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Is *Silybum Marianum* a Good Alternative to Atorvastatin on Atherosclerosis? In Rabbits using an Animal High Fat Diet Model

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Abstract

Background: Silybum marianum seed extract (SMSE) with antioxidative and antiatherosclerotic properties, contains flavonoids and Silymarin as its main active compounds.

Objective: The purpose of this study is to investigate the therapeutic effects of SMSE on atherosclerosis by evaluating the level of antiatherogenic apolipoprotein A-1, and B (ApoA-1, ApoB) and ApoB/ApoA-1 ratio, lipid profile, antioxidant system (OS) enzymes, and arterial wall thickness.

Methods: Thirty-six male white New Zealand rabbits were divided into six groups (n=6) as follows: control group and atherosclerosis groups (2-6) who used high-fat diet for 4 weeks. Groups 3 to 6, animals were fed with standard diet for the second eight weeks. Group 3, atherogenic control group (AC), group 4, Atorvastatin group (AV), group 5, SMSE extract 1 (SM1, daily gavage of 100 mg/kg), and SMSE extract 2 (SM2, daily gavage of 200 mg/kg). After 2 months, blood level of antiatherogenic lipoprotein particles, lipid profile, OS enzymes, and arterial wall thickness were evaluated.

Results: High fat diet affected rabbits' vascular thickness, lipoprotein particles, lipid profile, and OS enzymes. Administration high dose of SMSE significantly reduced the aorta thickness ($P<0.05$), compared to lower dose, AV and control groups. Treatment also decreased serum NADPH oxidase, Malondialdehyde, and lipids, whereas increased superoxide dismutase, catalase, and high-density lipoprotein in comparison with AC and AV groups. In contrast to AC and AV, treated rabbits showed an increase in the serum level of ApoA-1 and a decrease in ApoB and ApoB/ApoA-1 ratio.

Conclusion: These results concluded that SMSE probably has anti-atherosclerotic and cardioprotective effects by modifying the factors involved in the pathogenesis of atherosclerosis such as OS.

Key words: Atherosclerosis, Antioxidants, Lipid profile, Silymarin, Oxidative Stress.

Introduction

Atherosclerosis, as one of the main causes of mortality and morbidity [1,2], can cause coronary artery stenosis, myocardial infarction, and heart failure [2-4]. Disturbance in plasma lipoprotein, lipids metabolism, and modification of oxidative system are among the hypotheses investigated in the pathogenesis of atherosclerosis [2,5-8]. The role of oxidative stress (OS) in atherosclerosis is related to oxidative changes of lipids and proteins in vascular lesions [9]. Vascular dysfunction leads to the retention of LDL in the vascular intima and induces the production of oxidized LDL (Ox-LDL), which is an important indicator of OS [10,11].

Increased permeability to low-density lipoproteins (LDL) and, on the contrary, a decrease in high-density lipoprotein (HDL) particles causes the formation of atherosclerotic plaque [6,12,13]. Recent studies have focused on the association between atherosclerotic components and increased apolipoprotein B and lipoproteins, such as very-low-density lipoprotein (VLDL), LDL, and Lipoprotein (a) (Lp(a)) through the inflammation cycle; also, ApoA-1 acts as an anti-atherogenic component and prevents oxidation by increasing antioxidant activity [13-15].

As previously mentioned, vascular oxidative stress facilitates the initiation of key molecular events in atherogenesis, including oxidative modification of lipoproteins and phospholipids, endothelial cell activation, and macrophage infiltration/activation [16]; therefore, the "Oxidative Theory of Atherosclerosis" was investigated in many studies [17,18].

Despite the usefulness of statins, which are the most potent drugs used to treat CVD, liver dysfunction as a side effects of statins causes some patients to abandon treatment [19-21]. Therefore, it is necessary to investigate other methods with fewer side effects such as herbal therapy.

Silybum Marianum (Silymarin) seed extract (SMSE), consists of four flavonolignans, silybinin, isosylibinin, silychristin, and silydianin [22,23]. SMSE is mainly recommended for the treatment of liver disorders in traditional medicine [24,25]. Several studies show that SMSE has anti-oxidative and immunomodulatory effects [24,26], reduces inflammation, and inhibits oxidation of LDL [27]. Studies on the anti-atherosclerotic effect of SMSE on lipid profile are limited to its protective effect [28], but the present study was conducted to investigate the therapeutic effect of SMSE on ApoA, ApoB, and ApoB/ApoA ratio in male atherosclerotic rabbits.

