ABSTRACT

The Cefuroxime axetil has been used in treatment of wide range of infections but exhibits poor and variable bioavailability thus it is difficult to establish optimal oral dosage schedule. The purpose of this work was to prepare stable solid self-microemulsifying drug delivery system (S-SMEDDS) of cefuroxime to improve the solubility and dissolution. The saturation solubility of drug in oils, solvents, surfactants and co-surfactants were determined and ternary phase diagram was drawn. Based on the results SMEDDS were prepared and characterized for self-emulsification properties and in-vitro dissolution. One of the best SMEDDS formulations was converted to S-SMEDDS by adsorption technique using maltodextrin as adsorbent. SEM of the S-SMEDDS revealed that particles were well separated and were free flowing, characterization by DSC, XRD revealed no interaction between drug and excipients. In-vitro dissolution was rapid and complete and no marked changes in physical and emulsification property were observed on stability.

KEYWORDS: Self-emulsification; Adsorption technique; Scanning electron microscope.

Introduction

Cefuroxime (C) is a second generation cephalosporin used against different kinds of bacterial infections. The prodrug, 1-acetyloxyethyl (axetil) ester of C known as Cefuroxime axetil (CA) has been used in oral dosage forms. CA is an acid stable lipophilic oral prodrug hydrolyzed to C by intestinal and or plasma enzymes. It is reported to have bioavailability of 35 to 50%, maximum drug concentration occurs at 1 to 4 hours and elimination half-life is 1 to 2 hours (Ruiz-Carretero et al., 2004; Ravindra et al., 2009; Anna Szlagowska et al., 2010). It is difficult to establish optimal oral dosage schedule due to its poor and variable bioavailability.

Very limited work has been published on increasing the solubility and dissolution of CA. The approaches reported for increasing the dissolution are preparation of solid dispersion using urea as carrier (Arora SC et al., 2010) and preparation of gastro retentive mucoadhesive tablets for controlled release (Gudigennavar et al., 2013).

Self-microemulsifying drug delivery systems (SMEDDS) are the preferred method for enhancing solubility and bioavailability of poorly bio available drugs. But these formulations are having low stability, shows irreversible drugs/excipients precipitation, interaction of the content with capsule shell, capsule leaking and on storage dissolved drug or excipient reprecipitate leads to slow release or partial release of drug (Bo Tang et al., 2008).

To address these problems, S-SMEDDS have been investigated as alternative technique. Such system involves conversion of SMEDDS into powder; these can be further compressed into tablets or filled in to capsules. The S-SMEDDS are self emulsifiable, exhibits higher solubility, bioavailability and stability (Karanakar Reddy et al., 2011; Karanakar Reddy et al., 2010).

Different methods have been used for manufacture of S-SMEDDS, they are adsorptions on to solid carriers, spray drying, melt extrusion etc. Among these methods, adsorption process is preferred as it involves mixing of liquid formulation with carriers in a blender to convert in to powder. The powder can be filled into capsules or mixed with suitable excipients and compressed into tablets (Puttachari et al., 2013; Katteboina et al., 2009; Katteboina et al., 2008: Koushik et al., 2013). The objective of this study was to prepare stable solid form of Cefuroxime with self-emulsifying properties to overcome the poor bioavailability.

Materials and Methods

CA was received from Indoco Remedies, Mumbai. Labrasol and Gelucire were received from Gattefosse and PEG 400 (Lutrol E-400) from Signet. Hard gelatin capsules were received from Associated Capsules, Mumbai, India and all other reagents were purchased from SD fine chemicals. All the excipients and reagents