Biochemical role of *asparagus* in regulation of cholesterol metabolism and improvement of antioxidants status in hypercholesterolemic rats.

Yakout, A. El-senosi[1]; Yousef Mohamed Ali[2]; Wasfi, A.A[3]and Aboalella, M.S.

[1]*Biochemistry Department, faculty of veterinary medicine, Benha University.* [2] *Biochemistry Department, faculty of veterinary medicine, Zagazig University.*[3] *Chemistry Department, faculty of Science, Benha University.*

A B S T R A C T

Hypercholesterolemia are well-recognized major risk factors of atherosclerosis and cardiovascular diseases. Root of Asparagus racemosus (AR) is widely used in Ayurvedic system of medicine in India and is known for its steroidal saponin content. This study was designed to investigate the possible hypocholesterolemic effect and antioxidant potential of AR root in normal and hypercholesterolemic rats. Hypercholesterolemia was induced in normal rats by fed a normal diet containing 0.75% cholesterol and 1.5 g % bile salt for 8 weeks. Dried root powder of Asparagus racemosus was administrated to the hypercholesterolemic and normal rats as feed supplement a dose level of 200mg/kg/B.W and 400mg/Kg/B.W for a duration of 6 weeks. Serum and hepatic lipid profiles, serum HMG-CoA reductase and antioxidants enzymatic status determined. Feed supplementation with AR root powder resulted in a significant decrease in serum and hepatic lipid profiles in hypercholesterolemic rats and HMG-CoA reductase activity. However, the activities of catalase, SOD, Glutathione peroxidase and Glutathione reductase were significantly increased in both the experimental groups. The results of the present study indicate that the addition of AR root as feed supplement reduced serum and hepatic lipid concentration and elevated of hepatic antioxidant status in hypercholesterolemic rats. It could be concluded that AR root administration could ameliorate hypercholesterolemia and oxidative stress in hypercholesterolemic condition.

Keywords: antioxidant, *Asparagus racemosus*, cholesterol metabolism, hyper-cholesterolemia.

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1. INTRODUCTION:

Hypercholesterolemia is a metabolic condition that determines the onset of chronic degenerative diseases such as atherosclerosis (Devi and Sharma, 2004; Kim et al., 2008). It characterized by the elevation of cholesterol and lipid parameters (LDL-cholesterol, triacylglycerol). It estimated provoke about 4.4 million deaths (7.9%) in the world. Scientists often cite lifestyle: unhealthy diet, physical inactivity, lack of exercise, stress, smoking, and obesity as predisposing factors (Callias, 2007). Moreover, Hypercholesterolemia was observed when cholesterol (LDL) in the blood was higher than the actual needs. The excess not used by the cells then tend to settle against the vessel walls, causing, if not recovered and returned to the liver by HDL, obstruction of the arteries, leading to infarction (Callias, 2007). There are three types of these triglyceride-containing lipoproteins: chylomicrons produced by the small intestine after meals, very low

density lipoprotein, or VLDL (Very Low Density Lipoproteins) produced by the liver from sugars, and intermediate density lipoproteins or IDL from the conversion of VLDL. (Callias, 2007). These lipoproteins spread into the bloodstream where degradation system turns them into free fatty acids, which are in turn used by tissues as an energy source. The excess is stored as energy reserves in fat cells called adipocytes. The elevation of triglycerides promotes the cardiovascular diseases (Callias, 2007). Atherosclerosis is a complex chronic disease characterized by the accumulation of lipids within arterial walls that eventually go on to form plaques, which can cause narrowing, hardening, and/or complete blockage of arteries. (Maton., et al., 1993). Many studies have been made to propose alternative treatment based on plant species (Kothiyal and Gupta, 2011; Patel et al., 2012; Sodipo et al., 2012, Ghorbani, 2013). *Asparagus racemosus* is a Wild variety. Belongs to the family Liliaceae, known as 'Shatavari'. The name Shatavari means "curer of a hundred diseases" (shat: "hundred"; vari: "curer"). (Michigan Asparagus Advisory Board., 2012). *Asparagus racemosus* is a well-known Ayurvedic rasayana that prevent ageing, increase longevity, impart immunity, improve mental function, vigor and add vitality to the body and it is also used in nervous disorders, dyspepsia, tumors, inflammation, neuropathy, hepatopathy (Sharma and Charaka, 2001). Studies indicate that the pharmacological activities of *Asparagus racemosus* root extract include antiulcer (Sairam et al., 2003), antidiarrhoeal, antidiabetic and immunomodulatory activities. Moreover, Root of *A.racemosus* referred as bittersweet, emollient, cooling, nervine tonic, constipating, galactogogue, aphrodisiac, diuretic, rejuvenating, carminative, stomachic, antiseptic and as tonic (Chopra, et al., 1994), it also has anti-tussive, antibacterial activities and antioxidant (Mandal , et al., 2000). Visavadiya and Narasimhacharya also studied the effect of *A. racemosus* on the lowering of cholesterol in hypercholesterolemia in rats. (Visavadiya and Narasimhacharya, 2005). The present study established to investigate the potential of AR root (powder) as a dietary supplement in normalizing the hypercholesteremic and oxidative stress conditions induced by chronic intake of cholesterol-rich diets with regard to serum and hepatic lipid profiles, cholesterol metabolism and antioxidant status.

