CHAPTER 3

AIMS AND OBJECTIVES

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Cardiovascular disease (CVD) results in approximately 7 million deaths per annum world-wide. Many of these result from sequelae following myocardial ischemia / reperfusion (I/R) injury. In recent years, more than 6 million people died of ischemic heart disease (IHD). It is predicted to be the leading cause of deaths in the world over in the near future, although treatments for ischemic heart disease such as recanalization therapy have progressed, reperfusion treatment often makes way for myocardial injury by increasing inflammatory responses. There is a growing body of evidence that inflammation is one of the major contributors to myocardial infarction and to ischemic reperfusion injury (IRI). Research findings are unveiling the potential role of inflammatory mediators in ischemic-reperfusion injury.

Recent developments in immunology and cell biology have demonstrated the importance of inflammation in IRI. Since available treatment for IHD is minimally effective, substantial efforts are being directed towards the discovery of new drugs for IHD. In this context, pyrazolone derivatives have been developed and proved as a strong novel free radical scavenger. Moreover, it has been shown that pyrazolone has preventive effects on myocardial injury following ischemia and reperfusion in the rat heart and in patients with acute myocardial infarction. As the literature revealed that 3-methyl pyrazol-5-one is a versatile lead molecule for synthesizing newer drug candidates, the main object of the project is designed as follows.

3.1. Synthesis of novel 3-methyl pyrazol-5-one derivatives as heterocyclic scaffold

3.2. Characterization of synthesized compounds by modern physio chemical methods

viz Melting Point , TLC and by spectroscopic methods such as UV-Visible Spectroscopy, FTIR Spectroscopy, NMR Spectroscopy, Mass Spectroscopy and elemental analysis.

3.3 Evaluation of cardio protective activities by chemical methods.

3.3.1. Estimation of Plasma lipid profile

Plasma total cholesterol (TC), total protein (TP), triglycerides (TG), high density lipoprotein (HDL), low density lipoprotein (LDL) and very low density lipoproteins (VLDL).

3.3.2. Estimation of Plasma cardiac specific injury markers

Activity levels of creatine phospokinase (CPK) lactate dehydrogenase (LDH), alanine transaminase (ALT), aspartate transaminase (AST) and alkaline phosphate (ALP) in plasma.

3.3.3. Estimation of Cardiac endogenous antioxidant

Superoxide dismutase (SOD); Catalase (CAT) and reduced glutathione (GSH).

3.4. Evaluation of cardio protective activities by using Langendorff's apparatus

3.4.1. Estimation of Myocardial tissue injury markers

Malonaldehyde (MDA) and 4- Hydroxy- 2- Noneal (4-HNE).

3.5. Histopathology

Light microscopic Haematoxylin and Eosin stained sections are studied.

3.6. Analgesic and anti inflammatory activity studies

Study of analgesic and anti inflammatory activity.

3.7. Statistical analysis to verify the significance of the results

Data were analysed for statistical significance using one way analysis of variance (ANOVA) followed by Dunnets test and results are expressed as mean±S.E.M using Graph Pad Prism version 3.0 for Windows, Graph Pad Software, San Diego California USA.