FORMULATION AND EVALUATION OF FLOATING TABLETS OF NORFLOXACIN

Ms. Jyoti Rathore[1*], Mr. Hitesh Kumar Parmar[1]

Ujjain Institute of Pharmaceutical Sciences, Ujjain.
Email- hkparmar7@rediffmail.com

ABSTRACT

The oral route is considered as the most promising route of drug delivery. Several approaches have been attempted in the preparation of gastro-retentive drug delivery systems. These include floating systems, swell able and expandable systems, high density systems, bioadhesive systems, altered shape systems, gel forming solution or suspension systems and sachet systems. Various approaches have been followed to encourage gastric retention of an oral dosage form. Floating systems have low bulk density so that they can float on the gastric juice in the stomach. The problem arises when the stomach is completely emptied of gastric fluid. In such a situation, there is nothing to float on.

Key words: Floating drug, Bioavailability, Sustain release, Gastric fluid.

INTRODUCTION

The oral route is considered as the most promising route of drug delivery. Effective oral drug delivery may depend upon the factors such as gastric emptying process, gastrointestinal transit time of dosage form, drug release from the dosage form and site of absorption of drugs. Most of the oral dosage forms possess several physiological limitations such as variable gastrointestinal transit, because of variable gastric emptying leading to non-uniform absorption profiles, incomplete drug release and shorter residence time of the dosage form in the stomach. This leads to incomplete absorption of drugs having absorption window especially in the upper part of the small intestine, as once the drug passes down the absorption site, the remaining quantity goes unabsorbed. The gastric emptying of dosage forms in humans is affected by several factors because of which wide inter- and intra-subject variations are observed. Since many drugs are well absorbed in the upper part of the gastrointestinal tract, such high variability may lead to non-uniform absorption and makes the bioavailability unpredictable. Hence a beneficial delivery system would be one which possesses the ability to control and prolong the gastric emptying time and can deliver drugs in higher concentrations to the absorption site (i.e. upper part of the small intestine).[1-7] The identification of new diseases and the resistance shown towards the existing drugs called for the introduction of new therapeutic molecules. In response, a large number of chemical entities have been introduced, of which some have absorption all over the gastrointestinal tract (GIT), some have absorption windows (i.e. absorption sites, especially the upper part of the small intestine) and some drugs have poor solubility in intestinal media. The drugs belonging to the second and third categories, and the drugs which are required for local action in the stomach, require a specialized delivery system. All the above requirements can be met and effective delivery of the drugs to the absorption window, for local action and for the treatment of gastric disorders such as gastro-esophageal reflux, can be achieved by floating drug delivery systems (FDDS).[8-12]

MATERIAL AND METHOD

Chemicals are use: Norfloxacin, Lactose, Talc, Magnesium stearate, Starch, CMC (Carboxy Methyl Cellulose),

PREFORMULATION STUDIES

A) Appearance: The color, odor, smell and other physical parameters were observed by visual inspection only.

B) Solubility: The solubility of ibuprofen was determined in different solvents. 10 ml of each solvent (water, ethanol, methanol etc.) were taken in beaker. Excess of drug was dissolved in the solvents and shaken for 72 hours and filtered. The solubility was determined by UV spectrophotometer.

C) Melting point: It was determined by melting point apparatus.

D) UV Spectrophotometric methods for estimation of drugs: Preparation of Standard Curve

a) Preparation of stock solution: Stock solution of celecoxib was prepared in 0.1N HCl by first dissolving 10 mg of the drug in 10 ml of 0.1 N HCl and then making up the final volume to 100 ml with 0.1 N HCl.

b) Determination of λ_{max} : From the stock solution, 0.5 ml of stock solution was transferred to 10 ml volumetric flask and volume was adjusted to the mark using of 0.1 N HCl to obtain strength of 5µg/ml. The solution was scanned in the UV range of 200-400 nm.

c) Study of linearity: Appropriate volumes of aliquots from standard celecoxib stock solution were transferred to five separate 10 ml volumetric flask. The volume was adjusted to the mark with 0.1 N HCl to obtain concentrations of 2, 5, 10, 15 and 20 µg/ml.

i) Preparation of stock solution: - 100 mg of drug was dissolved in 100 ml 0.1 N HCl to prepare 1000 µg/ml of stock solution.

ii) Preparation of dilutions: - From the stock solution, dilutions were made of 10, 20, 30, 40 and 50 µg/ml.

iii) UV estimation: - The solutions were subjected to UV estimation in the range of 200-400 nm to determine λ_{max}. The beer's range was determined.