2. MATERIALS AND METHODS:

2.1 Experimental animals:

Sixty male albino rats of 10-12 weeks old and weighing 170 – 200g used for the experimented investigation of this study. Rats were obtained from the laboratory animal's research center, faculty of veterinary medicine, Benha University. Rats were housed under standard conditions of light and temperature and allowed free access of standard pellet diet and tape water was provided ad libitum. The animals were left 10 days for acclimatization before the beginning of the experiment.

2.2 Chemicals and Plant material used

All chemicals were of analytical grade and obtained from standard commercial suppliers. The chemicals used in the present study were: Cholesterol and bile acid powders were purchased from El-Gomhouria Co. For Trading Chemicals, Medicines and Medical Appliances, Egypt. The AR roots Powder were obtained from Shaanxi Pioneer Biotech Co.,Ltd from China and used as feed supplement.

2.3 Induction of hypercholesterolemia:

Hypercholesterolemia was induced by addition of 0.75 g% cholesterol and 1.5 g% bile acid to the basal diet for (8 weeks). The basal diet contained carbohydrates (56 g %), proteins (22 g %), fat (4 g %), fiber (4 g %) and mineral mixture (6 g %).

2.4 Experimental Design:

After 10 days adaptation period, Animals were randomly divided into six groups: Group I Normal Control (NC): included 6 healthy rats received normal diet daily. Group II (N+200 mg AR): included 12 healthy rats received normal diet + 200mg/kg/b.w AR root powder daily. Group III (N+400 mg AR): included 12 healthy rats received normal diet + 400mg/kg/b.w AR root powder daily. Group IV Positive control (HC): included 6 rats received hypercholestrolemic diet daily. Group V (H+200 mg AR): included 12 healthy rats received hypercholestrolemic diet + 200mg/kg/b.w AR root powder daily. Group VI (H+200 mg AR): included 12 healthy rats received hypercholestrolemic diet + 400mg/kg/b.w AR root powder daily.

2.5 Sampling:

Blood samples and liver tissue specimens were collected from all animals groups, after overnight fasting, sacrificed under light anesthesia three times during the experiment at 2nd, 4th and 6th weeks.

2.5.1 Blood samples:

Blood samples were collected by ocular vein puncture in dry, clean and screw capped tubes and serum were separated by centrifugation at 3500 r.p.m for 15 minutes. The clean, clear serum was separated by Pasteur pipette and kept in a deep freeze at -20°C until used for subsequent biochemical analysis.

2.5.2 Preparation of erythrocyte lysate:

Blood samples were collected in dry, clean and screw capped heparinized tubes and plasma were separated by centrifugation at 3500 r.p.m for 15 minutes. after plasma separation, erythrocytes were washed three times with an equal volume of cold saline, then 1ml RBCs lysed with 4 ml distilled water in dry sterile caped tubes. The samples were kept at -20 ºC for the determination of superoxide dismutase (SOD) and catalase (CAT).

