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The Curative Hypolipidemic Effect, Antioxidant Activity, and Atherogenic Indexes of Methanolic Extract of Arbutus Pavarii Leaves

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Abstract **Original Research Article**

The aim of the study was to investigate the antioxidant activity and curative effect of (MEAPL) and its role in the treatment of hypercholesterolemia in male albino rats. The effect of (MEAPL) against hypercholesterolemia in rats was analyzed via examination of various types of parameters, (LDL), (HDL), (TC), and (TG), also liver enzymes (ALT, AST, G-GT, LDH, and ALP) besides proteins and MDA. Antioxidant enzymes (SOD, GR, GPx, and CAT), were measured in control and (HFD). We have found that the level of TC, LDL, TG, and liver enzymes were increased but the level of HDL decreased in HFD rats compared with control. Lipid peroxidation was determined by the level of MDA, which increased in HFD compared with control while antioxidant enzymes SOD, GR, GPx, and CAT were decreased. The results obtained revealed that MEAPL has a healing effect against hypercholesterolemia compared with the reference standard agent ″Atorvastatin″ and standard antioxidant vitamin C.

Keywords: Hypolipidemic Activity, Antioxidant Enzymes, Atherogenic Indexes, Atorvastatin.

INTRODUCTION

Hyperlipidemia and hyperlipoproteinemia, are abnormal blood levels of lipids and lipoproteins, associated with obesity prevalence, a major public health concern. Elevated blood lipid and cholesterol levels are indicator of hyperlipidemia and may imply many issues related to lipoprotein metabolism [1]. When there is an unusually high quantity of triglyceride-protein complexes in the blood, the condition known as hyperlipoproteinemia happens. Elevated plasma concentrations of different lipid and lipoprotein fractions, which are major risk factors for cardiovascular disease (CVD), are the defining factor of this lipid metabolic disorder. Triglycerides, phospholipids, and cholesterol esters also increase. A healthy lifestyle that includes a diet rich in fruits and vegetables can help prevent heart disease [2]. Hyperlipidemia is defined as changes in the serum lipid and lipoprotein profiles brought on by decreased levels of HDL-C and increased levels of Triglycerides (TG), Total Cholesterol (TC), Low-Density Lipoprotein-Cholesterol (LDL-C), and Very Low-Density Lipoprotein-Cholesterol (VLDL-C), as well as LDL-C and LDL-C, respectively. A list of 21,000 medicinal plants utilized in various parts of the world has been prepared by the WHO [3]. Natural materials have long been a valuable source of innovative molecules with biological activity and prospective use in agriculture, medicine, and food chemistry. The secondary metabolites found in plants can be categorized based on their common chemical-physical properties, origin in biosynthesis, or structure as mentioned before. Metabolites with potential medical applications include those that are anti-inflammatory, antioxidant, anticancer, antimicrobial, antiviral, and antidiabetic among all these types of natural substances. Plant extracts can display significant activity on their own, or as being the sources of antimicrobial compounds effective against human infections [4].

The Arbutus pavarii Pamp. (Family Ericaceae), also referred as "Shmeri" or "Libyan Strawberry," is an indigenous medicinal plant found in Libya that is currently listed as an endangered shrub or tree species. Its conservation has drawn public attention. It is a source of a particular kind of honey that is mostly limited to Libya's Al-Akhdar mountain region. In addition to its ecological significance in the production of honey, A. pavarii has been utilized in Libyan traditional medicine to treat a variety of human conditions, such as renal and gastritis. Berries of this plant are a good source of

minerals, nutrients, carbohydrates and most importantly, vitamin C. Limited phytochemical studies on this plant revealed predominantly the presence of simple phenolics e.g., arbutin, gallic acid and polyphenolics, including flavonoids and tannins e.g., apigenin, epicatechin, hesperidin, kaempferol, naringin, quercetin and rutin, and some triterpenes and sterols [5, 6].

