

*Full Length Research Paper*

# Protective potential of *Avena sativa* seed mucilaginous extract against hyperlipidemia indicated by improved biomarkers and histopathology

Ibtsam M. Gheith<sup>1,2</sup> and Abubakr M. El-Mahmoudy<sup>3\*</sup>

<sup>1</sup>Department of Clinical Laboratory Sciences, Faculty of Applied Medical Sciences, Taibah University, 344 Medinah, Saudi Arabia.

<sup>2</sup>Department of Biotechnology, Animal Health Research Institute, 11843 Dokki, Egypt.

<sup>3</sup>Department of Pharmacology, Faculty of Veterinary, Medicine, Benha University 13736 Moshtohor, Egypt.

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**Hyperlipidemia is one of the major health concerns worldwide. The present study aimed at utilizing clinicopathological tools to investigate the possible improving effect of *Avena sativa* mucilaginous extract (ASE) on lipid metabolic and liver function profiles in albino rats. The rats were rendered hyperlipidemic by 6-week supplementation of high-fat diet *ad libitum*. The rats were grouped into seven groups; with different treatment applications. Rats of group-I received normal diet and served as normal control; those of group-II were kept on high-fat (cholesterol 1% + coconut oil 2%) diet for 6 weeks and served as diseased control. Rats in group-III were kept on high-fat diet and received ezetimibe (1 mg/Kg B. Wt, orally, daily) and served as standard. Those in group-IV and V were kept on high-fat diet and received ASE at doses of 25 and 50 mg/Kg B. Wt., orally, daily (small and high doses, SD and HD, respectively) and served as treated-SD and treated-HD, respectively. While the last two groups (VI and VII) were kept on normal diet and received SD and HD of ASE. Blood samples for serum were taken for clinicochemical analysis on days 28 (4 weeks) and 42 (6 weeks) of the experiment and tissue specimens were taken for histopathology. ASE significantly ( $P<0.05$ ) decreased the elevated serum lipid profile parameters, including total lipids, tri-acylglycerols (TAGs), cholesterol, LDL-C, VLDL-C, but significantly ( $P<0.05$ ) normalized the serum HDL-C concentrations of rats kept on high-fat diet. Administration of *A. sativa* extract significantly decreased elevated serum liver enzyme activities in samples taken from animals kept on high-fat diet compared to the diseased untreated ones. Observations from histopathological examination were parallel and explanatory to clinicochemical analytical results. These data may suggest that the aqueous mucilaginous extract of *A. sativa* seed has a good health impact in cases associated with hyperlipidemia indicated by clinical pathology.**

**Key words:** *Avena sativa*, antihyperlipidemic, clinical pathology, liver function, phytotherapy, phytomedicine.

## INTRODUCTION

Among metabolic disorders, dyslipidemia, particularly hypercholesterolemia is considered as a major contributor in cardiovascular disease, including athero-sclerosis and atherosclerosis- associated conditions as coronary heart disease, ischemic cerebrovascular disease and peripheral

vascular disease (Nelson, 2013). The best target for therapy in these conditions is to normalize blood and/or tissue cholesterol and lipid values. The conventional anti-hyperlipidemic chemical drugs are, usually, associated with some common adverse effects such as malaise,

gastric irritation, nausea/vomiting/diarrhea, hyperuricemia, muscle aches, red dry skin, and altered liver function; Kumar et al., 2008). Natural products with health improving impacts constitute, therefore, an interesting research area in minds of concerned personnel, including patients, physicians and researchers based on their safety, efficacy and easy access (Ververidis et al., 2007).

*Avena sativa* (Oat; Kingdom: *Plantae*; Family: *Poaceae*) and its constituents were reported to possess variable beneficial health activities like antimicrobial (Maizel et al., 1964), antiparkinsonian (Zhou and Panchuk-Voloshina, 1997), topical anti-inflammatory (Boyer et al., 1998; Capasso, 2003). Also included are wound healing (Aries et al., 1999), antidiabetic (Jenkins et al., 2002), antioxidant (Bratt et al., 2003; Xu et al., 2009), anti-atherogenic (Liu et al., 2004), vasodilating (Nie et al., 2006), anti-asthmatic (Tabak et al., 2006), immunomodulatory (Ramakers et al., 2007; Dhillon and Bhatia, 2008), and anticancer (Anderson et al., 2009) activities.

