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Research Article

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STUDIES ON FORMULATION AND EVALUATION OF FLOATING TABLETS OF CIPROFLOXACIN HCl

Ajay Bagherwal*, Dinesh Kumar Patidar and Pradeep Sharma

Dr. Shri R.M.S. Institute of Science & Technology, College of Pharmacy, Bhanpura, Dist. Mandsaur, Madhya Pradesh, India.

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ABSTRACT

Ciprofloxacin HCl belong to the fluoroquinoline derivatives which is widely used in the long term therapy for treatment of a wide range of infections including anthrax, biliary tract infection, bone and joint infection, gastrointestinal including traveler's diarrhoea and *Campylobacter enteritis*, *Shiegella*, meningococcal meningitis prophylaxis, surgical infection prophylaxis, tuberculosis, leprosy and topically in the treatment of eye infections. Hence there is a potential need for floating tablet as sustained release dosage form for this drug. HPMC and carbomer are the polymers, used as suspending agent, viscosity increasing agent and tablet binder coating agents. In the present study, it was aimed to formulate floating tablet of ciprofloxacin HCl with HPMC and carbomer in different proportion (4%, 8% and 12%) by direct compression techniques using polymers lactose, Magnesium Streate, talc with sodium bicarbonate. All the prepared formulation were found to complies with the official tests like precompression parameter like angle of repose and post compression parameters like Shape, tablet dimensions, hardness, friability test, weight variation test, floating test, content uniformity and *in-vitro* dissolution study. *In-vitro* release studies were carried out using USP XXII dissolution test apparatus. The mean percentage of ciprofloxacin released at various time intervals was calculated and plotted against time. The mechanism of drug release with all the formulations was dominantly diffusion and followed zero order kinetics. It was observed that the integrity of the drug is not affected by formulation procedure. The results revealed the drug polymer ratio showed greater drug release than other formulations.

Keywords: Ciprofloxacin HCl, HPMC, Carbomer.

INTRODUCTION

For achieving a prolonged and predictable drug delivery profile in the gastrointestinal tract is to control the gastric residence time using a gastro retentive dosage forms that will provide as with new and important therapeutic options. The design of oral controlled drug delivery system primarily be aimed at achieving more predictable and increase availability of drugs. However, the development process is precluded by several physiological difficulties such as inability to restarin and locates the controlled drug delivery system within the desired region of gastrointestinal tract due to the variable gastric emptying and motility.[1]

The concept of floating drug delivery system offers experiencing engaging or choking by some person while swallowing medicinal pills. The researcher suggested that difficulty could overcome by providing pills having a density of less than 1.0g/ml. So that pill will float on water surface since then several approaches have been proposed for ideal floating delivery system. This buoyant delivery system includes hollow microspheres powder granules, tablet, capsules and laminated films. The FDDS also called as hydro dynamically balanced system or gastro retentive system. Sustained release dosage form design embodies this approach to the control of drug action i.e. through a process either drug modification or dosage form modification. The absorption process and subsequently drug action can be controlled.[1, 2]

HPMC and carbomer is a positively charge natural biodegradable and biocompatible polymer. The chemical name of HPMC and carbomer are cellulose, 2-hydroxy methyl ether and carboxypolymethylene.It is a synthetic high molecular weight, cross linked polymer of acrylic acid copolymerized with approximately 0.75-2% w/w of polyalkyl sucrose. There are numerous report highlighting the low toxicity and biocompatibility of HPMC and carbomer respectively. In recent years, chitosan is in interest to be used in the medical field. Especially in biomedical and pharmaceutical application has been increasing.[3, 4]

Ciprofloxacin HCl belong to fluoroquinoline derivative which is widely used in the long term therapy for treatment of wide range infection including anthrax, biliary tract infection, bone and joint infection, gastrointestinal including traveler's diarrhea and *Campylobacter enteritis* and *Shiegella*. It is also used in *meningococcal* meningitis prophylaxis, surgical infection prophylaxis, tuberculosis, leprosy and topically in the

***Corresponding Author:**
Ajay Bagherwal
Dr. Shri R.M.S. Institute of Science & Technology, College of Pharmacy,
Bhanpura- 458775, Dist. Mandsaur, Madhya Pradesh, India.
Contact no: +91-9425949575,
Email: ajaybagherwal25@gmail.com

treatment of eye infections. Hence there is a potential need for floating tablet as well as sustained release dosage form for prolonged action and to improve patient's compliance.

The aim of current research work is to study the release characteristics of a polymer such as HPMC and carbomer containing ciprofloxacin by direct compression using lactose, Magnesium streate, Talc with sodium bicarbonate as alkalizing agent.[3-6]

MATERIALS AND METHODS

Ciprofloxacin HCl was obtaining as gift sample from Micro Lab Ltd. Bangalore. HPMCK_4M was obtaining from Sri Dev Pharmaceuticals Hyderabad and Carbopol 934 was obtaining from Central Drug house New Delhi. Sodium bicarbonate, Magnesium Streate, lactose and hydrochloric acid was obtained from S.D. Fine Chem. Ltd. All materials used were of analytical grade procured from commercial sources.