2.5.3 Liver tissue samples:

At the end of the each experimental period, rats were sacrificed by cervical decapitation. The liver specimen was quickly removed and weighted, then perfused with cold saline to exclude the blood cells and then blotted on filter paper; and stored at -20°C. Briefly, liver tissues were cut, weighed and minced into small pieces, homogenized with a glass homogenizer in 9 volume of ice-cold 0.05 mM potassium phosphate buffer (pH7.4) to make 10% homogenates. The homogenates were centrifuged at 5,000 r.p.m for 15 minutes at 4°C then the supernatant was used for the determination of superoxide dismutase (SOD), catalase (CAT) , glutathione peroxidase (GPx) and glutathione reductase (GSH).

2.6 Biochemical Analysis:

Total cholesterol (TC), triacylglycerol (TG), HDL-cholesterol (HDL-C), LDL-C, very low-density lipoprotein cholesterol (VLDL-C) were determined according to the methods of (Young et al., 2001), (Gordon et al., 1977) and (Friedewald W, et al., 1972) respectively. Moreover, HMG-CoA reductase was determined according to the method of (Rao and Ramakrishnan, 1952). Moreover, the supernatant of hepatic tissue homogenate were used for the determination of Catalase (CAT), Superoxide dismutase (SOD), Glutathione reductase (GSH) and Glutathione peroxidase (GPx) activities was estimated according to the methods of (Sinha, 1972), (Kakkar, et al., 1984), (Beutler, et al., 1963) and (Paglia and Valentine ,1967) respectively.

2.7 Statistical Analysis:

Results data were analyzed using two way analysis of variance (ANOVA) using SPSS Statistical package for social science,;ver.10.0), and the significance among the samples was compared at *P*<

0.05. Results were represented as mean ± SD.

3. RESULTS:

The obtained data table (1), (2) and (3) demonstrate that a dietary supplement of AR root powder to normal rat groups, (N+200mg AR) and (N+400 mg AR), revealed a significant decreased in serum TG, TC, LDL-C and VLDL concentration with highly significant increase in HDL-C level as compared to NC group. Moreover, Hypercholesterolemic rats supplemented with (H+200mg AR) and (H+400 mg AR) showed a highly significant decreased in serum TG, TC, LDL-C and VLDL with high significant increase in HDL-C as compared to HC group. Hepatic TC, TG showed no significant difference in normal rats administrated with (N+200mg AR) and (N+400 mg AR) as compared to NC , however, there was significant reduction in hepatic TC, TG concentration were observed in hypercholesterolemic rats supplemented with (H+200mg AR) and (H+400 mg AR). (Table 6). There was no significant change in serum HMG-CoA reductase activity in rats groups supplemented with (N+200mg AR) and (N+400 mg AR) as compared to NC, However there was a significant decrease in serum HMG-CoA reductase activity was observed in (H+200mg AR) and (H+400 mg AR) supplemented rats group when compared to HC. Table (3). Enzymatic antioxidant status (Erythrocytelysate of catalase and SOD) activities showed a significant increase in both normal and hypercholesterolemic rats groups as shown in table (4).While**,** (hepatic catalase, SOD, GSH and GPx) activities were significantly increased in both normal and hypercholesterolemic groups as presented in table (5).