Although effect of *Avena sativa* was tried on lipid profile in earlier studies (Karmally et al., 2005; Robitaille et al., 2005), yet, most of them used it as cereal as a whole or a part of the diet; and at least to our information, no studies have been performed using it as mucilaginous aqueous extract with adjusted doses. Moreover, Kerckhoffs et al. (2003) reported that the cholesterol lowering effect of  $\beta$ -glucan from oat bran in mildly hyper-cholesterolemic subjects may decrease when  $\beta$ -glucan is incorporated into bread and cookies. Therefore, the present study was designed to assess, using clinicopathological tools, the hyperlipidemia improving profile of *A. sativa* mucilaginous aqueous extract as a natural remedy to the control of dyslipidemia in rats prepared as hyperlipidemic model by high-fat diet supplementation.

## MATERIALS AND METHODS

### A. *sativa* mucilaginous extract

The extract was obtained and standardized according to the classical methodological stepwise described by Harborne (1973) with minor modifications. The green seeds with aerial parts of *A. sativa* (Figure 1) were collected from the local environment (Qaliubeya Governorate, 2016) and identified by a plant specialist. Plant parts were refluxed in running tap water and then with bi-distilled water, shade dried at room temperature and chopped. Extract was prepared by macerating a weighed amount of the chopped plant parts (200 g) in a known volume (1.5 L) of water/ethanol (70:30, v/v). Maceration continued for 48 hours in refrigerator with occasional shaking. The hydro-ethanolic extract was then strained through muslin mesh and then concentrated using a shaking water bath at 56°C in a wide-mouthed containers and the mucilage obtained (yield) was then weighed and re-

constituted freshly every day by dissolving in measured amount of bi-distilled water. Two stock solutions were prepared, 5 and 10 mg/ml. *Avena sativa* extract (ASE) was administered to rats at dosage rate of 25 (small dose; SD) and 50 (high dose; HD) mg/Kg B. Wt daily adjusted so that each rat (weighing 200 g) receives 1 ml of ASE orally using a rat gastric tube to the corresponding groups as explained below.

### Ezetimibe

EZE, a standard inhibitor of cholesterol absorption, (Lipka, 2003) used in the present study was kindly gifted by SIGMA pharmaceuticals, Quesna Industrial Zone, Egypt. It was obtained as a pure powder. EZE was dissolved in 20% ethanol; where 10 mg of EZE were dissolved firstly in 10 ml absolute alcohol, and then the alcoholic solution of EZE was completed up to 50 ml by bi-distilled water. Each rat within the target group received 1 ml of the prepared solution which is equivalent to a dosage rate of 1 mg/Kg B. Wt., orally, once daily (Patel, 2004).

### Experimental animals and protocol

Forty-two white male rats, of age 6-8 weeks and of average weight of 200 g were used in a parallel study design. Rats were divided in separate cages and gained access to clean water and diets *ad libitum* at room temperature. A week later (for acclimatization), rats were subjected to various experimental treatments, as follows:

**Group-I:** Rats kept on normal balanced diet and administered no drugs but their vehicles; served as normal control.

**Group-II:** Rats kept on high-fat diet and administered no drugs but their vehicles; served as diseased control.

**Group-III:** Rats kept on high-fat diet and administered EZE at a dose rate of 1 mg/Kg B. Wt.; used as a standard anti-hyperlipidemic.

**Group-IV:** Rats kept on high-fat diet and administered ASE at a dose of 25 mg/Kg.

**Group-V:** Rats kept on high-fat diet and administered ASE at a dose of 50 mg/Kg.

**Group-VI:** Rats kept on normal balanced diet and administered ASE at a dose of 25 mg/Kg.

**Group-VII:** Rats kept on normal balanced diet and administered ASE at a dose of 50 mg/Kg.

Treatments were conducted simultaneously from the first day of the experiment and continued for 6 weeks with continuous observation. All procedures were ethical to animals, and were performed with merciful and humane manner under light ether anesthesia, and adhered to principles published by International Council for Laboratory Animal Science (ICLAS) and those of Benha University Animal Care and Use Committee.

### Sampling

Blood for serum was collected on the 28th and the 42th days from the start of the experiment. Blood was harvested into plain sampling tubes from the ocular medial canthus venous plexus using heparinized capillary tubes. The harvested blood was left to

\*Corresponding author. E-mail: a.elmahmoudy@fvfm.bu.edu.eg.