MATERIALS AND METHODS

Plant Material

A sample of leaves from Arbutus Pavarii that were obtained from the Wadi Al-Kuf area of Al-Jabal Al Akhdar. Arbutus pavarii leaves were dried in a lab and ground into a powder. The leaves were extracted by a hot continuous Soxhlation process, which involved extracting the leaves with methanol. A rotary evaporator was used to evaporate the methanolic extract.

Animals

Twenty-eight healthy adult male albino rats weighing between 100 -120 g were used for this study. The animals were kept in cages and maintained at 25 ± 2ºC and normal photoperiod (12:12 h dark: light cycle). The animals were allowed free access to standard commercial rat chow (pellet form, in the sack, Benghazi Animal Feed Company, Benghazi, Libya) and water ad libitum. The animal experiment was approved by the research committee of Benghazi University, Libya.

Induction of Hypercholesterolemia

Hypercholesterolemia was achieved in rats through a cholesterol/cholic acid mixture (3:1) and mixed with the synthetic diet each rat received 0.5g of this mixture/kg body weight daily for 8 weeks. 10% Saturated fat was used in the diet instead of the corn oil in addition, 50% of sucrose (Carbohydrate source) used to accelerate the incidence of hypercholesterolemia [7].

Experimental Design

Curative Effect of Different Treatments on Hypercholesterolemic Rats

In this experiment, a total of 36 rats were used. Six rats were fed on the standard synthetic diet and served as negative control (-ve) "**group I**". The other rats were subjected to the induction of experimental hypercholesterolemia for 8 weeks as described above and treated for 8 weeks. The hypercholesterolemia rats (30 rats) were divided randomly into equal 5 sub-groups (6 rats each) as follows:

Group II: Rats were served as hypercholesterolemic animals (+ ve).

Group III: Rats daily received vitamin C at a dose of 300 mg/kg body weight (orally).

Group IV: Rats were daily received methanolic extract of leaves of *Arbutus pavarii* at a dose of 300 mg/kg b.w. (oral).

Group V: Rats daily received a methanolic extract of leaves of *Arbutus pavarii* at a dose of 500 mg/kg body weight (orally).

Group VI: Rats daily received 1mg/kg body weight of Atorvastatin as a standard hypolipidaemic agent (orally).

Sample Collection and Biochemical Assays

The blood samples obtained were collected into plain sample tubes and centrifuged at 1000 rev/min. for 5 minutes to separate the serum. The serum was carefully withdrawn and kept in Eppendorf tubes for the determination of the biochemical parameters.

Assessment of Liver Marker Enzymes

The activities of Serum Alanine Transaminase (ALT). Aspartate Transaminase (AST). Lactate Dehydrogenase (LDH). Gama glutamyl transferase (GGT). Serum total protein (T. Protein). Serum albumin (ALB). Serum total bilirubin (T. BIL). And Alkaline phosphatase (ALP). Were all assayed using standard Diagnostic kits at Benghazi Medical Center.

Assessment of Antioxidant Enzymes

The activities of Glutathione reductase (GR), Glutathione peroxidase (GPx), Catalase (CAT), Superoxide dismutase (SOD), and Malondialdehyde (MDA).

Atherogenic Indices

After determining the concentration in mmol/L of total cholesterol (TC), total triglyceride (TG), HDL-c, and LDL-c fractions, atherogenic indices [AIP, CRR, AC, and cardioprotective index (CPI)] were calculated by using the values of lipid profile parameters in the following way [8]. Atherogenic index of plasma (AIP) = Log [TG/HDL]. Atherogenic coefficient (AC): AC = [TC-HDL/HDL]. Cardiac risk ratio (CRR): CRR = [TC/HDL]

Cardioprotective index (CPI): CPI= [HDL-c/LDL-c]

Statistical Analysis

Statistical data was analyzed by T test, between control vs all treated groups. A probability level of less than 5% ($p<0.05$) was considered significant. † Insignificant at $P> 0.1$; * Significant at $P<0.05$; ** Highly significant at $P<0.01$; *** Very highly significant at $P<0.001$.