E) Flow properties of drug and granules:-

a) Bulk Density: - It was determined by taking 50 gm of the powder. It was poured into a graduated measuring cylinder. The bulk volume was determined.

Bulk Density (gm/cm^3) = Mass/Bulk Volume

b) Tapped Density: - It was determined by taking 50 gm of the powder. It was poured into a graduated measuring cylinder. Tap the measuring cylinder about 100 times. Then determine the tapped volume.

Tapped Density (gm/cm^3) = Mass/Tapped Volume

c) Hausner's Ratio:- It is defined as the ratio as the ratio of tapped density to that of bulk density.

Hausner ratio = Tapped density/Bulk Density

d) Angle of repose:- It is defined as the maximum possible between the surface of the pile of the powder and the horizontal plane.

tan = h/r

Where = angle of repose

h and r are the height and radius of base of pile of powder.

e) Loss on drying: - Weigh accurately a weighing bottle that has been dried for 30 minutes. Take about 1-2 gm of powder and pour it into the weighing bottle. Place the bottle in hot air oven at 105°C for 4 hours. After 4 hours, determine the loss in weight.

Loss on drying (%) = $(w_1 - w_2)/ w_1$ x 100

Where, w_1 and w_2 are the initial and final weights of powder.

PREAPRATION OF GRANULES

Talc, magnesium stearate, lactose were taken in pestle mortar. Then starch solution in water was added to above ingredients to prepare wet mass. This wet mass was passed through mesh # 8 to prepare wet granules. These granules were allowed to dry in hot air oven at 50°C for 1 hour. The dried granules were again passed through mesh # 24.

PREAPRATION OF TABLET These granules were punched in form of tablets by tablet punching machine.

Table 5.2- Formulation of tablet

INGREDIENTS	**FORMUALTIONS**		
	F1	F2	F3
Lactose	35 mg	25 mg	15 mg
Magnesium stearate	10 mg	10 mg	10 mg
Starch	5 mg	5 mg	5 mg
Talc	10 mg	10 mg	10 mg
CMC	90 mg	100 mg	110 mg
Norfloxacin	200 mg	200 mg	200 mg

EVALUTION OF TABLETS

a) Weight variation: - Twenty tablets were weighed. Average weight was determined. Individual tablets were weighed and their % deviation from average weight was determined.

b) Hardness: - It was determined by hardness tester.

c) Friability: - It was determined by Roche friabilator. 10 tablets were taken and their initial weight (w_1) was determined. The friabliator was operated at 100 rpm. Then final weight (w_2) was determined.

% Friability = $[[(w_1)- (w_2)]/ (w_2)]*100]$

d) Thickness: It was determined by vernier calliper's scale.

e) Disintegration: - It was determined by disintegration apparatus. 6 tablets were taken in apparatus with 0.1 N HCl as the medium. The disintegration time was determined for all the tablets.

f) In-vitro Drug release studies: The release rate of Norfloxacin from floating tablets was determined using USP Dissolution Testing Apparatus type-II (paddle method). The dissolution test was performed using 900 ml of 0.1N HCl, at 37 ± 0.5°C and 100 rpm. The samples were withdrawn and replaced with fresh medium at specific time intervals. The samples withdrawn were diluted and the amount of drug released was estimated using UV Spectrophotometer..

g) Buoyancy time: The time taken for tablet to emerge on the surface of the medium is called the floating lag time or buoyancy time and duration of time the dosage form constantly remains on the surface of the medium is called total floating time. The buoyancy of the tablets was performed by using 0.1 N HCl. The time of duration of floatation was observed visually.

