JOURNAL OF PHARMACOLOGY AND BIOMEDICINE
E-ISSN: 2456-8244
www.rbscience.co.in

Formulation and Evaluation of Sustained Release Matrix Tablets of Ciprofloxacin

Roshani Khan*, Urvesh Narwariya

IPS College of Pharmacy, Gwalior, Madhya Pradesh

*Corresponding Author

Email ID – khan.ros0751@gmail.com

Abstract

The objective of the current investigation was to formulate matrix tablets of ciprofloxacin with an ability to sustain the release of the drug for a period of 12 h. The objective was accomplished by preparation of the matrix tablets employing wet granulation method for formulating the tablets using HPMC and sodium CMC as the matrix forming polymers. The angle of repose for all formulations was found to be within the range from 25°64' to 27°54' indicating good flow property of powder blend. The bulk density and tapped density values were found to be within the range from 0.366 to 0.404 and 0.404 to 0.436 respectively. The Hausner's ratio values were found to be within the range from 1.02 to 1.12. The thickness of all formulation was ranged in between 4.1 to 4.2 mm while the hardness of the formulations ranged from 6.1 to 6.6 Kg/cm^2. The friability of all formulation was in the range of 0.23% to 0.61% and the weight variation was in the range of 1.2 to 4.4 %. Swelling study was performed on all the formulation for 9 h. All formulation was in the range of 2.06 to 6.21. The highest degree of swelling was achieved by F7.

Keywords: Ciprofloxacin, sustained release, matrix tablets, swelling, HPMC, CMC

Received 23/08/2021; Revised 31/08/2021; Accepted 03/09/2021

Scan QR Code to visit Website

Introduction

The oral route is the most popular route used for administration of drugs, owing in part to the ease of administration and to the fact that gastrointestinal physiology offers more flexibility in dosage form design than most other routes (Gutpa and Robinson, 1992). The terms sustained release, prolonged release, modified release, extended release or depot formulations are used to identify drug delivery systems that are designed to achieve or extend therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose (Jantez and Robinson, 1995).

Introduction of matrix tablet as sustained release (SR) has given a new breakthrough for novel drug delivery system (NDDS) 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. Hydrophilic polymer matrix is widely used for formulating an SR dosage form [Altaf and Friend, 2003; Vidyadhara et al., 2004; Reddy et al., 2003; Mohammad et al., 1999; Lee et al., 1995).

Ciprofloxacin is a second generation fluoroquinolone used for oral, intravenous, intratympanic, ophthalmic, and otic administration for a number of bacterial infections. The oral bioavailability of the drug is 60-80% with a half life of 4 h (Wikipedia, 2021). Ciprofloxacin is eliminated by renal and non-renal mechanisms. The drug is metabolized in the liver by modification of the piperazinyl group to at least four metabolites. Ciprofloxacin and its metabolites are excreted in urine by both glomerular filtration and by tubular secretion. Also the drug is found to be excreted 27-30% unchanged in urine after oral administration. Thus preventing the metabolism and excretion of the drug would be helpful in reducing the required dosing of the drug.

The current work was undertaken with an objective to delay and control the release of the drug through the matrix tablet formulations which would eventually help in decreased metabolism and excretion and reduce the dosage of the drug required.

Material and Methods

Ciprofloxacin was obtained as a generous gift sample from Medreich Pharmaceuticals, Bengaluru, India. All the chemical and reagents used in the study were procured from various suppliers and used as obtained.

Preformulation Studies

Color: A small quantity of pure ciprofloxacin hydrochloride powder was taken in a butter paper and viewed in well illuminated place.

Taste and odor: Very less quantity of ciprofloxacin hydrochloride was used to get taste with the help of tongue as well as smelled to get the odour.

Solubility analysis: Solubility of ciprofloxacin hydrochloride was qualitatively determined in methanol, ethanol, dimethyl fluoride, methylchloride, 0.1N hydrochloric acid.

Melting point: The melting point of ciprofloxacin hydrochloride was determined by capillary method, using small quantity of ciprofloxacin hydrochloride was taken and placed in apparatus and determined the melting point and matched with standards.

Loss on drying: It was determined by drying the pure drug in an oven at 100°C to 105°C for 3 hours. The percent loss of moisture was calculated by the difference between the initial and final weight of the drug.