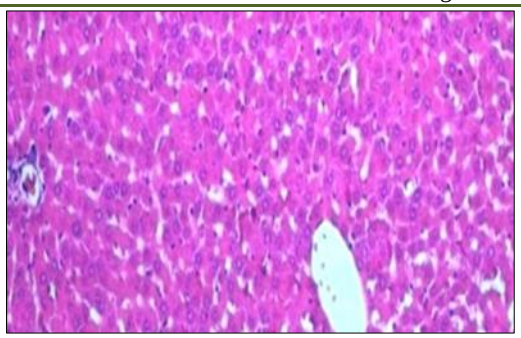

Fig. 1: The control group of animals

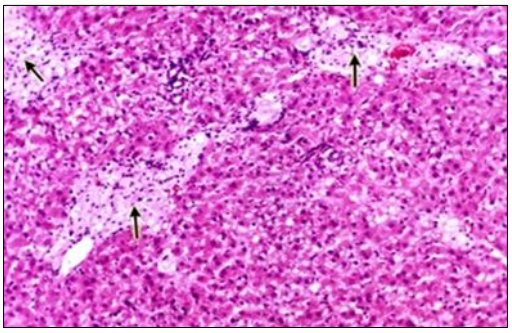

Fig. 2: Representing the liver of positive rats

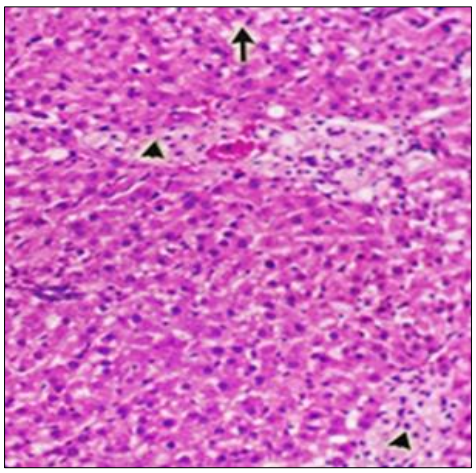

Fig. 3: Treated group of MEAPL

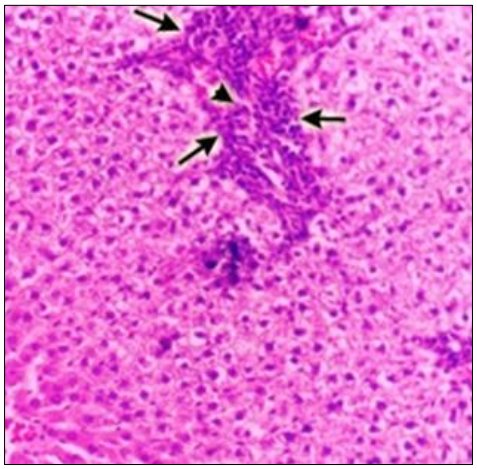

Fig. 4: Treated group of Vit C

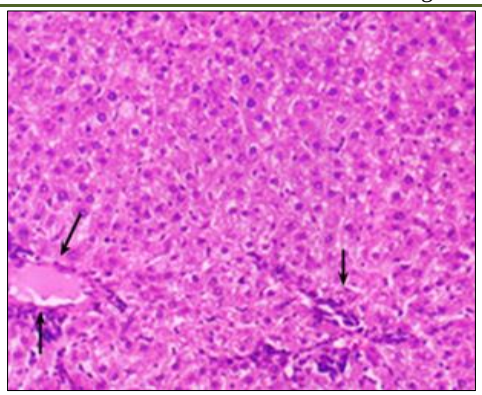

Fig. 5: Treated group of Atorvastatin.

RESULTS AND DISCUSSION

Numerous studies show that a close relationship exists between high blood cholesterol and atherosclerosis, it has also been suggested that this relationship may be dependent on enhanced oxidative stress. Studies have also shown that a cholesterol-rich diet increases the formation of peroxynitrile, a toxic reaction product of superoxide and nitric oxide in the rat [8]. Rats fed on a hypercholesterolemia diet developed hypercholesterolemia marked by significant increase in serum lipid profile TL, TC, LDL-C, VLDL-C, and TG compared with normal control rats. besides the activity of (ALT), (AST), (G-GT), (LDH), (ALP) (MDA). But the level of (HDL-C), total protein, and albumin decreased in addition to antioxidant enzymes (GR), (GPx), (CAT) and (SOD) also decreased when compared with normal control trail rats.

