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Formulation and evaluation of matrix tablets of Norfloxacin

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Abstract

The objective of the current investigation was to formulate matrix tablets of norfloxacin that could control the release of the drug thereby reducing its dosing frequency and improving the bioavailability. The objective was accomplished by preparation of the matrix tablets using HPMC and xanthan gum as the matrix forming polymers. The angle of repose for all formulations was found to be within the range from 24°22 to 26°18. The bulk density and tapped density values were found to be within the range from 0.42 to 0.58 and 0.53 to 0.67 respectively. The Hausner's ratio values were found to be within the range from 1.06 to 1.21.The thickness of all formulation was ranged in between 4.1 to 4.3 mm while the hardness of the formulations ranged from 4.1 to 4.6 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 0.48 to 0.56 %. Swelling study was performed on all the formulation for 9 h. The results of swelling index were shown in table. All formulation was in the range of 1.37 to 5.31. The highest degree of swelling was achieved by F9 that contained highest concentration of HPMC and xanthan gum. The formulation F7-F9 were able to release almost 100% of the drug at the end of 12 h duration.

Keywords: Norfloxacin, controlled release, matrix tablet, xanthan gum, HPMC, precompression

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Introduction

Drug delivery is the system of administering a pharmaceutical product for achieving a therapeutic effect (Vyas and Khar, 2002). Most of the products currently available in the market are immediate release products. For achieving and maintaining the concentration of the drug within therapeutically effective range, it usually becomes necessary to administer the drug dosage many times and this causes in a fluctuating drug level in the blood (Chien, 1982). Controlled drug delivery is a technique that delivers the drug at a preset rate, for a specified period of time. Sustained release is a form of controlled release that allows extended delivery of the drug, thereby decreasing the number of times the medication is to be taken while maintaining a steady state of drug in the bloodstream (Xiaoling and Jasti, 2005).

Matrix tablet is a type of controlled release dosage form that doesnot involve the complex procedures such as coating and pelletization, rather the drug release is controlled by the use of polymeric material during the formulation (Jantenz and Robinson, 1995). Matrix drug delivery systems release the drug in continuous manner, controlling the release drug by dissolution as well as diffusion controlled mechanisms (Chugh et al., 2012).

Norfloxacin is a drug with oral bioavailability of 30-40% (drugbank, 2021). This makes it a potential candidate for improvement by appropriate formulation design. Matrix tablets are known to improve the biovailability of drug molecules as the drug substance is homogenously mixed into the rate controlling material as crystalline, amorphous or in sometimes as molecular dispersion. A few reports of matrix tablets of norfloxacin were found in literature with promising results (Suja and Sismy, 2018; Oliveira et al., 2013; Bomma et al., 2009; Karthik et al., 2018; Gul and Sajid, 2015; Madhuri et al., 2017; Al-Dhubiab, 2018; Gadade et al., 2016; Radhika et al., 2009)

The objective of the current work was to prepare sustained release matrix tablets of norfloxacin in order to reduce dosing frequency.

Material and Methods

Norfloxacin was obtained as a generous gift sample from Medreich Pharmaceuticals, Bengaluru, India. Xanthan gum was purchased from Oxford Fine Chemicals; all other excipients, reagents and chemical were procured from various local suppliers.

Preformulation study

Organoleptic properties

A small quantity of pure norfloxacin powder was taken in a butter paper and viewed in well illuminated place to observe its color; the taste and odor were observed using tasting and smelling the drug.

Solubility analysis

Solubility of norfloxacin was determined in methanol, ethanol, dimethyl fluoride, methylchloride, 0.1N hydrochloric acid. Solubility studies were performed

by shaking small amount of norfloxacin in test tubes containing the solvent and observing for undissolved particles (if any).

Melting point

The melting point of norfloxacin was determined by open capillary method. The pure drug was filled in a capillary tube sealed at one end and placed in the melting point apparatus to observe the temperature at which melting occurs.

Loss on drying

It was determined by drying the pure drug in an oven at 100°C to 105°C for 3 h. 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-IR. Spectra were recorded for pure drug, pure excipients, and physical mixture of drug and polymer, drug, polymer and excipients.