**Figure 1.** Green seeds and some aerial parts of *Avena sativa* plant used for extraction.

coagulate at 37°C for an hour; and then the clot was allowed to shrink by refrigeration for further an hour. Centrifugation at 1000 × g for 10 min were performed to separate clean sera, which were collected into Eppendorf's tubes using Pasteur pipettes. The obtained samples were at -50°C until analysis of the following clinicochemical parameters: Total lipids (TL), total cholesterol (TC), tri-aclyglycerols (TAGs), high-density lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C), very low-density lipoprotein-cholesterol (VLDL-C), aspartate amino transferase (AST), and alanine amino transferase (ALT). On the last day of the experiment, and after blood collection, animals were sacrificed by slaughtering using sharp scalpels under ether anesthesia, and tissue specimens from the liver were taken into 10% formalin solution for histopathological examination.

#### Clinicochemical analysis

The serum total lipids were determined according to the method described by Chabrol and Castellano (1961) using a kit supplied by Spinreact® (Sant Esteve De Bas, Spain); total cholesterol was determined enzymatically according to the method described by Meattini et al. (1978) using a kit supplied by Spinreact®; HDL-L was determined according to the precipitation method described by Friedewald et al. (1972) using a kit supplied by Spectrum® (Obour city, Egypt); TAGs were measured enzymatically depending on the method explained after Young et al. (1975) using a kit Spinreact®. LDL-C and VLDL-C values were calculated using the formulae described by Friedewald et al. (1972) and Bauer (1982), respectively. Serum AST and ALT were quantitatively determined according to the method described by Murray (1984) using kits supplied by Diamond® (Cairo, Egypt). All laboratory steps were according to the instructions supplied by the kit manufacturers.

#### Histopathological examination

Liver specimens picked out from dissected rats in all groups were immediately placed in 10% formalin solution; processed for sectioning, staining and microscopical examining as described by Bancroft and Gamble (2008). Samples were allowed to fix for a 24

h period. The fixed samples were then gently washed under slowly running water for over-night. The clean fixed samples were then allowed to dehydrate in a series of increased-concentrations of ethanol starting in 70% and finalizing in absolute alcohol. The fixed, clean, dehydrated samples were placed in xylol for 3 h to clear and then placed in melted paraffin wax tissue boxes. The wax containing tissue specimens was left to solidify and then sections of 4 - 6 μm thickness were obtained using a rotary microtome. Staining procedure started with removal of wax from the microsections by two changes in ethanol (absolute; 5 minutes each). Ethanol was washed away with water. Sections were stained with Haematoxylin and Eosin (HandE) for 10 minutes, and then the extra stains were gently flushed under running water for 15 minutes. The stained microsections were dehydrated by alcohol series as mentioned above, then allowed to clear in xylol and finally covered with Dibutylphthalate Polystyrene Xylene (DBX). The prepared microsection slides were examined microscopically and interpreted by a specialist.

#### Data analysis and presentation

Data were presented as mean ± S.E of 6 observations. The obtained data were statistically analyzed using repeated-measures ANOVA at two timing points (4 and 6 weeks) with Tukey's post-hoc to determine differences between groups at probability level of 5%. All statistical procedure was done by SPSS software, version 20. The sample size for each group was adjusted according to principles stated in literature, where value of  $\alpha = 1.96$ ,  $\beta = 0.842$ , a difference of 15 in each parameter is proposed between the groups as significant (Mean1- Mean2) and be detected with 80% beta power at a significance level alpha of 0.05 (Das et al., 2016).

## RESULTS

### Effect of ASE on serum lipid profile:

As shown in Tables 1, 2, 3, 5, 6, there were significant

**Table 1.** Serum total lipids concentration (mg/dL) in rats under different treatments, Normal Control (I), Hyperlipidemic (II), Hyperlipidemic with Ezetimibe 1 mg/Kg B. Wt., orally (III), Hyperlipidemic with ASE 25 and 50 mg ASE/Kg B. Wt. orally (IV and V), and Normal with ASE 25 and 50 mg ASE/Kg B. Wt. orally (VI and VII) daily for 42 days ( $\bar{X} \pm S.E$ ; n=6).

