Efficacy of Sesamol on Plasma and Tissue Lipids in Isoproterenol-Induced Cardiotoxicity in Wistar Rats

Lakshmanan Vennila and Kodukkur Viswanathan Pugalendi
Department of Biochemistry and Biotechnology, Faculty of Science, Annamalai University, Annamalainagar-608 002, Tamil Nadu, India

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Myocardial infarction is the leading cause of death all over the world. Sesamol is a potent phenolic antioxidant contained only in processed sesame oil and possesses potent chemopreventive, antimitogenic, and antioxidant properties. This study was undertaken to investigate the effect of sesamol on plasma and tissue lipid profiles in isoproterenol (ISO)-induced rats. Myocardial infarction was induced in adult male albino rats of the Wistar strain, weighing 180–200 g, by administration of isoproterenol (85 mg/kg of body weight), subcutaneously for 2 consecutive days. Sesamol dissolved in saline (0.9% NaCl) was administered intraperitoneally once in a day in the morning for 7 days. Increased levels of total cholesterol, phospholipids, triglycerides, and free fatty acids in the plasma and the decreased levels of phospholipids in tissues were observed in ISO-induced rats. Very low density lipoprotein cholesterol (VLDL-C) and low density lipoprotein cholesterol (LDL-C) increased while high density lipoprotein cholesterol (HDL-C) decreased in the plasma of ISO-induced rats. Administration of sesamol (50, 100 and 200 mg/kg of body weight) improved the above changes and brought towards normal level. The protective role of sesamol against isoproterenol-induced myocardial infarction was further confirmed by histopathological examination. These results suggest that sesamol has antihyperlipidaemic effect against cardiotoxicity.

Key words: Myocardial infarction, Isoproterenol, Sesamol, Lipid profile

INTRODUCTION

Cardiovascular diseases (CVDs) have a high prevalence in developing and developed countries and MI accounts for majority of deaths and disabilities (Wafaa et al., 2012). Myocardial infarction (MI) is caused due to the disruption in blood supply to any part of heart, resulting in death of cardiac tissue (Myocardial necrosis). Consequences of MI include hyperlipidemia, peroxidation of membrane lipids and loss of plasma membrane integrity (Krushna et al., 2009).

Isoproterenol [1-(3, 4-dihydroxyphenyl 2-isopropylamino ethanol) hydrochloride] a synthetic catecholamine and β-adrenergic agonist, has been found to cause a severe stress in the myocardium resulting in infarct like necrosis of the heart muscle (Sunmonu and Afolayan, 2010). Isoproterenol-induced myocardial infarction serves as a well standardized model to study the beneficial effects of many drugs and cardiac function (Upaganlawar et al., 2011).

High level of blood cholesterol is a contributory factor of atherosclerosis and many lipid associated ailments like obesity, heart attacks and stroke. The plasma cholesterol level can generally be regulated by the absorption of dietary cholesterol, the excretion of cholesterol via fecal sterol or bile acid, the cholesterol biosynthesis, and the removal of cholesterol from circulation. In the regulation of cholesterol metabolism, the liver is an important organ for maintaining the cholesterol homeostasis of the whole body. Decrease in plasma cholesterol may lower the incidence of coronary
heart disease through the reduction of esterified cholesterol in the atherosclerotic lesion. Recent studies have shown that lipid associated disorders are not only attributed to the total serum cholesterol, but also to its distribution among different lipoproteins (Noorani et al., 2011). The low density lipoproteins are the major carriers of cholesterol towards tissues having atherogenic potential, while the high density lipoproteins carry cholesterol from peripheral tissues to the liver. High density lipoproteins thus give protection against many cardiac problems and obesity (Noorani et al., 2011). Accumulation of TG is also one of the risk factors for CVD.

