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FORMULATION AND EVALUATION OF LANSOPRAZOLE FLOATING TABLETS

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ABSTRACT

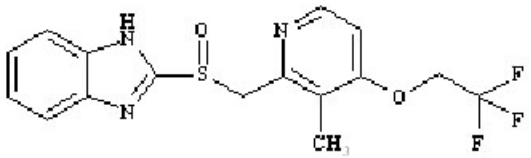
Floating tablets were designed to prolong the gastric residence time after oral administration and to achieve controlled release of Lansoprazole to treat gastric ulcers. A combination of effervescent and non-effervescent mechanism is used. HPMC (Hydroxy propyl methyl cellulose) was used as swelling polymer and sodium bicarbonate as gas generating agent to reduce the floating lag time. Floating tablets with varying proportions of sodium bicarbonate and HPMC were prepared. The prepared formulations were evaluated for various tablet and floating parameters. Tablet properties were found to be within the limits according to procedures prescribed in USP. They had a floating lag time around 3-7 seconds and floating time more than 24 hours. The cumulative % drug release in simulated gastric fluids after 10 hours was 70% - 95%. The mechanism of drug release was analyzed by fitting the release data into various kinetic models. It was found that all the formulations best fit the Higuchi's model.

Keywords: *Floating drug delivery system; Lansoprazole; HPMC; Kinetic model fitting.*

INTRODUCTION

Rapid gastrointestinal transit could result in incomplete drug release from the device beyond the absorption zone leading to diminished efficacy of the administered dose. Relatively brief gastric residence time in major absorption window results in incomplete drug release from the dosage form. Floating systems float over the gastric contents and remain buoyant in stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. Floating drug delivery also has the applications in site specific drug delivery, sustained drug delivery and also in enhancement of absorption[1].

Therefore, different approaches have been proposed to retain the dosage form in the stomach. These include bio-adhesive systems, swelling and expanding systems, and floating systems[2]. The swelling and expanding systems may show hazard of permanent retention. Bioadhesive systems may cause problems such as irritation to the mucous layer owing to high localized concentration of the drug. Hydrodynamically balanced systems, designed using effervescent mixtures alone have achieved commercial success but require a high drug:excipients ratio, and are unsuitable for drugs degrading in basic pH due to the alkaline microenvironment[3]. In the present study, we have prepared the floating system with swelling polymer in combination with the effervescent mixture. Lansoprazole is a proton pump inhibitor with a bioavailability of 80% or more and protein binding of 97%. Its metabolism is mainly by liver (CYP3A4 and CYP2C19 mediated) and excretion by renal and fecal. Its dose is usually 30 mg. It acts by irreversibly blocking the hydrogen/potassium adenosine triphosphatase enzyme system of the gastric parietal cell[4].



Previously Lansoprazole micropellets were prepared by using the non-effervescent polymers like HPMC, Methyl cellulose and chitosan without the incorporation of gas liberating agent[5]. Its half life is 1–1.5 hours with poor absorption may be because of poor solubility or degradation. It can be assumed that the solubility and absorption can be improved with an increase in the gastric residence time and also by creating basic pH due to the alkaline microenvironment with the release of sodium bicarbonate. Our main aim of the study was to prepare the gastric retentive drug delivery system for the drug Lansoprazole and at the same time to sustain the drug release for longer time to overcome the short half life of the drug.

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MATERIALS AND METHODS

Lansoprazole (99.5%w/w on assay by HPLC) was a gift sample from Dr. Reddy's Laboratories Ltd, Bachupally and HPMC K4M, Sodium bicarbonate, talc and magnesium stearate were purchased from Sd Fine chem Limited, Mumbai. All other chemicals and solvents used were of analytical grade.

Preparation of Lansoprazole GFDDS

In this work direct compression was employed to prepare the GFDDS of Lansoprazole. Total five formulations were prepared and coded as F1 to F5. Powder mixtures were prepared, weighed and compressed into 100mg tablets by using 3mm flat faced punches with a compression force of 2.5 Kg/cm^3. The formulation details are given in Table 1.

