FORMULATION AND EVALUATION OF CEFPODOXIME PROXETIL SUSTAINED RELEASE MATRIX TABLETS

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ABSTRACT

Formulation of Cefpodoxime proxetil extended release matrix tablets. The aim of the present study is to develop a pharmaceutically stable, once a day robust formulation which will have similar clinical efficacy as that of twice a day formulation of 200mg strength and can reduce dosage frequency. Cefpodoxime proxetil is used in the treatment of respiratory and urinary tract infections. In the present study, the polysaccharides guargum and xanthum gum were evaluated as carriers for colon targeting by formulating matrix tablets of cefpodoxime proxetil with different concentrations (5%,10%,20%,40%) of the above polysaccharides. Tablets were prepared by wet granulation method. Formulation containing 40% guargum is considered as optimized formulation as it releases less amount of drug in first 2 hours compared to other formulations. The optimized formulation was subjected to stability studies as per ICH guidelines at accelerated condition for 3 months and was found to be stable.

Key words: Cefpodoxime Proxetil, Sustained Release, Polysaccharides, Drug Release

INTRODUCTION

Oral drug delivery is the most desirable and preferred method of administering therapeutic agents for their systemic effects. Oral delivery can be classified into three categories, immediate release is designed for immediate release of drug for rapid absorption, sustained release pharmaceutical products which are designed on the basis of spansule coating technology for extended absorption and sustained release systems include any drug delivery system that achieves slow release of drug over an extended period of time. The onset of its pharmacologic action is often delayed and the duration of its therapeutic effect is sustained.

Matrix tablets: Matrix tablet has given a new breakthrough for novel drug delivery system in the field of pharmaceutical technology. It excludes complex production procedures such as coating and pelletization during manufacturing and drug release rate from the dosage form is controlled mainly by the type and proportion of polymer used in the preparations. These are the type of controlled drug delivery systems, which release the drug in continuous manner by dissolution controlled as well as diffusion controlled mechanisms. The drug is dispersed in swellable hydrophilic substances, an insoluble matrix of rigid swellable hydrophobic materials or plastic materials. The materials most widely used in preparing matrix systems include both hydrophilic and hydrophobic polymers. Commonly available polymers include hydroxyethyl cellulose, hydroxy propyl methyl cellulose, hydroxyl propyl cellulose, xanthan gum, sodium alginate, polyethylene oxide and cross linked homopolymers and copolymers of Acrylic acid.

Cefpodoxime is a broad spectrum oral third generation cephalosporin antibiotic. Cefpodoxime proxetil is a prodrug of cefpodoxime. It is well tolerated and is one of the third generation cephalosporins to be available in oral form. Cefpodoxime is bactericidal and acts by inhibition of bacterial synthesis. It passes through ion channels in the bacterial cell wall and binds to the penicillin binding proteins (PBP) in the cell membrane causing acylation of membrane bound transpeptidase enzymes; this prevents cross linkage of peptidoglycan chains, which is necessary for bacterial cell wall strength and rigidity. This leads to reduced synthesis of peptidoglycans and result in damage to cell wall. Cefpodoxime is stable in the presence of beta-lactamase enzymes.

MATERIALS AND METHODS

Guar Gum, Xanthan Gum, Lactose, Magnesium Stearate, Talc and Cefpodoxime proxetil

Preparation of matrix tablet by Wet granulation method: The ingredients were weighed accurately and mixed thoroughly. Granulation was done with a solvent blend of water and methanol (1:1). The wet mass was passed through sieve no.12 for the preparation of granules. The granules were dried in a conventional hot air oven at 40 c. The dried granules were subjected to dry screening by passing through mesh no.22, blended with a mixture of talc and magnesium stearate and compressed into tablets using 6 station rotary tablet punching machine. The total weight of each tablet was 500mg.

Table.1. Composition of matrix tablets of Cefpodoxime proxetil

Ingredients (mg)	F4
Cefpodoximeproxetil	200
Guar gum	200
Xanthan gum	-
Lactose	80
Magnesium stearate	10
Talc	10

RESULTS AND DISCUSSION

Evaluation of precompression parameters:

Angle of repose: The height and the radius of the pile were measured and the angle of repose was calculated using the equation, $\theta = \tan^{-1}(h/r)$; where θ is the angle of repose, h and r are the height and radius of the pile.

Bulk density and tapped density: The bulk density and tapped density were calculated by the following formula:

Bulk density (ρ_b) = Weight of granules (g)/Bulk volume (ml) (V_b)Tapped density (ρ_t) = Weight of granules (g)/tapped volume (ml) (V_t)Where (V_b) is bulk volume of the powder and (V_t) is tapped volume of the powder.

