.05) of all liver enzyme comparedto the(+ve) controlgroup (table 4). The best result was found in rats received mixture seeds (5%).

Table (4)

Effect of feeding Purslane, Chia, Garden cress and Seeds Mixture on serum(aspartate amino transferase and alanine amino transferase, Alkaline phosphatase, and Total bilirubin) in rats

Groups \ Parameters		AST (IU/L)	ALT (IU/L)	ALP (IU/L)	BIL (IU/L)
(-ve) Control		55.8±6.8^{c}	23.8±4.2^{d}	82.5±14.9^{d}	.39±.12^{c}
Ccl_4 injected groups	(+ve) Control	206.5±32.8^{a}	58±6.2^{a}	206.1±1.6.1^{a}	.87±.09^{a}
	Purslane Seeds	80.5±7.7^{b}	35.5±4.5^{bc}	125.6±5.31^{b}	.57±.05^{b}
	Chia Seeds	83.1±7.1^{b}	38±5.3^{b}	106.8±8.8^{c}	.62±.06^{b}
	Garden cress Seeds	84.3±8.1^{b}	37.1±5.6^{bc}	100.5±10.07^{c}	.59±.06^{b}
	Seed Mixture	66.3±7.4^{bc}	31.1±4.6^{c}	82.6±6.8^{d}	.42±.11^{c}

Values are expressed as mean ± S.D.

Significance difference is expressed at p<0.05 using one-way ANOVA test and LSD test.

Values which have different letters in each column differ significantly, while the difference among those with similar letters completely or partially not significant.

Serum Albumin, Globulin and Total protein

Data presented in Table (5) showed the effect of feeding Purslane, Chia, Garden cress and their Mixture on serumTotal protein, albumin and Globulin and in CCl_4-intoxicated rats. The mean values of total protein, albumin and globulin in the (+ve) control group showed significant decrease compared to the (-ve) control group. The rats that received purslane, chia and garden cress seeds as a powder (5%) showed significant increase ($P<0.05$) of total protein,albumin and globulin as compared tothe (+ve) control group as shown in table (5). The best result was found in rats that received seeds mixture (5%).

Table (5)

Effect of feeding Purslane, Chia, Garden cress seeds and Seed Mixture on serum (Total protein, Albumin and Globulin) in rats .

Groups \ Parameters		Total protein (g/dl)	Albumin (g/dl)	Globulin (g/dl)
(-ve) Control		$7.3 \pm .40^{a}$	$4.2 \pm .47^{a}$	$3.1 \pm .54^{a}$
Ccl_4 injected groups	(+ve) control	$3.0 \pm .47^{c}$	$1.3 \pm .25^{d}$	$1.7 \pm .43^{c}$
	Purslane Seeds	$4.2 \pm .47^{b}$	$2.1 \pm .27^{c}$	$2.1 \pm .47^{b}$
	Chia Seeds	$5.7 \pm .30^{b}$	$3.5 \pm .14^{b}$	$2.2 \pm .63^{b}$
	Garden cress	$5.8 \pm .31^{b}$	$3.3 \pm .35^{bc}$	$2.5 \pm .91^{b}$
	Seed Mixture	$6.2 \pm .17^{a}$	$3.1 \pm .24^{c}$	$3.1 \pm .47^{a}$

Values are expressed as mean ± S.D.

Significancedifference is expressed at $p<0.05$ using one-way ANOVA test and LSD test.

Values which have different letters in each column differ significantly, while thedifference among those with similar letters completely or partially not significant.

Serum lipid profile:

Data presented in Table (6) showed the effect of feedingPurslane , Chia , Garden cress seeds and Seeds Mixture on serum Cholesterol , Triglyceride ,high-density lipoprotein, low-density lipoprotein,Very low-density lipoprotein in CCl_4-intoxicated rats.The mean values of cholesterol and triglyceride were significantly increased in the (+ve) control rats compared with the (-ve) control group . All supplemented diets with purslane, chia and garden cress seeds powder(5%)showed significant decrease ($P<0.05$) comparing with the(+ve) control rats. The best result was obtained in rats fed on seeds mixture (5%) .