Materials and Methods

Silybum Marianum seed Extraction procedure

After collecting and drying seeds, each 100 gr of seeds powder was soaked in 96% and 70% ethanol, respectively. Then, we concentrated the filtered solution to about ⅓ volume by vacuum distillation at 50°C. The aqueous phase was dried under sterile conditions at 50°C and the final dry SMSE was stored at 4°C.

Determination of extract purification

First, 1ml of phenol solution was mixed with 200 µl of SMSE and kept in a dark place (6 minutes). After that, 2ml of Naco3 (7%) was added for 120 minutes. The absorbance of the solution was measured at a wavelength of 765µm, and finally, the total phenolic content of the extract was calculated using the standard curve of gallic acid and reported 9.28 mg/(GAE)4/g [29]. Total flavonoid measurement was calculated by Dharmadasa's method, and 44.32mg of (QE) 5/g extract was reported based on quercetin standard curve [30].

Antioxidant activity was evaluated using DPPH. 1ml of SMSE was mixed with 3 ml of methanolic DPPH solution for 30 minutes. Then, the absorbance of the solution was read at a wavelength of 517µm and methanol was used as blank sample [31]. Finally, inhibitory activity was calculated based on the following formula:

% inhibitory activity= [(Acontrol-Asample)/Aconntrol]*100

The measurement of DPPH (%) with this formula was reported as 28.16.

Animals and Ethical Approval

Thirty-six adult male white New Zealand rabbits (1.6-1.8 Kg) were housed in the animal house, under standard condition, without any restrictions on food and water. All ethical issues of working with animals were registered with ethic code (IR.JUMS.REC.1395.096) in the Ethics Council of Jahrom University of Medical Science, Iran.

Grouping of Animals

After a 2-weeks adaptation period, the rabbits were randomly divided into six equal groups as follows (Fig. 1).

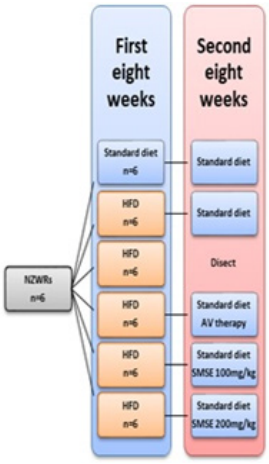

Figure 1: Grouping of Animals.

NZWRs: New Zealand White Rabbits; HFD: High-Fat Diet; AV: Atorvastatin, SMSE: Silybum Marianum seed extract

Animals were fed a standard diet and an atherosclerotic diet (a high-fat diet); the standard diet contains 20% protein, 10% Cellulose, 15% fat, and supplements such as vitamins, and the atherosclerotic diet contains 2% cholesterol and 14% coconut oil [32]. Group 1, control group (C), rabbits were fed with standard food for two months. Group 2 to 6, animals were fed with an atherosclerotic diet for the first four weeks. Group 2, after 4 weeks, animals were dissected and groups 3 to 6, animals were fed with standard diet for the second 4 weeks. Group 3, Atherogenic control (AC) group, animals received no treatment. Group 4, Atorvastatin (AV) group, atherosclerotic rabbits were gavaged daily with Atorvastatin (5 mg/kg) during the second 4 weeks. Groups 5 (SM1) and 6 (SM2), atherosclerotic rabbits were gavaged daily with SMSE (100 and 200 mg/kg, respectively) during the second 4 weeks.

Serum Evaluation

After 2 months, fasting venous blood samples were collected from the aorta and centrifuged at 3000×g for 20 minutes. Serum concentration of OX-LDL, apolipoprotein A-1 (ApoA-1), apolipoprotein B (ApoB), and ApoB/ApoA-1 ratio were evaluated by Immunoturbidometric method (Crystal Day Company, China). Serum Lipid profile (TG, TC, LDL, VLDL, HDL) was measured using kits from ParsAzmoon Company, Iran.