Carr's index and Hausner's ratio: Carr's index and hausner ratio are calculated by using following formula:

Carr's index = [(Tapped density – Bulk density)/(Tapped density)] * 100

Hausner's ratio = ρ_t / ρ_b Where ρ_t is tapped density, ρ_b is bulk density

Evaluation of tablets: Tablets were tested for hardness using Monsanto hardness tester,thickness using verniercalipers,friability using roche friabilator ,weight variation usinga electronic balance .

Estimation of drug content: Ten tablets from each formulation were powdered. The powder equivalent to 100mg of cefpodoxime proxetil was weighed and transferred into 100ml volumetric flask. The powder was dissolved in ph 6.8 phosphate buffer. The solution was filtered and suitable dilutions were prepared and the solution was analysed spectrophotometrically at 236nm using uv visible spectrophotometer.

Swelling behavior of matrix tablets: Percent weight gain by the tablet was calculated using formula:

S.I = {(Mt –M0) / M0} x 100Where S.I is swelling index, Mt is weight of tablet at time t and M0 is weight of tablet at time t=0

In-vitro drug release studies: Dissolution studies of all the batches were performed employing USP type II Dissolution testing apparatus (LABINDIA DS 8000). The dissolution test was performed using 900 ml of 0.1 N HCL(for 2hrs) followed by phosphate buffer pH 6.8 up to 24 hrs at 37°C ±0.5°C and 50 rpm. A 5ml aliquot of the sample was withdrawn periodically at suitable time intervals andvolume replaced with an equivalent amount of the dissolution medium. The samples were analyzed spectrophotometrically at 236nm using UV Visible spectrophotometer.

Table.2. In-vitro drug release data of formulation F4

Time (Hours)	Cumulative % Drug Release ± SD of Formulation 4
1	15.25±0.26
2	23.00±0.15
3	31.42±0.34
4	34.46±0.28
5	38.28±0.21
6	42.20±0.13
7	50.72±0.41
8	52.12±0.15
9	53.28±0.39
10	54.78±0.34
11	56.78±0.27
12	57.71±0.34
14	62.32±0.16
16	67.52±0.31
20	73.77±0.24
24	79.80±0.15

Table.3. Characterization of drug release from Cefpodoxime proxetil matrix tablets

Formulation Code	Correlation Co-efficient (r) value				Korsmeyer - Peppas	
	Zero order	First order	Higuchi	Hixon crowell	r value	n value
F4	0.868	0.977	0.989	0.952	0.985	0.533

The angle of repose was found to be in the range of 21.43 ± 0.32 to 27.82 ± 2.14 having good flow property.The bulk density and tapped density were found to be in the range of 0.31 ± 0.01 to 0.40 ±0.02 gm/cc and

0.34 ± 0.02 to 0.44±_0.02 gm/cc respectively. The compressibility index and hausner's ratio were found to be 6.23 ± 2.08 to 13.02 ± 2.53 and 1.07 ± 0.02 to 1.15 ± 0.03.All the results of precompression parameters were within the prescribed limits indicating good flow properties of granules. The thickness of the tablet ranged from 2.70 ± 0.10 to 2.90 ± 0.10 mm showed uniform thickness. The hardness of the tablet was found between 4.17 ± 0.29 to 5.33 ± 0.29 kg/cm^2. The friability was found to be 0.30±0.06 to 0.49 ± 0.36%, which indicates satisfactory mechanical resistance of tablets. The drug content estimation values range of 97.57±0.12 to 100.01 ± 0.39% which reflects good uniformity in drug content.

The in-vitro drug release studies it was observed that increasing the amount of gum in the formulation, resulted in slower rate and decreased amount of drug release from the tablet. The formulations containing low concentration of gums failed to control the drug release in first 2hrs in ph 1.2.The formulations F4, F8, F12 containing polymer in the concentration of 40% succeeded in the drug release up to 24hrs. However formulation F4 containing 40% Guar gum is considered as optimized formulation as it released less amount of drug in first 2hrs in ph 1.2 compared to other formulations. This shows that Guar gum is capable of protecting the drug from being completely released in the physiological environment of stomach.

CONCLUSION

The present study was aimed to develop once a day formulation which will have similar clinical efficacy as that of twice a day formulation of 200mg strength and can reduce dosage frequency which proved to be an ideal formulation, F4 containing polymer in the concentration of 40% succeeded in sustaining the drug release upto 24hrs. Therefore the formulation F4 was found to be stable.

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