The mean values of HDL were low in the (+ve) control group compared with the (-ve) control rats. All supplemented diets with purslane, chia and garden cress seeds powder(5%)showed significant increase ($P<0.05$) compared with the (+ve)control rats. The best result was obtained in rats fed on seeds mixture (5%). the mean values of LDL were significantly increased in the(+ve) control rats compared with the (-ve) control group . All supplemented diets with purslane, chia and garden cress seeds powder(5%) lowered the level of LDL ($P<0.05$) compared with the (+ve) control rats. The best result was found in rats fed on seeds mixture (5%) .The mean value of VLDL in the (+ve) control was significantly higher than the (-ve) control group. The rats that received diets supplemented with purslane, chia and garden cress seeds powder (5%)showed significant decrease ($P<0.05$) compared with the (+ve) control rats. The best result was obtained in rats fed on seeds mixture (5%).

Table (6)

Effect of feeding Purslane, Chia, Garden cress seeds and Seeds mixture on serum (Cholesterol , Triglyceride ,high-density lipoprotein , low-density lipoprotein and Very low-density lipoprotein) in rats .

Groups \ Parameters		Chol. (mg/dl)	T.G (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
(-ve) Control		88.1±7.7[c]	132±9.1[c]	49.1±4.7[a]	12.6±6.9[c]	26.5±1.8[c]
Ccl_4 injected groups	(+ve) control	238±12.8[a]	238±12.8[a]	33.1±2.6[c]	157.3±11.2[a]	47.6±2.5[a]
	Purslane Seeds	118.9±13.3[b]	174.3±4.5[b]	45.0±4.7[b]	39.1±14.7[b]	34.8±.98[b]
	Chia Seeds	123.7±12.1[b]	179.5±4.6[b]	47.0±4.8[ab]	40.8±15.3[b]	36.0±.89[b]
	Garden cress seeds	131.3±6.5[b]	171.1±6.04[b]	48.6±2.9[ab]	48.5±5.1[b]	34.1±1.3[b]
	Seed Mixture	98.5±5.4[c]	137.8±6.5[c]	52.0±4.8[a]	19.0±6.1[c]	27.5±1.3[c]

Values are expressed as mean ± S.D.

Significancedifference is expressed at p<0.05 using one-way ANOVA test and LSD test.

Values which have different letters in each column differ significantly, while thedifference among those with similar letters completely or partially not significant.

Kidney functions :

Data presented in Table (7) showed the effect of feeding Purslane , Chia , Garden cress seeds and their Mixture on kidney functions in the intoxicated rats .The mean values of urea, creatinine and uric acid the(+ve) control group revealed significant increase compared with the (-ve) control group. On supplementing diets withPurslane , Chia and Garden cress seeds induced (5%) significant decrease(P<0.05) compared with the (+ve) control rats. For all markers, the best results were noticed as a result of feeding seeds mixture (5%). For serum urea, chia seeds –fed group showed also normal value,while garden cress seeds –fed group showed normal uric acid value.

Table(7)

Effect of feeding Purslane, Chia, Garden cress seeds and Seed mixture on kidney functions in rats .

Groups \ Parameters		Urea (mg/dl)	Creatinine (mg/dl)	U.A (mg/dl)
(-ve) control		21.17±3.06[d]	.70±.06[c]	2.48±.27[c]
Ccl_4 injected groups	(+ve) control	35.6±3.32[a]	1.45±.18[a]	4.23±.21[a]
	Purslane Seeds	27.8±2.31[b]	.89±.065[b]	3.08±.40[b]
	Chia Seeds	23.8±3.31[cd]	.86±.070[b]	3.03±.65[b]
	Garden cress Seeds	26±4.19[bc]	.86±.073[b]	2.93±.33[bc]
	Seed mixture	20.83±2.7[d]	.73±.037[c]	2.50±.25[c]

Values are expressed as mean ± S.D.