4. DISCUSSION:

The lipid-lowering effects of AR root in hypercholesteremic rats demonstrated in the present investigation related primarily to an increased excretion of cholesterol, neutral sterols, bile acid and an increase in hepatic bile acid content. The phytosterol (0.79 g %) and saponin (8.83g%) contents of AR root besides polyphenols (1.69 g%) flavonoids (0.47 g%) ascorbic acid (0.76 g%) could be responsible for increased fecal sterol excretion and decreased cholesterol levels in the hypercholesteremic rats. Although the main component of the Asparagus root is a steroidal saponin, the root also contains alkaloids, flavonoids, sterols, terpenes, tannins, phenolics and mucilage. (Gupta and Tandon, 2004). Also, phytosterols have ability to compete and displace cholesterol from the intestinal bile acid micelles and decrease the cholesterol circulation, (Ikeda and Sugano, 1998), (Quilez, et al., 2003). On the other hand, saponins precipitate cholesterol from micelles and interfere with enterohepatic circulation of bile acids making it unavailable for intestinal absorption of cholesterol leading to a reduction in serum cholesterol levels (Harwood, et al., 1993, Kostenr, et al., 1989). Visavadiya and Narasimhacharya (2005) investigated the efficacy of Asparagus racemosus in reducing the cholesterol levels and as an antioxidant in hyperlipidemic rats. The study demonstrated that addition of Asparagus racemosus root powder at 5 gm% and 10 gm% level as feed supplement reduced the plasma lipid profile including serum triacyglycerol as well as VLDL. Who added that, there was no significant changes in serum TG and VLDL (Visavadiya and Narsimhacharya, 2009) also, steroid glycosides such as digitonin and tomatine bind to cholesterol to induce its precipitation in vitro (Malinow, et al., 1978) and inhibit cholesterol absorption without affecting bile acid absorption in vivo (Cayen, 1971). Many of the triterpenoid saponins interfere with micelle size, structure (Sidhu, Oakenfull, 1986), and alter bile acid absorption in addition to inhibiting

Table (1): Effect of *Asparagus racemosus* root powder on Serum total cholesterol and LDL concentrations.

Animal Groups	Cholesterol*(mg/dl)*			LDL*(mg/dl)*		
	2nd	4th	6th	2nd	4th	6th
NC	93.21±0.79	93.54±0.42	91.54±1.10	44.76±1.13	45.13±0.57	42.36±1.58
(N+200mgAR)	90.10±1.6 ^{d,e,f}	82.67 ±2.4^{d,e,f}	79.20 ±1.38^{d,e,f}	42.46±1.2^{d,e,f}	30.32±1.69^{d,e,f}	27.1±4.02^{d,e,f}
(N+400mgAR)	86.14±2.4^{d,e,}	79.71±3.7^{d,e,f}	73.14 ±1.95^{a,c,d,e,f}	36.59±2.4^{d,e,f}	24.56±2.5^{d,e,f}	19.5±2.0a^{,c,d,e,f}
HC	268.36±0.4^{a,b,c,d,e,f}	268.21 ±0.4^{a,b,c,d,e,f}	268.27 ±0.51^{a,b,c,d,e,f}	200.73±0.2^{a,b,c,d,e,f}	200.8±0.4^{a,b,c,d,e,}	201±1.18^{a,b,c,d,e,f}
(H+200mgAR)	205.82±0.3^{a,b,c,d,e,f}	202.02±1.3^{a,b,c,d,e,f}	190.41±2.4^{a,b,c,d,e,f}	143.64±0.2^{a,b,c,d,e,f}	138.8±1.2^{a,b,c,d,e,f}	128.8±2.0^{a,b,c,d,e,f}
(H+400mgAR)	171.85±0.7^{a,b,c,d,e,f}	168.22±1.3^{a,b,c,d,e,f}	153.90±1.5^{a,b,c,d,e,f}	110.2±1.4^{a,b,c,d,e,f}	105.59±2.0^{a,b,c,d,e,f}	93.9±1.7^{a,b,c,d,e,f}

Table (2): Effect of *Asparagus racemosus* root powder on Serum triacylglycerol and VLDL concentrations.