Effect of Different Treatments in the Curative Groups

Elevations indicated in the serum lipid profile seem to be logical and run parallel with the excess of saturated fat and sugar available in the diet. Elevations in the total lipids were also indicated after the induction of experimental hypercholesterolemia [9].

The results concerning the effect of methanolic extract of Arbutus Pavarii leaves on healing effect against hypercholesterolemia. It has an amelioration effect against the incidence of hypercholesterolemia. The decrease of TL, TC, LDL-C, VLDL-C, and TG and increase of HDL-C in rats fed on a high-cholesterol diet when orally treated with 500 mg/kg of Arbutus Pavarii leaves in healing groups. This significant effect of the methanolic extract of Arbutus Pavarii leaves is due to its contents of very important substances which in general act as antioxidant substances such as flavonoids, and phenolic compounds. Flavonoids decreased LDL-cholesterol and increased HDL-cholesterol. High-density lipoprotein may hasten the removal of cholesterol from peripheral tissue to the liver for catabolism and excretion in vivo [10].

Supplementation of vitamin C (300 mg/kg) and Atorvastatin (1mg/kg) reduced total lipids, triglycerides, total cholesterol, LDL-C, and insignificant alteration in HDL-C compared with the hypercholesterolemic group. Atorvastatin belongs to 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-COA) reductase inhibitors, potent inhibitors of cholesterol biosynthesis that are used extensively to treat hypercholesterolemia [11]. The levels of total lipids, total cholesterol, triglycerides, and LDL-C were decreased, but the level of HDL-C increased. Effect of different treatments on serum of total lipid, total cholesterol, HDL-C, LDL.C., VLDL-C, and T.G. Oral administration of hypercholesterolemic diet significantly increased the activities of the serum of T. lipid, T. Chol. , LDL.C., VLDL-C., and T.G. by (109.5%, 152.4%, 635.3%, 147.8 and 147.8 %), but the level of HDL-C. decreased by 46.9%respectively after the post-treatment of rats with methanolic extract of Arbutus Pavarii leaves at 500 mg/kg leading to decreases by (34%, 25%, 37.2%, 40.4%, and 40.4%), in T. lipid, T. Chol ., LDL.C., VLDL-C. and T.G., respectively, but the level of HDL-C. increased by 51.6%, when compared with the positive group as illustrated in Table (1).

Table 1: Effect of MEAP, Vit. C and Atorvastatin on serum lipid profile in hypercholesterolemic subjects

Parameters	Control Zero	Positive 8 weeks (HCD)	MEAPL 8 weeks (HCD)	Atorvastatin 8 weeks (HCD)	Vit. C week (HCD)
TC (mg/dL)	63.45 ± 3.64	160.17^{***} ±5.5	120 ±18*	103^{**} ±27	135^{***} ±26
TL (mg/dL)	$295.28^{\dagger}$±8.5	$618{\cdot}52^{***}$ ±7.4	408.37^{***}±7.6	395.58^{***}±8.2	$430.33^{a,***}$ ±8.1
TG (mg/dL)	$52.54^{\dagger}$±8.84	130.16^{***}± 16	77.50^{***}± 17	79.94^{***}± 9.78	89.7^{***}± 11
LDL-C (mg/dL)	$17.3^{\dagger}$± 3.20	125.56^{***}±11	78.59^{*}±81	58.42^{***}±7.86	92.31^{***}±8.17
VLDL-C (mg/dL)	$10.55^{\dagger}$± 2.33	26.31^{*}± 3.56	15.5^{*}± 3.76	16.58^{*}± 5.12	$18.13^{\dagger}$± 3.55
HDL-C (mg/dL)	$35.81^{\dagger}$±4.11	19.85^{*}± 3.25	$26.41^{\dagger}$± 3.91	$28.52^{\dagger}$± 2.53	$24.8^{\dagger}$± 3.22

TC: Total Cholesterol, TL: Total Lipid, TG: Triglyceride, LDL-C: Low-density lipoprotein cholesterol, VLDL-C: Very low-density lipoprotein cholesterol, HDL-C: High-density lipoproteins cholesterol.