Significance is expressed at p<0.05 using one way ANOVA test and LSD test.

Values which have different letters in each column differ significantly, while thedifference among those with similar letters completely or partially not significant

Lipids peroxidation malondialdehyde (MDA), nitric oxide (NO) and tumor necrosis factor -α in liver tissues.

Data presented in Table (8) showed the effect of feeding Purslane , Chia , Garden cress seeds and Seeds Mixture on lipids peroxidation malondialdehyde (MDA) , nitric oxide (NO) and tumor necrosis factor -α (TNF-α) in liver tissues of hepatotoxic rats. It could be noticed that positive control group recorded a significant increase (p<0.05) in the mean value of MDA, NO and TNF-α compared with the negative control group.On supplementing the rats diet with purslane ,chia , garden cress seeds and seeds mixture as a powder (5%) the parameters showed significant decrease, (P<0.05) compared with the (+ve)control rats.

Table(8)

Effect offeeding Purslane , Chia, Garden cress seeds and Seed mixture on lipids peroxidation malondialdehyde , nitric oxide and tumor necrosis factor -α in liver tissues in rats.

Groups \ Parameters		MDA (mmol/ g)	NO (U/g)	TNF-α (pg/ml)
(-ve) Control		0.15±.010[c]	0.136±.009[C]	0.14±.018[c]
Ccl_4 injected groups	(+ve) control	0.27±.007[a]	0.35±.004[a]	0.27±.007[a]
	Purslane Seeds	0.15±.006[c]	0.17±.007[b]	0.15±.006[c]
	Chia Seeds	0.17±.003[b]	0.17±.006[b]	0.17±.003[b]
	Garden cress Seeds	0.17±.006[b]	0.17±.011[b]	0.17±.006[b]
	Seed mixture	0.15±.005[c]	0.14±.006[c]	0.15±.005[c]

Values are expressed as mean ± S.D.

Significance is expressed at p<0.05 using one way ANOVA test and LSD test.

Values which have different letters in each column differ significantly, while thedifference among those with similar letters completely or partially not significant

Discussion

Purslane , Chia and Garden cress seeds have a different phenolic compounds in different proportions such as Gallic ,Caffeine , Ellagic and coumarin .This agreed with the study ***Martínez and Paredes(2014)*** who showed that Caffeic acid is among the phenolic compounds already identified in chia products, and they play an important role in the prevention and management of different neurological disorders, such as epilepsy. ***Abd El azizet al., (2014)*** showed that purslane contain of phenolic compound fractionated to catechein, chlorogenic, salycillic and pyrogallol.Elagic resulted in maximum concentration of phenolic, followed by salicylic, chlorogenic and catechein. In addition to these results in agreement with ***Abd El Salamet al.,(2019)*** who showed The extract of (Garden Cress) GC seeds had high level of total phenols and total flavonoids. Gallic acid and hisperidin were the most abundant phenolic and flavonoid compounds in GC seed extract.

Injection by CCl_4 is associated with reduced nutrient digestion and absorption as a result of low bile secretion and associated with loss of appetite leading to , leading to weight loss .***Behboodiet al., (2017)*** showed that CCl_4 caused significant reduction infeed intake and body wight gain .Feeding on Purslane, Chia and Garden cress seeds with the rats diet injected with ccl_4 which induced hepatotoxicity , led to significant increase in feed intake , body weight gain and efficiency ratio of rats.These results in agreement with ***Akramet al.,(2014)*** who studied the effect of purslane ethanolic extract administration on the body weightsof CCl_4-treated rats **.** The results were the body weights of the rats significantly decreased in the CCl_4-treated group, but increased in the normal control and purslane extract-treated groups .Also results are in agreement with ***Poudyal et al., (2012)*** who showed **t**he intake of chia seeds by the Wistar ratsimprove the food consumption and body weight .Also results are in agreement with ***Abuelgasimet al., (2008)*** who demonstrated the protective ability of seed extracts of *Lepidium sativum*on liver injury induced by Ccl_4.The anorexic effect produced by Ccl_4 due to its hepatotoxicity was masked by the use of *Lepidium sativum*.

