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Original Article

Formulation evaluation and stability studies of hydrogel tablets containing Cefditoren Pivoxil

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ABSTRACT

Aim: Cefditoren Pivoxil hydrogel tablets were prepared to achieve the gastro retentive effect in order to improve its absorption and bioavailability.
Methods: The formulations were made by varying the concentrations of carbopol and sodium alginate. The prepared blends were compressed directly using a 16-station rotary punch tablet machine (Cadmach, Germany) having caplet shaped concave punches. Stability studies for the selected formulation were performed as per the ICH protocol.
Results: The pre-compression parameters and post compression parameters were within acceptable pharmacopeial limits. The tablets prepared with sodium carbonate showed good porosity in the swelling index studies. The *in-vitro* dissolution behavior shows that the formulations that contain carbopol (100 mg) and sodium alginate (30 mg) were found to have good controlled release of 95.012% at 24th hour.
Conclusion: By preparing Cefditoren Pivoxil hydrogels with the above mentioned polymers gastro retentive effect was achieved, further the drug release can be controlled.

1. Introduction

Oral administration is still a common convenient method for introducing drugs in to the systemic circulation and because of ease of administration and low cost therapy leads to higher levels of patient compliance.[1] However, this approach is not has been suited to a variety of active pharmaceutical ingredients (API) which are of having a narrow therapeutic absorption window in the upper GIT (gastro intestinal tract). This is due to short transit time of the selected dosage form in the segments of upper GIT leads to lesser bioavailability. It was suggested that novel drug deliveries like gastro retentive dosage forms like oral hydrogels were the recent advances for delivering the drug molecules to the upper gastro intestinal tract for prolonging the drug release and to improve the absorption.[2]

The development of oral hydrogels was formulated with an aim to hold the dosage form in the gastric environment.[3] These drug delivery systems maintain its uniformity throughout the stomach and swells up rapidly in the stomach environment for a controlled drug release.[4] Hydrogel is a three dimensional polymeric network of hydrophilic chains which are cross-linked either through physical or chemical bonding. Hydrogel absorbs water to swell in the presence of surplus water because of the hydrophilic nature of polymeric chains.

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Cefditoren Pivoxil (CP) is a semi synthetic, third generation cephalosporin exhibiting bactericidal action by inhibiting cell wall synthesis.[5] Cefditoren Pivoxil is a prodrug which can be hydrolyzed by esterase during absorption to Cefditoren as an active drug and is distributed in the blood circulation. Cefditoren is used for the treatment of uncomplicated skin and structure skin infections. CP has a broad spectrum of activity against Gram negative and Gram positive bacterial infections including strains of *Staphylococcus pyrogenes*, *Haemophilus influenza*, *Klebsiella pneumonia* and *Staphylococcus aureus*.[6] CP is the most frequently used drug for the treatment of tonsillitis, pharyngitis and acute exacerbations of chronic bronchitis.[7]

The present research was mainly focused to formulate the swellable hydrogel matrix formulations for controlled drug delivery and to study the drug release pattern of Cefditoren Pivoxil. Further the pre-compression and post compression parameters were evaluated. The swelling index and stability studies were also performed.[8]

2. Materials and methods

2.1. Materials

Cefditoren Pivoxil (CP) was obtained as a gift sample from Hetero drugs (Hyderabad, India), Carbopol 940 and sodium alginate was procured from Pure Chem Laboratory. Magnesium-stearate, lactose and all other solvents and reagents used were of analytical reagent grade were procured from SDFCL, India.

2.2. Experimental

2.2.1. Drug-polymer interaction study

Assessment of possible incompatibilities between an active drug substance and different excipients forms an important part of the pre-formulation stage during the development of solid dosage form. Therefore FTIR spectra of the drug and the polymer-drug mixture were recorded on Thermo Nicolet FTIR 330, spectrometer using a thin film supported on KBr pellets in order to find out the physico–chemical interactions between the polymer and drug-polymer mixture.[9]

2.2.2. Evaluation of tablet blend

Before compressing into the tablets the tablet blend was evaluated for its rheological properties like angle of repose (Θ), bulk density (B.D), tapped density (T.D), Carr's index (C.I) and Hausner's ratio (H.R).[10]

2.2.3. Preparation of Cefditoren Pivoxil tablets

The tablet ingredients were weighed accurately as mentioned in Table 1. The above ingredients were then passed through a 20-mesh sieve and properly mixed. Finally the blends were mixed for 5 min after the addition of magnesium-stearate and talc. The blends were compressed using a 16 station rotary punch tablet machine (Cadmach, Germany) having caplet shaped concave punches.

2.2.4. Evaluation of hydrogel tablet characteristics

Hydrogel tablets were evaluated for drug content uniformity, weight variation, friability, thickness and hardness according to the specifications of British pharmacopoeia. Drug content was analyzed using Shimadzu UV–Visible spectrophotometer (1700) at 271 nm and the % of the drug content was estimated.[11]

2.2.5. Water uptake studies

The swelling index for the formulation 5 was calculated by placing the weighed tablets in the medium (900 mL of 0.1 N HCl) at 37 ± 0.5 °C. Periodically the tablets were removed from the medium and were re-weighed. Percentage swelling of the tablet was stated as percentage water uptake.[12]

$$\text{Water Uptake \%} = \frac{\text{Weight of swollen tablet} - \text{Initial weight of the tablet}}{\text{Initial weight of the tablet}} \times 100$$

2.2.6. In-vitro dissolution study

The release of CP from hydrogel matrix tablets was carried out using a USP apparatus II (Electrolab Disso 8000) in 900 mL of 0.1N HCl at 75 rpm maintained at 37 °C ± 0.5°. Samples of 5 ml were taken at regular 1 h time intervals and the absorbance was measured at 271 nm with UV–Visible spectrophotometer of JASCO V 670. The sink condition was maintained by replacing with fresh buffer medium. The dissolution study was carried out for 24 h.

2.2.7. Stability studies

For all the pharmaceutical dosage forms it is important to determine the stability of the dosage form .The stability studies were carried out for the most satisfactory formulation as per the ICH guidelines to estimate the stability of the prepared drug dosage formulation. The formulation sealed in aluminum package and kept in humidity chamber maintained at 40 ± 2 °C, 75 ± 5% RH and at 30 ± 2 °C, 65 ± 5% for 3 months. At the end of studies *in-vitro* drug release and post compression parameters were evaluated to the samples.[13]

Table 1 – Formulation composition of hydrogel tablets.

Ingredients (mg/tablet)	F1	F2	F3	F4	F5	F6	F7
Drug	200	200	200	200	200	200	200
Carbopol	50	75	100	100	100	150	150
NaHCO3	30	30	30	30	30	30	30
Lactose	212	187	162	142	132	92	82
Sodiumalginate	–	–	–	20	30	20	30
Mgstearate	5	5	5	5	5	5	5
Talc	3	3	3	3	3	3	3