Protective Effect of *Lepidium sativum L.* Seeds Powder and Extract on Hypercholesterolemic Rats

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Abstract: The present study was designed to investigate the effects of *Lepidium sativum L* (LS) on the nutritional status and some biochemical analyses of serum and liver in hypercholesterolemic rats. Forty-two adult albino male rats Sprague Dawley strain were classified into six groups. One was fed on standard diet and kept as control (-ve) group. The other five hypercholesterolemic rat groups were control (+ve), drug, LS extract, 5 % or 10 % LS powder rat groups. In comparison to control (- ve) group, the control (+ve) group showed a significant higher value of weight gain , feed efficiency ratio (FER), serum cholesterol, triglycerides , LDL-c ,VLDL-c, cholesterol/ HDL-c and LDL-c/ HDL-c, serum (AST& ALT) ,creatinine ,urea, liver cholesterol and total lipids but significant decrease in HDL-c, globulin and liver triglycerides .Also, LS extract and 5% LS powder rat groups showed a significant increase in weight gain, cholesterol/ HDL-c and LDL-c/ HDL-c, serum (AST& ALT) however, drug and 10% LS powder rat groups showed a significant increase in cholesterol/ HDL-c. On the other hand, The drug, LS extract , 5% and 10% LS powder rat groups showed a significant increase in serum cholesterol ,triglycerides VLDL-c , LDL-c ,serum creatinine and urea level when compared to control (- ve) group. In comparing with control (+ ve) group, The drug, LS extract , 5% and 10% LS powder rat groups showed a significant lower value of weight gain , feed efficiency ratio, serum cholesterol ,triglycerides VLDL-c , LDL-c level, cholesterol/ HDL-c , LDL-c/ HDL-c , serum (AST& ALT) ,serum creatinine, urea, liver cholesterol and total lipids with a significant increase in both serum globulin and liver triglycerides.

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Key wards *:* Lepidium sativum – aqua extract- cholesterol and rats

1. Introduction:

Hypercholesterolemia refers to elevated serum LDL cholesterol or a combination of high levels of LDL cholesterol and triglycerides. Hypercholesterolemia, a significant cardiovascular risk factor, is one of the major oxidative stresses that generate excess of highly reactive free radicals. This exacerbates the development and progression of atherogenesis Hypercholesterolemia increased the risk of increased LDL-c or more occurately LDL-c/ HDL-c ratio. The atherogenic index decreased as a result of the reduction in LDL-c and increment in HDL-c (Durrington, 1995 and Abd El-Ghanny et al., 2007).

Plants still remain a major source for drug discovery in spite of the great development of synthetic molecules. Consequently, the uses of traditional plant extract in the treatment of various diseases have been flourished (Jouad et al., 2001).The garden cress seed oil, Lepidium sativum L.,(LS) is a fast growing annual herb belonging to the Brassicaceae family that is native to Egypt and west Asia The seeds are wildly consumed as salad and spice (Gokavi et al .,2004). Previous studies have demonstrated the protective action of LS against carcinogenic compounds and growth inhibition of *Pseudomonas aeruginosa*, a bacteria strain with a potent antibiotic resistance (Abuja et al., 2001 and Kassie et al., 2003). LS recommended in the treatment of hypertension, diabetes and renal disease (Kirtkar and Basu 2005 and Tahraoui et al., 2007).

The present study was designed to investigate the effect of powder or aqua extract from Lepidium sativum L. seeds (LS) either on the nutritional status and some biochemical analyses of serum and liver in hypercholesterolemic rats.

2. Materials and methods

I.– Materials:

1- Garden cress *(Lepidium sativum* L.) seeds:

Lepidium sativum L. seeds (LS) were purchased from Agricultural Research Center. Garden cress seeds were dried with hot air (40–60 ^{o}C) and grinded to powder. Garden cress seeds powder was used in preparation of aquatic extract and also added to the diet as 5 % and 10% of the constituent of fiber.

2- Gemfiibrozil capsules:

It was obtained from Amoun Pharmaceutical Industries Company. Each tablet contains 100 mg. It is lipid regulating agent which decrease lipid elevated serum lipids by lowering serum triglycerides and total cholesterol. Human therapeutic dose was 100 mg which converted to rat dose that was 9 mg/kg body weight daily which dissolved in distilled water and given to rats by oral intubations according to Paget and Barnes (1964).

