ABSTRACT

The role of oxidative stress in genesis of heart disease is well studied. In pathological or disease condition the production of free radicals may outweigh the scavenging effect of antioxidants and leads to oxidative stress. Reports from several studies had shown beneficial effects of antioxidant therapy in hypertension, atherosclerosis, ischemic heart disease, cardiomyopathies and congestive heart failure. In addition, epidemiological data as well as *in vitro* studies strongly suggest that functional food enriched with antioxidant phytochemicals have strong protective effects against major degenerative diseases including cancer and cardiovascular diseases. Previous study on hypolipidemic activity of anthocyanin rich red cabbage (*Brassica olereacea* var. capitata F. Rubra; ARCE) from our lab had laid the foundation of the study envisaged herein. The aim of this study was to decipher the role of ARCE in preventing the oxidative stress induced pathogenesis in heart. Cardioprotective potential of ARCE was assessed in H_2O_2 treated rat neonatal cardiomyoblasts (H9c2 cells) and isoproterenol (ISO) induced rodent model of myocardial infarction. H_2O_2 treated H9c2 cells recorded cytotoxicity (48-50%) and apoptosis (57.3%). However, ARCE treatment reduced cytotoxicity and apoptosis in H9c2 cells. Also, ARCE pretreatment reduced the intracellular oxidative stress, prevented the loss in mitochondrial membrane potential and prevented apoptosis in H9c2 cells as evident by DCF-DA staining, RHO-123 staining and mRNA expression level of *sod, catalase, caveolin-3, bax* and *bcl-2*. Rats pretreated with ARCE for 30 days followed by ISO treatment recorded decrease in heart: body weight ratio with improved levels of enzymatic antioxidants (*sod* and *catalase*) and apoptotic genes (*bax* and *bcl-2*) similar to the control group suggesting that ARCE pretreatment prevents ISO induced depletion of

enzymatic antioxidants and apoptosis. ARCE+ISO treated group accounted for upregulation of *caveolin-3*and *SERCA2a* and downregualtion of *ANKRD1* expression as compared to the ISO treated group implying towards ARCE mediated regulation in membrane damage, mechanosensing machinery and calcium imbalance. Histoarchitechture of ventricular tissue of ISO treated group was marked by infracted areas, derangement of myocardium, loss of nuclei and distortion of collagen fibres as observed in TTC, HXE and picrosirus red staining. Whereas, histoarchitechture of ventricular tissue of ARCE+ISO treated group was similar to that of normal control. Thus, this study provides an evidence on potential of ARCE in preventing myocardial infarction (MI). Molecular docking scores and Ligplot analysis of cyanidin-3-glucoside (-36.40 kJ/mol), cyanidin-3,5-diglucoside (-26.22 kJ/mol), delphinidin-3-glucoside (-35.56 kJ/mol) and isoproterenol (-30.54 kJ/mol) showed stable hydrophobic and electrostatic interactions with β1 adrenergic receptor (AR). Cyanidin-3,5-diglucoside required more free energy to bind β1AR then cyanidin-3-glucoside and delphinidin-3-glucoside. Also, cyanidin-3-glucoside and isoproterenol were found to interact with similar amino acid residue of β1AR. This study throws light on the underlying mechanism of cyanidin-3-glucoside as a cardioprotectant in ARCE and its subsequent ability in protecting myocardium from further pathogenesis. Overall this study elucidates the mechanism of ARCE mediated prevention of experimentally induced myocardial damage.