histopathological alterations
Results

Histopathological examination of myocardial tissue of saline administered normal control rats (CON group) depicted clear integrity of myocardial cell membrane. Endocardium and pericardium were seen within the normal limits. No necrosis, edema, inflammatory cells infiltration was seen. Flavonoid rich AIE treatment alone (AIE group) at 200 mg/kg.bw dose showed the normal architecture of rat with no sign of inflammation, but at the same with few interstitial spaces. In 85 mg/kg.bw ISO administered (ISO) group, extensive myofibrillar degeneration, which was associated with infiltration of neutrophil granulocytes and interstitial edema, vacuolar changes with focal myonecrosis, myophagocytosis was observed.

Pretreatment with flavonoid rich AIE modulated the myocardial degeneration effects of isoproterenol. Most of outstanding pathological findings in ISO+AIE group were slight degree of inflammation in subendocardial area but without any severe tissue destruction. Moreover, there was intact myocardial tissue in this group. Mild myofibrillar degeneration, which is associated with interstitial edema were seen in myocardial tissue of rat receiving amlodipine 9 mg/kg.bw+isoproterenol (ISO+AML).

Discussion

The pathophysiological changes following ISO administration are comparable to those taking place in human myocardial alterations (Fatih et al., 2009). On histopathological examination, the ISO administered group demonstrated focal myonecrosis and chronic infiltration of inflammatory cells. Marked vacuolar changes and edema were seen. Moreover significant increase in the heart weight and hypertrophic index of ISO treated rats has been attributed to increased water content,
formation of oedematous intramuscular spaces, extensive necrosis of cardiac muscle fibres and invasion by inflammatory cells (Thounaojam et al., 2011).

In the present study, pretreatment with flavonoid rich AIE significantly minimised increase in heart weight and hypertrophic index possibly due to prevention of edema (Devika and Prince, 2008). Our results are also in consistent with the earlier reports (Ravirajsinh et al., 2010). AIE pretreatment at dose of 200 mg/kg.bw showed only mild inflammation without edema, infarction and the myocardial fibers were within normal limits. This observation is suggestive of salvation of higher viable area in AIE pretreated rats and protection against ISO induced cardiac damage. These results can be attributed to the high content of flavonoids in AIE that helps in the protection of the cardiac tissue against ISO induced oxidative damage (Devika and Prince, 2008).

The histoarchitecture of cardiac tissue of CON rats appeared to be normal as there was no visible necrotic damage to the myocytes. Decrease in myocardial CK-MB, LDH, endogenous antioxidants and increased lipid peroxidation during ISO induced necrosis is a sensitive index of the degree of ischemic damage and corroborated with histological results (Jennings et al., 1990; Mohanty et al., 2004). Flavonoid rich AIE pretreatment restored the endogenous antioxidants and controlling lipid peroxide formation and preserving activities of CK-MB, LDH enzymes demonstrated its protection of the myocardium against ISO induced myocardial injury. Furthermore, histopathology of myocardium correlated with the biochemical findings of our study. It is concluded that flavonoid rich fraction AIE has a potential to inhibit the cardiotoxic effects induced by ISO and possesses a significant therapeutic value in the prophylactic treatment of MI.
Fig: 5.1. Effect of flavonoid rich AIE on the histological morphology of myocardium shown by hematoxylin and eosin staining: (A) control group; (B) AIE only; (C) isoproterenol induced; (D) AIE + isoproterenol; (E) amlodipine + isoproterenol. (i interstitium, cm cardiac myocytes, in inflammatory cell infiltration, ed edema)