3-Biochemical kits:

BioMeriuex Kits were purchased from Alkan Co. for Chemicals and Biodignostics, Dokki,, Egypt.

4-Experimental animals:

A total of forty-two Sprague –Dawley adult male rats were purchased from the Agricultural Research Center, Giza, Egypt. The average weight was 205 ±5 g. The animals were kept under observation for five days before experiment and supplied with standard diet and water *ad libitum*. The standard diet comprised of casein (200g/kg), corn starch (497g/kg), sucrose (100g/kg) , cellulose (30 g/kg) ,corn oil (50g/kg), mineral mixture (100g/kg) , vitamin mixture (20g/kg) and DL-methionine (3g/kg).The standard diet was performed according to NRC (1995).

II. -Methods:

1. Preparation of the garden cress aqueous extract:

The aqueous extract was prepared in a standardized manner by boiling 1 g of dried powdered seeds of LS in 100 ml of distilled water for 10 min and left for 15 min to infuse then cooled and filtered. The filtrate was lyophilized and the desired dose was then prepared and reconstituted in 10 ml of distilled water per kilogram body weight just before oral administration. The aqueous extract dose was 20 mg/kg body weight daily by oral intubations (Eddouks et al., 2005).

2- Grouping of rats and experimental design:

The experimental rats were divided into six groups (n= 7 rats). The first group which kept as normal control (-ve) group which fed on standard diet only. The rest of rats were fed on standard diet with 2 % cholesterol for 3 weeks to be hypercholesterolemic, then classified into 5 groups and remained fed on hypercholeslerolemic diet during the experimental period (8 weeks). One of them acted as control (+ve) and the other groups were drug, LS seeds extract, 5% and 10% LS powder.

3 –Calculation of some parameters:

Feeding and growth performance were carried out by determination of daily feed intake, body weight gain and feed efficiency ratio (FER) according to Chapman et al., (1950) using the following Formula

FER = Body weight gain / Feed intake.

5 –Collection of samples:

The rats were sacrificed at the end of the experiment (8 weeks). The collected blood samples were centrifuged at 3000 rpm/ 10 minutes to obtain serum. Livers of rats were also collected for some biochemical analysis.

5 -Biochemical analysis:

A- Serum analysis

Serum cholesterol, triglycerides (TG) and high density lipoprotein cholesterol (HDL-c) were determined by using enzymatic colorimetric methods (Allain et al., 1974, Buccolo and David (1973) and Kostener, 1977, respectively). Very low density lipoprotein cholesterol (VLDL-c) was calculated as TG/5 while low density lipoprotein cholesterol (LDL-c) was calculated as following [LDL-$_C$= Total cholesterol –HDL-$_C$ –VLDL-$_C$] according to Fruchart, (1982). Serum aspartate and alanine amino transferase (AST&ALT) enzymes, total protein, and albumin were estimated according to Reitman and Frankel (1957), Weichselbaum (1946) and Bartholomev and Delany (1966), respectively. Serum globulin (G) value was determined by subtracting the albumin from the total proteins according to Coles (1974). In addition, creatinine and urea were estimated according to Bonsens and Taussky, (1984), and Patton and Crouch, (1977) respectively. Atherogenic indexes (cholesterol/ HDL-c & LDL-c/ HDL-c) were calculated according to Castelli and levitar, (1977).

B- Liver analysis:

Livers of rats were rapidly removed and parts of them perfuse with 50 to 100 of ice cold 0.9%NaCL solution for estimation of cholesterol, triglycerides , and total lipids, according to Abell et al., (1952) , Seheletter and Nussel, (1975), Folch et al., (1957), respectively.

III.- Statistical analysis:

Collected data were subjected to analysis according to SPSS Program Differences were considered significant at $p< 0.05$ (Artimage and Berry, 1987).

3. Results:

Data recorded in table (1)showed that the control (+ve) group showed a significant higher value of weight gain and feed efficiency ratio (PER) at p<0.01 while the LS extract, 5% and 10% LS powder rat groups showed a significant higher value of weight gain at p<0.05 compared to control (- ve) group. The drug, LS extract , 5% and 10% LS powder rat groups showed a significant lower value of weight gain and feed efficiency ratio compared to control (+ ve) group.