Time/Group	I	II	III	IV	V	VI	VII
Day 28	355.20±12.55	650.67 <sup>a</sup> ±22.13	410.04 <sup>b</sup> ±15.61	457.33 <sup>b</sup> ±23.33	421.33 <sup>b</sup> ±21.82	351.20 <sup>b</sup> ±17.65	335.20 <sup>b</sup> ±16.52
Day 42	362.15±19.25	714.61 <sup>a</sup> ±25.33	430.25 <sup>b</sup> ±25.33	475.66 <sup>b</sup> ±24.84	443.00 <sup>b</sup> ±22.67	345.15 <sup>b</sup> ±15.85	332.15 <sup>b</sup> ±16.66

Superscripts <sup>a</sup> and <sup>b</sup> mean significantly ( $P < 0.05$ ) different from corresponding Control (I) and Diseased (II), respectively.

increases in serum total lipids, cholesterol, tri-acylglycerols, LDL-C, VLDL-C values in samples obtained from rats kept on high-fat diet, compared to those obtained from rats on balanced diet. While administration of ASE to control rats revealed insignificant alterations in these parameters throughout the experimental period, yet, its administration significantly ( $P < 0.05$ ) decreased their serum levels in samples of rats kept on high-fat diet in a dose-dependent manner. Nevertheless, as presented in Table 4, there was a significant ( $P < 0.05$ ) decrease in HDL-C values of samples of rats kept on high-fat diet. Such decrease was significantly ( $P < 0.05$ ) not only improved but also increased upon administration of ASE. Again, there was no significant changes in rats kept on basal diet.

#### Effect of ASE on Liver function profile

Data of the present study (Tables 7 and 8) demonstrate a significant elevation in serum ALT and AST activities in samples taken from rats kept on high-fat diet throughout the experiment, compared to those in samples taken from the normal control rats which were kept on balanced diet. Although administration of ASE to normal rats revealed insignificant alterations in liver enzyme activities throughout the experimental period; yet, it significantly ( $P < 0.05$ ) decreased their elevated serum activities in animals kept on high-fat diet compared to the diseased ones, upon its administration.

#### Effect of ASE on Liver structure

Data of the present study showed that there were no changes in liver samples picked out from rats of normal control group. Yet, subjecting experimental rats to high-fat diet (diseased-control group) resulted in some hepatic degenerative changes as hydropic and vacuolar degenerations and peri-portal fatty change of hepatocytes, as well as congestion of hepatic blood vessels. The severity and development of such changes were inhibited largely, in liver specimens picked out from ASE-treated groups and EZE-treated rats, as well (Figure 2a, b, c and d).