Animal Groups	Triacylglycerol *(mg/dl)*			VLDL *(mg/dl)*		
	2nd	4th	6th	2nd	4th	6th
NC	79.67±0.30	80.70±0.18	80.54±0.28	15.91±0.047	16.14±0.03	16.11±0.05
(N+200mgAR)	79.73±1.1^{c,d,e,f}	82.67 ±1.3^{d,e,f}	71.78±0.8^{d,e,f}	15.94±0.27^{d,e,f}	15.12±0.26^{d,e,f}	14.36±0.14^{d,e,f}
(N+400mgAR)	75.97±2.1^{b,d,e,f}	71.66±0.7^{d,e,f}	69.40±0.4^{a,c,d,e,f}	15.37±0.48^{d,e,f}	14.37±0.14^{d,e,f}	13.80±0.13 ^{a,c,d,e,f}
HC	242.78±1.86^{a,b,c,d,e,f}	242.51±0.9^{a,b,c,d,e,f}	242.07±0.6^{a,b,c,d,e,f}	48.50±0.41^{a,b,c,d,e,f}	48.4±0.2^{a,b,c,d,e,f}	48.40±0.17^{a,b,c,d,e,f}
(H+200mgAR)	191.00±2.1^{a,b,c,d,e,f}	182.74±1.7^{a,b,c,d,e,f}	173.00±2.1^{a,b,c,d,e,f}	38.18±0.41^{a,b,c,d,e,f}	36.5±0.31^{a,b,c,d,e,f}	34.35±0.39^{a,b,c,d,e,f}
(H+400mgAR)	174.85±2.4^{a,b,c,d,e,f}	166.03±3.2^{a,b,c,d,e,f}	157.71±3.5^{a,b,c,d,e,f}	34.88±0.47^{a,b,c,d,e,f}	33.50±0.6^{a,b,c,d,e,f}	31.50±0.63^{a,b,c,d,e,f}

Table (3): Effect of *Asparagus racemosus* root powder on Serum HDL-C and HMG-COA R concentrations.

Animal Groups	HMG-CoA Reductase			HDL *(mg/dl)*		
	2nd	4th	6th	2nd	4th	6th
NC	157.09±0.56	157.22±0.60	156.91±0.39	32.2±0.25	32.17±0.35	33.81±0.92
(N+200mgAR)	155.67±0.94^{d,e,f}	153.87±2.16^{d,e,f}	149.1±4.22^{d,e,f}	31.9±1.68^{d,e,f}	35.5±0.39^{d,e,f}	35.9±4.0^{d,e,f}
(N+400mgAR)				33.9±0.85^{d,e,f}		39.4±0.4^{a,c,d,e,f}
HC	156.92±0.90^{d,e,f}	153.00±2.94^{d,e,f}	149.1±2.28^{a,c,d,e,f}	19.2±0.2^{a,b,c,d,e,f}	37.5±0.42^{d,e,f}	18.5±0.6^{a,b,c,d,e,f}
(H+200mgAR)						27.1±0.2^{a,b,c,d,e,f}
(H+400mgAR)	385.95±0.56^{a,b,c,d,e,f}	386.18±1.34^{a,b,c,d,e,f}	386.5±0.44^{a,b,c,d,e,f}	24.2±0.44^{a,b,c,d,e,f}	18.8±0.2^{a,b,c,d,e,f}	29.0±0.1^{a,b,c,d,e,f}
	296.04±0.20^{a,b,c,d,e,f}	292.96±0.17^{a,b,c,d,e,f}	289.5±1.61^{a,b,c,d,e,f}	27.1±1.1^{a,b,c,d,e,f}	26.4±0.4^{a,b,c,d,e,f}	
	253.56±2.7^{a,b,c,d,e,f}	249.20±0.86^{a,b,c,d,e,f}	245.5±1.44^{a,b,c,d,e,f}		28.5±0.4^{a,b,c,d,e,f}	

a significant compared to negative control *b significant compared to negative control+200 mg AR*
c significant compared to negative control +400 mg AR *d significant compared to positive control*
e significant compared to positive control + 200 mg AR *f significant compared to positive control + 400 mg AR*

Table (4): Effect of *Asparagus racemosus* root powder on SOD erythrocyte cell lysate and Catalase erythrocyte cell lysate activities.