Dietary factors play a very important role in various human diseases including CVDs. Phenolic compounds form a substantial part of plant foods. Phenolic compounds are considered to be capable of regenerating endogenous tocopherol in the phospholipid bilayer of lipoprotein particles and changing back into its active antioxidant form (Israel and Okoro, 2012). Sesamol is a potent phenolic antioxidant contained only in processed sesame oil. Sesamol has been generally regarded as the main antioxidative component in sesame seeds (Kakkar et al., 2011). Previous studies show that sesamol possesses chemopreventive, antimutagenic and antineoplastic properties (Alencar et al., 2009). No work has been carried out on its role in the hyperlipidaemia of ISO-induced rats.

The aim of the present study was to understand ISO-induced myocardial damage in relation to myocardial lipids and to study the overall effect of sesamol on such parameters.

MATERIALS AND METHODS

Animals

Male Albino rats of Wistar strain with a body weight ranging from (180-200 g), were procured from the Central Animal House, Department of Experimental Medicine, Rajah Muthiah Medical College and Hospital, Annamalai University, and maintained in an air-conditioned room (25 ± 3°C) with a 12 h light/12 h dark cycle. Feed and water were provided ad libitum. All experimental studies were conducted in the Department of Biochemistry, Faculty of Science, Annamalai University. The experimental study protocol was approved by the Animal Ethics Committee of Rajah Muthiah Medical College and Hospital (Reg No.160/1999/CPCSEA, Pro. No.579), Annamalainagar.

Chemicals

Isoproterenol hydrochloride and sesamol were purchased from Sigma-Aldrich Chemical Co., St. Louis, Missouri, USA. The purity of sesamol is ≥99% (TLC). All other chemicals and reagents used were of analytical grade from E. Merck, Mumbai, India.

Experimental induction of myocardial ischemia

Myocardial ischemia was induced by subcutaneous injection of isoproterenol hydrochloride (ISO, 85 mg/kg BW), dissolved in physiological saline, for 2 consecutive days (Seth et al., 1998).

Experimental design

The rats were randomly divided into six groups of eight rats each. Sesamol dissolved in saline (0.9% NaCl) was administered intraperitoneally once in a day in the morning for 7 days.

- Group I : Control (0.9% saline only)
- Group II : Control + sesamol (200 mg/kg BW)
- Group III : ISO control (85 mg/kg BW, sc, twice at an interval of 24 h on 1st and 2nd day)
- Group IV : ISO + sesamol (50 mg/kg BW)
- Group V : ISO + sesamol (100 mg/kg BW)
- Group VI : ISO + sesamol (200 mg/kg BW)

The total experimental duration was 9 days. After treatment, the animals were anaesthetized between 8:00 am and 9:00 am using ketamine (24 mg/kg BW, intramuscular injection), and sacrificed by cervical dislocation. The blood was collected in a heparinized centrifuge tube, centrifuged at 2000 rpm for 10 min and the plasma was separated. The separated plasma was used for estimations. The tissues (heart & liver) were excised, washed in ice-cold isotonic saline and blotted with a filter paper. A portion of the tissue was weighed, homogenized in 0.1 M Tris-HCl buffer (pH 7.4) and the homogenate was used for tissue lipid estimations.

Estimation of plasma and tissue lipids

Plasma and tissue lipids were extracted by the method of Folch et al. (1957). To a known volume of plasma or tissue homogenate, 10.0 mL of chloroform-methanol (2:1 v/v) mixture was added and mixed well for 30 min and was filtered through Whatmann filter paper (No. 42, pore size: 8 µm) into a separating funnel. The filtrate was mixed with 0.2 mL of physiological saline and the mixture was kept undisturbed overnight. The lower phase containing the lipid was drained off into preweighed beakers. The upper phase was re-extracted with more of chloroform-methanol mixture; the extracts were pooled and evaporated under vacuum at room temperature. The lipid extract was re-dissolved in 3.0 mL of chloroform-methanol (2:1) mixture and aliquots were taken for the estimation of lipids. Total cholesterol, triglycerides (TG), free fatty acids (FFA), and phospho-