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DESIGN AND EVALUATION OF GASTRORETENTIVE TABLETS FOR CONTROLLED DELIVERY OF NORFLOXOCIN

Ganesh Kumar Gudas*, Subal Debnath, Parameshwar Pabba, Nilesh P Babre, N Santhosh Kumar, D Vamshi Krishna
Sri Krupa Institute of Pharmaceutical Sciences, Vill-Velkatta, Kondapak(mdl), Siddipet, Dist. Medak, A.P., Pin- 502 277.
E-mail: *subal_2007@yahoo.co.in*

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Abstract

Floating matrix tablets were designed to prolong the gastric residence time after oral administration and to achieve the controlled release of norfloxocin to treat urinary tract infections. Norfloxocin was chosen a model drug because it is poorly absorbed from the lower gastrointestinal tract. The tablets were prepared by wet granulation technique, using polymers such as Hydroxyl Propyl Methyl Cellulose (HPMC), Carbopol 934P. Sodium bicarbonate used as a gas generating agent was kept constant for all the formulations. The rate of release of Norfloxocin was controlled by quantity of Hydroxyl Propyl Methyl Cellulose (HPMC) and Carbopol 934P where as, HPMC and Sodium carbonate was added to achieve buoyancy in 0.1N HCl. Further; tablets were evaluated for *in vitro* release characteristics for 24 h, buoyancy lag-time and swelling index were evaluated.

Key Words: Floating lag time, floating matrix tablet, norfloxocin, total floating time,

Introduction

Oral sustained release dosage forms have been developed for the past three decades due to there considerable therapeutic advantages this approach is suitable for a variety of drugs, characterized by a

narrow absorption window in the upper part of the gastrointestinal tract, due to relatively short transit time of the sustained release dosage forms in these anatomical segments[1]. Thus, after a only a short period (<5h), the sustained release dosage form lefts the upper GIT and the drug is released. This results in a short absorption phase i.e. often accompanied by lesser bioavailability[2]. It was suggested that compounding narrow absorption window drugs in a unique pharmaceutical dosage form with gastro retentive properties would enable an extended absorption phase of these drugs. After oral administration these dosage forms would be retained in the stomach and release the drug in a sustained manner, so that the drug could supplied continuously to its absorption site in the upper GIT[3]. The need for gastro retentive dosage forms (GRDFs) has led to extensive efforts in both academic and industry to wards the development of such drug delivery systems. The GRDFs were designed based on low density form of the dosage form that causes buoyancy and gastric fluid in the stomach and expansion by swelling or unfolding to a large size which limits emptying of the dosage form through the pyloric sphincter[4].

Materials and Methods

Norfloxocin was obtained gift sample lupin pharma, pune, Hydoxy Propyl Methyl Cellose (HPMC), Carbopol 934P were received as gift sample from Torrent research center (Gandhi nagar, India) Sodium bicarbonate, Poly vinyl pyrrolidine, Lactose, magnesium stearate, Talc were obtained commercially from S.D. Fine chemicals (Mumbai, India).

Preparation of Norfloxocin Floating tablets

Norfloxocin was mixed with required quantity of polymer (Hydoxy Propyl Methyl Cellose, Carbopol 934P), Sodium bicarbonate and Lactose in mortar for 5 min by using a spatula. Isopropyl alcohol was added drop wise till suitable mass for granulation was obtained. The wet mass granulated through sieve 40#. The granules were dried at room temperature for 1 hr and then blended with talc and magnesium stearate in the

weight proportion as mentioned in table 1 and compressed on 8 station rotary tablet compression machine (Cadmach, India) using 8 mm standard flat face die punch set[5].

Physical Properties of floating tablets

The prepared floating tablets were tested for weight variation, hardness and friability as per standard procedure.

