# 1. ABSTRACT

**Aim:** To evaluate 2-APB, Eugenol, *Piper betle ethyl acetate* and *Rubia cordifolia* in various cardiovascular disorders like Hypertension, Myocardial ischemia and reperfusion injury through Store operated calcium channel blocker.

**Material and Methods:** Phytochemical screening, in-vitro antioxidant activity of plant extracts were measured and standardized by GC-FID analysis. RP-HPLC method and pharmacokinetic study of 2-APB was performed. Drugs were evaluated on H9c2 cell through cytoprotective assay, Intra cellular ROS and Apoptosis assay. In-vivo experiment was performed in three pharmacological models. First model, Angiotensin-II induced acute hypertension in vagotomized rat, in which blood pressure, serum electrolyte level, antioxidant status in heart and kidney were measured. Second model, Isoproterenol induced global ischemia, in which electrocardiography, hemodynamic parameter, cardiac markers, serum electrolytes, membrane bounded enzyme, antioxidant status, anti-inflammatory markers and histopathology were performed. Third model, Left anterior descending coronary artery ligation induced reperfusion injury cardiac marker was evaluated. In all the models STIM1 and Orai1 protein expression in heart were measured by western blot analysis. For the safety concern, drugs were evaluated on H9c2 cell and doxorubicin induced cardiotoxicity. Moreover, plant extracts were evaluated for acute and sub-acute toxicity study by OECD guidelines.

**Results:** Selected plant extracts have high total phenolics and total flavonoids content. PBEA had strong in-vitro antioxidant and free radical scavenging activity as compare to RCHA. Selected drugs 2-APB (150 µM), Eugenol (50 mM), PBEA (10 µg/ml) and RCHA (100 ng/ml) dose had significantly cytoprotectivity activity, ROS scavenging activity, antioxidant activity and apoptotic activity. In in-vivo models, selected drugs were significantly improved the antioxidant activity, electrocardiographic pattern, hemodynamic parameter, electrolyte level, ATPase activity and histopathology. STIM1 and Orai1 protein expression were suppressed by all drugs depends upon severity of the disease. Moreover, PBEA was found to be safe drug in the acute and sub-acute study.

**Conclusion:** PBEA may work safely in cardiovascular disorders through blocking SOCE channel.