Effect of Different Treatments on Serum ALT, AST, ALP, G-GT, LDH, Total Protein, and Albumin

In our study, it was observed that enzymes such as AST, ALT, G-GT, LDH, and ALP were released into the blood as a result of hypercholesterolemia. Their increase in the serum activities of these enzymes was directly proportional to the degree of cellular damage. These values decreased by the effect of methanolic extract of Arbutus Pavarii leaves at 500 mg/kg when compared with the positive group. Besides, the serum levels of liver enzymes declined toward the normal value this indicates that vitamin C has stabilized the plasma membrane as well as helped in the healing of the hepatic tissue damage, resulting in lower levels of ALT, AST, ALP, G-GT, LDH, and ALP than the hypercholesterolemic rats in both prophylactic and curative groups. The activity of vitamin C and Atorvastatin improved the decrease in total protein and albumin activity by increasing their levels in serum especially when compared with positive groups. The effect of a hypercholesterolemic diet on the serum enzymes ALT, AST, ALP, G-GT, and LDH, as illustrated in tables (2), led to significantly increased activities of these enzymes by (102.3%, 116.4%, 22.4%, 254.8%, and 38.1%), respectively in vice versa the level of total protein and albumin significantly decreased by (32.8%, and 43.4%), conversely, post-treatment of the rats with methanolic extract of Arbutus Pavarii leaves at 500 mg/kg led to decreases by (36.4%, 22.8%, 11%, 40.2%, and 17.3%), in ALT, AST, ALP, G-GT, and LDH, respectively, the total protein and albumin increased by 9.7%, and 14.6% after treatment when compared with the hypercholesterolemic diet treated group.

Table 2: Effect of MEAP, Vit. C, and Atorvastatin on serum liver function in hypercholesterolemic animals

Periods	Control Zero	Positive 8 weeks (HCD)	MEAPL 8 weeks (HCD)	Atorvastatin 8 weeks (HCD)	Vit. C 8 weeks (HCD)
ALT (u/ml)	$34.22^{\dagger}\pm 4.2$	$70.27^{***}\pm 3.52$	$44.32^{**}\pm 3.8$	$46.63^{*}\pm 3.6$	$44.17^{**}\pm 4.3$
AST (u/ml)	$65.84^{\dagger}\pm 2.4$	$142.58^{***}\pm 2.68$	$95.77^{***}\pm 3.1$	$110.2^{***}\pm 2.9$	$115.54^{**}\pm 3.1$
ALP(u/l)	$133.12^{\dagger}\pm 5.77$	$165.32^{**}\pm 6.14$	$142.58^{*}\pm 5.43$	$144.85^{*}\pm 5.62$	$149.26^{*}\pm 4.83$
G-GT (u/l)	$3.22^{\dagger}\pm 1.12$	$11.14^{***}\pm 1.68$	$6.58^{\dagger}\pm 2.04$	$7.44^{\dagger}\pm 1.36$	$8.56^{\dagger}\pm 1.52$
LDH (u/l)	$631.55^{\dagger}\pm 48$	$871.48^{***}\pm 72$	$721.84^{***}\pm 63$	$744.68^{***}\pm 64$	$748.78^{***}\pm 72$
TP (g/dL)	$5.83^{\dagger}\pm 1.84$	$3.22^{\dagger}\pm 1.75$	$4.62^{\dagger}\pm 2.14$	$4.31^{\dagger}\pm 2.65$	$4.12^{\dagger}\pm 1.52$
Alb (g/dL)	$5.69^{\dagger}\pm 2.21$	$3.22^{\dagger}\pm 1.84$	$4.12^{\dagger}\pm 2.56$	$3.88^{\dagger}\pm 2.15$	$3.34^{\dagger}\pm 1.78$

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase ALP: Alkaline phosphatase, G-GT: Gama glutamate transferase, TP: Total protein, Alb: Albumin.