Animal Groups	SOD *(U/ml)*			Catalase *(U/L)*		
	2nd	4th	6th	2nd	4th	6th
NC	47.20±0.21	47.13±0.45	47.81±0.22	33.14±0.38	33.31±0.33	32.44±0.51
(N+200mgAR)	47.21±0.92^{d,e,f}	48.95±0.68^{d,e,f}	51.27±0.70^{d,e,f}	35.07±0.31^{d,e,f}	37.95±0.7^{d,e,f}	40.32±0.23^{d,e,f}
(N+400mgAR)	49.21±0.52^{d,e,f}	51.09±0.14^{d,e,f}	53.87±0.42^{a,c,d,e,f}	37.07±0.62^{d,e,f}	40.08±0.4^{d,e,f}	43.12±0.3^{a,b,c,d,e,f}
HC	25.89±0.95^{a,b,c,d,e,f}	28.3±0.9^{a,b,c,d,e,f}	28.50±0.97^{a,b,c,d,e,f}	13.35±0.96^{a,b,c,d,e,f}	13.90±0.2^{a,b,c,d,e,f}	13.5±0.7^{a,b,c,d,e,f}
(H+200mgAR)	36.50±0.63^{a,b,c,d,e,f}	37.8±3.5^{a,b,c,d,e,f}	41.8±0.27^{a,b,c,d,e,f}	20.20±0.53^{a,b,c,d,e,f}	22.88 ±0.2^{a,b,c,d,e,f} 23.73±0.5^{a,b,c,d,e,f}	25.2±0.5^{a,b,c,d,e,f}
(H+400mgAR)	38.06±0.90^{a,b,c,d,e,f}	40.16±0.34^{a,b,c,d,e,f}	42.90±0.20^{a,b,c,d,e,f}	22.19±0.53^{a,b,c,d,e,f}		26.2±0.7^{a,b,c,d,e,f}

Table (5): Effect of *Asparagus racemosus* root powder on hepatic glutathione reductase (GSH), Glutathione peroxidase(GPx).

Animal Groups	Glutathione peroxidase *(mg/g)*			Glutathione reductase *(mU/g)*		
	2nd	4th	6th	2nd	4th	6th
NC	20.85±0.39	21.15±0.57	21.97±0.22	2.27±0.04	2.29±0.06	2.23±0.045
(N+200mgAR)	21.41±0.75^{d,e,}f	23.03±0.50^{d,e,f}	25.19±0.32^{d,e,f}	2.43±0.05^{d,e,f}	2.75± 0.10^{d,e,f}	3.05±0.08^{d,e,f}
(N+400mgAR)	23.05±0.20^{d,e,f}	24.49±0.38^{d,e,f}	27.12±0.4^{a,c,d,e,f}	2.61±0.07^{d,e,f}	3.07±0.13^{d,e,f}	3.40±0.1^{a,b,c,d,e,f}
HC	8.86±0.6^{a,b,c,d,e,f}	9.65±0.23^{a,b,c,d,e,f}	9.93±0.21^{a,b,c,d,e,f}	1.02±0.03^{a,b,c,d,e,f}	1.01±0.1^{a,b,c,d,e,f}	1.±0.03^{a,b,c,d,e,f}
(H+200mgAR)	13.92±0.5^{a,b,c,d,e,f}	15.29±0.4^{a,b,c,d,e,f}	17.08±0.34^{a,b,c,d,e,f}	1.23±0.03^{a,b,c,d,e,f}	1.34±0.04^{a,b,c,d,e,f}	1.6±0.016^{a,b,c,d,e,f}
(H+400mgAR)	14.86±0.6^{a,b,c,d,e,f}	16.94±0.3^{a,b,c,d,e,f}	18.87±0.36^{a,b,c,d,e,f}	1.34±0.04^{a,b,c,d,e,f}	1.50±0.04^{a,b,c,d,e,f}	1.77±0.03^{a,b,c,d,e,f}

Table (6): Effect of *Asparagus racemosus* root powder on hepatic cholesterol and hepatic triacylglycerol.

