Available online at www.pelagiaresearchlibrary.com

Pelagia Research Library

Der Pharmacia Sinica, 2013, 4(4):72-75

Der Pharmacia Sinica
ISSN: 0976-8688
CODEN (USA): PSHIBD

Formulation and evaluation of controlled release floating capsules of ciprofloxacin HCL

Anindya S. Das, Sudipta Das* and Arnab Samanta

Department of Pharmaceutics, Netaji Subhas Chandra Bose Institute of Pharmacy, Chakdaha, Nadia, West Bengal, India

---

ABSTRACT

The objective of the present study was to formulation and evaluation of controlled release floating capsule of ciprofloxacin HCL. The granules of ciprofloxacin were prepared by wet granulation method using polymers such as ethyl cellulose and HPMC. The prepared granules were evaluated to preformulation studies such as angle of repose (17.35^{0} to 24.22^{0}), bulk density, tapped density, compressibility index (11.235-12.751) and hausners ratio. All the parameters shows that the granules having good flow properties. Then the formulated Capsules were taken to evaluation studies such as weight variation, release study, buoyancy and floating duration (more than 6 hrs). All the parameters were within the acceptable limits.

Key words: Ciprofloxacin, Controlled release, Floating, capsule, EC and HPMC.

INTRODUCTION

Oral delivery of drugs is the most preferred route of drug delivery due to ease of administration, patient compliance and flexibility in formulation [1]. The design of oral controlled drug delivery systems is primarily aimed to achieve more predictable and increased bioavailability. Floating drug delivery systems were first described by Davis in 1968 [2, 3]. It is possible to prolong the gastric residence time of drugs using these systems. Floating Drug Delivery Systems have a bulk density is lower than gastric fluids and thus remain buoyant in stomach for a prolonged period of time, without affecting the gastric emptying rate. While the system is floating on gastric contents, drug is released slowly at a desired rate from the system. After the release of drug, the residual system is emptied from the stomach. This result is increase in GRT and a better control of fluctuations in plasma drug concentrations [4].

Ciprofloxacin comes under the category of Fluorinated 4-quinolones [5]. Ciprofloxacin HCL is a broad-spectrum antibiotic active against both Gram-positive and Gram-negative bacteria. The dosage is equivalent of 250 to 750 mg of ciprofloxacin twice daily (116 mg of ciprofloxacin hydrochloride is approximately equivalent to 100 mg of ciprofloxacin) [4,6]. The objective of the present study was to formulation and evaluation of controlled release floating capsule of ciprofloxacin HCL.

MATERIALS AND METHODS

Materials

Ciprofloxacin HCL was obtained as a gift sample from S. C. Biotechnology; Ethyl cellulose, HPMC, Sodium bicarbonate and Cetyl alcohol were obtained from Loba Chemie Pvt. Ltd. India.

Preparation of Granules

Ciprofloxacin HCL, Ethyl cellulose, HPMC, Cetyl alcohol and Sodium bi carbonate were weighed by electronic balance and mixed well in a mortar. Required amount of starch was taken in a beaker. Small amount of water was taken in it and stirred until thick past was formed without lumps. Excess water was boiled in a separate beaker for 15 mins and then added to the paste when stirring to form the mucilage. The mucilage was slowly added to the powder mix to form a damp mass that breaks with a snap when pressed between thumb and index finger. The damp mass was passed through the sieve and the granules were collected on a dry tray. The granules were dried in a hot air oven at 60^{o} c for 2 hrs. Then the dried granules were passed through sieve. The granules were filled in the empty gelatin capsule shell by hand filling capsule machine [3, 7].

Table-1 Composition of ciprofloxacin Controlled release floating capsules.

Ingredients (mg)	F1	F2	F3	F4	F5	F6
Ciprofloxacin	250	250	250	250	250	250
Cetyl alcohol	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Ethyl cellulose	125	100	75	50	25	-
HPMC	-	25	50	75	100	125
Starch	20	15	15	15	15	15
Sodium bicarbonate	25	25	25	25	25	25
Talc	2.5	2.5	2.5	2.5	2.5	2.5

F1=Formulation-1, F2= Formulation-2, F3= Formulation-3, F4= Formulation-4, F5= Formulation-5, F6= Formulation-6

Evaluation Granules Flow Characteristics [8, 11, 12]

Bulk Density:

A known quantity of granules was poured into the measuring cylinder carefully level the granules without compacting, if necessary and read the unsettled apparent volume (V), to the nearest graduated unit . Calculate the bulk density, in gm per ml, by the formula m / V.