Drug content

Drug content uniformity was carried out by calculating the average weight of 10 tablets and these tablets were triturated to get a fine powder. From the resulting powder a quantity equivalent to 50 mg of Norfloxocin was weighed and dissolved in little quantity of 0.1N HCl and volume was adjusted to 50 ml. The content of Norfloxocin was determined as per the procedure.

Floating property study

This test was performed in beaker containing 100 ml of 0.1N HCl as a testing medium maintained at 37^{o}C. The time required for a tablet to rise to the surface was noted to determine as floating lag time. Total floating time was also noted for each tablet and noted as floating time simultaneously by patel *et. al*. (2005).

Swelling characteristics

The swelling property of each tablet was determined by placing the individual tablet in the petridish containing 50 ml of 0.1N HCl .The tablets were removed periodically from petridish. After draining the water these were measured for weight gain, thickness and diameter. The percent weight gain by the tablet was calculated by the formula by deshpande et. al. (1997)[6].

% water uptake = Weight of the swallow tablet – Dry weight of the tablet x 100

***In vitro* release study**

The release rate of Norfloxocin from floating tablets was determined as per USP, using dissolution testing apparatus 2 (paddle method). The dissolution test was performed using 900 ml of 0.1N HCl, at 37±0.5^{o} C and 50 rpm. A 2 ml of sample was withdrawn from dissolution apparatus hourly for 24h, and the samples were replaced with fresh dissolution medium. The samples were filtered through whatman filter paper and diluted to a suitable concentration with 0.1N HCl. Absorbance of these solutions was measured at 278 nm using UV/Visible double beam spectrophotometer. Duration of time, the tablet consistently float on dissolution medium were noted as total floating time[7].

Results and Discussion

The present study was carried out to develop floating tablet of Norfloxocin in order to enhance the absorption and bioavailability of the drug by increasing the gastric retention time in the stomach. Eight formulations (F1 to F8) were prepared by varying concentration of various formulations **(*Table 1*).**

***Table 1*: Design of floating of Norfloxocin tablet formulations (F1-F8)**

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Norfloxocin	400	400	400	400	400	400	400	400
HPMC	110	120	130	140	110	120	130	140
Carbopol 934P	15	15	15	15	25	25	25	25
Sodium bicarbonate	30	30	30	30	30	30	30	30
Magnesium stearate	10	10	10	10	10	10	10	10
Lactose	80	70	60	50	70	60	50	40
Talc	5	5	5	5	5	5	5	5
Total weight (mg)	650	650	650	650	650	650	650	650

The shape of all formulations remained circular and no visible cracks. The percentage water uptake of all the formulations ranges 165.65% to 190.23% formulation F7 and F8 showed a maximum % swelling index because of high proportion of HPMC. This showed a higher % of water uptake. Swelling index for formulation F1 to F8 was found to be 175.45, 170.83, 182.12, 183.13, 182.06, 18436, 188.93 and 190.23% respectively. Evaluation parameters like weight variation, hardness, thickness and friability of all formulations, were found to be satisfactory and within IP limit shown in ***Table 2*.**

***Table 2*: Evaluation of Floating tablet of Norfloxocin**

Formulation Code	Weight variation (g)	Thickness ± S.D. (mm)	Friability ± S.D. (%)	Hardness ±S.D. (kg/cm^2)	Drug content (%)
F1	0.649±0.125	4.10±0.38	0.382±0.21	4.15±0.35	97.32
F2	0.650±0.084	4.10±0.42	0.376±0.25	4.24±0.29	98.53
F3	0.648±0.132	4.11±0.19	0.403±0.26	4.65±0.34	99.62
F4	0.648±0.095	4.10±0.63	0.498±0.32	4.56±0.42	97.23
F5	0.653±0.083	4.10±0.89	0.465±0.28	4.25±0.26	98.96
F6	0.648±0.164	4.10±0.42	0.512±0.26	4.85±0.35	99.90
F7	0.652±0.063	4.12±0.09	0.477±0.24	4.44±0.31	100.05
F8	0.652±0.136	4.11±0.442	0.485±0.33	4.35±0.32	99.85