Table (2) showed that the control (+ve) group showed a significant increase in serum cholesterol, triglycerides, LDL-c and VLDL-c (p< 0.001) but significant decrease in HDL-c (p<0.001) in comparison with control (-ve). On the other hand, the drug, LS extract , 5% and 10% LS powder rat groups showed a significant increase in serum cholesterol ,triglycerides LDL-c and VLDL-c level (p< 0.05&0.01) compared to control (- ve) group. The drug, LS extract , 5% and 10% LS powder rat groups showed a significant decrease in serum cholesterol ,triglycerides LDL-c and VLDL-c level in comparison with control (+ve).

Table (3) showed that, control (+ve), LS extract and 5% LS powder rat groups showed a significant increase in cholesterol/ HDL-c and LDL-c/ HDL-c (p< 0.01&0.05) while drug and 10% LS powder rat groups showed a significant increase in cholesterol/ HDL-c (p< 0.05) compared to control (- ve) group. The drug, LS extract, 5% and 10% LS powder rat groups showed a significant decrease in value of cholesterol/ HDL-c and LDL-c/ HDL-c in comparison with control (+ve).

From data presented in table (4), it could be noticed that control (+ve) ,drug, LS extract , and 5% LS powder rat groups showed a significant increase in serum alanine and aspartate aminotransferase (ALT &AST) at p<0.01 compared to control (- ve) group. The drug, LS extract , 5% and10% LS powder rat groups showed a significant decrease in serum alanine and aspartate aminotransferase enzymes in comparison with control (+ ve) group .

As shown in table (5), the control (+ve) showed a significant decrease in globuline (p<0.05) but a significant increase in creatinine and urea (p<0.01) compared to control (- ve) group. The drug, LS extract , 5% and 10% LS powder rat groups showed a significant increase in serum creatinine and urea (p< 0.05) compared to control (- ve) group. The drug, LS extract , 5% and 10% LS powder rat groups showed a significant increase in serum globulin and a significant decrease in serum creatinine and urea compared to control (+ ve) group.

As recorded in table (6) showed that control (+ve) group showed a significant increase in liver cholesterol and total lipids (p<0.01) but significant decrease in liver triglycerides (p<0.05) in comparison with control (- ve).The drug, LS extract, 5% and 10% LS powder rat groups showed a non significanjt difference in liver cholesterol, triglycerides and total lipids in comparison with control (- ve) group. The drug, LS extract , 5% and 10% LS powder rat groups showed a significant decrease in liver cholesterol and total lipids but significant increase in liver triglycerides in comparison with control (+ ve) group.

Table (1): Mean values ± SD of body weight gain, feed intake and feed efficiency ratio (FER) of experimental rat groups.

Groups / Variables	Control (-ve)	Hypercholesterolemic				
		Control (+ve)	Drug	LS		
				extract	5%	10%
Initial weight(g)	115.33± 3.41[a]	116.25± 3.77[a]	117.35± 4.12[a]	117.50± 4.81[a]	116.81± 4.99[a]	116.75 ± 4.71[a]
Final weight(g)	190.53± 11.22[a]	217.42± 10.33[a]	198.12± 11.44[a]	210.64± 13.77[a]	214.01±13 .25[a]	211.78± 14.61[a]
Weight gain(g)	75.20± 5.68[c]	101.17±8. 24[a**]	80.77± 7.69[bc]	93.14± 8.21[b*]	97.20± 9.11[b*]	95.03± 8.61[b*]
Feed intake(g/d)	15.11± 1.24[a]	16.22± 1.18[a]	15.75± 2.01[a]	16.53± 2.11[a]	16.31± 1.89[a]	16.41± 1.49[a]
FER	0.082± 0.003[b]	0.103± 0.002[a**]	0.085± 0.001[b]	0.093± 0.001[b]	0.099± 0.004[b]	0.096± 0.005[b]

Significant with control group * P<0.05 ** P<0.01 *** P<0.001
Mean values in each row having different superscript (a, b &c,) are significant.

Table (2) The Mean values ± SD of some serum lipid patterns of experimental rat groups.

