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Dysregulation of Lipid and Cholesterol Metabolism in High Fat Diet Fed Hyperlipidemic Rats: Protective Effect of *Sida rhomboidea. roxb* Leaf Extract

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The present study was undertaken to evaluate the efficacy of freeze dried extract of *Sida rhomboidea.roxb* leaves (FESR) on alteration in lipid and cholesterol metabolism in high fat diet induced hyperlipidemia in experimental rats. Plasma and hepatic lipid profiles, lipid and cholesterol metabolizing enzymes in target tissues and fecal total lipids and bile acid contents were evaluated in FESR treated normolipidemic and hyperlipidemic rats. These results were compared with synthetic hypolipidemic drug lovastatin (LVS). Results indicate that FESR was able to positively regulate induced experimental hyperlipidemia by significant alteration in plasma and tissue lipid profiles. These results can be attributed to reduced absorption, effective elimination and augmented catabolism of lipids and cholesterol possibly due to high content of saponin and phytosterols in *S. Rhomboidea.* roxb (SR). Use of SR extract as a potential therapeutic agent against hyperlipidemia is indicated.

Key words——*Sida rhomboidea. roxb*, hyperlipidemia, hypercholesterolemia

INTRODUCTION

Excessive dietary lipids and cholesterol are the major factors of relevance for the development of hypertriglyceridemia and hypercholesterolemia, two important cardiovascular risk factors.[1,2] Hyperlipidemia, hypercholesterolemia, obesity, sedentary lifestyle etc are the key risk factors leading to cardiovascular disorders (CVD)[3] and, also the most common causes of death in developed as well as developing countries.[4] Some of the major limitations in the effective pharmacological treatment of hyperlipidemia are the constraints imposed on healthcare resources, particularly in the low- and middle-income countries.[5] There is a need to tackle this physiological problem as it is attaining grave proportions globally. In this scenario, the problem may be tackled by the use of natural agents due to their cost effectiveness and minimal side-effects.[6] In recent times, much research interest has been focused on various herbs that possess hypolipidemic properties that may be useful in reducing the risk of cardiovascular diseases.[7] *Sida rhomboidea. roxb* (SR, Syn. *S. rhombifolia linn, fam.* Malvaceae) is a shrubby weed found growing throughout India. In ayurveda, it is known as "Mahabala."[8] Phytochemical analysis of the aerial parts has shown presence of *n*-alkanes, long chain alcohols, sterol, ephedrine, sterculic acid, linoleic acid, phenyl ethylamines, cellulose and lignin.[9,10] It has been shown to have significant anti-inflammatory cum antipyretic[11] and antibacterial[12] effects along with antinociceptive[13] and hepatoprotective abilities.[14] It is also considered beneficial in controlling fever, cardiovascular diseases and urinary disorders.[15] It is used in many parts of North Eastern India as a home remedy against obesity and diabetes. The present inventory is in this behest an attempt to evaluate the efficacy of SR extract on the induced alterations in lipid and cholesterol metabolisms in high fat diet fed hyperlipidemic rats.

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Article

Sida rhomboidea.Roxb leaf extract down-regulates expression of PPARγ2 and leptin genes in high fat diet fed C57BL/6J mice and retards *in vitro* 3T3L1 pre-adipocyte differentiation

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Abstract: *Sida rhomboidea*.Roxb leaf extract (SRLE) is being used by populace of North-East India to alleviate symptoms of diabetes and obesity. We have previously reported its hypolipidemic and anti-diabetic properties. In this study, we report effect of SRLE on (i) *in vivo* modulation of genes controlling high fat diet (HFD) induced obesity and (ii) *in vitro* 3T3L1 pre-adipocyte differentiation and leptin release. Supplementation with SRLE significantly prevented HFD induced increment in bodyweight, plasma lipids and leptin, visceral adiposity and adipocyte hypertrophy. Also, SRLE supplementation reduced food intake, down regulated PPARγ2, SREBP1c, FAS and LEP expressions and up-regulated CPT-1 in epididymal adipose tissue compared to obese mice. *In vitro* adipogenesis of 3T3L1 pre-adipocytes was significantly retarded in the presence of SRLE extract. Also decreased triglyceride accumulation, leptin release and glyceraldehyde-3-Phosphate dehydrogenase activity along