***Table 1** : Formulation ingredients.*

Ingredients	Weight of the ingredients in formulations (in mg)				
	F1	F2	F3	F4	F5
Lansoprazole	30	30	30	30	30
HP MC	50	40	30	20	10
Sodium Bi carbonate	17.5	27.5	37.5	47.5	57.5
Talc	1	1	1	1	1
Magnesium stearate	0.5	0.5	0.5	0.5	0.5
Starch	1	1	1	1	1
Total weight	100	100	100	100	100

FTIR study

FTIR studies (carried out in M/S Symphony Life Sciences Pvt. Ltd., Hyderabad.) for the compatibility of the drug with other ingredients were performed.

In vitro Characterization of GFDDS

The prepared floating tablets were tested for weight variation and friability as per standard procedure[6]. The hardness was tested using Pfizer hardness tester and friability was tested using Roche friabilator.

Floatation studies

This test was performed in beaker containing 100 mL 0.1 N HCl as testing medium maintained at 37^{0}C with 50 rpm. The time required for a tablet to rise to the surface was noted as floating lag time. The total floating time was also noted for each tablet simultaneously [7-9].

Swelling characteristics

The swelling property of each tablet was determined by placing the individual tablet in a beaker containing 50mL 0.1N HCl. The tablet was removed from beaker. After draining the excess 0.1N HCl, the tablets were measured for weight gain. The percentage weight gain was calculated by the formula[10],

% water uptake = (weight of the swollen tablet / dry weight of the tablet) × 100

In vitro drug release

The release rate of Lansoprazole from floating tablet was determined by using USP dissolution test apparatus – Electrolab TDT-08L (paddle type). The dissolution test was performed using 900 ml of 0.1N HCl at 37^{o}C±0.5^{o}C and 50 rpm. A sample of 1 mL solution was withdrawn from the dissolution media periodically up to 10 hrs and was replaced with fresh buffer. Samples were filtered through Whatman filter paper No. 1 and the content of Lansoprazole was determined by double beam UV spectrophotometer (Elico SL-159) at 278nm.

Model fitting for drug release

The suitability of several equations that are reported in the literature to identify the mechanisms for the release of drug was tested with respect to the release constraints between 20 to 80% of cumulative % drug release. The data was evaluated according to the following equations:

Zero order model [11]

$M_t = M_0 + K_0 t$

Higuchi model [12]

$M_t = M_0 + K_H t^{0.5}$

Korsmeyer - Peppas model [13]

$M_t / M_{á} = K_k t^n$

Where M_t is the amount of drug released in time t. M_0 is the initial amount of the drug. K_0 is the Zero order release constant, K_H is the Higuchi rate constant, K_k is a Korsmeyer – Peppas release constant and n is the release exponent that characterizes the mechanism of drug release.

RESULTS AND DISCUSSION

In the present study floating tablets of Lansoprazole were prepared in order to increase the gastric residence time and also to sustain the drug release rate. Five formulations (F1 to F5) were prepared by varying the concentrations of HPMC and sodium bicarbonate according to Table 1. From the results of FTIR studies it was found that Lansoprazole is compatible with all the other ingredients. FTIR spectra of the drug and with the major components (HPMC and Sodium bicarbonate) are presented in Figure 1.

