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Formulation and evaluation of Ciprofloxacin controlled release matrix tablets

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Abstract

The goal of this study was to formulate and evaluate ciprofloxacin controlled release matrix tablets. Ciprofloxacin controlled release tablets were prepared by wet granulation method using two polymers such as HPMC K 100M (hydrophilic polymer) and guar gum (natural polymer) and with three polymer ratios (0.5, 1.0 and 1.5). The prepared granules were evaluated to preformulation studies such as angle of repose, bulk density, tapped density, bulkiness, compressibility index and hausners ratio. All the parameters shows that the granules having good flow properties. Then the formulated tablets were taken to evaluation studies such as hardness, weight variation, friability, drug content and thickness. All the parameters were within the acceptable limits. IR spectral analysis showed that there was no interaction between the drug and polymers. The in vitro release study was performed in phosphate buffer pH 7.4 at 278 nm. The in vitro release study showed that if the polymer ratio is increased, then the release of the drug is prolonged. HPMC K 100M shows a prolonged release when compared to guar gum.

Keywords: Ciprofloxacin, Controlled release, HPMC K100M, Guar gum.

INTRODUCTION

Oral route has been the commonly adopted and most convenient route for the drug delivery. Tablets and capsules are the major preparation before the introduction of advanced controlled drug delivery system (1).

Among various dosage forms, matrix tablets are widely accepted for oral controlled release as they are simple to formulate and easy to make. Polymers and release retarding materials used as

matrix play a vital role in controlling the drug release from matrix tablets. Ideal, oral CR systems are reliant upon the dosage form to control the rate of drug release with little or no effect from the intrinsic properties of the drug or the condition prevalence with in the GI tract. Realistic drug candidates exhibit high permeability across the GI epithelium such that their absorption rate is controlled exclusively by the rate of release from the dosage form (2).

Though a variety of substances are available to serve as releasing retarding materials for matrix tablets. Natural gums and polysaccharides and their derivatives represent a group of polymers widely used in pharmaceutical dosage forms due to their non toxicity, low cost and free availability. Natural gums and hydrophilic polymers when in contact with water; they are hydrated to form a gel. Because of this property natural gums like karaya, xanthan gum and guar gum have been reported (1) as good matrix materials for controlled release tablets.

Ciprofloxacin comes under the category of Fluorinated 4-quinolones. It has a broad antimicrobial activity and is effective after oral administration for the treatment of a wide variety of infectious diseases (2). Ciprofloxacin is the most potent Flouroquinolone active against a broad range of bacteria the most susceptible ones are the aerobic gram negative bacilli (3).

The goal behind the development of oral controlled release formulations at that time were the achievement of a constant release rate of the entrapped drug. The aim of the study was to formulate and evaluate ciprofloxacin controlled release matrix tablets.

MATERIALS AND METHODS

Materials

Ciprofloxacin was obtained as a Gift sample from Micro Labs, Hosur, HPMC K100M and Guar gum were purchased from Loba Chemicals, Mumbai. Carboxy methyl cellulose (CMC) and Starch were purchased from Paxmy Chemicals Mumbai. Poly vinyl pyrolidine, magnesium stearate and iso propyl alcohol were obtained from S.D.Fine Chemicals, Mumbai. All other reagents used were of analytical grade.

Preparation of ciprofloxacin Tablets

The tablets were prepared by wet granulation method (5). Ciprofloxacin and the polymers HPMC K100M and guar gum were mixed (0.5, 1.0 and 1.5) uniformly. CMC and starch was added to the drug and polymer mixture and blended thoroughly for 5 minutes. PVP K30 was dissolved in sufficient quantity of iso propyl alcohol and was added to the drug, polymer and lactose mixture to form a coherent mass. Then the formed coherent mass was sieved manually through sieve no. 16 to form granules. Then the granules are collected and dried at $40^0C \pm 2^0C$ for 2 hours. The dried granules were passed through sieve no. 20. The granules are then subjected to preformulation studies. After preformulation studies, the granules were mixed with magnesium stearate uniformly and are compressed into tablets.