Drug excipient compatibility studies by FT-IR

IR spectra of drug, polymer and drug and polymers, individual excipients, drug and polymers and excipients were obtained using FT-R by KBr pellet method in the region 400-4000 cm^{-1}. Spectra were recorded for pure drug, pure excipients, and physical mixture of drug and polymer, drug, polymer and excipients.

Standard Curve of Ciprofloxacin Hydrochloride

The maximum absorption of ciprofloxacin was observed at 276 nm. The calibration curve was obtained using different concentrations of the drug at the above wave length.

The stock solution was freshly prepared by dissolving 100mg of ciprofloxacin hydrochloride in few ml of methanol (5ml) in a 100ml volumetric flask and then made up the solution upto the mark using 0.1N hydrochloric acid for obtaining the solution of strength 1000 μg/mL (stock I). 10ml of this solution is diluted to 100ml with 0.1N hydrochloric acid to obtain a solution of strength 100 μg/mL (stock II).

10 ml stock solution was taken from stock solution-2 and volume made up to 100 ml by using 0.1N hydrochloric acid to get 10 μg/ml concentrations. From this solution with draw 2, 4, 6, 8, 10 ml of solution in to the 10 ml volumetric flask and volume made up to 10 ml by using 0.1N hydrochloric acid to get the concentrations 2, 4, 6, 8, 10 μg/ml.

Formulation of Ciprofloxacin Matrix tablets

The formulation of the matrix tablets was performed using wet granulation method by employing HPMC and sodium CMC as the matrix forming polymers (Table 1). Mannitol was used as the bulk forming agent for the matrix tablets.

Table 1 Composition of matrix tablets

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ciprofloxacin	250	250	250	250	250	250	250	250	250
HPMC	120	180	240	120	180	240	120	180	240
CMC sodium	30	30	30	60	60	60	90	90	90
Avicel	50	50	50	50	50	50	50	50	50
Mannitol	190	130	70	160	100	40	130	70	10
Magnesium stearate	5	5	5	5	5	5	5	5	5
Purified talc	5	5	5	5	5	5	5	5	5

Ciprofloxacin hydrochloride and a 75% amount of HPMC and sodium CMC were passed through #40 sieve and mixed thoroughly. The remaining amount of the polymers was dissolved in 30 mL of an isopropyl alcohol and dichloromethane (1:1) mixture. The resultant solution was used as a binding agent to prepare a wet mass. The wet mass was passed through #12 sieve to form granules. The wet granules were dried in a hot air oven at 45 ±5°C for 1 h. The dried granules were passed through #20 sieve and mixed with the remaining ingredients previously passed through #40 sieve (Soumya et al., 2013). The matrix tablets were punched using single punch tablet compression machine using 8 mm diameter flat punch.

Evaluation of matrix tablets (Jalonya et al., 2018)

The tablets were evaluated for in process and finished product quality control tests i.e. appearance, thickness, weight variation, hardness, friability, swelling index, dissolution study.

Hardness test: The hardness of the formulated tablets was tested using Monsanto type hardness tester.

Friability test: The friability test of the formulations was performed using a Roche type friability test apparatus. Twenty tablets were initially weighed ($W_{initial}$) and transferred into 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 percentage friability was then calculated by the formula

$$\% \text{ Friability} = \frac{W_{initial} - W_{final}}{W_{initial}} X\ 100$$

Weight variation test: 20 tablets were randomly taken and weighed to calculate the average weight of the tablets. Each of these tablets was individually weighed and the difference from average weight was calculated. The percent weight variation was calculated to determine the deviation from the average weight.

Thickness: The thickness of randomly selected tablets from each batch of formulation was measured using a digital vernier caliper.

Drug content: Five tablets from each formulation were weighed to determine the average weight. These tablets were crushed in a mortar then the amount of powder equivalent to 100 mg of drug was dissolved in phosphate buffer pH 7.4 and suitably diluted. The absorbance of the resulting solution was measured at 276 nm using UV spectrophotometer.

In vitro disintegration time: The *in-vitro* disintegration time of a tablet was determined using disintegration test apparatus. The time required for complete disintegration of the tablet with no palpable mass remaining in the apparatus was recorded.