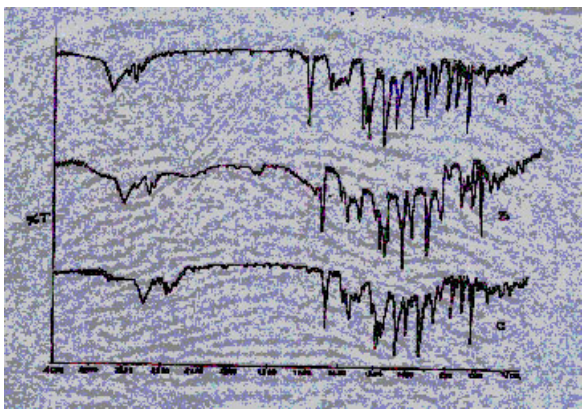

***Fig.1:** FTIR spectra of Lansoprazole alone (A), Lansoprazole with Sodium bicarbonate (B) and Lansoprazole along with HPMC (C).*

Evaluation parameters like weight variation, hardness, friability and disintegration are shown in Table 2. The % deviation from the mean weight of all the formulations, disintegration time and % weight loss in friability (less than 1%) were found to be within the prescribed limits of USP. The hardness of the prepared tablets was found to be in the range of 3 – 3.5 kg/cm^2. Disintegration time was found be increased with the increase in the HPMC content. The cumulative % drug release of the formulation was at the order of 75-95% (Figure 2) and was found to be sustained with the content of HPMC. This indicates the formation of swollen gelatinous mass by HPMC which slows down the drug release.

***Table 2** : Evaluation of Tablets.*

S. No.	Parameters	F1	F2	F3	F4	F5
1	Weight variation ± SD (mg)	93.3 ± 7.0	93.5 ± 7.01	91.1 ± 6.82	93.0 ± 6.97	93.2 ± 6.98
2	Hardness ± SD (kg/ cm^2)	3.2 ±0.312	3.4 ±0.155	3.3 ±0.653	3.4 ±0.713	3.5 ±0.288
3	Friability ± SD	0.74 ±0.31	0.69 ±0.96	0.75 ±0.12	0.61 ±0.24	0.65 ±0.81
4	Floating lag time ± SD (Sec)	6.25 ±0.3	5.56 ±0.22	5 ± 0.54	3.7 ±0.41	3.02 ± 0.31
5	Swelling Index (%)	188.22	186.35	192.54	196.78	201.96
6	Disintegration time (Minutes)	12	13	12	10	10
7	Floating time (Hours)	>24H	>24H	>24H	>24H	>24H

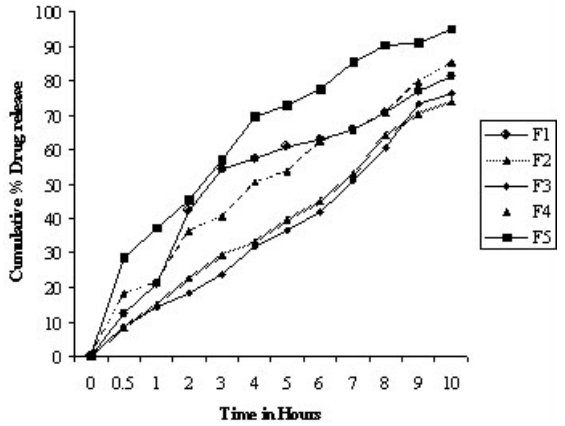

***Fig. 2:** Drug release profile of Lansoprazole gastric floating tablets F1 to F5.*

For all the formulations the floating lag time was found to be between 3-7 seconds. This lag time was decreased with an increase in the sodium bicarbonate content. All formulations have shown a floating time more than 24 hours. The swelling index which was in the order of 185% - 200% also increased with increase in the HPMC content. Among the prepared formulations both F2 and F3 were found to have the optimum properties of floating lag time, swelling index and sustained property.

In this study *in vitro* release profiles of all the formulations could be best expressed by Higuchi's matrix model as they showed a good linearity with 'R' value of 0.9996 to 0.9946. The 'n' value for the Korsmeyer and Peppas model were between 0.5- 0.9 which indicates, that non- fickcian diffusion is the dominant mechanism of drug release.

CONCLUSION

For the drugs like Lansoprazole whose mechanism of action is proton pump inhibition gastric floating systems are best suited. When a swelling polymer is also included along with the gas generating agent it helps in extension of gastric retention and also shows slow release of the drug for prolonged period.

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