Summary and Conclusion
Isoproterenol induced myocardial infarction serve as a well-standardized model. This experimental model was used in the present study to evaluate the efficacy of mangiferin on myocardial ischemia. The main objective of this study was to determine whether pretreatment with mangiferin could improve resistance (tolerance) of myocardium to the ischemic necrosis induced by isoproterenol hydrochloride. The results obtained from the experimental study are summarized as below.

Isoproterenol induced MI rats showed significant increase in heart weight to body weight ratio when compared to normal rats whereas mangiferin pretreated rats showed significant decrease in this ratio when compared with MI induced rats.

Histopathological studies of heart tissue of MI rats revealed degenerative changes in the heart on isoproterenol induction when compared to normal rats and the protective efficacy of mangiferin was established from the maintenance of normal architecture of heart myocardium when compared with myocardial damaged rats.

ECG studies showed significant ST elevation in isoproterenol induced MI rats and it was found to be reduced to near normal in mangiferin pretreated rats showing the cardio protective nature of mangiferin.

Serum and heart tissue markers such as AST, ALT, CPK, LDH and CK-MB showed significant changes in MI induced rats when compared to normal rats. These changes were altered significantly upon pretreatment with mangiferin when compared with MI induced rats. This was further established
by TTC assay. Electrophoretic separation of serum LDH isoenzymes and plasma protein also confirmed the cardiotonic action of mangiferin. The plasma protein and A/G ratio of the ISPH induced MI rats showed significantly decreased level when compared to normal rats, whereas mangiferin pretreatment increased these parameters significantly when compared with ISPH induced rats.

The LPO level in serum, heart, mitochondria and lysosome of ISPH induced rats showed significant increase when compared to normal rats and it was found to be decreased upon pretreatment with mangiferin. A significant decrease in antioxidant status of serum, heart tissue and mitochondria in isoproterenol induced MI rats were observed when compared to normal rats whereas pretreatment with mangiferin significantly increased the antioxidant status. This might be due to its anti free radical, anti lipid peroxidation and oxidant-antioxidant balance maintaining property of mangiferin.

Pretreatment with mangiferin decreased the level of heart tissue nucleic acids, blood glucose and heart tissue protein levels when compared to MI induced rats. Similarly, increased level of heart tissue glycogen was observed in mangiferin pretreatment when compared with ISPH induced MI rats.

Isoproterenol administration significantly increased the levels of lipid and lipoprotein profiles except phospholipids and HDL₄ in MI induced rats when compared to normal rats. Mangiferin pretreatment offered significant decrease in these parameters with significant increase in
phospholipids and HDL-C levels when compared with ISPH induced MI rats revealing the anti lipid peroxidative and hypolipidemic activity of mangiferin.

In ISPH induced MI rats, the extent of mitochondrial membrane damage was revealed from the decreased activities of ATPases and increased activities of proteases, phospholipases as compared to normal rats which were altered significantly upon pretreatment with mangiferin when compared to ISPH induced MI rats. Mangiferin pretreatment significantly reduced Na\(^+\) and Ca\(^{2+}\) levels in heart tissue and mitochondria and significantly increased Mg\(^{2+}\) and K\(^+\) levels, when compared with ISPH induced MI rats where the levels were altered revealing the antioxidant property of mangiferin.

The decreased activities of mitochondrial respiratory enzymes and ETC process during ISPH administration were observed when compared to normal rats and mangiferin pretreatment significantly increased these parameters when compared with ISPH induced MI rats. Mangiferin pretreatment reduced plasma lactate significantly when compared to MI induced rats where its levels were altered.

Electron microscopy studies on mitochondrial structure of ISPH induced MI rats showed extensive damage when compared to normal rats whereas mangiferin pretreatment protected mitochondria from ISPH induced damage. The cardioprotective nature of mangiferin was revealed from this study.

A significant increase in serum Na\(^+\) and Ca\(^{2+}\) level with significant decrease in serum Mg\(^{2+}\) and K\(^+\) levels were observed with mangiferin
pretreatment, when compared to ISPH induced MI rats. Trace elements such as serum Zn^{2+} were increased significantly with significant decrease in serum Cu^{2+} when compared with MI induced rats showing the cardio tonic action of mangiferin.

The activities of lysosomal hydrolase enzymes were decreased in lysosomes with significant increase in serum lysosomal hydrolase enzymes during ISPH administration when compared to normal rats. These parameters were altered significantly upon pretreatment with mangiferin when compared with ISPH induced MI rats.

Mangiferin pretreatment reduced the level of RBC cells, Hb content, packed cell volume (haematocrit), neutrophils, platelet count, fibrinogen level and increased the level of lymphocyte content, cosinophil content, basophil amount, ESR, prothrombin time, bleeding time and clotting time when compared to ISPH administrated MI rats.

**CONCLUSION**

The study shows that oxidative damage appears to play a major role in isoproterenol induced myocardial infarction as evidenced by significant inhibition of antioxidant defense mechanism in cardiac tissue accompanied by an elevation of lipid peroxidation, lipids, lipoprotein levels and decrease of mitochondrial, lysosomal functions in heart. Intraperitoneal administration of mangiferin, ameliorated the extensive damage and exhibited a potent antioxidant effect in cytosol, mitochondria, lysosomes and serum in the myocardial infarcted animals. The therapeutic efficacy of mangiferin might be
due to its antioxidant, anti lipid peroxidative, free radical scavenging, immunomodulatory, antidiabetic and cardiotonic property which could have prevented ISPH generated free radical mediated tissue injury. In conclusion, it could be stated that pretreatment with mangiferin plays a significant role in reducing the infarct size in experimental myocardial infarction without any adverse effect and its possible use as a cardiotonic drug for cardiovascular diseases may not be far off for human beings and for clinical use in future.