h) Swelling index: The extent of swelling was measured in terms of percentage weight gain by the tablet. The swelling behaviour of formulation F1-F3 was studied. One tablet from each formulation was kept in a petritdish containing 0.1N HCl. The tablet was withdrawn in time intervals, soaked with tissue paper, and weighed. Weights of the tablet were noted and the process was continued till the end 12 hrs. Percentage weight gain by the tablet was calculated by formula:

$$\text{Swelling index} = \frac{\text{Weight of swollen tablet-Initial weight of tablet}}{\text{Initial weight of tablet}}$$

RESULT

We intended to develop floating tablets of norfloxacin. The main aim is to enhance the retention time of the drugs by increasing the buoyancy time of the drugs. The results have shown that tablets were found to have good properties as well as enhanced buoyancy time which provides good retention time of the drug in the body.

PREFORMULATION STUDIES

a) Appearance:-

Color	Clay colored powder
Odor	Odourless
Taste	Bitter

b) Solubility:-

SOLVENTS	SOLUBILITY OF NORFLOXACIN
Water	+
Ethanol	+
Methanol	+
Acetone	++

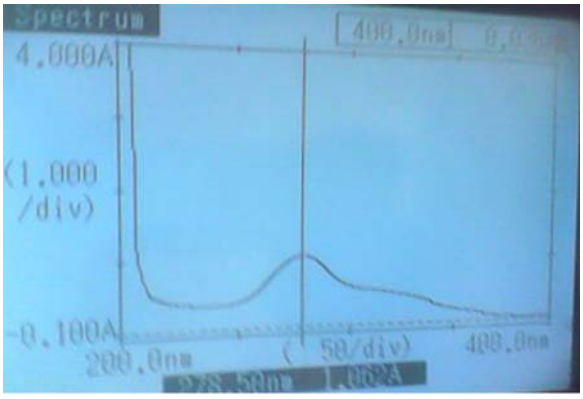
+ = very slightly soluble, ++ = slightly soluble

c) Melting point:- The melting point was found to be 220°C.

d) UV estimation of drug:-

1. Determination of λ_{max}

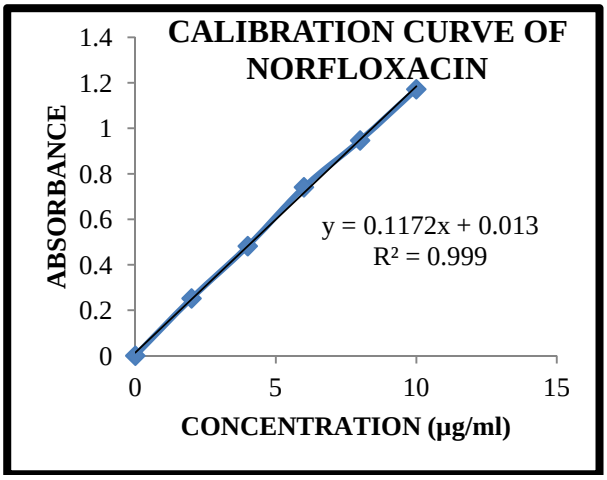
The absorption maxima of norfloxacin (5µg/ml) were determined in 0.1 N HCl. The λ_{max} was found to be 278.5 nm.



2. PREAPRATION OF CALIBRATION CURVE:

The calibration curve of norfloxacin was prepared in 0.1 N HCl. at 278.5 nm and the absorbance values of different concentrations of ibuprofen solutions are shown in the Table. The beer's law was found to obey in the range of 2-10 µg/ml.

S.No.	Concentration (µg/ml)	Absorbance
1	0	0
2	2	0.252
3	4	0.482
4	6	0.741
5	8	0.947
6	10	1.172



e) FLOW PROPERTY

Ingredient	*Bulk density (g/ml)	*Tapped density (g/ml)	*Carrs index	*Hausner ratio	*Angle of repose	*Flow behaviour
Norfloxacin	0.301	0.464	35	1.4	46	Poor

From the flow properties of norfloxacin, it was found that norfloxacin has poor flow properties.