Morphometric Analysis

Finally, rabbits were anesthetized with ketamine (70 mg/kg) and xylazine (10 mg/kg), a portion of the aortic artery was dissected, and fixed with 10% buffered formalin for 24 hour, the aortas were immersed in Sudan IV for 2–3 minutes. Then the tissues were washed consecutively in running tap water for 1 hour. The sections were stained with hematoxylin-eosin.

Statistical Analysis

All values were reported as Mean±SD. Data were analyzed using one-way ANOVA of variance and Tukey's post-hoc test for multiple comparisons using SPSS 18 software. Significance was defined as $P<0.05$.

Results

Evaluation of apolipoproteins and ApoB/ApoA-1 ratio

We observed neither death nor any significant toxicity in clinical and histopathologic observation. High-fat diet significantly decreased ApoA-1 in the AC group; AV and SM1 groups could affect this reduction, while SM2 successfully compensates for this decrease. ApoB evaluation showed that despite the effectiveness of the treatments compared to the AC group, none of the treatments could reduce the increase in ApoB caused by high fat diet compared to the control. ApoB/ApoA-1 ratio results were consistent with ApoA-1 (Fig. 2). The most effective dose of SMSE was 200 mg/kg.

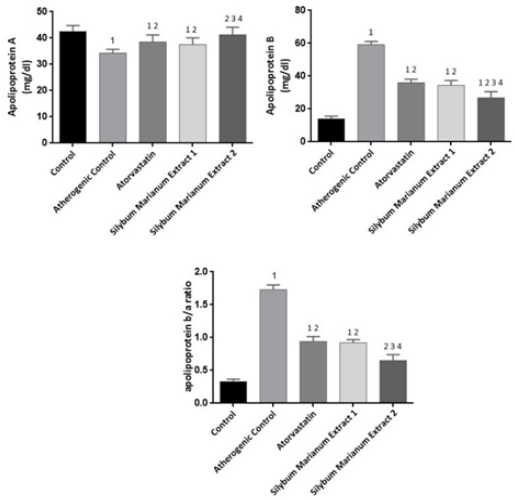

Figure 2: Evaluation of apolipoproteins and ApoB/apoA-1 ratio at the end of the sixteenth week (end of treatment).

Evaluation of the Levels of Oxidative Stress Factors

Overall, AC group had significantly ($P<0.05$) lower antioxidants level and higher oxidants level, and no treatment could significantly reverse this. The Use of atorvastatin in AV group did not affects CAT and SOD compared to AC, but significantly reduced MDA and NADPH oxidase (Fig. 3). SMSE consumption significantly affected OS; it significantly increased SOD and CAT, and decreased NADPH oxidase and MDA compared to AV and AC. Higher dose of SMSE was significantly more effective (Fig. 3).

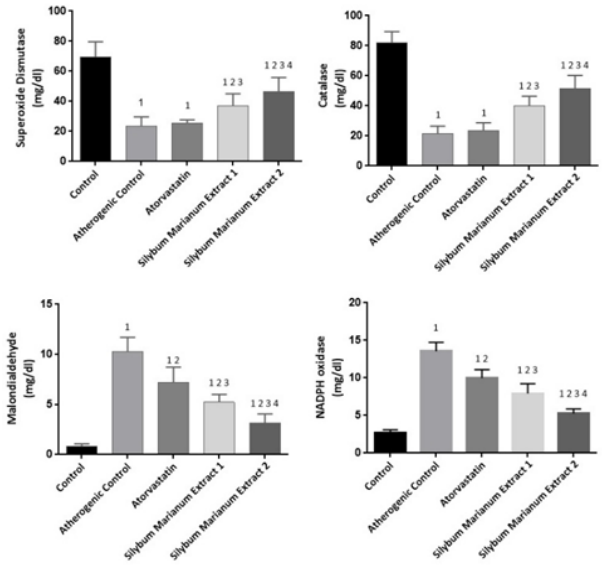

Figure 3: Evaluation of oxidative stress factors (Superoxide Dismutase, Malondealdehide, Catalase and NADPH oxidase) at the end of the sixteenth week (end of treatment).

Evaluation the levels of oxidative stress factors

The mean concentration of TC, TG, HDL, LDL, and VLDL in the AC, AV, and SM2 groups had a statistically significant increase (P< 0.05) compared to the control group, while there was no significant differences between the control and SM1 group in TC, TG, and LDL levels. These results indicated the effectiveness of higher dose of SMSE. The serum lipid profile of the SMSE groups showed that they performed better than AV-treated group (Table 1).

