2. SCOPE AND OBJECTIVES

The prevalence of MS is increasing throughout the world in parallel with a rise in obesity and sedentary lifestyle. MS increases the risk of CVD by 2-fold and T2D by 5-fold which emphasizes the need for improved treatment options for this growing group of patients. A better understanding of the pathophysiology of MS-related heart disease is essential to prevent this emerging global epidemic. The cardiac manifestation of MS involves insulin resistance, a shift in substrate metabolism, oxidative stress, mitochondrial dysfunction, diminished cardiac performance, LVH and diastolic dysfunction. Recently altered mitochondrial dynamics and biogenesis and apoptosis are reported to be the major molecular mechanisms contributing to myocardial remodeling.

Consumption of high calorie diet results in insulin resistance, obesity, lipid accumulation, dyslipidemia, hyperinsulinemia, impaired glucose tolerance, hypertension and inflammatory response that favour the progression of MS to T2D and CVD. High carbohydrate, high fat diet-fed rodents develop a phenotype similar to the MS. The diet is similar to the Western-type high calorie diet and this model is regarded to be a useful model to study insulin resistance and MS.

Many of the drugs used for MS-associated cardiac disease have been proved to cause side effects and it is mandatory to provide a safe and effective drug without or with minimal side effects. Natural compounds have been proposed as potential therapeutic agents in the prevention and treatment of cardiac diseases. Examples include fish oil, curcumin, garlic, Danshen and Psyllium. The impacts of such agents are explored in order to provide scientific data that validate their therapeutic use. On this note, TX, a trihydroxyethylated derivative of the natural biflavonoid rutin has been selected for this study. TX is
used in the treatment of chronic venous insufficiency, varicose veins and hemorrhoids. TX has been reported to have anti-oxidative, anti-inflammatory, anti-thrombotic, fibrinolytic and edema-protective activities.

On the basis of the reported effects, TX could represent a candidate agent. The study hypothesizes that TX may have ameliorative effect on insulin signaling and the components of MS and thereby cardioprotection. The present study investigates the potential of TX to ameliorate insulin resistance-associated cardiac disease. The objective of the study is to characterize the potential effects of TX on metabolic remodeling in the myocardium, hypertrophic cardiac remodeling and mitochondrial abnormalities in HFFD- induced insulin resistant mice. For this, insulin signaling molecules, lipid metabolism, biomarkers of cardiac damage, oxidative stress, myocardial fibrosis and apoptosis were analyzed.

It is hoped that the study will throw light on the underlying mechanisms of TX in improving cardiac function in the chosen dietary model of MS.