## DISCUSSION

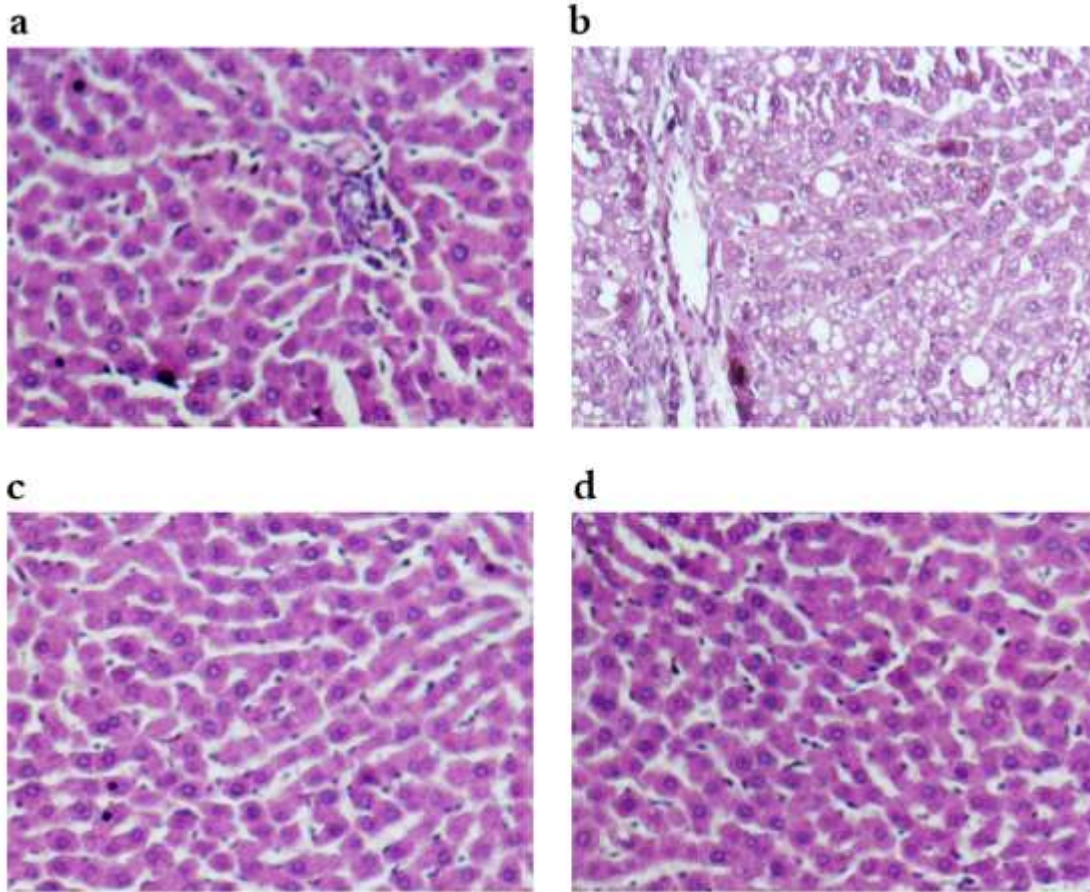
It is well established that alteration in lipid metabolic profile, especially long standing hyperlipidemia is a direct cause to various disease conditions including atherosclerosis, ischemic heart disease (Ross and Harker, 1976). This fact is later supported by Ross (1986) and Crowther (2005). Findings of the current experiment show that hyperlipidemia, induced by 42-day supplementation of high-fat (cholesterol and coconut oil 1 and 2% wt/wt, respectively) diet caused, as expected, marked alterations in the measured lipid parameters (Tables 1 to 6) of rat groups kept on such diet. In addition, the established dyslipidemia was associated with abnormally elevated liver function markers (AST and ALT; Tables 7 and 8), together with considerable hepatic histopathological changes (Figure 2). These rats were applied, in the present study, as a model for hyperlipidemia to evaluate the possible anti-hyperlipidemic potential of a mucilage extract prepared from *Avena sativa* green seeds and leaves.

Data presented in this study (Table 1) show a significant ( $P < 0.05$ ) increase in serum total lipid value of rats received high-fat diet throughout the 42 days of the experiment, compared to the normal control rats fed on a balanced diet. Similar findings were reported previously in rats (Csont et al., 2002; El-Mahmoudy et al., 2013; El-Mahmoudy et al., 2014) and rabbits (Diaz et al., 2000).

Administration of ASE significantly decreased serum total lipid concentration in animals received high-fat diet compared to the diseased untreated ones. The decrease in serum total lipid concentration in ASE-treated animals is logic after recording the improved serum values of TAGs, TC, LDL-C and VLDL-C that were observed simultaneously in this study. Lowering serum lipid profile recorded in the present study may be parallel with that reported by (Czerwiński et al., 2004) who found that oat and amaranth meals positively affect plasma lipid profile in rats fed cholesterol-containing diets. The authors attributed such effect to the contents of the bioactive components and the antioxidant activities of the studied plant samples.

Findings presented in the current study (Table 2) show a significant ( $P < 0.05$ ) elevation in serum TC concentration in samples from rats kept on high-fat diet throughout the 42-day experimental period, compared to





**Figure 2.** Histopathological picture of a liver sections from normal (a), diseased (b, showing fatty change and vacuolar degeneration), EZE-treated (c, almost normalized) and ASE-treated (d, almost normalized) rats.

that of the normal control animals. This finding is in accordance with that achieved by (Diaz et al., 2000) who found that rabbits kept on atherogenic diet exhibited marked elevation in TC in plasma.

Elevated serum cholesterol level is expected after high-fat diet supplementation and the inhibited clearing rate of LDL-C from the blood due to some defect in LDL receptors associated with elevated plasma total cholesterol values above normal levels (Zulet et al., 1999). Although administration of ASE to control rats revealed insignificant alteration in serum total cholesterol value throughout the experiment; yet, it significantly ( $P < 0.05$ ) decreased serum cholesterol concentration in animals received high-fat diet compared to the diseased untreated ones. The hypo-cholesterolemic effect of ASE may be explained based on decreasing cholesterol intestinal absorption with less dietary cholesterol is delivered to the pool of cholesterol to the liver; and/or greater clearance of LDL-cholesterol particles by the liver.