Table 1: Comparing serum lipid profile of rabbits at the end of the sixteenth week (end of treatment).

	Control	Atherogenic Control	Atorvastatin	Silymarin (100mg/kg)	Silymarin (200mg/kg)
Triglycerides	71.50±7.2	162.16±11.2[1]	99.00±4.6[12]	102.83±5.9[12]	79.83±12.0[234]
Total Cholesterol	29.50±4.0	220.00±18.3[1]	51.83±7.8[12]	55.16±7.2[12]	37.33±5.3[234]
HDL	17.16±2.8	53.66±7.5[1]	39.00±5.7[12]	36.33±2.2[12]	35.00±6.3[12]
LDL	31.00±3.9	67.00±5.4[1]	44.16±4.9[12]	40.16±4.7[12]	33.66±3.9[234]
VLDL	8.50±1.9	25.50±1.9[1]	17.00±1.4[12]	19.16±1.7[123]	14.66±1.61[234]
OX-LDL	12.83±2.3	43.50±3.3[1]	29.33±3.3[12]	24.33±2.8[123]	15.33±2.4[234]

TG: Triglyceride; C: Cholesterol; VLDL: Very-low-density lipoprotein; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; IDL: Intermediate-density lipoprotein

1. P<0.05, level of significance compared with the control (c) group
2. P<0.05, level of significance compared with the atherogenic control (AC) group
3. P<0.05, level of significance compared with the Atorvastatin (AV) group
4. P<0.05, level of significance compared with the Silybum Marianum seed extract (SM1) group.

Histologic Assessment of Aorta

The thickness of aorta wall, intima, media, adventitia, and intima-media are shown in Table 2. Administration of SMSE decreased the thickness of these layers in SM2 more than SM1 and AV and reached the control thickness in artery intima-media.

Table 2: Comparing aorta wall thickness of rabbits at the end of the sixteenth week (end of treatment).

	Control	Atherogenic Control	Atorvastatin	Silybum Marianum Extract (100mg/kg)	Silybum Marianum Extract (200mg/kg)
Intima thickness	38.00±3.1	118.16±5.2[1]	78.00±7.4[12]	70.00±6.0[123]	49.66±3.5[1234]
media thickness	480.00±16.0	1017.83±32.6[1]	779.83±23.6[12]	722.00±23.0[123]	645.66±16.1[1234]
Adventitia layer thickness	441.83±13.8	867.66±16.5[1]	639.83±17.9[12]	611.00±20.6[123]	528.66±11.9[1234]
Intima–media thickness	0.08±0.0	0.13±0.01	0.12±0.0[1]	0.11±0.0[123]	0.09±0.0[234]

Discussion

Induction of atherogenic model using high fat diet showed that Silymarin affected lipid profile and 200 mg/kg SMSE is more effective than Atorvastatin and even controlled TG, TC, LDL, and X-LDL. SMSE also decreased oxidant enzymes and increased antioxidants more than Atorvastatin. The results indicated the effects of SMSE on ApoA and ApoB.

Our results showed that rabbits treated with SMSE and AV experienced a significant increase in serum HDL and a decreased in TC, TG, LDL, and VLDL compared to atherosclerosis; according to Radjabian study, SMSE can alter lipoprotein profiles in a dose-dependent manner [33]. Other articles have shown that Silymarin improves metabolism and blood lipids concentration by inhibiting 3-hydroxy-3-methylglutheryl coenzyme-A (HMG-CoA) reductase as well as by lowering blood cholesterol by inhibiting its absorption in the digestive system [16,25,34].

We demonstrated that Silymarin not only reduced oxidative stress markers, NADPH oxidase, MDA, and Ox-LDL, but also increased SOD and CAT. SMSE compounds, such as flavonoids, have antioxidant and cell membrane stabilizing properties [35,36]. Studies have shown that Silymarin plays a protective role by removing free radicals, increasing the activity of SOD, CAT, and pancreatic antioxidant enzymes, and preventing the release of glutathione [8,19]; Silymarin prevents lipid peroxidation by inhibiting the enzyme 5-lipo oxygenase [37,38]. Free radicals adversely alter lipids and have shown to be the underlying pathogenic processes of atherosclerosis and vascular inflammatory [39,40]. Antioxidants facilitate the treatment of atherosclerosis by inhibiting LDL oxidation, reactive oxygen production, and cytokine secretion [41].

