Original article

Gastro retentive microencapsulated Cefpodoxime Proxetil to improve oral bioavailability

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Abstract

Objective: The objective of the present study was to develop floating microspheres of Cefpodoxime Proxetil in order to achieve an extended retention in the upper GIT, which may result in enhanced absorption and there by improved bioavailability. **Methods**: The microspheres were prepared by non – aqueous solvent evaporation method using polymers such as Hydroxyl Propyl Methyl Cellulose (HPMC K15M), Ethyl Cellulose (EC) in different ratios, and Cefpodoxime Proxetil contain in each formulation. *In vitro* drug release were performed by USP apparatus type I andthe microspheres were characterized by calculating percentage yield, particle size analysis, buoyancy percentage, drug entrapment efficiencyand *in vitro* drug release studies. **Results**: The result showed microspheres yield were 50.50 %-72.21 %, particle size were distributed between75-600 μm, drug entrapment efficiency were 14.1 %-28.2 %, buoyancy percentage were 70.10 %-88.25 %. **Conclusion**: Cefpodoxime Proxetil floating microspheres, at the lower polymer to drug ratio, there was a significant drug release. The better drug release profile was seen with FA_2 with ratio of drug polymer (1∶2).

Keywords: Hydroxyl Propyl Methyl Cellulose; Ethyl Cellulose; Drug release; Bioavailability; Non-aqueous solvent evaporation; Floating microspheres

INTRODUCTION

Gastro retentive floating microspheres have emerged as an efficient means of enhancing the bioavailability and controlled delivery of many drugs. The increasing sophistication of delivery technology will ensure the development of increasing number of gastro-retentive drug delivery systems to optimize the delivery of molecules that exhibit absorption window, low bioavailability, and extensive first pass metabolism. a gastric floating drug delivery system can overcome at least some of these problems and is particularly useful for drug that are primarily absorbed in the duodenum and upper jejunum segments and it can prolong the retention time of a dosage form in the GIT tract, there by improve the oral bioavailability[1]. The control of gastro intestinal transit could be the focus of the next decade and may result in new therapeutic possibilities with substantial benefits for patients.

Cefpodoxime Proxetil is a prodrug which orally administered third generation cephalosporin with only 50 % absolute bioavailability[2]. By formulating the drug as sustained action dosage form especially, as floating dosage form the bioavailability may be improved because of the low bioavailability of Cefpodoxime Proxetil due to intestinal lumen hydrolysis

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may be to some extent prevented. Moreover the absorption of the Cefpodoxime Proxetil in the upper GIT is more [3,4].

Floating drug delivery is able to prolong the gastric retention of microspheres, thereby improving oral bioavailability of Cefpodoxime Proxetil. Some studies have been contented to evaluate the suitability of various excipient to achieve floating dosage forms[5,6].

MATERIALS AND METHODS

Materials

Cefpodoxime Proxetil was provided by Orchid Pharma. Hydroxyl Propyl Methyl Cellulose (HPMC K 15M) was purchased from Coloron Private Ltd, Asia, Ethyl Cellulose (EC) from S. D. Fine Chemicals Ltd., Dichloro methane (DCM), ethanol and Tween 80 were from Merck.

Preparation of floating microspheres

Microspheres containing Cefpodoxime Proxetil drug as a core material were prepared by a non-aqueous solvent evaporation method. Drug and HPMC and EC were mixed in the mixture DCM and ethanol at 1∶1 ratio. The slurry was slowly introduced into 30 mL of liquid paraffin containing 0.01 % Tween 80 while being stirred at 1 200 rpm using mechanical stirrer equipped with three bladed propellers at room temperature. The solution was stirred for 2 h and allowed the solvent to evaporate completely and filtered by using filter paper. The microspheres obtained were washed repeatedly with petroleum ether (40 ℃-60 ℃) until free from oil. The collected microspheres were dried at room temperature and subsequently stored in desiccators[7].

Buoyancy percentage

The microspheres weighed about 0.3 g were spread over the surface of USP XXIV dissolution apparatus (Type II) filled with 900 mL of 0.1 mol/ L Hcl containing 0.02 % of Tween 80. The medium was agitated with a paddle rotating at 100 rpm for 12 h. The floating and the settled portions of microspheres were recovered separately. The microspheres were dried and weighed. Buoyancy percentage was calculated as the ratio of the mass of the microspheres that remained floating and the total mass of the microspheres[8].