Animal Groups	Hepatic total Cholesterol *(mg/g)*			Hepatic triacylglycerol *(mg/g)*		
	2nd	4th	6th	2nd	4th	6th
NC	0.53±0.008	0.52±0.007	0.53±0.01	0.758±0.008	0.755±0.003	0.745±0.004
(N+200mgAR)	0.51±0.009^{d,e,f}	0.495±0.009^{d,e,f}	0.42±0.016^{d,e,f}	0.71±0.014^{d,e,f}	0.69±0.013^{d,e,f}	0.65±0.017^{d,e,f}
(N+400mgAR)	0.49±0.006^{d,e,f}	0.457±0.018^{d,e,f}	0.39±0.016^{a,c,d,e,f}	0.70±0.008^{d,e,f}	0.67±0.02^{d,e,f}	0.61±0.02^{a,c,d,e,f}
HC	15.54±0.35^{a,b,c,d,e,f}	15.55±0.21^{a,b,c,d,e,f}	15.84±0.18^{a,b,c,d,e,f}	6.94±0.051^{a,b,c,d,e,f}	6.9±0.04^{a,b,c,d,e,f}	6.9±0.01^{a,b,c,d,e,f}
(H+200mgAR)	12.43±0.3^{a,b,c,d,e,f}	11.96±0.24^{a,b,c,d,e,f}	10.99±0.19^{a,b,c,d,e,f}	6.49±0.065^{a,b,c,d,e,f}	6.18±0.1^{a,b,c,d,e,f}	5.8±0.17^{a,b,c,d,e,f}
(H+400mgAR)	10.14±0.233^{a,b,c,d,e,f}	9.15±0.50^{a,b,c,d,e,f}	8.46±0.27^{a,b,c,d,e,f}	6.194±0.083^{a,b,c,d,e,f}	5.82±0.2^{a,b,c,d,e,f}	5.41±0.2^{a,b,c,d,e,f}

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c significant compared to negative control +400 mg AR *d significant compared to positive control*
e significant compared to positive control + 200 mg AR *f significant compared to positive control + 400 mg AR*

cholesterol absorption. Saponins reported to lower TG by inhibiting pancreatic lipase activity (Han, et al., 2002) and the subsequent decline in vLDL levels could be directly correlated to a decline in TG levels (Howell, et al., 1998). The enzyme HMG-CoA reductase catalysis the rate-limiting step in cholesterol biosynthesis in the tissues and its activity closely correlates with cholesterogenesis in the tissues. Defective regulation of HMG-CoA reductase has been demonstrated in hypercholesteremia. The increased activity of the enzyme in the liver of rats fed with high fat diet corresponds with increased cholesterogensis, as indicated by the higher incorporation of serum total cholesterol and LDL cholesterol observed in current study. The hypercholesterolemic animals treated with AR root powder (H+200mg AR) and (H+400 mg AR) had shown decreased activity of enzymes as evidenced by the reduction in serum TC and LDL. By inhibiting HMG-CoA reductase, saponins reduce the hepatocyte cholesterol content and increase expression of low-density lipoprotein (LDL) receptors, responsible for LDL cholesterol uptake via receptor-mediated endocytosis. Additionally, a second mechanism of LDL reduction may relate to LDL and very-low-density lipoprotein (vLDL) interactions. However, increases in HMG-CoA reductase synthesis shortly after saponins therapy restore cellular VLDL levels, and the ultimate effect of reductase inhibition is enhanced LDL receptor expression and lower plasma LDL in the setting of normal cellular cholesterol content. (Kostner, 1989). In addition, the normocholesterolemic rats (NC) under AR treatment, exhibited significant variations in serum and hepatic cholesterol, Triacylglycerol, HDL, LDL and VLDL. It is well documented that while a low level of HDL is indicative of high risk for cardiovascular disease, an increase in HDL level could potentially contribute to antiatherogenicity, inhibit LDL oxidation and protect endothelial cells from the cytotoxic effects of oxidized LDL (Howell, et al., 1998.Wilson et al., 1988). In the present study, a significant increase in plasma HDL levels with a concurrent decline in serum total cholesterol level of (H+200mg AR) and (H+400 mg AR) clearly indicate the beneficial role of AR root administration to hypercholesteremic animals. Reduced bioavailability of antioxidants causes oxidative damage to cells and tissues. An imbalance between prooxidant and antioxidant levels in the body gives rise to cellular oxidative stress that plays an important role in the genesis of cardiovascular diseases (Dhalla, et al., 2000). An increased oxidized LDL levels leading to atherosclerotic plaque formation (Tiwar, 1999). Several studies suggest that naturally occurring antioxidants such as polyphenols, flavonoids and vitamin C in diet may play a role as antiatherogenic agents (Vinson, et al., 1998, Tripathi, 2005). Both these are also known to stimulate catalase and SOD gene transcription and decrease malondialdehyde concentration (Toyokuni, et al., 2003, Ranaivo, et al. 2004). Additionally, Asparagus root extract possesses in vivo antioxidant activity in rats although the principles responsible for this antioxidant activity were not reported (Bhatnagar, et al 2005). Presently noted higher levels of hepatic catalase and SOD activities in (H+200mg AR) and (H+400 mg AR) groups indicate the possible role of polyphenols and flavonoids of AR root, in modulating the expression of both catalase and SOD activities. Taken together, these observations indicate that AR root powder administration to HC animals can reduce lipid levels in both blood and liver, increase bile acid production and modulate antioxidant enzyme activities.