Tapped Density:

A known quantity of granules were taken in a measuring cylinder and tapped on mechanical tapping apparatus for 5 mins. The initial and final volumes were noted.

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

Angle of Repose:

The frictional forces in a loose powder or granules can be measured by angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane.

The value of angle of repose are calculated by using the following formula,

$\tan \theta = h/r$

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

Where,

θ = Angle of repose, h = height of the heap and r = radius of the heap

Compressibility index and Hausner ratio:
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.

$$\text{Compressibility index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \text{X } 100$$

$$\text{Hausner ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Evaluation of Capsules
Weight variation [7, 8]
Twenty capsules were randomly selected and individually weighted (shimdzu). The average weight of capsules were calculated and compared with individual weight.

Determination of *In-Vitro* Dissolution Study [9]
Dissolution study was carried out in USP–II type dissolution apparatus (paddle type). Dissolution study was performed at 50 rpm in 900 ml 0.1(N) HCl 5ml of sample was withdrawn at a predetermined interval and the volume of dissolution medium was maintained by adding same volume of dissolution medium. Absorbance of these solutions was measured using a UV-Visible spectrophotometer.

Floating capacity [3, 10]
Floating characteristics of the prepared formulations were determined by using USP 2 paddle apparatus at a paddle speed of 50 rpm in 900 ml of a 0.1 N HCl solution (pH=1.2) at 37±0.5°C for 12 h. The time between the introduction of tablet and its buoyancy on the simulated gastric fluid (floating lag time) and the time during which the dosage form remain buoyant (floating duration) were measured.

RESULTS AND DISCUSSION

In the present study, ciprofloxacin controlled release floating capsules were prepared by using polymer such as ethyl cellulose (EC) and HPMC. A total number of six formulations were prepared by wet granulation method. Angle of repose for F1- F6 is between 17.35$^{\theta}$ to 24.22$^{\theta}$, bulk density is between 0.390-0.398, tapped density is between 0.442-0.450, compressibility index is between 11.235-12.751 and hausners ratio is between 1.126-1.146 are within the acceptable limits (Table 2). The above values of pre compression parameters show the prepared granules having good flow property. From the preformulation studies for drug excipients compatibility, it was observed that no physical incompatibility existed between the drug and excipients. The weight variation was within ±5%, it was within the acceptable limit. The floating duration was greater than 6 hrs in F1- F6 (Table 3). Different ratio of both polymers exhibited different release pattern. *In-vitro* drug release showed (Fig. 1) that the variation of release pattern of different batches (F1-F6) of the ciprofloxacin hydrochloride in 6 hrs study period. The increase trend in release was observed as concentration of EC decrease.