The marked increase in relative liver and kidney weights in CCl 4 –treated group which was reversed by supplementation with antioxidant sources, as in the present study, is in harmony with ***Akramet al., (2014)*** who noticed marked elevations in organ weights in CCl_4 -treated groups. These elevations were reversed by administration with purslane extract.Also results agreed with ***Bárbara et al., (2016)*** who found that Chia seeds decreased the percentage of liver fat and liver weights due to lower accumulation of lipids in the body, which may have led to increased excretion of fat in the feces, since animals fed with chia showed an increase in fecal weight compared to the control one. ***Shukla and Bigoniya (2013)*** showed hepatoprotective effect of *Lepidium Sativum Linn* (Cruciferae) by reducing the liver weight of ccl_4 intoxicated rats.

CCl_4-induced liver injury is the best-characterized model of xenobiotic-induced hepatotoxicity***(Brautbarand Williams, 2002; Brent and Rumack, 1993).*** The bio-activation of CCl_4, primarily through the activity of CYP2E1, generates the free radicals $^{\bullet}CCl_3$ and $CCl_3OO^{\bullet}$, which results in hepatic damage. These free radicals initiate lipid peroxidation by abstracting a hydrogen atom from the polyunsaturated fatty acid of a phospholipid ***(Recknagelet al., 1989; Weber et al., 2003).*** The CCl_4-induced lipid peroxidation in turn increases the permeability of plasma membrane to Ca^{2+}, leading to severe disruption of calcium homeostasis and necrotic cell death ***(Weber et al., 2003).*** The extent of hepatic damage is assessed by the increase in serum levels of the cytoplasmic enzymes AST, ALT, ALP,Bil and by histopathological examination. The increased serum levels of AST and ALT have been attributed to damages in the structural integrity of the liver, as these cytoplasmic enzymes are released into circulation after cellular damage ***(Recknagelet al., 1989)*** Elevation of AST has been reported to be an index of hepatocellular injury in rats, whereas ALT elevation is more commonly associated with the necrotic state ***(Navarro and Senior, 2006).*** Serum ALP and GGT, which are important enzymes for assessing obstructive liver injury ***(Bulleet al., 1990; Kaplan, 1986),*** were also found to be significantly elevated in CCl_4-treated rats. ALP activity is related to the functioning of hepatocytes. Suppression of increased ALP activity is indicative of the stabilization of biliary dysfunction in rat liver during chronic hepatic injury induced by CCl_4 **(*Mukherjee, 2002).***The increase in serum total bilirubin in ccl_4 treated rats may be owing to blockage of bile ductules as a result of the inflammation and fibrosis in the portal triads and/ or due to regurgitation of conjugated bilirubin from the necrotic hepatocytes to sinusoids ***(Ahmed, 2001).***

All supplemented diet with purslane , chia and garden cress seeds in the present study decrease liver enzyme including transaminases (ALT and AST) ,alkaline phosphatase (ALP) and total bilirubin of rats injected with ccl_4.These results are in agreement with ***Vogel(2002)*** who reported that treatment with purslane extract restored the liver enzymes to near normal level indicating protection against liver damage.