As we documented a decrease in ApoB and ApoB/ApoA-1 ratio, we demonstrate that SMSE treatment can dramatically increase HDL and apoA-1, which prohibits inflammation, OS, and promotes cholesterol efflux. Many studies have represented that ApoB, ApoA-1, and especially ApoB/ApoA-1 ratio are better risk indicators of heart diseases and atherosclerosis than LDL and HDL [42,43]. ApoB is a component of atherogenic particles such as VLDL, IDL, and small dense LDL, while ApoA-1 is the major apolipoprotein found in HDL particles [44,45]. Skottova et al. proved that hypercholesterolemia treatment with Silymarin lead to reduction of HDL-cholesterol, apolipoproteins A and pre-beta lipoproteins [46]. On the other hand, the more apoB particles are inside the artery, the more they are trapped in the arterial wall, and the level of atherosclerosis increases [47,48]; therefore Silymarin by affecting Apolipoproteins can reduce atherosclerosis rate.

Histological studies of vessels have shown that SMSE prevents the formation of atherosclerotic plaques. Today, measuring the thickness of artery intima-media has been raised as a reliable marker for the diagnosis of atherosclerosis [49,50]. Since measuring the thickness of intima, media, adventitia, and intima-media showed a decrease in these layers thickness, we approaches achieving normal size with using high dose of SMSE. The arterial-wall thickness is not assessed in the majority of studies of SMSE.

Conclusion

This study indicates that SMSE may have good therapeutic effects due to its potency in reducing ApoB/ApoA-1 ratio, as a lipid-lowering treatment, by decreasing ApoB which presents at atherogenic particles such as LDL, VLDL and by increasing ApoA-1 which is an anti-atherogenic agent. It also raises antioxidant enzymes level and decreases oxidative stress markers. The results suggest that higher dose of SMSE is more effective than lower dose and even than AV.

References

1. L.Kasper, D., et al., Harrison principles of internal medicine. 16 ed. Vol. 3. 2005. 1426.
2. Wu, M.-Y., et al., New insights into the role of inflammation in the pathogenesis of atherosclerosis. IJMS, 2017. 18(10): p. 2034.
3. Milutinovic, A., D. Suput, and R.J.B.j.o.b.m.s. Zorc-Pleskovic, Pathogenesis of atherosclerosis in the tunica intima, media, and adventitia of coronary arteries: An updated review. BJBMS, 2020. 20(1): p. 21.
4. Jaberi, N., et al., Role of thrombin in the pathogenesis of atherosclerosis. J Cell Biochem, 2019. 120(4): p. 4757-4765.
5. Khosravi, M., et al., The effects of oxidative stress on the development of atherosclerosis. Biol Chem, 2019. 400(6): p. 711-732.
6. Steinberg, D., The LDL modification hypothesis of atherogenesis: an update. J Lipid Res, 2009. 50 Suppl: p. S376-81.
7. Steinberg, D. and J.L.J.C. Witztum, Is the oxidative modification hypothesis relevant to human atherosclerosis? Do the antioxidant trials conducted to date refute the hypothesis? CIRC, 2002. 105(17): p. 2107-2111.

8. Zalat, Z., et al., Silymarin: A promising cardioprotective agent. Al-Azhar j. pharm. sci., 2021. 1(1): p. 13-21.

9. Stocker, R. and J.F. Keaney, Jr., Role of oxidative modifications in atherosclerosis. Physiol Rev, 2004. 84(4): p. 1381-478.

10. Gimbrone, M.A., Jr. and G. Garcia-Cardena, Endothelial Cell Dysfunction and the Pathobiology of Atherosclerosis. Circ Res, 2016. 118(4): p. 620-36.

11. Pirillo, A., G.D. Norata, and A.L. Catapano, LOX-1, OxLDL, and atherosclerosis. Mediators Inflamm, 2013. 2013: p. 152786.

12. Hao, W. and A. Friedman, The LDL-HDL profile determines the risk of atherosclerosis: a mathematical model. PLoS One, 2014. 9(3): p. e90497.