Antioxidant Enzymes in the Curative Group

Our results showed that a high-cholesterol diet might lead to a reduction in antioxidant enzymes including SOD, CAT, GR, and GPx when compared with the normal control group. Whereas orally treated with methanolic extract of Arbutus Pavarii leaves at 500 mg/kg could increase the serum antioxidant capacity in rats. In the current study, antioxidant enzymes (SOD, CAT, GPx, and GR) activities decreased in rats fed a cholesterol-rich diet compared to those in the control group. The decrease in the activities of these enzymes could be attributed to the excessive utilization of these enzymes in inactivating the free radicals generated due to the high-cholesterol diet [12]. Vitamin C and Atorvastatin administration to HCD-fed rats increased the levels of SOD, GAT, GPx, and GR and decreased the serum of MDA, compared with the positive group. Results of the present study suggest vitamin C ameliorating effects to be likely mediated via inhibition of free radical generation and/or free radical scavenging activity. We can notice these effects in prophylactic and curative groups when compared to the "positive group". After the exposure of rats to a hypercholesterolemic diet only a significant decrease in the activities of the antioxidant enzymes SOD, GR, GPx, and CAT, and, in comparison to the control group by (46.1%, 48%, 26.9%, and 31.6%), respectively, but the MDA level shows a significant increase by 59.6%. After treatment of the rats with methanolic extract of Arbutus Pavarii leaves at 500 mg/kg increase the activity of these enzymes SOD, GR, GPx, and CAT by (39.7%, 42.4%, 16.6%, and 20%), respectively, and a significant decrease in MDA by 30.9% when compared with the hypercholesterolemic diet treated group as appear in tables (3).

Table 3: Effect of MEAP Vit C and Atorvastatin on antioxidant enzymes in hypercholesterolemic subjects

Periods	Control Zero	Positive 8 weeks (HCD)	MEAPL 8 weeks (HCD)	Atorvastatin 8 weeks (HCD)	Vit. C week (HCD)
GPx (mu/ml)	$33.81^{\dagger}\pm 2.45$	$24.71^{\dagger}\pm 3.62$	$30.16^{\dagger}\pm 3.85$	$27.37^{\dagger}\pm 3.21$	$28.81^{\dagger}\pm 3.42$
GR (u/l)	$25.30^{\dagger}\pm 3.11$	$13.15^{*}\pm 2.89$	$20.31^{\dagger}\pm 2.5$	$18.87^{\dagger}\pm 3.05$	$18.20^{\dagger}\pm 2.94$
CAT (u/l)	$53.22^{\dagger}\pm 5.17$	$36.45^{*}\pm 4.38$	$44.15^{\dagger}\pm 4.67^{*}$	$42.71^{\dagger}\pm 4.13$	$43.26^{\dagger}\pm 3.88$
SOD (u/mol)	$7.39^{\dagger}\pm 2.18$	$3.58^{*}\pm 2.41$	$5.68^{\dagger}\pm 3.19$	$5.21^{\dagger}\pm 2.89$	$5.33^{\dagger}\pm 2.58$
MDA (nmol/ml)	$15.68^{\dagger}\pm 4.32$	$25.68^{*}\pm 4.26$	$17.13^{\dagger}\pm 3.79$	$18.98^{\dagger}\pm 4.12$	$18.06^{\dagger}\pm 3.59$

GR: Glutathione reductase, GPx: Glutathione peroxidase, CAT: Catalase, SOD: Superoxide dismutase, MDA: Malondialdehyde.

