ABSTRACT

Myocardial infarction (MI) is one of the leading cause of death in India and worldwide. MI, commonly known as heart attack is a disorder where blood supply to a region of heart is interrupted. Decreased blood supply results in prolonged ischemia and death (necrosis) of heart muscle (myocardium). A plant named \textit{Crataegus oxyacantha} (COC) is widely used in traditional medicine in the treatment of various cardiovascular disorders. In the current study, we evaluated the effect of COC on MI and endothelial dysfunction in rats. The study was carried out in three phases. In phase-I, acute and sub-acute toxicity of COC was investigated. In the Phase-II, the Isoproterenol dose was standardised. In Phase-III, the comparative therapeutic potential of COC with metoprolol in the prevention of myocardial infarction was evaluated in Isoproterenol (ISO) induced MI in rats.

The Phase – I study was designed to investigate the acute and sub-acute toxicities of \textit{Crataegus oxyacantha} dry fruit extract. Dose dependent toxicity studies was carried out, where biochemical analysis of liver enzymes (ALT, AST, total bilirubin), proteins, Urea, K$^+$, Na$^+$, Cl$^-$ and whole blood analysis (RBC, WBC, Hct, Hg, MCV, MCH, MCHC, PLT, Clotting time, PT and APTT) were performed.

We observed that Ethanolic fruit extract of COC did not produce any toxicity when administered up to the dose of 2000mg/kg body weight, as per the OECD guidelines.

In Phase –II, the ISO effects were studied to standardise the exact dose for induction of Myocardial infarction and tissue necrosis. Upon examining three different doses of ISO, based on serum troponin-I levels and histopathological observations, subcutaneous injection of 85 mg/Kg BW was proven to produce myocardial infarction in rats.
The Phase-III study was designed to compare the cardio protective effect of various doses of COC (50,100 and 200 mg/Kg BW) vs 50 mg/ Kg BW of metoprolol on ISO induced MI in rats.

Biochemical profile including Serum Troponin-I, CKMB, ALT, AST, LDH, and Lipid profile were done. Endothelial markers like V-CAM, CRP and TNF-α were measured to determine endothelial dysfunction. Anti oxidant status and cardiac enzymes were studied in tissue homogenate. The changes in the myocardium was examined by histopathological analysis and TTC staining. Heart weight, left ventricle weight and left ventricle wall thickness was measured.

In comparison with ISO treated animals the COC 100 mg/kg BW and 200 mg/kg BW showed positive effects on cardiac enzymes, antioxidants, lipid profile as well as no myocardial tissue damage in histopathological examination and TTC staining and COC significantly reduced Left ventricle wall thickness, Heart and left ventricle weight in comparision with ISO treated group. It does not produced toxicity in other vital organs.

However, when COC was used in combination with metoprolol showed significant improvement in myocardial and endothelial functions were observed in comparision to metoprolol or COC when used alone.

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.