CHAPTER 3
AIM AND OBJECTIVE

Aceclofenac is one of the well tolerated COX-2 inhibitor and is often the drug of choice in the treatment of osteoarthritis, rheumatic arthritis and other related conditions. However, because of its short half life (2-4 hrs) it requires dosing of 100 mg twice daily. Missing of dose, which is often common, would cause inconsistence in drug level in the blood, which would in turn reflect in poor therapeutic outcome. It has been reported that more than 50% of patients fail to take medicine as advised. Extended release formulations are the tools useful in promoting medication adherence and improving therapeutic outcomes. Medication adherence in chronic conditions like arthritis improves the quality of life of the patients.

The present study is an attempt to develop extended release formulation of aceclofenac to addresses the above issues.

The objectives for the present study are -

- To identify formulation excipients based on compatibility studies.
- To Optimize formulation and processing parameters (Stirring speed, Viscosity of oil phase and Percentage of emulsifying agent, etc.) using optimization technique (Response Surface Methodology) to get the desired response (particle size, entrapment efficiency and drug release).
- To predict the optimized formulation based on the desired response obtained.
- To prepare the aceclofenac microparticles based on predicted optimized formulation.
- To evaluate the product through various in-vitro (entrapment efficiency, drug content, surface characteristics, particle size, drug release & stability) and in-vivo (safety, bioavailability & efficacy) studies.
PLAN OF THE WORK

1. Selection of drug and polymers through literature search
2. Assessment of suitability of polymer based on the drug-excipient compatibility studies using DSC, XRD and FTIR.
3. Formulation of trial run of extended release aceclofenac microparticles using emulsion solvent evaporation technique.
4. Optimization of formulation and processing parameters (polymer ratio, stirring speed, Viscosity of oil phase [polymer ratio] and proportion of emulsifying agent, etc.)
5. As function of the desired responses (particle size, entrapment efficiency and drug release).
6. Predicting the optimized formulation based on the optimized formulation and processing parameters using derringer’s desirability method.
7. Validation and in vitro evaluation of optimized formulation entrapment efficiency, assay (drug content), and dissolution release profile, release mechanisms, surface morphology and particle size analysis.
8. Stability studies of optimized formulations as per ICH guidelines.
9. In vivo study of final products (acute toxicity, bioavailability, anti-inflammatory and analgesic activity studies in animal model)
CHAPTER 4
PREFORMULATION STUDIES

4.1 INTRODUCTION

Preformulation as a stage of development of a new formulation and characterise the physicochemical properties of drugs. All these parameters are studied prior to the formulation were carried out by Differential Scanning Calorimetry (DSC), X-ray diffractometry (XRD), and Fourier Transmission Infra Red (FTIR) Spectroscopy. Estimation of aceclofenac by Spectrophometric method and Estimation of aceclofenac in plasma by HPLC method. When these studies are completed the results obtained are analysed and utilised for the development of the microparticle formulation.

4.1.1 DRUG EXCIPIENT COMPATIBILITY STUDIES

Drug polymer compatibility studies were carried out by Differential Scanning Calorimetry (DSC), X-ray diffractometry (XRD), and Fourier Transmission Infra Red (FTIR) Spectroscopy.

4.1.1.1 Differential Scanning Calorimetry

DSC thermograms of aceclofenac, individual polymers Ethyl cellulose, Eudragit RSPO, Aerosil and physical mixtures of aceclofenac and polymers were recorded in a Differential Scanning Calorimeter (Shimadzu, Model no: DSC-60).

Pure drug, pure excipients and physical mixtures of pure drug and excipients (1:1) were sealed in aluminum pan, and scanned between 25°C and 300°C with heating rate of 10°C per minute under an atmosphere of dry nitrogen. The thermograms obtained were observed for any interaction.

4.1.1.2 X-ray diffractometry (XRD)

X-ray diffractometry is one of crystallography characterization tools. It is employed by researchers for a wide variety of applications. It is used as an analytical tool in identification of the constituents of mixtures of crystalline phases and for the