Findings presented in the current study (Table 3) show a significant ( $P < 0.05$ ) increase in TAGs in samples from

animals kept on high-fat diet if compared with those of the normal control. Such significant elevation in serum TAGs may be explained on the basis of the diminished activity of lipase -insulin-dependent enzyme- contributing in TAGs clearance from blood by enhancing their hydrolysis to glycerol and free fatty acids (Yost et al., 1995). Daily oral administration of ASE significantly decreased serum TAGs concentration in animals received high-fat diet compared to that of diseased untreated ones. This finding may be parallel to those of Maier et al. (2000) and Czerwiński et al. (2004) in women and rats, respectively. The significant decrease in plasma TAGs has been explained previously by Bennani-Kabchi et al. (2000) who related that decrease to the higher rate of lipolysis mediated by enhanced plasma lipase activity. Nevertheless, more earlier, Griffin et al. (1982) stated that the lower level plasma TAGs might also reflect a lower rate of lipogenesis in the liver.

Tables 4, 5 and 6 present significant increases in serum LDL-C and VLDL-C and a significant decrease in HDL-C in rats kept on high-fat diet, compared to the corresponding normal control ones. The elevated serum

**Table 2.** Serum cholesterol concentration (mg/dL) in rats under different treatments, Normal Control (I), Hyperlipidemic (II), Hyperlipidemic with Ezetimibe 1 mg/Kg B. Wt., orally (III), Hyperlipidemic with ASE 25 and 50 mg ASE/Kg B. Wt. orally (IV and V), and Normal with ASE 25 and 50 mg ASE/Kg B. Wt. orally (VI and VII) daily for 42 days ( $\bar{X} \pm S.E$ ; n=6).

Time/Group	I	II	III	IV	V	VI	VII
Day 28	73.17±6.20	151.18 <sup>a</sup> ±8.06	93.33 <sup>b</sup> ±8.40	107.33 <sup>b</sup> ±7.66	98.22 <sup>b</sup> ±7.85	70.17 <sup>b</sup> ±6.10	68.37 <sup>b</sup> ±7.20
Day 42	75.35±7.88	198.35 <sup>a</sup> ±14.69	117.34 <sup>b</sup> ±10.35	138.21 <sup>b</sup> ±9.78	125.22 <sup>b</sup> ±6.80	68.35 <sup>b</sup> ±6.78	65.55 <sup>b</sup> ±6.89

Superscripts <sup>a</sup> and <sup>b</sup> mean significantly ( $P<0.05$ ) different from corresponding Control (I) and Diseased (II), respectively.

**Table 3.** Serum Triacylglycerols concentration (mg/dL) in rats under different treatments, Normal Control (I), Hyperlipidemic (II), Hyperlipidemic with Ezetimibe 1 mg/Kg B. Wt., orally (III), Hyperlipidemic with ASE 25 and 50 mg ASE/Kg B. Wt. orally (IV and V), and Normal with ASE 25 and 50 mg ASE/Kg B. Wt. orally (VI and VII) daily for 42 days ( $\bar{X} \pm S.E$ ; n=6).

Time/Group	I	II	III	IV	V	VI	VII
Day 28	92.75±8.94	186.35 <sup>a</sup> ±17.33	116.66 <sup>b</sup> ±24.53	140.55 <sup>b</sup> ±14.70	125.98 <sup>b</sup> ±10.06	90.75 <sup>b</sup> ±8.96	85.75 <sup>b</sup> ±7.94
Day 42	98.2±11.33	195.66 <sup>a</sup> ±19.24	124.16 <sup>b</sup> ±10.48	147.33 <sup>b</sup> ±14.24	134.12 <sup>b</sup> ±11.21	93.2 <sup>b</sup> ±10.03	84.2 <sup>b</sup> ±8.33

Superscripts <sup>a</sup> and <sup>b</sup> mean significantly ( $P<0.05$ ) different from corresponding Control (I) and Diseased (II), respectively.