Elkhayatet al., (2008) found that 70% alcohol extract of *P. oleracea* significantly restored the hepatic marker enzymes and total bilirubin in hepatic injured rats to near-normal values.***Ahmida (2010)***reported that the hepato protective effective effect of *portulaca oleracea* was due to the phytochemical present in it, including omega-3-fatty acids, β-carotene, flavonoids and alkaloids. ***Rafaela et al.,(2015)*** confirmed that the consumption of white and black chia seeds was found to be effective for reducing liver damage and improvement in liver function.***Sheisaet al.,(2019)***attributed these effects to itscontent of high level of omega-3 fatty acids. Additionally**,**another substance that has been found to improve both lipids and liver enzymes is a-linolenic acid. This substance is present at high levels in chia seeds, ranging from 14 to 20 g/100 g (55 to 65.8%)***Heinze et al.,(2012).***The antioxidant in chia seeds such as Caffeic and Chlorogenic acid can improve both lipids and liver enzymes ***Kweonet al., (2001).*** On the other hand,***Abaelgasimet al., (2008)***found that the use of seed extracts of *Lepidium sativum* protect the liver from damage and improved histologic picture and biochemical markers of liver damage.The Ccl4 induced hepatotoxicity produced in rats leading to hepatic injury triggers the generation of toxic radicals which can be masked by using a correct antioxidant in adequate amount. The mechanism of the hepatoprotective action of the plant may be related to the ability of the plant to inhibit lipid peroxidation in the liver. The presence of flavanoids triterpens, alkaloid, tannin and coumarins in *Lepidium sativum* explain its role in hepatoprotection by inhibiting the free radicals mediated damage.Moreover, the improvement in liver functions markers status in seeds–fed groups, in the present study, may be attributed to the presence of not onlyphenolic compounds, but also dietary fibers and polyunsaturated fatty acids.

Feeding on diet supplemented purslane ,chia and garden cress seeds in the present study , led to significant increase in serum total protein, albumin and globulin of rats injected with ccl_4 that induced hepatotoxicity . These findings are in agreement with ***Anushaet al., (2011)*** showed the hepatoprotective effect of *Portulaca oleracea* (*P. oleracea*) by significantly restoring the levels of serum enzymes to normal and increase in albumin and total protein .CCl_4 impaired protein metabolism in the injured hepatocytes causing a release of non-protein and protein nitrogenous substances. This is associated with a decrease in the level of protein synthesis along with an increase in the activities of hepatic enzymes ***Anusha et al., (2011).*** The ability of purslane extract to restore the levels of TP, Alb might be due to its effect on the functional statues of the poisoned liver and to protect against hepatotoxicity.***Zamzamiet al., (2019)*** evaluated the hepatoprotective efficacy of *L. sativum* seeds in white male New-Zealand rabbits. The results revealed that treatment of rabbits administered with CCl_4 with *L. sativum* seeds significantly repaired their liver injurious marker enzymes as well as bilirubin, total protein, and albumin, hence approving its hepatoprotective effect . *Lepidium sativum* improved the degree of structural damage and reduced inflammatory infiltration in hepatic cells. ***Balgoon(2019)*** assessed the protective role of *Salvia officinalis* essential oil (SO) against carbon tetrachloride (CCl_4)-induced liver and kidney damage in mice.The activity of SO was associated with increasing total protein, albumin, globulin, and prothrombin. SO is a potential candidate for counteracting hepato/renal injury associating CCl_4..

Feeding on purslane ,chia and garden cress seeds in the present study , led to significant decrease in triglycerides ,LDLc ,VLDLc and significant increase in HDLc of rats injected with CCl4 induced hepatotoxicity conducted by ***Gatrehet al., (2011),*** they found that The serum levels of LDL-C, and TG decreased significantly in purslane group .All the therapeutic values of purslane (*P. oleracea*) are attributed to the presence of many biologically active compounds including flavonoids, Alkaloids, Coumarins, and high content of ω-3 fatty acids were considerable beneficial in preventing heart attacks and strengthening the immune system ***Okafor and Ezejindu (2014)***. Predominantly containing poly-unsaturated (omega-3) fatty acids, make purslane medicinal plant to have favorable effects on cholesterol and triglyceride levels ***Yokoyamaet al., (2007).***