Angle of repose values	
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Compressibility Index	Percentage Flowability
5-15	free-flowing to excellent flow
12-16	free-flowing to good flow — powders
18-21	fair to passable powdered granule flow
23-28	easily fluidizable powders — poor flow
28-35	cohesive powders — poor flow
33-38	cohesive powders — very poor flow
>40	cohesive powders — very very poor flow

The Carr's index was found to be 35 which show poor flow of norfloxacin.

EVALUATION OF GRANNULES

S.No.	Evaluation parameters	Formulations		
		F1	F2	F3
1	*Carrs index	21	26	28
2	*Hausner ratio	1.11	1.12	1.14
3	*Angle of repose	16	19	17
4	*Flow behaviour	Excellent	Good	Good

Evaluation Parameters of Tablets

PARAMETERS	FORMUALTIONS		
	F1	F2	F3
Weight Variation[a]	349 mg	352 mg	350 mg
Hardness[a]	5.3	5.9	6
Friability[b]	0.38	0.30	0.27
Swelling index	0.06	0.07	0.08
Buoyancy time	10 mins.	11 mins.	15 mins.
Disintegration time			

a:- mean of 20 tablets, b:- mean of 10 tablets

In vitro drug release studies

Time (hours)	% Cumulative drug release		
	F1	F2	F3
0	0	0	0
1	18.07	17.37	16.20
2	36.52	29.10	29.60
3	47.90	37.09	35.40
4	59.67	48.60	43.64
5	72.71	61.24	58.40
6	87.63	78.24	65.74

CONCLUSION

Among all the three tablet formulations, F3 was found to be having the most appropriate parameters. Thus the study shows that the tablets containing more amount of carboxy methyl cellulose (CMC) was found to be having good properties specially the buoyancy time. The tablet F3 was found to show delayed release with time which shows that it provides more retention as compared to F1 and F2. Thus the formulation F3 will provide best retention time of norfloxacin among all the three formulations.

REFERENCES

[1] Chien, Y.W., "Novel drug delivery system", Marcel Dekker, 2nd Edi. Rev. Expand., 50, 139-196.
[2] Chungi, V.S., Dittert, L.W., Smith, R.B., "Gastrointestinal sites of furosemide absorption in rats", Int. J. Pharm., 1979, 4, 27-38.
[3] Sheth, P.R., Tossounian, J., "The hydrodynamically balanced system (HBS™): a novel drug delivery system for oral use", Drug Dev. Ind. Pharm., 1984, 10, 313-339.
[4] Gutierrez-rocca, J., Omidian, H., Shah, K., "Progress in Gastroretentive drug delivery systems", Business Briefing, Pharmatech, 2003, 152-156.
[5] Hou, S.Y., Cowles, V.E., Berner, B., "Gastric retentive dosage forms: a review", Crit. Rev. Ther. Drug Carrier Syst., 2003, 20(6), 459-97.
[6] Cremer, K., "Drug delivery: gastro-remaining dosage forms", The Pharm. Journal 1997, 259, 108.
[7] Garg, S., Shringi, S., "Gastroretentive drug delivery systems", Business briefing, Pharmatech, 5thedition, Available on: http://www.touchbriefings.com., 2003, 160-166.
[8] Robinson, J., Lee, R., "In Controlled drug delivery", 2nfd edition, 1987, 418.
[9] Kalus, Florey, "Analytical profile of drug substances", Academicpree, Florida , l-9, 1987, 87.
[10] Jain, S.K., Jain, N.K., Agrawal, G.P., "Gastro retentive floating drug delivery: an overview",www.drugdeliverytech.com, 5(7), 2005.
[11] Rouge, N., Buri. P., Doelker, E., "Drug absorption sites in the gastrointestinal tract and dosage forms for site-specific delivery", Int. J. Pharm., 1996, 136, 117-139.
[12] Reddy, L., Murthy, R., "Floating dosage systems in drug delivery", Crit. Rev. Ther. Drug Carrier Syst., 2002, 19, 553-585.