Introduction
1. INTRODUCTION

Despite improved clinical care, heightened public awareness, and widespread use of health innovations, myocardial infarction remains a leading cause of death all over the world. It is estimated that by the year A. D. 2020, up to three quarters of deaths in developing countries would result from non-communicable diseases and in that myocardial infarction will top the list of killers (Gupta & Gupta, 1998). With changing life style in developing countries like India, particularly in urban areas, myocardial infarction is making an increasingly important contribution to mortality statistics of such countries (Farvin et al., 2004). In India, the number of patients being hospitalized for myocardial infarction is on the increase over the past 35 years, more strikingly among male patients. It is predicted that by the year 2020, India will have the highest incidence of myocardial infarction in the world (Krishnaswami, 1998). There are an estimated 45 million patients of coronary heart disease in India. This increased prevalence of myocardial infarction is contributed largely to adoption of "western" life-style and its accompanying risk factors such as smoking, high fat diet, obesity and lack of exercises.

Myocardial infarction (MI) is the medical term for heart attack. "Myocardia" refers to the heart muscle, "Infarction" means an irreversible injury to a portion of the heart tissue resulting from lack of oxygen and blood supply, which occurs 98% of the time from a process called atherosclerosis (commonly called "hardening of the arteries") in coronary vessels (Ye et al., 1997). Myocardial infarction and the resultant abnormalities in cardiac function are well recognized and it is a complex phenomenon affecting the mechanical, electrical, structural and biochemical properties of the heart. Earlier it was felt that most heart attacks were caused from the slow closure of artery, now it is clear that this process
can occur even in minor blockages where there is rupture of cholesterol plaque. This in turn causes blood clotting within the artery, blocking the blood flow.

Extensive research is being carried out to understand the major factors responsible for myocardial infarction. The relationship between lipid levels and myocardial infarction has been studied in detail and it has contributed enormously to the literature. Higher cholesterol level especially of low-density lipoprotein (LDL) cholesterol is a recognized potent risk factor for heart attack (Griffin et al., 1994). Reports suggest that hypertriglyceridemia also contribute to myocardial dysfunction regardless of cholesterol levels (Fredrickson, 1969; Ryder et al., 1984). In addition to it, low HDL cholesterol confers great risk compared to high serum triglycerides (Castelli, 1988). The lipid abnormalities seen in myocardial infarction appear to correlate with changes in cellular and cell membrane functions. The rise in the intracellular calcium efflux, an inducer of phospholipase A₂, which degrades membrane phospholipids, is also designated as a destructive factor involved in the myocardial damage (Zhang et al., 1995). A considerable body of clinical and experimental evidence is now emerging which suggests that reactive oxygen-derived radicals play an important role in the pathogenesis of acute myocardial infarction (Kukreja & Hess, 1992). Also reports indicate that reduction in free radical scavengers and altered myocardial antioxidant status worsens myocardial injury.

Despite this complexity, impressive recent progress has been achieved in advancing our understanding and appreciation of the cellular processes and mechanistic bases underlying cardiac dysfunction associated with myocardial infarction and most importantly applying this knowledge to therapeutic interventions (Karmazyn, 1996). As myocardial injury is irreversible in nature, most of the drugs available are effective in the prevention of spreading or dispersal of necrotic damage to the adjacent cells. Drugs
available for the treatment of myocardial infarction includes thrombolytic agents, anti-platelet agents, the anti-coagulants, vasodilators, ACE (angiotensin converting enzyme) inhibitors, β-blocking agents and blood-thinning agents. But all these drugs are having their own adverse effects and limitations. Hence, it is important to search for drugs capable of protecting myocardial cells from necrotic damage especially by strengthening the cardiac cell membrane.

Early in this century, Thomas A. Edison predicted "the doctor of the future will give no medicine, but will interest his patients in the care of the human frame, in diet, and in the cause and prevention of disease." In the years ahead physicians and patients alike have embraced Mr. Edison's prediction and looked to natural sources for healing and wellness. Employing natural substances including vitamins, minerals, trace elements, amino acids, fatty acids, and phytonutrients (substances derived from plant sources) in optimal supplemental quantities can produce efficacious therapeutic results.

Much information has been disseminated in the past two decades regarding nutrition and cardiovascular diseases, mainly myocardial infarction. There are numerous interconnections between nutrients and biochemical pathways, which are involved in the prevention of myocardial infarction and its treatment. Ensuring more efficient functioning of the biochemical pathways by promoting proper diet and or supplementation can have a significant positive impact on this multi-factorial disease process. The major abnormalities noticed in myocardial infarction are lipidaemia, peroxidation and loss of plasma membrane integrity. Hence the drug should possess antilipidemic, antiperoxidative and membrane stabilizing properties. Also, it should be devoid of any adverse side effects. So it is better to be a biological molecule. If that molecule possesses
all the desired properties and also involved in the biochemical pathways related to cardiovascular function, it could be of significance.