Groups / Variables	Control (-ve)	Hypercholesterolemic				
		Control (+ve)	Drug	LS		
				extract	5%	10%
Cholesterol (mg/dl)	80.34± 7.88 c	199.77±11.43 a***	106.78±10.18 b*	110.01± 11.33 b*	113.24±12.14 b*	105.35± 10.61 b*
Triglyceride (mg/dl)	70.31 ± 6.12 c	155.14± 18.48 a***	95.67± 10.11 b*	98.01± 11.31 b*	96.18± 10.15 b*	94.31± 9.96 b*
HDLc (mg/dl)	32.32± 3.47 a	20.11± 2.87 b***	29.75± 2.78 a	28.88± 3.11 a	31.14± 2.99 a	30.91± 3.03 a
LDLc (mg/dl)	33.06± 4.01 c	104.01± 10.22 a***	57.90± 6.08 b**	61.53± 7.18 b**	62.87± 7.33 b**	55.58 ± 6.14 b**
VLDLc (mg/dl)	14.01± 1.81 c	31.02± 3.17 a***	19.13± 2.15 b*	19.60± 2.11 b*	19.23± 2.16 b*	18.86± 2.22 b*

Significant with control group * P<0.05 ** P<0.01 *** P<0.001
Mean values in each row having different superscript (a, b &c,) are significant.

Table (3) The Mean values ± SD of atherogenic indexes of experimental rat groups.

Groups / Variables	Control (-ve)	Hypercholesterolemic				
		Control (+ve)	Drug	LS		
				extract	5%	10%
Cholesterol/HDLc	2.42± 0.38 c	9.93± 1.77 a***	3.58± 0.77 b*	3.80± 0.75 b*	3.63± 0.65 b*	3.40 ± 0.54 b*
LDLc/ HDLc	1.05± 0.16 c	5.17± 1.14 a***	1.94± 0.18 bc	2.13± 0.47 b*	2.01± 0.32 b*	1.79± 0.18 bc

Significant with control group * P<0.05 ** P<0.01 *** P<0.001
Mean values in each row having different superscript (a, b &c,) are significant.

Table (4) The Mean values ± SD of serum amino transferase (ALT & AST) enzymes of experimental rat groups.

Groups / Variables	Control (-ve)	Hypercholesterolemic				
		Control (+ve)	Drug	LS		
				extract	5%	10%
ALT (µ /ml)	27.69± 2.81c	49.14± 4.31a**	34.41± 3.27 b*	33.47± 3.61 b*	34.21± 3.11 b*	31.78± 3.18 bc
AST (µ /ml)	41.27± 4.22C	67.71± 5.91 a**	51.17± 5.15 b*	49.39± 5.31 b*	48.11± 3.92 b*	40.31± 4.16 c

Significant with control group * P<0.05 ** P<0.01 *** P<0.001
Mean values in each row having different superscript (a, b &c,) are significant.

Table (5) The Mean values ± SD of serum total protein, albumin, globulin, creatinine and urea of experimental rat groups.

Groups / Variables	Control (-ve)	Hypercholesterolemic				
		Control (+ve)	Drug	LS		
				extract	5%	10%
T. protein (g/dl)	7.30± 1.21 [a]	6.11± 1.31 [a]	6.81± 1.30 [a]	6.87± 1.41 [a]	6.91± 1.35 [a]	6.90± 1.40 [a]
Albumin (g/dl)	3.71± 0.55 [a]	3.99± 0.45 [a]	3.59± 0.13 [a]	3.24± 0.19 [a]	3.49 ± 0.23 [a]	3.11± 0.16 [a]
Globulin (g/dl)	3.59± 0.22 [a]	2.12± 0.13 [b*]	3.22± 0.66 [a]	3.63± 0.45 [a]	3.42± 0.48 [a]	3.79± 0.55 [a]
Creatinine (mg/dl)	0.75± 0.01 [c]	1.01± 0.15 [a**]	0.98± 0.06 [b*]	0.97± 0.11 [b*]	0.95± 0.12 [b*]	0.92± o.14 [b*]
Urea (mg/dl)	40.14± 4.77 [c]	55.79± 7.11 [a**]	50.17± 6.18 [ab*]	49.31± 5.11 [b*]	48.20± 4.25 [b*]	47.32± 4.60 [b*]

Significant with control group * P<0.05 ** P<0.01 *** P<0.001
Mean values in each row having different superscript (a, b &c,) are significant.

Table (6) The Mean values ± SD of liver cholesterol, total lipids and triglyceride of experimental rat groups.