Atherogenic Indexes in the Curative Group

A ratio of lipids is more valuable than standard lipid components utilized alone because it more accurately represents the risk of cardiovascular diseases. It is assumed that animals with HCD levels have a high TC/HDL-C ratio and are more likely to suffer stroke or atherosclerosis. Through Atherogenic rations which include the Atherogenic index of plasma AIP, Atherogenic coefficient AC, cardiac risk ratio CRR, and cardiac protective index CPI. Among those ratios, AIP has been reported to be a better biomarker for coronary artery disease [13]. A ratio of lipids is more valuable than standard lipid components utilized alone because it more accurately represents the risk of cardiovascular diseases. It is assumed that animals with high lipid diet levels have a high TC/ HDL-C ratio, represented by the Cardiac risk ratio (CRR), and are more likely to suffer stroke or atherosclerosis. Through Atherogenic rations which include the Atherogenic index of plasma AIP, Atherogenic coefficient AC, cardiac risk ratio CRR, or a combination with other parameters, like TC - HDL-C/HDL-C as an Atherogenic coefficient (AC) is the best lipid-related predictor of future cardiovascular events, and cardiac protective index CPI=[HDL-c/LDL-c], CRR related indicators hold of very strong correlation with TC. Among those ratios, AIP has been suggested that AIP was a reliable indicator in the prediction of atherosclerosis and cardiovascular complications. Cai *et al*., observed a significant decrease in the atherogenic index of plasma (AIP) in the control group compared with coronary artery disease (CAD) [14]. All ratios of lipids decreased with treatment by MEAPL, Atorvastatin, and vitamin C in comparison to positive with the HCD group except for cardiac protective indexes CPI which decreased in treatment groups.

Table 4: Effect of MEAP Vit. C and Atorvastatin on serum cardiac marker and lipoprotein ratios in hypercholesterolemic subjects

Periods	Control Zero	Positive 8 weeks (HCD)	MEAPL 8 weeks (HCD)	Atorvastatin 8 weeks (HCD)	Vit. C 8 weeks (HCD)
AIP	0.166 ±0.42	0.816±0.53	0.484 ± 0.18	0.436 ± 0.31	0.558 ± 0.27
AC	0.772 ±0.73	5.054±1.87	2.529 ± 1.91	2.132 ± 1.13	3.274 ± 1.54
HDL/LDL "CPI"	1.60 ±0.17	0.158±0.09	0.336 ± 0.28	0.490 ± 0.43	0.267 ± 0.07
TC/HDL "CRR"	1.772 ±0.96	8.069 ± 2.20	3.529 ± 1.31	3.132± 1.49	4.274 ± 1.06

AIP: Atherogenic index of plasma, AC: Atherogenic coefficient, CRR: Cardiac risk ratio, CPI: Cardioprotective index.

Histopathological Studies of Liver tissue

In the control group of animals, the parenchyma of the liver in all animals showed normal patterns regarding size, shape, arrangement, and staining characters. Also, the portal tract and control area were normal (fig. 1). In all examined animals of the (+ve) control group, histopathological changes of liver tissue revealed diffuse vacuolar degenerative changes of hepatocytes varying from mild to marked in severity. Ballooning of hepatocytes together with focal lymphocytic cell aggregates in portal areas was seen in (fig. 2). The hepatocyte distortion was ameliorated where near normal appearance of hepatocytes in methanolic extract of Arbutus pavarii leaves at (500 µg/ml) in treated livers (fig. 3), also at the 300 mg/kg of vitamin C, in addition to Atorvastatin at 1mg/kg which illustrated in (fig. 4 and 5).