The effect of HPMC and Carbopol 934P content on the hardness was studied. A difference in tablet hardness reflects differences in tablet density and porosity, which results in different release pattern of the drug by affecting the rate penetration of the dissolution fluid at the surface of the tablet and formation of the

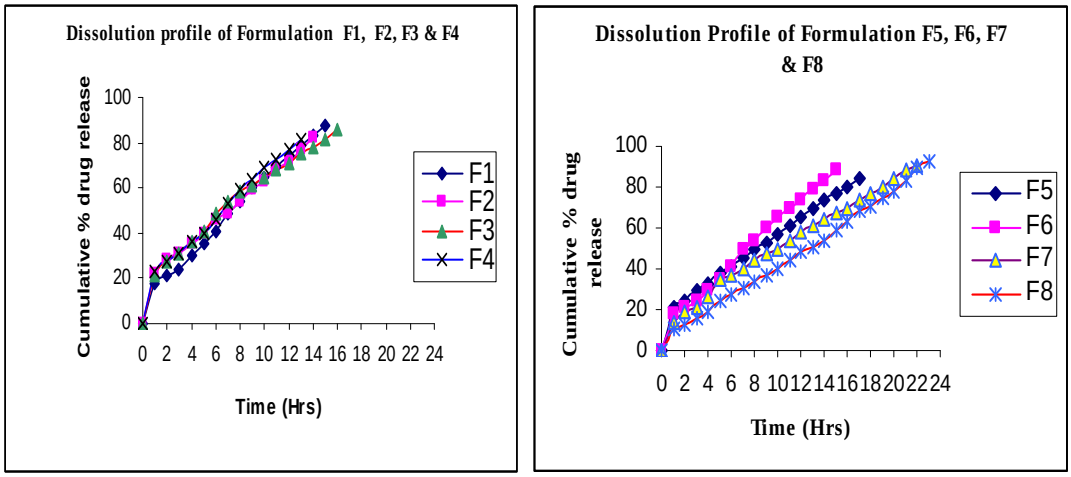
gel barrier. Therefore, such an effect is expected to be prominent during the initial face of the dissolution curve. However the results reported until now by many researchers suggest that tablet hardness has no or little effect on the release profile.

Floating lag time studies of the tablets with different hardness between 4-5 Kg/cm^2. It was observed that with increase in the hardness of the tablet the floating lag time was increased. Results of floating properties study reveal that all tablets had good floating properties are shown in *Table 3.* The incorporation of sodium bicarbonate helps to improve floating properties by reacting with gastric fluid when dosage form comes in contact and produce carbon dioxide gas which entrapped inside the hydrophilic matrixes leads to increase in volume of dosage form resulting in lowering of density and dosage form stars to float. Formulation F7 and F8 showed a floating lag time 1.55 and 1.42 , total floating time of 22 and 23 hrs respectively ***(Fig. 1(a &b))***

***Table 3*: Floating property and Swelling of formulations F1-F8**

Formulation Code	Floating Lag Time (Min)	Total Floating time (Hrs)	Swelling Index (%)
F1	2.56±0.4	14	178.42
F2	3.31±0.2	16	169.92
F3	2.57±0.6	13	182.95
F4	2.32±0.6	19	185.48
F5	2.62±0.8	17	186.09
F6	4.50±0.4	15	183.37
F7	1.55±0.6	22	188.26
F8	1.42±0.4	23	188.62

Fig. 1



(a) (b)

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For Correspondence

[*]**Ganesh Kumar Gudas., M.Pharm, Asst.Professor**

Sri Krupa Institute of Pharmaceutical Sciences,

Vill-Velkatta, Kondapak (mdl),

Siddipet, Dist. Medak, A.P., Pin- 502 277.

E-mail: *subal_2007@yahoo.co.in*