Standard Curve of norfloxacin

The maximum absorption of norfloxacin was observed at 295 nm using 0.1N HCl as the solvent for analysis. The calibration curve was obtained using different concentrations of the drug at the above wave length.

Formulation of norfloxacin matrix tablets

The formulation of the matrix tablets was performed using direct compression method by employing HPMC and xanthan gum as the matrix forming polymers (Table 1). Lactose 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**
Norfloxacin	400	400	400	400	400	400	400	400	400
HPMC	50	60	70	50	60	70	50	60	70
Xanthan gum	60	60	60	80	80	80	100	100	100
Sodium bicarbonate	50	50	50	50	50	50	50	50	50
Citric acid	30	30	30	30	30	30	30	30	30
Lactose	96	86	76	76	66	56	56	46	36
Magnesium stearate	7	7	7	7	7	7	7	7	7
Purified talc	7	7	7	7	7	7	7	7	7

The quantity of the drug, matrix forming polymers and all other excipients was accurately weighed and passed through sieve no. 22. The ingredients were mixed together manually using tumbling action in large poly bags. The powder blend was again sieved using sieve no. 22 and mixed with talc and magnesium stearate. The blend was evaluated for precompression parameters and compressed into 8

mm tablets using single punch tablet punching machine.

Evaluation of precompression blends

Angle of repose, Carr's Index, Bulk density, Tapped density and Hausner's ration were determined to assess the flow ability of the prepared granules.

Evaluation of matrix tablets

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. Three tablets from each batch of formulation were randomly taken and the force required to break the tablets was measured using 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 10 mg of drug was dissolved in 0.1M HCl and volume was made up to 100 ml using 0.1M HCl. 10ml of the filtrate was made up to 100ml with 0.1M HCL. 10µg/ml solution was prepared from the above solution and analyzed for drug content.

In vitro buoyancy studies

The tablets were placed in a beaker containing 250 ml of 0.1M HCl maintained at 37°C. The time required for the tablet to rise to the surface was determined as floating lag time and the time period up to which the tablet remained floating was determined as total floating time.

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 293 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 Study

The results of organoleptic characterization, melting point and solubility analysis are presented in table 2.

Table 2 Preformulation study

Test	Observation	Melting Point (°C)	Solubility	LOD
Color	White	221-224	freely soluble in glacial acetic acid, 0.1 M HCl and very slightly soluble in ethanol, methanol and water	0.21%
Odor	Odorless			
Taste	Bitter			

The linear regression analysis for the calibration curve was Abs = 0.057(conc) – 0.004 with a regression coefficient of 0.999.

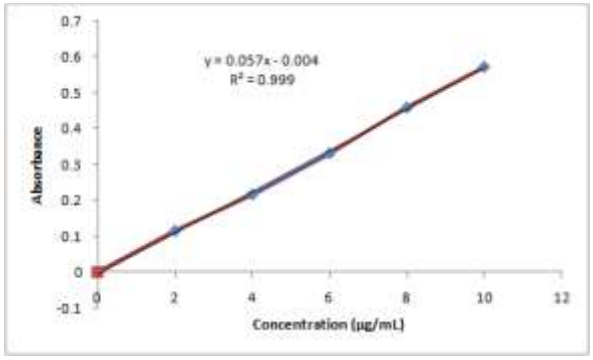

Figure 1 Calibration curve of norfloxacin in 0.1M HCl

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). Deletion of the peaks of the pure drug in the mixture spectra is usually taken as an indication of incompatibility of the drug and excipients. On comparison of the FTIR

spectra of the drug and the mixture it was observed that no peak was deleted and only the intensities of the existing peaks changed which might be due to the coupling of absorption frequencies. This provides an evidence of compatibility between the drug and the matrix forming polymers.