**Table 4.** Serum HDL-C concentration (mg/dL) in rats under different treatments, Normal Control (I), Hyperlipidemic (II), Hyperlipidemic with Ezetimibe 1 mg/Kg B. Wt., orally (III), Hyperlipidemic with ASE 25 and 50 mg ASE/Kg B. Wt. orally (IV and V), and Normal with ASE 25 and 50 mg ASE/Kg B. Wt. orally (VI and VII) daily for 42 days ( $\bar{X} \pm S.E$ ; n=6).

Time/Group	I	II	III	IV	V	VI	VII
Day 28	38.85±3.35	21.72 <sup>a</sup> ±1.67	30.46 <sup>b</sup> ±1.49	23.89±3.48	25.53 <sup>b</sup> ±1.87	39.85 <sup>b</sup> ±3.35	41.85 <sup>b</sup> ±3.35
Day 42	41.73±3.81	16.53 <sup>a</sup> ±1.33	31.62 <sup>b</sup> ±1.80	25.16±3.14	27.97 <sup>b</sup> ±2.49	41.73 <sup>b</sup> ±3.71	43.73 <sup>b</sup> ±3.66

Superscripts <sup>a</sup> and <sup>b</sup> mean significantly ( $P<0.05$ ) different from corresponding Control (I) and Diseased (II), respectively.

**Table 5.** Serum LDL-C concentration (mg/dL) in rats under different treatments, Normal Control (I), Hyperlipidemic (II), Hyperlipidemic with Ezetimibe 1 mg/Kg B. Wt., orally (III), Hyperlipidemic with ASE 25 and 50 mg ASE/Kg B. Wt. orally (IV and V), and Normal with ASE 25 and 50 mg ASE/Kg B. Wt. orally (VI and VII) daily for 42 days ( $\bar{X} \pm S.E$ ; n=6).

Time/Group	I	II	III	IV	V	VI	VII
Day 28	15.66±1.66	63.33 <sup>a</sup> ±3.88	31.66 <sup>b</sup> ±7.33	45.79 <sup>b</sup> ±4.85	39.01 <sup>b</sup> ±4.00	14.67 <sup>b</sup> ±1.67	13.63 <sup>b</sup> ±1.67
Day 42	16.02±1.33	75.12 <sup>a</sup> ±8.82	35.91 <sup>b</sup> ±9.05	48.10 <sup>b</sup> ±4.54	42.89 <sup>b</sup> ±4.65	15.32 <sup>b</sup> ±1.33	14.32 <sup>b</sup> ±1.33

Superscripts <sup>a</sup> and <sup>b</sup> mean significantly ( $P<0.05$ ) different from corresponding Control (I) and Diseased (II), respectively.

LDL-C and VLDL-C seemed to occur upon over-production of LDL beyond the capacity of LDL-receptors expressed on hepatocyte cell membranes. In addition, the dietary fat and cholesterol may alter the serum lipoprotein pattern and increases the cholesterol content in VLDL (Mahley and Holcombe, 1977). ASE administration revealed significant decreases in serum LDL-C and VLDL-C concentrations with a significant increase in HDL-C when compared to those of the rats received high-fat diet. Such improving effect of ASE may be attributed to the decreased absorption of fats supplemented to rats and/or increased peripheral and hepatic breakdown of cholesterol esters from VLDL-C and LDL-C. The compositional change of HDL-C might

be speculated due to a probable activation of Lecithin-cholesterol acyltransferase (LCAT) that is stimulated firstly by exogenous cholesterol.

Tables 7 and 8 present significant ( $P<0.05$ ) elevations in ALT and AST activities in samples taken from rats kept on high-fat diet, if compared with those of the control. ASE administration significantly protected against elevations of these hepatic function biomarkers compared to the diseased untreated rats. This protecting effect may be explained on the bases of improved cholesterol hepatic metabolism as well as inhibiting its intestinal cholesterol absorption. Histopathological findings come supportive to the biochemical analysis, where the fatty degenerative changes observed in liver

**Table 6.** Serum VLDL-C concentration (mg/dL) in rats under different treatments, Normal Control (I), Hyperlipidemic (II), Hyperlipidemic with Ezetimibe 1 mg/Kg B. Wt., orally (III), Hyperlipidemic with ASE 25 and 50 mg ASE/Kg B. Wt. orally (IV and V), and Normal with ASE 25 and 50 mg ASE/Kg B. Wt. orally (VI and VII) daily for 42 days ( $\bar{X} \pm S.E$ ; n=6).

