3. AIM & SCOPE OF THE STUDY

The objective of the present study is to establish an experimental model of NASH and identify safe and effective agents to treat NASH. The present study is concerned with exploring the potential effects of the three drugs of choice viz. Pioglitazone – an insulin sensitizer, Quercetin – hepatoprotectant, an antioxidant and hydroxy citric acid – lipid regulator in experimental model of non alcoholic steatohepatitis (NASH).

Hence a study on the following topics has been considered appropriate and this study was undertaken in two distinct phases.

3.1. PHASE – I: ESTABLISHMENT OF EXPERIMENTAL MODEL OF NASH IN RATS

A high-fat diet (HFD) is used to create a model of NASH. Thus, this model mimics the most common features of NASH in humans and provides an ideal tool to study the role of events involved in the pathogenesis of NASH and to define any future experimental therapy, which ameliorated the degree of liver injury. Liver biopsy is the only way to confirm the presence or absence of NASH in a person with features of NASH. It also remains the “gold standard” for fibrotic severity.

3.2. PHASE – II: COMPARATIVE STUDY OF PROTECTIVE ROLE OF PIOGLITAZONE, QUERCITIN AND HYDROXY CITRIC ACID

Since the pathogenesis of NASH involved interplay of three possible mechanisms such as hyper insulinemia, lipotoxicity and oxidative
stress, three categories of drugs, pioglitazone as insulin sensitizer, quercetin as hepatoprotectant & antioxidant and hydroxy citric acid as an lipid lowering agent & antiobesity agent, have been chosen in this study.

This study is designed to study the comparative protective role of the three drugs of choice by histopathological studies, scanning electron microscopy (SEM) studies and other important NASH biomarkers. Various biochemical experiments have also been carried out to analyze the possible mechanisms involved in the pathology of NASH by assessing serum liver function test parameters, general biochemical parameters, hepatic lipid profile, lipoprotein levels, enzymatic and non enzymatic antioxidants levels in liver tissue, components of the extra cellular matrix (ECM), various inflammatory markers and other immunogenic related parameters with regard to liver diseases. The study is also designed to separation analysis of phospholipids by thin layer chromatography (TLC), Real time – polymerase chain reaction (RT-PCR) analysis to assess expression of vascular endothelial growth factor messenger RNA (VEGF mRNA), assay of cytochrome P450 2E1 (CYP2E1) enzyme levels by immunoblot analysis, immune histochemistry of cytokeratin – 18 (CK-18), and comparison with alcoholic liver disease (ALD), estimation of tissue polypeptide specific antigen (TPSA) as a non invasive biomarker to diagnose NASH by enzyme linked immunosorbent assay (ELISA) and comparison with ALD were also carried out.