Preparation of Matrix Tablet of Ciprofloxacin HCl

Floating matrix tablets containing ciprofloxacin HCl were prepared by direct compression technique using varying concentration of different grade of polymer such as HPMCK_4M (4%, 8% and 12%) and carbopol (4%, 8% and 12%) with sodium bicarbonate. All the ingredients except magnesium stereate were blended in glass mortar uniformly. After sufficient mixing of drug as well as other component, magnesium stereate was added and further mixed for additional 2 to 3 minutes as shown in table **1**. The tablets were compressed by single punch machine. The weight of the tablet was kept constant for all formulations. A minimum of 100 tablets were prepared for each batch.[7,8]

Table 1. Composition of Hydrodynamically Balanced Tablets of Ciprofloxacin HCl

S.No.	Formulation code	Polymer ratio	Ingredients						
			Ciprofloxacin HCl	HPMCK_4M	Carbopol 934	Sodium Bicarbonate	Lactose	Mg- Streate	Talc
1.	F1	4%	300	24	-	70	178	4	24
2.	F2	8%	300	48	-	70	156	4	24
3.	F3	12%	300	72	-	70	132	4	24
4.	F4	4%	300	-	24	70	178	4	24
5.	F5	8%	300	-	48	70	156	4	24
6.	F6	12%	300	-	72	70	132	4	24

EVALUATION OF TABLETS

Evaluation was performed to assess the physiochemical properties and release characteristics of developed formulation.[9-12]

Precompression Parameters

Angle of repose: The powder was allowed to flow through the funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of granules formed.

$$\tan \varphi = \frac{h}{r}$$

$$\varphi = \tan^{-1}\frac{h}{r}$$

Where φ- Angle of repose, h- height and r- radius

The relationship between angle of repose and powder flow is as follows in given table **2**.

Table 2. Standard value of powder flow property test

S.No.	Angle of repose	Powder flow
1	<25	Excellent
2	25-30	good
3	30-40	passable
4	>40	very poor

Post compression parameters

Shape of tablets: Directly compressed tablets were examined under magnifying lens for the shape of the tablet.

Tablet Dimension: Thickness and diameter were measured using a calibrated screw gauge. Three tablets of each formulation were picked randomly and thickness was measured individually.

Hardness: Hardness indicates the ability of a tablet to withstand mechanical shocks while handling the hardness of the tablets was determined using Pfizer hardness tester. It is expressed in kg/cm^2. Three tablets were randomly picked and hardness of the tablets was determined.

Friability test: The friability of tablets was determined using Roche Friabilator. It is expressed in percentage (%). Ten tablets were initially weighed ($W_{initial}$) and transferred in to the friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again (W_{final}). The % friability was then calculated by

$$\% F = \frac{W - W_0}{W_0} \times 100$$

Where,

$\%F$= Friability in percent

W= Initial weight of tablets

W_o= weights of tablets after test

% friability of tablets <1% were considered acceptable.

Weight variation Test: Ten tablets were selected randomly from each batch and weighed individually to check for weight variation. A little variation is allowed in the weight of tablet by U.S. Pharmacopoeia. (Table **3**)

Table 3. Standard limit value in weight variation test

Average Weight of a tablet	Percentage Deviation
130mg or less	±10
>130mg and <324mg	±7.5
324mg or more	±5.0

In all formulations, the tablet weight is 310mg. hence 7.5% maximum difference allowed.

Floating Test: The time between introduction of dosage form and its buoyancy on simulated gastric fluid and the time during which the dosage form remain buoyant were measured. The time taken for dosage form to emerge on surface of medium called floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and total duration of time (TFT).

Test for Content Uniformity: Tablet containing 300mg of drug is dissolved in 100 ml of 0.1N HCl taken in volumetric flask. The drug is allowed to dissolve in the solvent. The solution was filtered, 1 ml of filtrate was taken in 50 ml of volumetric flask and diluted up to mark with 0.1N HCl and analyzed spectrophotometrically at 278nm. The concentration of ciprofloxacin in mg/ml was obtained by using standard calibration curve of the drug. Claimed drug content was 300mg per tablet. Drug content studies were carried out in triplicate for each formulation batch.

