CHAPTER 7

CONCLUSION

Cardiovascular disease is the chief health concern among medical practitioners. MI is one of the CVD which has to be addressed on emergency basis. It is essential to understand the underlying pathology, advancement of the disease and to find out possible therapeutic interventions to treat the disease. *Crataegus oxyacantha* is well known for its cardio protective potential in the literature. In the present study, we have evaluated the potential anti-oxidant, cardiotonic and endothelial protective effect of the ethanolic extract of COC in MI induced rats. Our results indicate that COC could be used as adjuvant therapy in the prevention of MI along with established pharmacological agents.

In the acute toxicity study, rats were treated with different doses of *Crataegus oxyacantha* fruit extract from 100mg/kg B.W to 2000mg/kg B.W which did not produce any signs of toxicity, behavioural changes, and mortality in the test Groups as compared with controls. In the present study, oral administration of ethanolic extract of COC did not produce any death or signs of acute toxicity up to dose of 2000 mg/kg B.W during the period of observation, indicating the high margin of safety. There was no significant changes in the body weight, organ weight, haematological parameters and biochemical parameters with different doses of COC showing high safety margin of *Crataegus oxyacantha* among rats which was found to be statistically significant (P<0.05).

In the present study, Isoproterenol was used in 3 different doses such as 5 mg/kg B.W, 85 mg/kg B.W and 150 mg/kg B.W CK –MB levels were 186 IU/L, 223 IU/L and 411 IU/L and serum Troponin-I levels were found to be 0.76 ng/ml, 1.06 ng/ml and 1.85 ng/ml at 5mg/kg B.W, 85mg/kg B.W and 150mg/kg B.W of Isoproterenol respectively.
Even though levels of serum cardiac markers were highest at 150 mg/kg body weight of Isoproterenol, histopathological findings showed that complete tissue destruction at this dose which was fatal for the animal and it is impossible to carry out the further research with above said dose of Isoproterenol. So in the present study, 85mg/kg body weight of Isoproterenol was chosen to induce MI and to carry out the effect of ethanolic extract of *Crataegus oxycantha* in rats.

Present study is one of its first to evaluate the effect of *Crataegus oxycantha* on the levels of V-CAM and revealed that there was significant decline in the V-CAM levels in the post treatment Groups compared to Isoproterenol Group further adding to its cardio protective potential.

Since the levels of ICAM-1 and E-selectin is reduced by *Crataegus oxycantha*, there should be associated decrease in inflammatory factors like CRP and TNFα. In the present study, alcoholic extract of *Crataegus oxycantha* considerably reduced the levels of CRP and TNFα confirming its anti-inflammatory, anti-atherosclerotic and endothelial protection.

In the present study, effect of different doses of *Crataegus oxycantha* was compared with control, Isoproterenol and metoprolol Group. Study showed that, effects on body weight decreased in Isoproterenol Group compared to control and was improved in metoprolol and combination of metoprolol with *Crataegus* Group. Heart weight, left ventricular weight of the animals were increased in Isoproterenol Group. Combination of metoprolol with *Crataegus* Group reduced the heart weight and left ventricular weight compared to Isoproterenol Group.

In the present study, left ventricular wall thickness was increased evidencing the cardiac hypertrophy in Isoproterenol. However, upon treatment with COC, metoprolol and combination of COC and metoprolol, a decrease in left ventricular wall thickness was observed. Further, our results showed that the COC extract had beneficial effects, in the prevention of endothelial dysfunction and myocardial necrosis. We observed reduction in the endothelial and myocardial markers. This may be due to the effect of *Crataegus oxycantha* extract and the synergistic effect on Co-administration with metoprolol.
In the present study, in Isoproterenol group there was necrosis and waviness of myocardial fibers with accumulation of neutrophils seen. However, following the treatment normal cardiac muscle fibers with little neutrophils and normal histo architecture was observed, indicating the cardioprotective effect of *Crataegus oxycantha* and its synergistic effect with metoprolol. Biochemical findings supported the histopathological results of *Crataegus oxycantha*, which further confirmed the cardio protective effect of the ethanolic plant extract during myocardial infarction (Figure No.5.16). Necrotic areas indicated by TTC-negative regions in heart sections of Isoproterenol treated groups was significantly reduced with the treatment of COC alone and with combination of COC and metoprolol. These findings, clearly establish the therapeutic potential of COC in the prevention of myocardial infarction as pre-treatment and its synergistic action while co-administering with metoprolol.

In the present study, myocardial markers such as Troponin-I, lactate dehydrogenase, CK-MB, AST and ALT levels increased in Isoproterenol group compared to control. However upon treatment with metoprolol alone or combination of metoprolol with *Crataegus oxycantha*, there was marked decline in the levels of Troponin-I, LDH, CK-MB, AST and ALT compared to Isoproterenol Group.

In the present study, in Group II there was necrosis and waviness of myocardial fibers with accumulation of neutrophils seen. However, upon treatment normal cardiac muscle fibers with little neutrophils and normal histo architecture of the nucleus was observed, suggesting cardioprotective effect of combination of *Crataegus oxycantha* with metoprolol.

In the present study, body weight of rats were decreased in Isoproterenol Group. And was improved in metoprolol and combination of metoprolol with *Crataegus* Group. Heart weight, left ventricular weight of the animals were increased in Isoproterenol Group compared to controls and combination of metoprolol with *Crataegus* Group reduced the heart weight and left ventricular weight compared to ISO group. Present study concludes that, phytophenolic content of COC extract is accountable for anti-cardiac remodelling effect in the present study. It could be due to preventing the oxidative damage and scavenging free radicals produced by Isoproterenol.
The heart after staining with TTC showed a pale staining area which represented the area of myocardial infarction. The area of infarction was reduced in COC 200mg/kg BW and metoprolol Group. Co-administration of COC 200 mg/kg and metoprolol showed normal tissue with no necrotic regions confirming the cardioprotective effect of *Crataegus oxycantha* against tissue necrosis induced by Isoproterenol.

The present study revealed that *Crataegus oxycantha* pretreatment attenuated oxidative stress and inflammatory mediators as well as decreased tissue damage in ISO induced MI in rats. The effect of COC on endothelial dysfunction and the synergistic effect with metoprolol was evaluated for the first time and the antioxidant levels were increased in the treatment groups which proved its beneficial effects and outcome of the study has highly illuminated these effects.

Present study suggests that 200 mg/kg BW of COC exhibits cardio protective and endothelial protective effect and in combination with metoprolol, COC shows synergistic effect necessitating its use as adjuvant therapy in prevention of myocardial infarction and endothelial dysfunction.

To conclude, in the light of the above findings the COC produced cardio protective effect on myocardium and endothelium and also it produces synergistic effect with metoprolol in the prevention and treatment of MI. Further experiments on higher order of animals and clinical studies may be required to demonstrate the cardio protective effects of *Crategus oxycantha*.