Time/Group	I	II	III	IV	V	VI	VII
Day 28	26.6±1.70	39.12 <sup>a</sup> ±1.43	31.83 <sup>b</sup> ±1.74	35.99 <sup>b</sup> ±1.91	33.33 <sup>b</sup> ±1.28	25.33 <sup>b</sup> ±1.70	22.42 <sup>b</sup> ±1.70
Day 42	25.66±2.77	46.24 <sup>a</sup> ±2.20	33.1 <sup>b</sup> ±1.64	39.12 <sup>b</sup> ±1.67	36.31 <sup>b</sup> ±1.58	24.67 <sup>b</sup> ±1.33	21.67 <sup>b</sup> ±1.77

Superscripts <sup>a</sup> and <sup>b</sup> mean significantly ( $P<0.05$ ) different from corresponding Control (I) and Diseased (II), respectively.

**Table 7.** Serum ALT concentration (U/L) in rats under different treatments, Normal Control (I), Hyperlipidemic (II), Hyperlipidemic with Ezetimibe 1 mg/Kg B. Wt., orally (III), Hyperlipidemic with ASE 25 and 50 mg ASE/Kg B. Wt. orally (IV and V), and Normal with ASE 25 and 50 mg ASE/Kg B. Wt. orally (VI and VII) daily for 42 days ( $\bar{X} \pm S.E$ ; n=6).

Time/Group	I	II	III	IV	V	VI	VII
Day 28	24.32±3.19	65.12 <sup>a</sup> ±1.25	29.53 <sup>b</sup> ±3.04	36.78 <sup>b</sup> ±1.25	34.13 <sup>b</sup> ±1.00	23.76 <sup>b</sup> ±1.33	22.53 <sup>b</sup> ±1.44
Day 42	25.66±2.82	86.25 <sup>a</sup> ±1.86	35.73 <sup>b</sup> ±3.66	43.66 <sup>b</sup> ±2.75	38.01 <sup>b</sup> ±1.66	24.61 <sup>b</sup> ±1.33	21.73 <sup>b</sup> ±3.66

Superscripts <sup>a</sup> and <sup>b</sup> mean significantly ( $P<0.05$ ) different from corresponding Control (I) and Diseased (II), respectively.

**Table 8.** Serum AST concentration (U/L) in rats under different treatments, Normal Control (I), Hyperlipidemic (II), Hyperlipidemic with Ezetimibe 1 mg/Kg B. Wt., orally (III), Hyperlipidemic with ASE 25 and 50 mg ASE/Kg B. Wt. orally (IV and V), and Normal with ASE 25 and 50 mg ASE/Kg B. Wt. orally (VI and VII) daily for 42 days ( $\bar{X} \pm S.E$ ; n=6).

Time/Group	I	II	III	IV	V	VI	VII
Day 28	33.17±3.60	88.35 <sup>a</sup> ±5.33	41.25 <sup>b</sup> ±2.39	57.70 <sup>b</sup> ±4.22	50.50 <sup>b</sup> ±2.59	32.50 <sup>b</sup> ±1.98	30.25 <sup>b</sup> ±1.39
Day 42	36.33±4.31	97.50 <sup>a</sup> ±7.68	52.66 <sup>b</sup> ±4.09	62.12 <sup>b</sup> ±3.90	58.25 <sup>b</sup> ±3.39	33.51 <sup>b</sup> ±1.98	32.66 <sup>b</sup> ±2.09

Superscripts <sup>a</sup> and <sup>b</sup> mean significantly ( $P<0.05$ ) different from corresponding Control (I) and Diseased (II), respectively.

specimens from rats kept on high-fat diet were almost not observed upon concurrent administration of ASE (Figure 2). The recorded beneficial effects of ASE may be related to the active pharmacological constituents present in the extract, including  $\beta$ -glucan, avenanthramides, flavonoids, flavonolignans, triterpenoid saponins, sterols, and tocopherols. In addition, the mucilaginous nature of the extract may impede lipid absorption from the intestines upon oral administration (Singh et al., 2013; Miraj and Kiani, 2016).

## Conclusion

The present findings suggest that *A. sativa* mucilage extract may protect the liver and the body against development of hyperlipidemia, indicated by clinicopathological analysis. The extract, therefore, may have a good health impact in dyslipidemia and concurrent illnesses.

## CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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