In-vitro dissolution: The USP type II paddle apparatus with a paddle speed of 50 rpm was used for dissolution testing for the formulated matrix tablets. The dissolution media used consisted of 900 mL of 0.1 N HCl and distilled water. 5 mL of samples were collected at time points of every hour until 12 h and

the media was replenished with the same volume of fresh media. The free drug concentration was estimated using a UV spectrophotometer at a wavelength of 276 nm.

Swelling Index: One tablet from each formulation was kept in a Petri dish containing phosphate buffer pH 7.2. At the end of 2 h, the tablet was withdrawn, kept on tissue paper and weighed. The weighing was continued for every 2 hr, till the end of 9 h. The % weight gain by the tablet was calculated by formula

$$S.I = \frac{Mt - Mo}{Mo} * 100$$

Where, S.I = swelling index, M_t = weight of tablet at the time (t) and M_0 = weight of tablet at time 0.

Results and Discussion

Preformulation Studies

The ciprofloxacin pure drug obtained as gift sample was pale yellow in color, odorless and exhibited no particular taste. Its melting point was found to be 255°C with a LOD of 0.42%. It was soluble in water dimethyl formamide, 0.1N NaOH, 0.1N HCl and slightly soluble methanol.

Drug-polymer compatibility study

The FTIR spectra of the pure drug and physical mixture of drug and excipient were recorded in between 400-4000 wave number (cm-1). No peaks are observed which interfere with the main drug peaks. Hence drug was found to be compatibles with excipients.

Calibration curve of ciprofloxacin hydrochloride was determined by plotting absorbance (nm) versus concentration (µg/ml) at 276 nm (Figure 1).

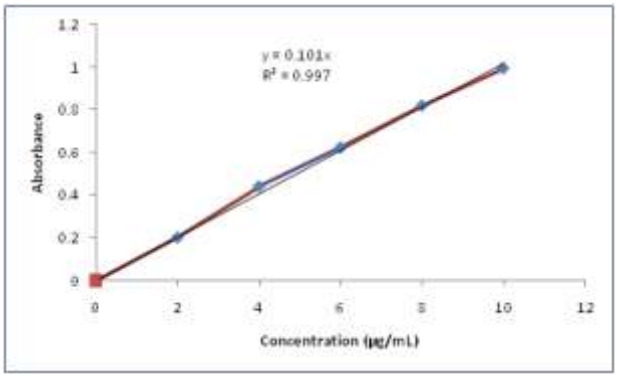

Figure 1 Calibration curve of ciprofloxacin

Evaluation of matrix tablets

The tablets were evaluated for appearance, thickness, hardness, weight variation, friability, swelling index, dissolution study (Table 2).

Table 2 Quality parameters of matrix tablets

Formulation code	Thickness (mm)	Hardness (Kg/cm2)	Weight variation (%)	Friability (%)	Swelling Index
F1	4.2	6.3	1.2	0.25	2.06
F2	4.1	6.5	2.3	0.23	2.18
F3	4.2	6.1	1.4	0.37	2.41
F4	4.2	6.2	3.1	0.41	3.96
F5	4.2	6.6	4.4	0.38	4.08
F6	4.1	6.1	2.7	0.29	4.27
F7	4.1	6.2	1.6	0.61	6.19
F8	4.2	6.1	2.4	0.27	6.21
F9	4.2	6.4	2.4	0.36	6.08

All prepared batches of tablets were checked by visual inspection. The tablet had uniformly texture and structure. There were no oily drops and no pin holes on the surface. There were small variations in between thickness of all formulation but in a particular formulation there was no variation. The thickness of all formulation was ranged in between 4.1 to 4.2 mm. The hardness of the compressed tablets was determined by using hardness tester (Monsanto) indicates that the tablets are of adequate strength. Hardness of tablet of all formulation ranged from 6.1 kg/cm^2 and 6.6 kg/cm^2. The hardness of all formulation showed variation because of formulation combination and powder properties. The friability of all formulation was in the range of 0.23% to 0.61%. All formulation exhibited less than 1% friability and hence passed the test for friability. The weight variation of all formulation was in the range of 1.2 to 4.4 %. The weight variation test was performed according to the procedure in the pharmacopoeia. The individual deviation of all the tablets formulation was found to be within the limit and hence passed the test for uniformity of weight.