Table: 1 Formula of CR Tablets containing Ciprofloxacin, HPMC K 100M and Guar gum as polymers with three ratios (1:0.5, 1:1 and 1:1.5)

Ingredients (mg)	F1	F2	F3	F4	F5	F6
Ciprofloxacin	100	100	100	100	100	100
HPMC K100M	50	100	150	-	-	-
Guar gum	-	-	-	50	100	150
Carboxy methyl cellulose	10	10	10	10	10	10
Starch	310	260	210	360	260	210
Poly vinyl pyrolidine K30	20	20	20	20	20	20
Magnesium stearate	10	10	10	10	10	10
Iso propyl alcohol	q.s	q.s	q.s	q.s	q.s	q.s

***Weight of each tablet was 500 mg*

Evaluation of Granules

Angle of repose

Angle of repose (θ) was determined using fixed funnel method. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the granules. The granules were allowed to flow through the funnel freely on to the surface. Angle of repose was calculated using the following equation (6).

$$\theta = \tan^{-1} (h/r)$$

Where h and r are the height and radius as of cone.

Bulk density (7)

Bulk density is the ratio between a mass of granules and its bulk volume. It is expressed by g/cc.

$$\text{Bulkdensity} = \frac{\text{Weightofpowder}}{\text{Bulkvolume}}$$

Tapped density (7)

Tapped density is the ratio between a mass of granules and volume of the granules after tapping. It is expressed by g/cc.

$$\text{Tapped density} = \frac{\text{Weight of granules}}{\text{Final volume after tapping}}$$

Bulkiness

Bulkiness is the reciprocal of bulk density. It is expressed by cc/g .

$$\text{Bulkiness} = \frac{1}{\text{Bulk density}}$$

Compressibility index and Hausner ratio (8)
The compressibility index and the closely related Hausner ratio have become the simple, fast and popular methods of predicting granules flow characteristics. The compressibility index and Hausner ratio were determined by measuring both the Bulk density and tapped density of granules.

Compressibility index = (Tapped density-Bulk density / Tapped density) × 100.
Hausner ratio = Tapped density / Bulk density

Evaluation of Tablets
Hardness (10, 11)
The strength of tablet is expressed as tensile strength (kg/cm^2). The tablet-crushing load, which is the force, required breaking tablet by compression. It was measured using a tablet hardness tester (Pfizer Hardness Tester).

Weight variation (9)
Twenty tablets ware randomly selected and individually weighted (shimdzu). The average weight of tablets was calculated.

Friability (11)
Ten tablets were placed in the Roche friabilator, which was then operated for 100 revolutions After 100 revolutions the tablets were dedusted and reweighed. Percentage friability was calculated by the following formula.

$$\text{Percentage friability} = \frac{\text{Initial weight - Final weight}}{\text{Initial weight}} \times 100$$

Estimation of drug content (12)
Ten tablets from each formulation were powdered. The powder equivalent to 100 mg of ciprofloxacin was weighed and dissolved in phosphate buffer pH 7.4 suitable dilutions was prepared and the solution was analyzed in UV-double beam spectrophotometer at 278nm using pH 7.4 as blank.

Thickness
Thickness of the tablet was tested using vernier caliper(Besto).

FT-IR Spectral analysis
IR Spectral analysis was used to study the interactions between the drug, polymer and the excipients. The drug and excipients must be compatible with one another to produce a product stable (13).

In vitro Release Studies, for all the formulated tablets were carried out using USP II paddle method at 50 rpm in 900 ml of pH 7.4 buffer solution as a dissolution medium, The dissolution medium was maintained at $37^0 \pm 0.5\ ^0$C.

10 ml of dissolution medium was withdrawn every 30 minutes intervals for 10 hrs. 10 ml of buffer solution (pH 7.4) was replaced to maintain the constant volume throughout the

experiment. The percentage of ciprofloxacin released from each formulation was measured at 278 nm using UV-visible spectrophotometer (Elico-SL164).