Also results agree with ***Ricardo and Wayne (2005)*** who assessed the effect chia seed, which is the highest vegetative source of a–linolenic fatty acid, has on plasma total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein(LDL), triacylglycerol content(T.G) , and fatty acid profile when fed to rats. They found that the chia diets dramatically decreased triacylglycerol (T.G) levels, (LDL) level ,cholesterol and increased HDL and omega -3 fatty acid contents in rat serum. These findings suggest that a-linolenic–rich chia may be an alternative to omega-3 sources for vegetarians and people allergic to fish and fish product.***Amawi andAljamal (2012)*** showed that the administration of *Lepidium sativum*improved lipid profile in hypercholesterolemic rats.

Supplementing rat diet with purslane ,chia and garden cress seeds in the present study, led to a marked improvement in the kidney function abnormalized by CCl_4 injection evidenced better levels of urea, creatinine and uric acid. These results agreed with ***AbdAlah et al.,(2018)***who investigated the effect of Purslane on kidney failure affected by copper toxicity in a rat model**.** They found thatPurslane administration decreased the elevated level of creatinine and BUN in rats which received toxic levels of copper due to its antioxidant and anti-inflammatory properties.The results agreed with ***Fahmy et***

al.,(2018) who ensured the protective role of *Salvia officinalis* essential oil (SO) against carbon tetrachloride (CCl_4)-induced liver and kidney damage in mice. The effect may occur via the antioxidant defense mechanism which in part related to the complexity of its chemical constituents. Also the result agreed with ***Loay and Wurood (2019)*** who reported that the ethanolic extract of garden cress has both renal protective and curative effects as it significantly reduced the blood levels of urea and creatinine which indicates increased glomerular filtration rate. In the present study rats diet supplemented with purslane,chia and garden cress seeds singly or as a mixture, led to significant decrease in lipids peroxidation and inflammation as manifested by decrease malondialdehyde (MDA) ,nitric oxide and TNF-α levels in liver tissues of rats.These findings were in line with ***Dkhil et al., (2011)*** who evaluated the anti- oxidative effects of *(Portulaca oleracea)* PO in adult male Waster albino rats. The results revealed that oral administration of PO improved liver and kidney functions .The improvement in all the indicators may be attributed to the presence of phenolic compound,which possess anti-oxidant, anti-diabetic and anti-inflammatory activities PO is the main source of anti-oxidant vitamins such as α-tocopherol, ascorbic acid, *β*-carotene and glutathione. ***Bárbaraet al., (2016)*** investigated the influence of chia consumption on inflammation and oxidative stress in adult female ovariectomized rats fed a high-fat diet . Chia intake improved the antioxidant activity by increasing SOD expression, PPAR-α expression and catalase activity . In addition, chia consumption decreased the concentrations of the inflammatory markers IL-1β .The improvement in all the indicators may be attributed to the presence of phenolic compounds, vitamins, minerals, dietary fiber, and polyunsaturated lipids***.(Silvaet al.,2017)***

Oliveira et al.,(2017) found that Chia intake increased catalase activity in the standard diet probably due to compounds present in the seeds including phenolic compounds and antioxidants. The main phenolic compounds found in chia are rosmarinic acid, quercertin, myricetin, kaempferol, caffeic acid, and galic acid. These compounds provide benefits to the human body due to the presence of hydroxyl groups that are readily oxidized to produce the corresponding *O*-quinones, which are effective scavengers of reactive oxygen species. Phenolic compounds can also alter the recruitment of inflammatory cells, decreasing the production of pro-inflammatory mediators. ***(Fraga ,et al 2010). Mazin et al., (2019)*** evaluated the hepatoprotective efficacy of *L. sativum* seeds in white male New-Zealand rabbits. The results revealed that concurrent treatment of rabbits administered with CCl_4 for 5 and 10 weeks with *L. sativum* seeds significantly reduction of lipid peroxidation and repaired the antioxidant enzymatic status and total protein restoring them to normal levels. The hepatoprotective action of L. sativum seeds could be due to down regulation of cytokines [TNF-α and interleukin-6 (IL-6)] and stress gene [inducible nitric oxide synthase (iNOS) and HO-1] messenger ribonucleic acid (mRNA) expression. Lepidium sativum ethanolic extract pre protection also improved the degree of structural damage and reduced inflammatory infiltrationin hepatic cells. These outcomes established that Lepidium sativum ethanolic extract alleviates hepatic impairments and structural injury through the decay ofoxidative stress, inflammation, and apoptosis in the liver ***(Raishet al., 2016).***