REFERANCES

1. Jain, P. G., & Surana, S. J. (2015). A review of Indian medicinal plants with hypolipidemic activity and their medicinal importance. *World J Pharm Pharm Sci*, *4*(3), 1477-93.
2. Bauman, A. E. (2004). Updating the evidence that physic activity is good for health: An epidemiological review 2000–2003. *J Sci Med Sport*, *7*(1), 6-19. DOI: 10 .1016/s1440-2440(04)80273-1
3. Ashim Kumar, S., Ramachandran, B., Dhanya, B. S., Dillip, K. D., & Rajesh, A. M. (2023). Medicinal Herbs as an Alternative Treatment in the Management of Hyperlipidemia. *Journal of Natural Remedies*, *23*(2). DOI: 10.18311/jnr/2023/32174
4. Di Lecce, R., Mérindol, N., Pérez, M.G., Karimzadegan, V., Berthoux, L., Boari, A., Zidorn, C., Vurro, M., Surico, G., & Desgagné-Penix, I. (2022). Biochemical Analyses of Bioactive Extracts from Plants Native to Lampedusa, Sicily Minor Island. *Plants*, *11*, 3447. DOI: 10.3390/plants11243447
5. Lutfun, N., Afaf, AL. G., & Satyajit, D. S. (2021). Arbutus pavarii Pamp. An updated profile., *Trends Phytochem. Res*, *5*(2), 45-46. DOI: 10.30495/tpr.2121.682277
6. Buzgaia, N., Awin, T., Elabbar, F., Abdusalam, K., Lee, S. Y., Rukayadi, Y., Abas, F., & Shaari, K. (2020). Antibacterial activity of *Arbutus pavarii* Pamp. against methicillin-resistant *Staphylococcus aureus* (MRSA) and UHPLCMS/MS profile of the bioactive fraction. *Plants*, *9*(11), 1359. DOI: 10.3390/plants.9111539
7. Said, M. M., Salim, H. M., Abdel-Rahim, E. A., & Badawi, A. M. (1990). Some biological aspects of propolis (Bee Glue): 1- propolis as hypolipidemic agents. *J. Drug Res. Egypt*, *19*(1-2), 237-242.
8. Nada Oršoli, ́C., Irena Landeka Jurˇcevic, Domagoj Đikic, Dunja Rogi ́c, Dyana Odeh, Vedran Balta, Eleonora Perak Junakovi ́c, Svjetlana Terzi ́c & David Jutri ́c. (2019). Effect of Propolis on Diet-Induced Hyperlipidemia and Atherogenic Indices in

Mice., *Antioxidants, 8*, 156. DOI: 10.3390/antiox8060156

9. Curtis Omar, G., Andrew O'Brien, W., Donovan Anthony, M., Lowell, L. D., & Helen, N. A. (2012). Modulation of antioxidant enzymes activities and lipid peroxidation products in diet-induced hypercholesterolemic rats fed ortanique peel polymethoxylated flavones extract., *J Appl Biomed, 10*, 91–101. DOI: 10.2478/v10136-011-0014-3
10. Lifeng Wang, J. S., Qida, Yi., Xuefeng, W., & Xingrong, Ju. (2012). Protective Effect of Polyphenols Extract of Adlay (Coix lachryma-jobi L. var. ma-yuen Stapf) on Hypercholesterolemia-Induced Oxidative Stress in Rats: *Molecules, 17*, 8886-8897. DOI: 10.3390/molecules17088886
11. Hermansen, K., Dinesen, B., Hoie, L. H., Morgenstern, E., & Gruenwald, J. (2003). Effects of soy and other natural products on LDL/HDL ratio and other lipid parameters. *Advanced Therapeutic, 20*, 50-78. DOI: 10.1007/bf02850119
12. Najah, R. H., Mohammed, A. A. H., & Ammar Rasuol, M. R. (2008). Effect of atorvastatin on oxidative stress parameters and lipid profile in type 2 diabetic patients; *The International Medical Journal, 2*, 44-51. DOI: 10.31436/imjm.v7i2.783
13. Ma, J., Qiao, Z., & Xiang, X. (2011). Aqueous extract of *Astragalus mongholicus* ameliorates high cholesterol diet induced oxidative injury in experimental rats models. *J. Med. Plants Res., 5*, 855–858. DOI: 10.5897/JMPR.9000260
14. El-Diwani, G., El-Rafie, S., & Hawash, S. (2009). Protection of biodiesel and oil from degradation by natural antioxidants of Egyptian Jatropha. *Int. J. Environ. Sci. Tech., 63*, 369-378. DOI: 10.1007/BF03326075
15. Peter, F. S. (2007). Natural Antioxidants in Poultry Nutrition: New Developments. 16th European Symposium on Poultry Nutrition, 669-676.