Drug entrapment efficiency

Microspheres equivalent to 50 mg of the drug were taken for evaluation. The amount of drug entrapped was estimated by crushing the microspheres and extracting with aliquots of 0.1N Hcl repeatedly. The extract was transferred to a 100 mL volumetric flask and the volume was made up using 0.1N Hcl. The solution was filtered and the absorbance was measured at 263 nm against appropriate blank. The amount of drug entrapped in the microspheres was calculated by the following formula:

$$\text{DEE} = \frac{\text{Amount of drug actually present}}{\text{Theoretical drug load expected}} \times 100$$

Yield of microspheres

The prepared microspheres with a size range of 251 μm were collected and weighed. The measured weight was divided by the total amount of all non-volatile components which were used for the preparation of the microspheres.

$$\%\,\text{Yield} = \frac{\text{Actual weight of product}}{\text{Total weight of excipients and drug}} \times 100$$

In vitro drug release study

In vitro drug release studies were carried out for all products by using USP type I (38) dissolution test apparatus. 100 mg of pure drug was used for the dissolution studies and microspheres equivalent to 270 mg of the pure drug were used. 5 mL of the aliquot was withdrawn at predetermined intervals a filtered. The required dilutions were made with 0.1N Hcl and the solution was analyzed for the drug content spectrophotometrically at 263 nm against suitable blank. Equal volume of the dissolution medium was replaced in the vessel after each withdrawal to maintain sink condition. Three trials were carried out for all formulations. From this percentage drug release was calculated and plotted against function of time to study the pattern of drug release.

RESULTS

Floating microspheres were prepared by non-aqueous solvent evaporation method with polymers such as HPMC and EC in various proportions of different formulations, namely FA_1, FA_2-FA_3, FA_4, FA_5 and FA_6. The microspheres were observed with ordinary microscope, and were found to be irregularly spherical shaped the exhibited a size of range from 75-600 μm all batch. Microspheres size distribution was approximately determined with the use of different grades of sieves. Each six formulation containing 270 mg of drug with various polymer ratios (EC/HPMC) ranging from 1∶1 to 1∶6 was taken for the preparation of floating microspheres.

The prepared microspheres were characterized by

calculating percentage yield, particle size analysis, buoyancy percentage, drug entrapment efficiency and in vitro drug release studies. The parameters evaluated Cefpodoxime Proxetil floating microspheres and its results were as shown in Table 1& Figure 1.

Table 1 Evaluation parameters of Cefpodoxime Proxetil floating microspheres.

Formulation code	Percentage of yield(%)	Drug entrapment efficiency(%)	Buoyancy percentage(%)	Percentage of cumulative drug release of microspheres after 12 h(%)
FA_1	50.5	14.1	70.1	–
FA_2	65.3	15.6	75.6	97.66
FA_3	66.5	16.4	76.4	90.80
FA_4	66.9	17.2	85.2	73.29
FA_5	76.9	28.9	87.9	66.29
FA_6	72.2	28.2	88.2	61.62

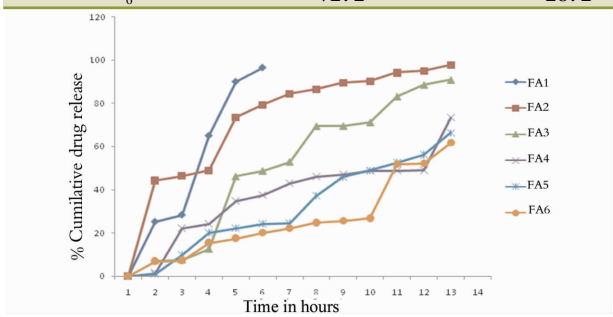

Figure 1 *In-vitro* drug release profile of Cefpodoxime Proxetil from FA_1-FA_6 formulation.

DISCUSSION

Percentage yield of formulations such as FA_1, FA_2-FA_3, FA_4, FA_5 and FA_6 were determined, it was found FA_5 yielded 76.9 %. In general with formulation (FA_5) percentage of yield was satisfied. The lowest yield was with FA_1 (50.5 %). The encapsulation efficiency was determined using the non-aqueous solvent evaporation method. The entrapment efficiency was found to be 14.1 % to 28.2 % for formulation FA_1 to FA_6, However the entrapment efficiency somewhat poor it may be attributed to mixing technique used, physical compatibility with polymer used, viscosity of media and particle size may also play a part in the entrapment of drug.

The buoyancy percentage for all batches almost was above 70 % which was studied for 12 hours. The highest percentage was obtained with formulation FA_6. Average buoyancy in percentage was found to be 70.1 % to 88.2 %. In general with increase in the amount of polymers there was an increase in the buoyancy percentage. The increase in the buoyancy percentage may be attributed to air and gel forming polymer HPMC K4M which caused swelling because of increased amount of the polymers present. Microspheres were subjected to *in vitro* release using USP dissolution apparatus Type I in 900 mL of simulated gastric pH medium. With all the formulation there was initial intermittent burst release. But the release seems to be somewhat sustained with increased in the amount of polymer. The release rate was found to be decreased in accordance with the increase in ratio of polymer used (FA_6).

Floating microsphere of Cefpodoxime Proxetil were prepared using HPMC and EC at the higher polymer to drug ratio improved the entrapment efficiency, percentage of yield as well as buoyancy percentage, whereas, in case of Cefpodoxime Proxetil floating microspheres, at the lower polymer to drug ratio there was a significant drug release, that is the 1: 2 ratio provides the desired drug release, so formulation FA_2 can be considered as best formulation.

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