13. Generoso, G., C. Janovsky, and M.S. Bittencourt, Triglycerides and triglyceride-rich lipoproteins in the development and progression of atherosclerosis. Curr Opin Endocrinol Diabetes Obes, 2019. 26(2): p. 109-116.

14. Kabiri, n., s. Asgary, and p. Rahimi, effects of hydroalcoholic extracts of amaranthus caudatus l. On reduction of some of risk factors of atherosclerosis in hypercholesterolemic rabbits. Ijmapr, 2012.

15. Linton, M.F., et al., The role of lipids and lipoproteins in atherosclerosis. 2019.

16. Giuseppe, D., et al., Effects of a combination of berberis aristata, silybum marianum and monacolin on lipid profile in subjects at low cardiovascular risk; a double-blind, randomized, placebo-controlled trial. ijms, 2017. 18(2): p. 343.

17. Forstermann, U., N. Xia, and H. Li, Roles of Vascular Oxidative Stress and Nitric Oxide in the Pathogenesis of Atherosclerosis. Circ Res, 2017. 120(4): p. 713-735.

18. Negre-Salvayre, A., et al., Role of reactive oxygen species in atherosclerosis: Lessons from murine genetic models. Free Radic Biol Med, 2020. 149: p. 8-22.

19. Al Batran, R., et al., Insights into the antiatherogenic molecular mechanisms of andrographolide against Porphyromonas gingivalis-induced atherosclerosis in rabbits. Naunyn Schmiedebergs Arch Pharmacol, 2014. 387(12): p. 1141-52.

20. Lankin, V.Z., et al., Antioxidants decreases the intensification of low density lipoprotein in vivo peroxidation during therapy with statins, in Biochemistry of Diabetes and Atherosclerosis. 2003, Springer. p. 129-140.

21. Patrick, L. and M. Uzick, Cardiovascular disease: C-reactive protein and the inflammatory disease paradigm: HMG-CoA reductase inhibitors, alpha-tocopherol, red yeast rice, and olive oil polyphenols. A review of the literature. Altern Med Rev, 2001. 6(3): p. 248-71.

22. Pferschy-Wenzig, E.M., et al., Identification of isosilybin a from milk thistle seeds as an agonist of peroxisome proliferator-activated receptor gamma. J Nat Prod, 2014. 77(4): p. 842-7.

23. Yadegari, H., et al., Flavonolignans of Milk Thistle (Silybum marianum L.) Seeds Affected by Fertilization Type and Plant Genotype. International Journal of Horticultural Science & Technology, 2021. 8(4).

24. Radjabian, T. and H.F. Huseini, Anti-hyperlipidemic and anti-atherosclerotic activities of silymarins from cultivated and wild plants of Silybum marianum L. with different content of flavonolignans. Iran. J. Pharmacol. Ther., 2010. 9: p. 63-67.

25. Skottova, N. and V. Krecman, Silymarin as a potential hypocholesterolaemic drug. Physiological research,1998. 47: p. 1-8.

26. Saller, R., et al., An updated systematic review of the pharmacology of silymarin. Forsch Komplementmed, 2007. 14(2): p. 70-80.

27. Pradhan, S. and C. Girish, Hepatoprotective herbal drug, silymarin from experimental pharmacology to clinical medicine. IJMR, 2013. 137(2): p. 423.

28. Radjabian, T. and H.H. FALLAH, Anti-hyperlipidemic and anti-atherosclerotic activities of silymarins from cultivated and wild plants of silybum marianum L. with different content of flavonolignans. 2010.

29. Alizadeh Behbahani, B., et al., Chemical Composition and Antioxidant, Antimicrobial, and Antiproliferative Activities of Cinnamomum zeylanicum Bark Essential Oil. Evid Based Complement Alternat Med, 2020. 2020: p. 5190603.

30. Dharmadasa, R., et al., Leaf essential oil composition, antioxidant activity, total phenolic content and total flavonoid content of Pimenta dioica (L.) Merr (Myrtaceae): A superior quality spice grown in Sri Lanka. Univers. J. Agric. Res., 2015. 3(2): p. 49-52.

31. Behbahani, B.A., M. Noshad, and F. Falah, Cumin essential oil: Phytochemical analysis, antimicrobial activity and investigation of its mechanism of action through scanning electron microscopy. Microbial pathogenesis,2019.136:p.103716.