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In Vitro Evidence for the Protective role of *Sida rhomboidea.* Roxb Extract Against LDL Oxidation and Oxidized LDL-Induced Apoptosis in Human Monocyte–Derived Macrophages

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Abstract The present study was undertaken to evaluate protective role of *S. rhomboidea.* Roxb (SR) leaf extract against in vitro low-density lipoprotein (LDL) oxidation and oxidized LDL (Ox-LDL) induced macrophage apoptosis. Copper and cell-mediated LDL oxidation, Ox-LDL-induced peroxyl radical generation, mitochondrial activity, and apoptosis in human monocyte-derived macrophages (HMDMs) were assessed in presence of SR extract. Results clearly indicated that SR was capable of reducing LDL oxidation and formation of intermediary oxidation products. Also, SR successfully attenuated peroxyl radical formation, mitochondrial dysfunction, nuclear condensation, and apoptosis in Ox-LDL-exposed HMDMs. This scientific report is the first detailed investigation that establishes anti-atherosclerotic potential of SR extract.

Keywords *S. rhomboidea.* Roxb · LDL oxidation · Macrophage apoptosis · Oxidative stress · Atheorsclerosis

Introduction

Cardiovascular diseases have become the leading cause of death in developed as well as developing countries in the past few decades [1]. Atherosclerosis, the leading cause of mortality in USA, shows increasing prevalence in Asian countries [2]. The onset of atherosclerosis is characterized by oxidative modification of LDL. Free radicals generated by endothelial cells, monocyte-derived macrophages, and smooth muscle cells reportedly oxidize the LDL [3]. Ox-LDL induces many biological effects, chiefly chemotaxis of monocytes and cytotoxicity to macrophage and endothelial cells [4, 5]. Apoptosis of macrophages caused due to cytotoxicity of Ox-LDL is the key event that triggers plaque formation [6]. Though mildly Ox-LDL favors proliferation, highly Ox-LDL induces apoptosis of macrophages in vitro [7]. Studies also suggest that formation of atherosclerotic plaques due to apoptosis of lipid laden macrophages in arterial walls is followed by secondary necrosis [8]. Various herbal extracts and dietary supplements have been shown to reduce risk of cardiovascular disease primarily by inhibiting LDL oxidation [9]. Recently, *Piper sarmentosum* and *Pinus pinaster* extracts have been shown to inhibit LDL oxidation, and the same has been attributed to high content of flavonoids and polyphenols in their extract [10, 11].

Sida rhomboidea. Roxb. (Fam. Malvaceae; SR) is a weed found in marshy places throughout India. Previous studies from our laboratory have shown that leaf extract of SR possesses significant anti-hypertriglyceridemic [12], anti-hyperlipidemic [13], anti-diabetic [14], anti-obesity (Thounaojam et al. 2011, personal communication), and nephroprotective [15] potentials. It has also been shown to be non-toxic up to a dose of 3,000 mg/kg body weight in mice [16] and ameliorate high-fat diet-induced steatohepatitis in C57BL/6 J mice [17]. Popular as "*Mahabala*" in Ayurveda, its efficacy against fever, cardiovascular diseases, burning sensation, urinary disorders, and inflammation has been reported [18]. In a previous study, we had reported the protective role of SR extract against isoproterenol-induced cardiac necrosis in rats [19]. The present study in continuation evaluates protective role of SR extract against in vitro LDL oxidation and Ox-LDL-induced apoptosis of human monocyte-derived macrophages (HMDMs).

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