Groups / Variables	Control (-ve)	Hypercholesterolemic				
		Control (+ve)	Drug	LS		
				extract	5%	10%
Cholesterol (mg/g)	3.66± 0.88 [b]	6.96± 1.41 [a**]	4.01± 0.89 [b]	4.35± 0.95 [b]	4.44± 0.58 [b]	4.25± 0.77 [b]
Total lipids (mg/g)	34.52± 3.21 [b]	48.99± 4.11 [a**]	36.11± 3.41 [b]	38.20± 2.71 [b]	38.77± 2.91 [b]	37.43± 3.11 [b]
Triglyceride (mg/g)	2.44± 0.11 [a]	1.65± 0.36 [b*]	2.11± 0.33 [a]	2.31± 0.35 [a]	2.01± 0.31 [a]	2.21± 0.30 [a]

Significant with control group * P<0.05 ** P<0.01 *** P<0.001
Mean values in each row having different superscript (a, b &c,) are significant.

4. Discussion:

Our investigation revealed that, consumption of Lepidium sativum L.(LS) seeds increase weight gain as LS seeds are found to contain 18–24% of fat which 34% of total fatty acids is alpha linolenic acid .It contains good amount of lignans and antioxidants, which can stabilize the n-3 polyunsaturated fatty acids in its seed oil. LS oil has alpha linoleic acid which could give it nutritional advantages (Gunstone, 2004 and Diwakara et al., 2008). The primary fatty acids in LS oil were oleic (30.6 wt %) and linolenic acids (29.3 wt %). LS seeds oil contained high concentrations of tocopherols. The primary phytosterols in L S were sitosterol and campesterol, with avenasterol (Bryan et al., 2009).

The results of lipid profile were agreed with results obtained by Das et al., (1997) who reported that the lipid profile of hypercholesterolemic animals were significantly higher than control rats for total lipid, total cholesterol , triglyceride, LDL-c and VLDL-c while only HDL-c was significantly lower in hypercholesterolemic rats than in control rats.

The increased plasma cholesterol, particularly LDL-c is one of the most important risk factor for coronary vascular disease. LDL-c particle are taken up by macrophage cells after oxidized or modified and then deposited in the arterial intima leading to formation of atheroma (Durrington, 1995). Low HDL-c levels are considered as a strong risk factor for coronary heart disease as HDL-c act as antioxidant and protect LDL-c from oxidation so that

reduce LDL-c from circulation (Boden and Pearson, 2000 and Glass and Witztum, 2001). Lepidium sativum L. seeds have revealed presence of glycoside, alkaloids, tannin (Phenolic compound), flavonoids, and amino acids like glutamine, cysteine, and glycine. The tannin and flavonoids may have antioxidant activity whenever glutamate, cysteine, glycine are intermediates for synthesis of the endogenous antioxidant glutathione. Diets rich in alpha linolenic acid have been associated with a reduced risk of fatal ischemic heart disease, a reduction in heart attacks and mortality from chronic vascular disease. Feeding alpha linolenic acid has also been shown to decrease platelet aggregation, total cholesterol, LDL cholesterol and triglycerides in humans and rats (Olsson, and Yuan 1996, Kirtkar and Basu 2005 and Hamer and Steptoe, 2006).

Protective and curative treatment of ethanolic extract of Lepidium sativum seeds L. in renal failure of rats significantly reduced the level of urea and creatinine that indicates increase glomerular filtration rate. Extract of Lepidium sativum L. seeds may be having nephroprotective and curative activity. Daily oral administration of aqueous LS extract for 3 weeks exhibited antihypertensive and diuretic activities. ALT and AST are closely correlated in most cases of liver diseases. Excessive storage of fat in the liver effects on liver functions and increases the susceptibility to free radical attack in hyporcholesterolemic rats resulting in liver damage as described by Tahri et al .,(2000), Mhamed et al .,(2005) and Yadav et al .,(2009). Feeding rats with 10% Garden cress seed oil lowered hepatic cholesterol by 12.3% and serum triglycerides by 40.4% compared to SFO fed group. Very low density lipoprotein cholesterol (VLDL-C) and low density lipoprotein cholesterol (LDL-C) levels decreased by 9.45% in serum of 10% LS oil fed rats, while HDL remained unchanged among LS oil fed rats (Diwakar et al .,2008)

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