In-vitro Dissolution Study: In-vitro release studies were carried out USP XXII dissolution test apparatus. 900 ml of 0.1 N HCl (PH 1.2) was filled in dissolution vessel and the temperature of the medium were set at 37° C ± 0.1°C. For the study, ring/mesh assembly was used. The tablet was put inside the ring assembly and placed inside the dissolution vessel. The speed was set at 100 rpm. 5 ml of sample was withdrawn at predetermined time intervals for 12 hrs and same volume of fresh medium was replaced. The samples were analyzed for drug content against 0.1N HCl as a blank at λ_{max} 278nm using spectrophotometer. The dissolution of the drug was expressed as percentage drug dissolved by using following formula.

$$\%\ drug\ Release = \frac{A_{Sample}}{A_{Standard}} \times \frac{W_{Standard}}{V} \times DF \times \frac{V}{Amt\ of\ Drug} \times DF \times \frac{Potency}{100} \times 100$$

Table 4. Physical Parameters of tablet of all formulation

Formulation	Angle of repose (φ)	Diameter (mm)	Thickness (mm)	Weight Variation (mg)	Drug Content Uniformity (%)	Hardness (kg/cm²)	Friability (%)
F1	24°.30'	10.19 ± 0.040	4.16 ± 0.010	500 ± 1.29	98.71	3.6 ± 0.21	0.631
F2	24°.77'	10.19 ± 0.040	4.16 ± 0.010	500 ± 1.29	98.71	3.8 ± 0.2	0.413
F3	25°.08'	10.19 ± 0.040	4.16 ±0.010	500 ± 1.29	99.21	3.9 ± 0.3	0.381
F4	24°.43'	10.19 ± 0.040	4.16 ± 0.010	500 ± 1.29	98.12	3.7 ± 0.01	0.481
F5	24°.91'	10.19 ± 0.040	4.16 ± 0.010	500 ± 1.29	98.51	4 .0± 0.21	0.381
F6	25°.30'	10.19 ± 0.040	4.16 ± 0.010	500 ± 1.29	98.02	4.2 ± 0.42	0.313

RESULTS AND DISCUSSION

The formulated floating tablets met the pharmacopoeial requirement of uniformity of weight. All the tablet confirmed to the requirement of assay as per I.P. Hardness, % Friability, Thickness, Weight Variation and content uniformity were within acceptable limit (Table **4**).

Hydrodynamically balanced tablets of ciprofloxacin were prepared and evaluated for their use as gastro retentive drug delivery system to increase its local action and bioavailability. Gastro retentive system of ciprofloxacin was prepared with HPMC K_4M and Carbopol 934 polymers. The granules were subjected to study the flow properties and all values obtained were within the range. The hardness of all tablets of each batch ranged between 3.6 to 4.3 kg/cm². This indicates good handling characteristics. All the evaluations parameter were within stated range.

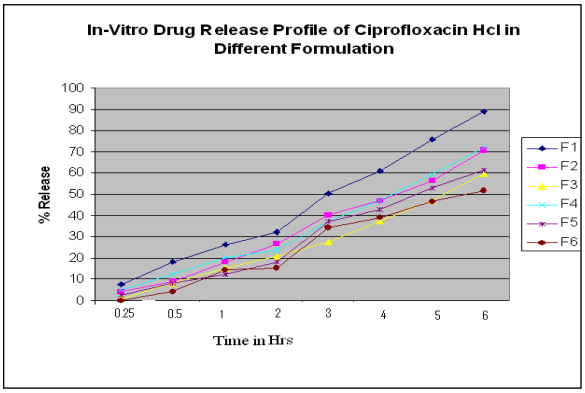
The drug release from all batches on floating tablets with HPMC polymer is found to be sustained over 6 hrs. The total amount of drug release in the formulation was found to be 89.94%, 70.74% and 59.67% for the formulation F1, F2 and F3 respectively and with carbopol 934 also sustain over 6 hr. The total amount of drug release in formulation was found to be 72%, 61.26% and 51.78% for formulation F4, F5 and F6 respectively.

When a plot is made between cumulative percent of drug release Vs time according to zero order equation. There is linearity, the linearity supported by regression value. This indicated the the main mechanism of drug release is diffusion.

Among the different formulation, tablets containing 12% of HPMC K_4M and carbopol 934 showed promising sustained release of drug for 6 hrs with 59.76% and 51.78% respectively. (Figure **1**)

The drug release from all the batches was diffusion control and followed zero order kinetics. From the result obtained it was observed that the presence of enteric polymer has greater influence over the release retardant ability of delivery system in acidic media. How the presence of enteric polymer controls the acidic release of system. Although the total amount of drug release was effectively controlled using enteric polymer as matrix agents based on the total amount of drug release at the end of 6th hour formulation F6 was selected as best *in-vitro* formulation since the release of drug to extent of 51.78% respectively.

Figure 1. *In-vitro* dissolution profile of Ciprofloxacin HCl in Different formulation



CONCLUSION

The result revealed that increase in the proportion of polymer (HPMC K_4M and carbopol 934) was associated with decreased in the overall cumulative drug release rate. Release profile of F6 in the % of polymer 12% was found to maximum release 51.78% at the end of 6 hrs. The drug release from the system was found to be concentration independent and diffusion mediated. The matrix tablet was found to have excellent physical characters. Hence the formulation F6 fulfils the objective of present study and may improve patient compliance.

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