A number of scientists have been investigating the connection between micronutrients such as vitamins, minerals, amino acids, flavonoids, coenzymes, and myocardial infarction. For example, vitamin E is a biological molecule possessing antioxidant (Amann et al., 1999) and membrane stabilizing (Mukherjee et al., 1997) properties but it is not directly involved in any of the metabolic pathways related to myocardial infarction. Though carotenoids have been found to be effective in counteracting free radical generation in myocardial infarction condition it is not directly involved in the myocardial function (Konovalova et al., 1989). L-Arginine and L-lysine are found to be effective in preventing myocardial damage and ensures normal myocardial function through nitrous oxide metabolism, but their membrane stabilizing capability is so far not clear (Ebenezar et al., 2003). Aspartate and glutamate have been shown to improve cardiac recovery after hypoxia or ischemia under normothermic conditions. Although these carboxylic amino acids have been reported to mediate the recovery of left ventricular pressure and contractile function of the myocardium, they are poor free radical scavengers in nature. Grape seed proanthocyanidine extract has been reported to attenuate oxidative stress and to improve cell survival and permit recovery of contractile function in myocardium, but it is not involved in any of the biochemical pathways of myocardium (Bagchi et al., 2000).

The pineal gland hormone, melatonin has been proved to provide protection for myocardium by its antioxidant and membrane stabilizing properties. Since it is involved in regulating the biological rhythm, a hormonal imbalance is often observed upon administration of melatonin (Acikel et al., 2003).
The consumption of diets rich in seafood is associated with a reduced risk of vascular diseases and certain cancers. The marine polyunsaturated fatty acids (PUFA) have been reported to exert cardioprotective effects through prostaglandin metabolism (Nair et al., 1997). PUFA are well known for its peroxidative properties, which is highly deleterious to the stabilization of membrane. Reports by Farvin et al. (2004) suggest that the cardioprotective effect of squalene, an antioxidant isoprenoid derived from shark liver oil is ascribable to its membrane stabilizing property and antioxidant nature. However, at lower supplementation rate it may lead to excess synthesis of cholesterol.

Taurine (2-aminoethanesulfonic acid), a non-protein sulfur containing amino acid, is the most abundant free amino acid and has been shown to play several essential roles in the human body (Lombardini., 1996). It is widely distributed in very high concentrations in brain, heart, kidney, lens and reproductive organs (Huxtable, 1992). Some sea foods are rich in taurine. It is involved in various important biological and physiological functions, which include cell membrane stabilization (Heller-Stilb et al., 2002), antioxidation (Atmaca, 2004), detoxification (Birdsall, 1998), osmoregulation (Timbrell et al., 1995), neuromodulation and brain (Renteria et al., 2004) and retinal development (Wright et al., 1986). Taurine makes up more than 50% of the total free amino acid pool in the mammalian heart (Lombardini, 1996). Earlier studies (Warskulat et al., 2004) demonstrated that pathology develops in the myocardium if the animal is depleted of taurine stores either through a taurine deficient diet or use of taurine transport antagonists. Pion et al. (1987) were the first to explain the role of dietary taurine deficiency associated with a dilated cardiomyopathy observed in experimental animals. Other studies by Keith et al. (2001) and Lake (1994) have explored the relationship between taurine deficiency and cardiac contractility, loss of cardiac myofibrils, and arrhythmogenesis. Though there is considerable evidence concerning the pharmacological significance of taurine in
maintaining the integrity of organism, the protective effect of taurine in experimentally induced myocardial infarction condition in rats have not explored in detail.

Intraperitoneal administration of isoproterenol [L-β-(3, 4-dihydroxyphenyl)-α-isopropyl amino ethanol hydrochloride], a β-adrenergic agonist, produces acute irreversible myocardial injury in rats that morphologically resembles myocardial infarction of human beings (Ravichandran et al., 1990). It induces myocardial necrosis by a multiple step mechanism (Chagoya de Sanchez et al., 1997). Peroxidation of endogenous lipids has been shown to be a major factor in the cardio toxic action of isoproterenol (Chattopadhyay et al., 2003). Isoproterenol-induced myocardial infarction is generally attributed to the formation of the highly reactive hydroxyl radical (OH'), stimulator of lipid peroxidation and source for the destruction and damage to cell membranes (Farvin et al., 2004). Alterations in tissue defense systems including chemical scavengers or antioxidant molecules and the antioxidant enzymes catalase, superoxide dismutase, glutathione peroxidase, glutathione-S-transferase have been reported in isoproterenol-induced myocardial infarction (Saravanan & Prakash, 2004).

In the present study, an attempt has been made to assess the preventive effects of taurine against isoproterenol-induced myocardial infarction in rats, an experimental animal model for myocardial infarction of human beings.

The main objectives of the work are

- To study the cardio protective effects of taurine in experimentally induced myocardial infarction by assaying the levels of serum diagnostic marker enzymes, troponin T, homocysteine, protein, glycoproteins and apolipoproteins.
To evaluate the antilipidemic effect of taurine against isoproterenol-induced myocardial infarction in rats by determining the levels of lipid components.

To study the antilipid peroxidative effect of taurine on tissue antioxidant defense system in isoproterenol-induced myocardial infarction in rats.

To determine the membrane stabilizing action of taurine by assaying the activities of lysosomal enzymes, membrane-bound ATPases and mineral status.

To study the effect of taurine on mitochondrial function in experimentally induced myocardial infarction by assaying the activities of TCA cycle enzymes and respiratory marker enzymes.

To investigate the electrophoretic pattern of serum proteins.

To study the effect of taurine on amino acid composition and fatty acid profile in experimentally induced myocardial infarction in rats.

To study the histopathological pattern to confirm the protective action of taurine against isoproterenol-induced myocardial infarction in rats.