32. Veseli, B.E., et al., Animal models of atherosclerosis. European Journal of Pharmacology 2017. 816: p. 3-13.

33. Radjabian, T. and H.H. FALLAH, Anti-hyperlipidemic and anti-atherosclerotic activities of silymarins from cultivated and wild plants of silybum marianum L. with different content of flavonolignans. Cell J 2010. 18.2 (70)

34. Tester, J.J.A.J.o.H.M., Berberis aristata and Silybum marianum combined with statin therapy. ASVD, 2015. 27(2): p. 74-76.

35. Gargari, B.P., et al., Effects of Silybum marianum (L.) Gaertn.(silymarin) extract supplementation on antioxidant status and hs-CRP in patients with type 2 diabetes mellitus: a randomized, triple-blind, placebo-controlled clinical trial. Randomized Controlled Trial, 2015. 22(2): p. 290-296.

36. Hassaan, M.S., et al., Effect of Silybum marianum seeds as a feed additive on growth performance, serum biochemical indices, antioxidant status, and gene expression of Nile tilapia, Oreochromis niloticus (L.) fingerlings. 2019. 509: p. 178-187.

37. Al-Jawad, F.K.H., et al., Protective effect of zinc sulfate, silymarin in thallium induced model of nephrotoxicity. Wjpps, 2017.

38. Taleb, A., et al., Antioxidant effects and mechanism of silymarin in oxidative stress induced cardiovascular diseases. Biomed Pharmacother, 2018. 102: p. 689-698.

39. Singh, R., S. Devi, and R. Gollen, Role of free radical in atherosclerosis, diabetes and dyslipidaemia: larger-than-life. Diabetes/metabolism research and reviews, 2015. 31(2): p. 113-126.

40. Salekeen, R., et al., Lipid oxidation in pathophysiology of atherosclerosis: Current understanding and therapeutic strategies. International Journal of Cardiology Cardiovascular Risk and Prevention, 2022: p. 200143.

41. Malekmohammad, K., R.D.E. Sewell, and M. Rafieian-Kopaei, Antioxidants and atherosclerosis: mechanistic aspects. Biomolecules, 2019. 9(8): p. 301.

42. Hong, L.F., et al., Is the ratio of apoB/apoA-1 the best predictor for the severity of coronary artery lesions in Chinese diabetics with stable angina pectoris? An assessment based on Gensini scores. J Geriatr Cardiol, 2015. 12(4): p. 402-9.

43. Tian, Y.F., et al., C-reactive Protein Level, Apolipoprotein B-to-apolipoprotein A-1 Ratio, and Risks of Ischemic Stroke and Coronary Heart Disease among Inner Mongolians in China. Biomed Environ Sci, 2016. 29(7): p. 467-74.

44. Mani, P., et al., Relation of high-density lipoprotein cholesterol:apolipoprotein a-I ratio to progression of coronary atherosclerosis in statin-treated patients. Am J Cardiol, 2014. 114(5): p. 681-5.

45. Walldius, G. and I. Jungner, Rationale for using apolipoprotein B and apolipoprotein A-I as indicators of cardiac risk and as targets for lipid-lowering therapy. Eur Heart J, 2005. 26(3): p. 210-2.

46. Skottova, N. and V.J.P.R. Krecman, Silymarin as a potential hypocholesterolaemic drug. Physiol. Res., 1998. 47(1): p. 1-7.

47. Sniderman, A.D., et al., Apolipoprotein B particles and cardiovascular disease: a narrative review. JAMA cardiology, 2019. 4(12): p. 1287-1295.

48. Glavinovic, T., et al., Physiological bases for the superiority of apolipoprotein B over low-density lipoprotein cholesterol and non–high-density lipoprotein cholesterol as a marker of cardiovascular risk. Journal of the American Heart Association, 2022. 11(20): p. e025858.

49. Mahdavi-Roshan, M., A. Salari, and T. Hasandokht, Decrease in artery intima-media thickness by garlic. Clinical Excellence, 2016. 4(2): p. 68-80.

50. Orekhov, A.N., et al., Anti-atherosclerotic therapy based on botanicals. Recent Pat Cardiovasc Drug Discov, 2013. 8(1): p. 56-66.

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