RESULTS AND DISCUSSION

In the present study, ciprofloxacin controlled release matrix tablets were prepared by using, two polymers HPMC K 100M and Guar gum, with three ratios (0.5, 1.0 and 1.5). A total number of six formulations were prepared by wet granulation method. Angle of repose for F1- F6 is between 30-35,bulk density is between 0.333-0.361,tapped density is between 0.399-0.407,bulkiness is between 2.49-3.00 ,compressibility index is between 11-18 is with in the acceptable limits, and hausners ratio is between 1.11-1.18 The above values of pre compression parameters shows the prepared granules having good flow property. weight variation was within ±5% it was within the acceptable limit ,hardness was with in 4-10 was within the acceptable limits, friability was within 1% it was within the limit, drug content was within 90-110 it was within the acceptable limits, all formulations showed uniform thickness.

Infra-red (IR) spectroscopy was used as means of studying drug – polymer compatibility and confirmed by comparing undisturbed structure of IR spectra of Ciprofloxacin, which indicated no drug- polymer interaction.

Table:2 Evaluation of granules

Formulation	Angle of Repose (θ)	Bulk density (g/cc)	Tapped density (g/cc)	Bulkiness(cc/g)	Compressibility index (%)	Hausners ratio
F1	3231 ±0.512	0.352 ±0.017	0.407 ±0.013	2.49 ±0.027	14.18 ±0.198	1.16 ±0.116
F2	33 39 ±0.731	0.355 ±0.031	0.399 ±0.073	2.70 ±0.032	14.13 ±0.410	1.16 ±0.451
F3	32 37 ±0.581	0.347 ±0.048	0.407 ±0.066	2.86 ±0.067	14.11 ±0.320	1.17 ±0.195
F4	34 36 ±0.629	0.342 ±0.069	0.399 ±0.091	2.89 ±0.051	14.28 ±0.237	1.16 ±0.305
F5	34 38 ±0.231	0.361 ±0.021	0.399 ±0.031	2.70 ±0.047	14.94 ±0.319	1.11 ±0.115
F6	31 38 ±0.310	0.333 ±0.051	0.407 ±0.049	3.00 ±0.063	14.28 ±0.210	1.18 ±0.216

All the reading are expressed as mean ± standard deviation (n=3)

Table -3 Evaluation of Controlled release matrix tablets of Ciprofloxacin

Formulation	Weight variation (mg)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)	Thickness (mm)
F1	498 ±2.5	5.08 ±0.13	0.501 ±0.04	96.2 ±0.58	4.2 ±0.02
F2	496 ±3.2	5 ±0.63	0.502 ±0.15	97.3 ±0.87	4.3 ±0.02
F3	497 ±2.7	4.94 ±0.30	0.602 ±0.03	97.4 ±0.20	4.3 ±0.03
F4	498 ±3.5	5.18 ±0.47	0.703 ±0.35	97.1 ±0.16	4.2 ±0.05
F5	494 ±4.3	4.98 ±0.29	0.201 ±0.04	96.8 ±0.23	4.02 ± 0.06
F6	497 ±4.2	5.12 ±0.31	0.401 ±0.26	97.2 ±0.30	4.3 ±0.03

All the reading are expressed as mean ± standard deviation (n=3)