Precompression blend characterization

Angle of repose for all formulations was examined and the values were found to be within the range from 24°22 to 26°18. This indicates that good flow property of powder blend. The bulk density and tapped density values were found to be within the range from 0.42 to 0.58 and 0.53 to 0.67 respectively. The Hausner's ratio values were found to be within the range from 1.06 to 1.21. All these parameters indicate that the powder blend had good flow property and is suitable for compression in to tablets. The compressibility index for formulation F9 was 5.36 which represented a very excellent flow character of the formulation.

Table 3 Precompression characterization

Formulation code	Angle of Repose	Bulk density	Tapped density	Carr's Index	Hausner's Ratio
F1	25.43	0.42	0.53	20.75	1.26
F2	25.11	0.50	0.56	10.71	1.12
F3	25.67	0.49	0.57	14.04	1.16
F4	25.22	0.47	0.54	12.96	1.15
F5	26.18	0.50	0.58	13.79	1.16
F6	25.43	0.51	0.59	13.56	1.16
F7	25.18	0.58	0.67	13.43	1.16
F8	25.21	0.49	0.59	16.95	1.20
F9	24.22	0.53	0.56	5.36	1.06

Evaluation of matrix tablets

The tablets were evaluated for appearance, thickness, hardness, weight variation, friability, swelling index, in vitro buoyancy and dissolution study (Table 4).

Table 4 Quality parameters of matrix tablets of norfloxacin

Formulation code	Thickness (mm)	Hardness (Kg/cm2)	Weight variation (%)	Friability (%)	Swelling Index	Drug content (%)	Buoyancy Lag Time (min)
F1	4.8	4.2	1.8	0.48	1.37	98.9	Immediate
F2	4.9	4.3	2.1	0.46	1.45	97.4	Immediate
F3	4.8	4.1	1.6	0.51	1.43	99.2	Immediate
F4	4.8	4.2	2.4	0.49	3.42	97.9	2.48
F5	4.9	4.2	2.6	0.54	3.36	98.7	3.06
F6	4.9	4.2	2.9	0.56	3.71	99	3.15
F7	4.7	4.3	3.3	0.54	5.18	99.2	3.54
F8	4.7	4.2	3.1	0.48	5.22	99.4	4.12
F9	4.8	4.2	2.8	0.49	5.31	99.3	4.25

The thickness of all formulation was ranged in between 4.1 to 4.3 mm. Hardness of tablet of all formulation ranged from 4.1 kg/cm^2 and 4.6 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 0.48% to 0.56%. 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 1.6 to 3.3 %.

Swelling study was performed on all the formulation for 9 h. The results of swelling index were shown in table. All formulation was in the range of 1.37 to 5.31. The highest degree of swelling was achieved by F9 that contained highest concentration of HPMC and xanthan gum. The results showed that the lower amounts of xanthan gum resulted in lower floating lag time and less swelling of the formulation.

The dissolution study was done in 0.1M HCl medium to check the release control profile of the matrix. It was observed that of all the formulations F1, F2, F3 and F4 could not control the release for even up to 6 h. On the other hand, the formulation F7-F9 were able to release almost 100% of the drug at the end of 12 h duration, formulations F5 & F6 were able to sustain the drug release upto 9 and 11 h respectively.

A plot of % cumulative drug release versus time for matrix tablet formulations is shown in Figure 2.

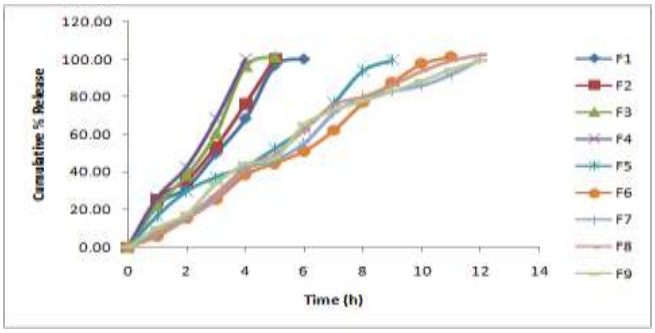

Figure 2 Release of norfloxacin from matrix tablets

Conclusion

The results obtained from the study indicate that use of HPMC and xanthan gum 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.

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