Conclusion

According to the results obtained in the present study, it appears that supplementing diet with purslane, chia and garden cress seeds singly or as amixture alleviated liver abnormalities and dysfunction associated with oxidative stress in liver tissues of CCl_4 –intoxicated rats.

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تأثير بذور بعض النباتات الطبية على التسمم الكبدى المحدث بواسطة رابع كلوريد الكربون فى جرزان التجارب

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الملخص العربى

كثير من النباتات يتم استخدامها كنباتات طبية بواسطة كثير من الناس. تم اجراء هذه الدراسة لمعرفة تأثيربذور الرجلة والشيا وحب الرشاد على التسمم الكبدى المحدث بواسطة رابع كلوريد الكربون فى جرزان التجارب. تم تقسيمالجرزان إلى مجموعتين رئيسيتين ، المجموعة الأولى (تتكون من 6 جرزان) وهمجموعه ضابطة سالبة تغذت على الغذاء القياسى فقط لمدة 6 أسابيع ، المجموعة الثانية الرئيسية تتكونمن 36جرز تم حقنهم تحت الجلد بمركب رابع كلويد الكربون المذاب فى زيت البرفين (50% حجم/حجم، 2مل/كجم من وزن الجسم) مرتين اسبوعيا ولمدة اسبوعين لاحداث تلف كبدى مزمن. بعد التأكد منالاصابة تبقى 30 جرز مصاب تم تقسيمهم إلى 5 مجموعات متساوية العدد تشمل المجموعة الثانية وهمجموعة ظابطة موجبة تغذت على الغذاء القياسى فقط ، وأما المجموعات الأربعة الأخرى (الثالثة والرابعة والخامسة والسادسة) فقد تم تغذيتهم على الغذاء القياسى مضافا اليه مسحوق أى من بذور الرجلة، الشيا ، حب الرشاد أو خليطهم على الترتيب (بنسبة 5%). استمرت مدة العلاج 4 أسابيع، وفى نهايتهاتم حساب الزيادة فى وزن الجسم والوزن النسبى لبعض الأعضاء الداخلية ، كما تم تحليل عينات السيرمونسيج الكبد بيوكميائيا. أظهرت النتائج حدوث خلل فى وظائف الكبد والكلى وارتفاع دهون الدم نتيجة التعرض لرابع كلوريد الكربون بسبب تأثيره المؤكسد. أدى استخدام بذور الرجلة والشيا وحب الرشاد كلعلى حدة أو فى صورة خليط إلى تحسن ملحوظ فى وظائف الكبد والكلى وانخفاض دهون الدم نتيجة لمحتواهم من المركبات الفينولية ومن ثم تأثيرهم المضاد للأكسدة. وطبقا لهذه النتائج يمكن للمرضى الذين يعانون من تسمم الكبد نتيجة التعرض لمصادر رابع كلويد الكربون استخدام هذه البذور كل على حدة أو فى صورة خليط (وهو الأفضل) لإختبار كفاءتها الممكنة فى تحسين حالتهم الصحية.

الكلمات المفتاحية: تسمم الكبد – رابع كلوريد الكربون - بذور الرجلة – بذور الشيا – بذور حب الرشاد – المركبات الفينولية – الجرزان