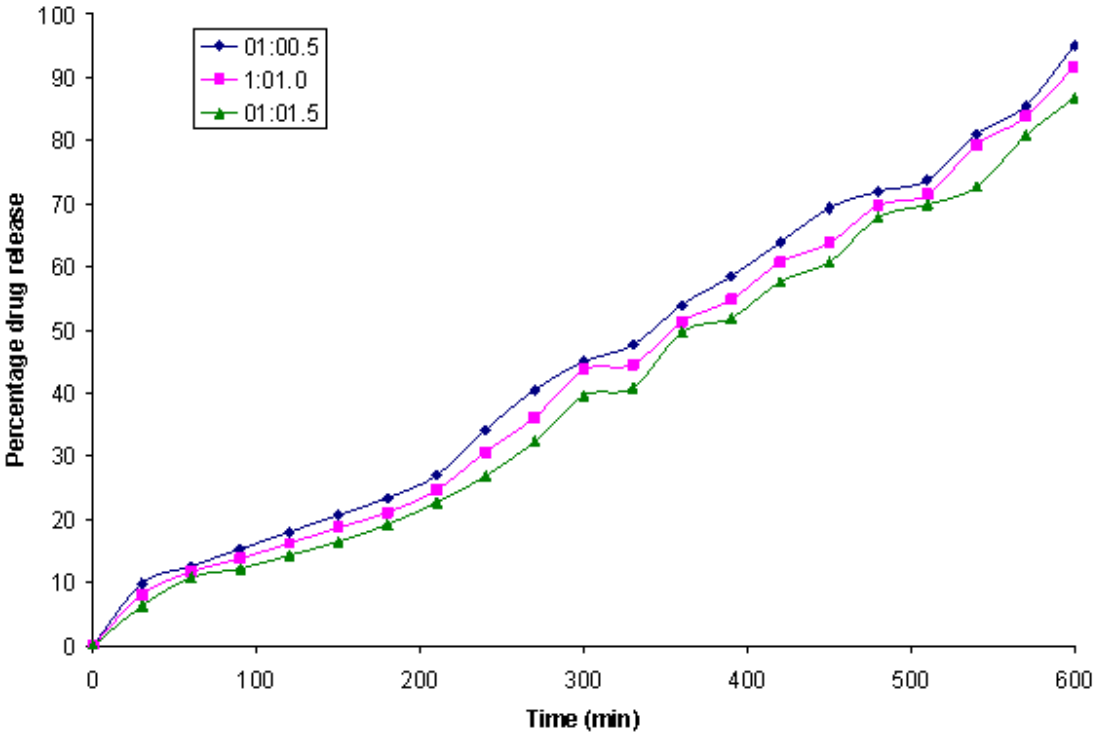

Fig. 1: *In-vitro* release study of ciprofloxacin with different ratio of HPMC K 100 M

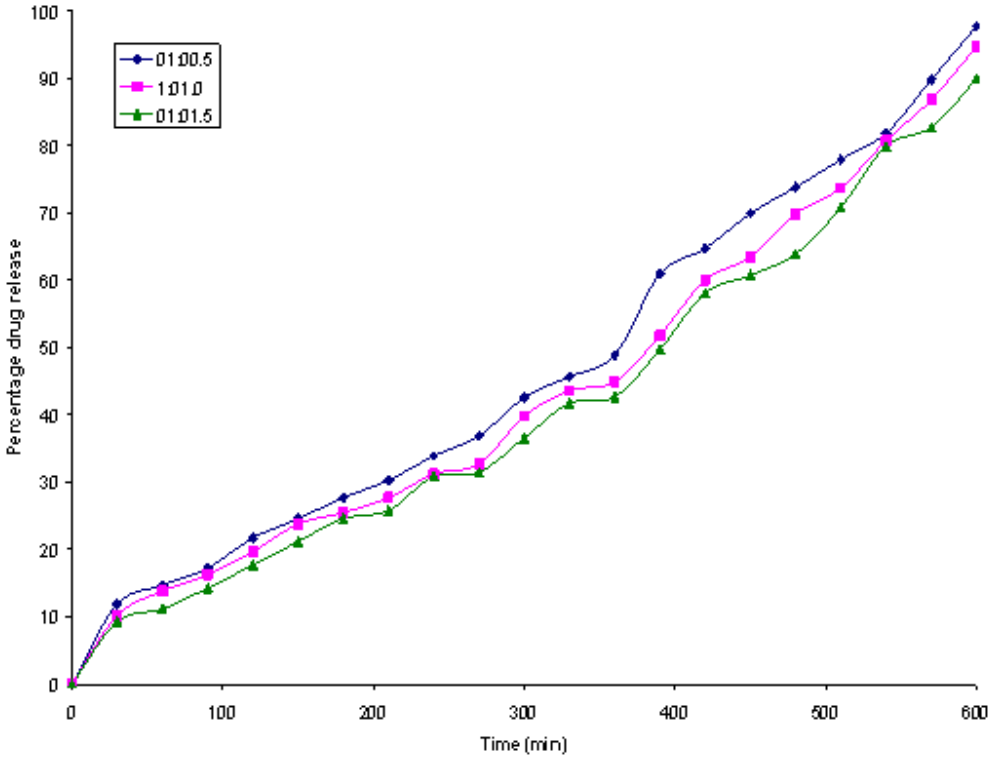

Fig. 2: *In-vitro* release study of ciprofloxacin with different ratio of Gaur Gum

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