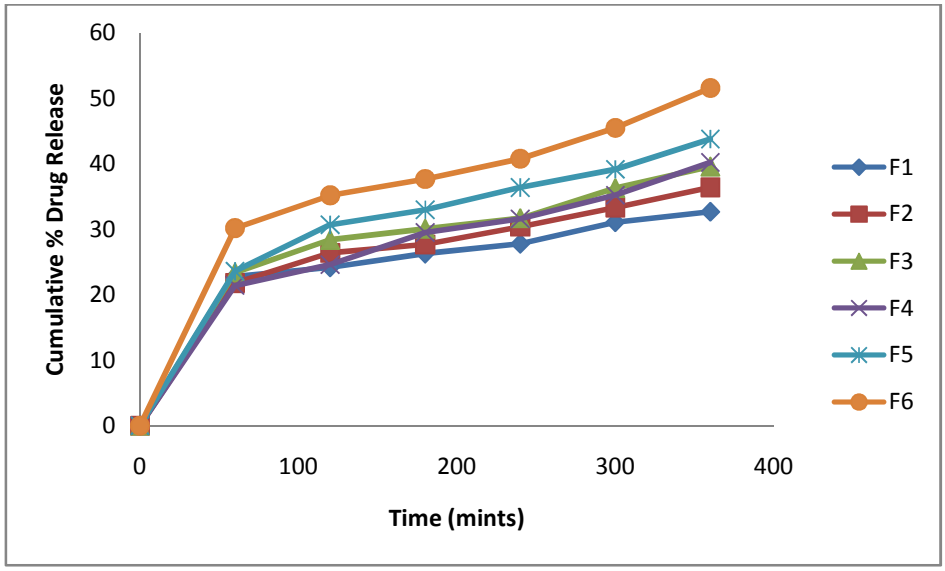
Table-2 Evaluation of Granules

Formulation	Angle of repose(θ)	Bulk density (g/cc)	Tapped density (g/cc)	Compressibility index (%)	Hausner ratio
F1	18.41 ± 1.32	0.392 ±0.012	0.442 ±0.034	11.312±0.423	1.127±0.245
F2	23.19 ± 1.46	0.395 ±0.014	0.445 ±0.037	11.235±0.487	1.126±0.216
F3	17.35 ± 1.57	0.390 ±0.024	0.447 ±0.032	12.751±0.324	1.146±0.176
F4	20.22 ± 1.69	0.393 ±0.021	0.444 ±0.041	11.486±0.419	1.129±0.234
F5	22.30 ± 1.25	0.395 ±0.017	0.449 ±0.036	12.026± 0.283	1.136±0.187
F6	24.22 ± 1.18	0.398 ±0.013	0.450 ±0.033	11.555±0.458	1.130±0.259

Table-3 Evaluation of Capsules

Formulation	Buoyancy Lag Time (sec)	Floating Duration(hrs)
F1	27	>6
F2	48	>6
F3	51	>6
F4	36	>6
F5	45	>6
F6	58	>6

Figure 1: *In-vitro* Dissolution study of formulated Capsules



CONCLUSION

From the present study it was concluded that controlled release floating capsules of ciprofloxacin hydrochloride can increase the gastric residence time as well as bioavailability and better patient compliance can be achieved.

Acknowledgement
The financial assistance of Netaji Subhas Chandra Bose Institute of Pharmacy, Chakdaha, West Bengal, India is gratefully acknowledged.

REFERENCES

[1] S Garg, S Sharma, *International J of Pharmaceutical Medicine*, **2004**, 21(2), 157-71.
[2] PG Yeole, S Khan, K Shah, *International J Pharm Sci.*, **2005**, 67, 265-72.
[3] R Manivannan, V Chakol, *International J of Recent Advances in Pharm. Research*, **2011**, 3, 25-30.
[4] R Devarajan, M Rangasamy, J Selvaraj, S Natesan, *IJPASA*, **2012**, 1 (1), 17-25.
[5] KD Tripathi, *Essentials of Medical Pharmacology*, Jaypee Brothers, 4th ed., Delhi; **1996**, pp 696.
[6] Government of India, Ministry of Health and Family Welfare, *Indian Pharmacopoeia* Ghaziabad, The Indian Pharmacopoeia Commission, **2010**, pp 1092-95.
[7] S Vachhani , J Patel , D Patel , S Prajapati, C Patel, *J Chem. and Pharma. Res.*, **2010**, 3–5.
[8] N Anjali Devi, M. Abdul Hadi, Venkateshwarulu, V. Priya, V. L. Babu, *International Research J of Pharmacy*, **2012**, 3(9), 185-193.
[9] K. Ravishankar., G V S. Sunil., V. Ramanarayana Reddy., K. Ramakrishna., G. Nagarjuna Reddy, P. Narayana Raju, *Current Pharma Research*, **2012**, 2(4), 655-658.
[10] D Patel, S Shivakumar, *International J of Pharm Tech Research*, **2012**, 4(3), 986-993.
[11] S Tamizharasi, T Sivakumar and J C Rathi, *Der Pharmacia Sinica*, **2011**, 2 (5), 43-53.
[12] Mohd. N Khan, J Suresh, K S Hemant Yadav, J Ahuja, *Der Pharmacia Sinica*, **2012**, 3 (2), 177-184.