Swelling study was performed on all the formulation for 9 h. The results of swelling index were shown in table 2. All formulation was in the range of 2.06 to 6.21. The highest degree of swelling was achieved by F7 that contained low amount of HPMC and high concentration of sodium CMC indicating that the carboxyl groups were involved in swelling of the matrix. The results show that low concentration of CMC resulted in lower swelling index.

The samples were withdrawn and estimated for the drug content at 1 h time interval for a total duration of 12 h of the dissolution study. A plot of % cumulative drug release versus time for sustained release matrix tablet formulations is shown in Figure 5.4. It was observed that of all the formulations F1, F2 and F4 could not sustain the release of ciprofloxacin up to 12 h. While the formulation F7 was able to release almost 100% of the drug at the end of 12 h duration, formulations F5 & F6 were able to release 96.11 & 97.99 % of ciprofloxacin. Formulations F3, F8 and F9 could not release more than 90% of ciprofloxacin at the end of the study duration.

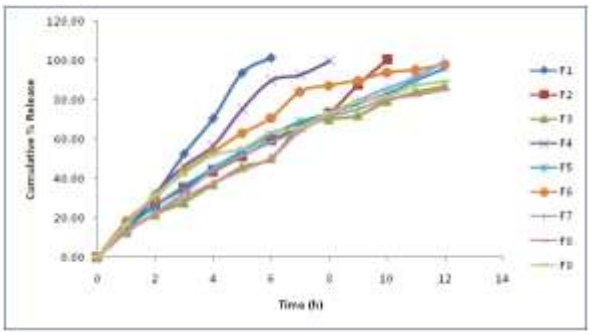

Figure 2 Release of ciprofloxacin from matrix tablets

Conclusion

The results obtained from the study conclusively indicate that use of HPMC and sodium CMC in equal ratio as the matrix forming substance could help in achieving sustained release over a longer duration and help in reducing the dose as well as frequency of administration of the medicaments. Further *in vivo*

release studies are needed to support for the conclusion of the present investigation.

Acknowledgement

The authors are thankful to the management of IPS College of Pharmacy, Gwalior for providing necessary facilities to carry the research work. The authors also thank Medreich Pharmaceuticals for providing the gift sample of Ciprofloxacin.

References

Gupta PK, Robinson JR. (1992) Oral controlled release delivery. Treatise on controlled drug delivery. 93(2): 545-555.

Jantzen GM, Robinson JR. (1995) Sustained and Controlled- Release Drug Delivery systems. Modern Pharmaceutics 121(4): 501-502.

Altaf AS, Friend DR. (2003) Sustained-Release Technology in Rathbone MJ, Hadgraft J, Robert MS, Modified Release Drug Delivery Technology, Marcell Dekker Inc., New York.

Vidyadhara S, Rao PR, Prasad JA. (2004) Formulation And Evaluation Of Propranolol Hydrochloride Oral Controlled Release Matrix Tablets. Indian Journal of Pharmaceutical Sciences 66: 188-192.

Reddy KR, Mutalik S, Reddy S. (2003) Once-daily sustained release matrix tablets of Nicorandil: Formulation and in vitro evaluation. AAPS PharmSciTech 4: 1-9.

Mohammed AD, James LF, Michael HR, John EH, Rajabi-Siahboomi AR. (1999) Release of Propranolol hydrochloride from matrix tablets containing sodium carboxy methylcellulose and Hydroxy propyl methyl cellulose. Pharmaceutical Development Technology 4: 313-24.

Lee BJ, Ryu SG, Cui JH. (1995) Formulation and release characteristics of hydroxypropyl methylcellulose matrix tablet containing melatonin. Drug Development and Industrial Pharmacy 25: 493-501.

en.wikipedia.org/wiki/Ciprofloxacin hydrochloride; last assessed 16/06/2021

Soumya P, Raghavendra Rao NG, Revathi K, Chawda B. (2013) Design and development of oral sustained release matrix tablets of didanosine using natural polymer blend. Journal of Chemical and Pharmaceutical Research. 5(12): 1398-1408.

Jalonya R, Soni P, Malviya K, Omray LK. (2018) Formulation and evaluation of bilayer tablets of diltiazem HCl. Journal of Pharmacology and Biomedicine 2(3): 189-198.