5. CONCLUSION &RECOMMENDATION:

The present study demonstrates that the addition of *Asparagus racemosus* root

powder at 200mg/kg/B.W and 400mg/Kg/B.W levels as feed supplement reduces the Serum and hepatic lipid and improves the enzymatic antioxidants status. Therefore, it can be conclude that AR root administration could ameliorate hypercholesterolemic and antioxidants status in hypercholesterolemic conditions.

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الدور الكيميائي الحيوي للأسبرجس في تحسين أيض الكوليسترول وحالة مضادات الأكسدة في الفئران التي تعاني من ارتفاع الكوليسترول

ياقوت عبدالفتاح السنوسي[1]،يوسف محمد علي[2]،أشرف وصفي[3]، محمد صابر أبو العلا

[1]قسم الكيمياء الحيويه-كليه الطب البيطري – جامعة بنها. [2]قسم الكيمياء الحيويه -كليه الطب البيطري – جامعة الزقازيق. [3]قسم الكيمياء -كليه العلوم – جامعة بنها

الملخص العربى

يعتبر ارتفاع الكوليسترول في الدم من أكبر المخاطر التي تؤدي لحدوث تصلب الشرايين وأمراض القلب وهناك العديد من النباتات التي تحتوي على مكونات علاجية مثل: الألياف والاستيرول والسابونين والبولي فينول والفلافينويد الى آخره من المواد التي يتم فحص قدرتها على خفض الدهون ومقاومة تصلب الشرايين ورفع كفاءة مضادات الأكسدة. من هذه النباتات بذور نبات الأسبرجس راسيموسس المستخدمة بطريقه منتشرة في الطب الهندي القديم لاحتوائها على مادة الاستيرويدال سابونين. الهدف من هذه الدراسة هو معرفة مقدرة جذور الاسبرجس على خفض نسبة الكوليسترول وتحسين كفاءة مضادات الأكسدة في الفئران المصابة بارتفاع الكوليسترول والغير مصابه أيضا. وقد تم رفع نسبة الكوليسترول في الفئران بواسطة إضافة 0.75% كوليسترول 1.50% أملاح الصفراء للغذاء المعد لهذه التجربة لمدة شهرين وتم استخدام مسحوق الجذور المجففة من نبات الأسبرجس كمكمل غذائي للفئران بجرعات: 200مجم/كجم/وزن و400مجم/كجم/وزن للفئران المصابة بارتفاع الكوليسترول في الدم والغير مصابة أيضا. تم تقدير معدل الدهون في مصل الدم والكبد وقياس نشاط انزيم HMG-Co A R في مصل الدم وقياس نشاط إنزيمات السوبر أوكسيد ديسميوتيز والكتاليزوالجلوتاثيون بيروكسيدازوالجلوتاثيون ريداكتيز باستخدام الطرق القياسية المحددة لذلك. وقد نتج عن ذلك انخفاض ملحوظ في نسب الدهون في مصل الدم والكبد وأعطى أيضا إنخفاض ملحوظ لنشاط إنزيم HMG-Co A R مع زيادة ملحوظه في نشاط مضادات الأكسدة في المجموعتين. ومن هذه الدراسة يمكن أن نستخلص ان المحتوى العلاجي الموجود في نبات الأسبرجس مثل الفيتو إستيرول السابونين والبولي فينول والفلافينويد وفيتامين سي مسؤولون عن زيادة إنتاج املاح الصفراء وإخراج الكوليسترول الزائد من الدم وزيادة نشاط مضادات الأكسدة في حالات زيادة الكوليسترول في الدم.

(مجلة بنها للعلوم الطبية البيطرية: عدد 26(2):40- 51, يونيو 2014)