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Formulation and evaluation of floating tablets of liquorice extract to improve bioavailability of Liquorice drug.

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ABSTRACT

Background: Floating tablets prolong the gastric residence time of drugs, improve bioavailability, and facilitate local drug delivery to the stomach. With this objective, floating tablets containing aqueous extract of liquorice as drug was prepared for the treatment of *Helicobacter pylori* and gastric ulcers. **Methods:** The aqueous extract of liquorice was standardized by HPTLC. Tablets containing HPMC K100M (hydrophilic polymer), liquorice extract, sodium bicarbonate (gas generating agent), talc, and magnesium stearate were prepared using direct compression method. The formulations were evaluated for physical parameters like diameter, thickness, hardness, friability, uniformity of weight, drug content, buoyancy time, dissolution, and drug release mechanism. The formulations were optimized on the basis of buoyancy time and *in vitro* drug release.

Results: The diameter of all formulations was in the range 11.166–11.933 mm; thickness was in the range 4.02–4.086 mm. The hardness ranged from 3.1 to 3.5 kg/cm2. All formulations passed the USP requirements for friability and uniformity of weight. The buoyancy time of all tablet formulations was less than 5 min and tablet remained in floating condition throughout the study. All the tablet formulations followed zero-order kinetics and Korsemeyer–Peppas model in drug release.

Conclusion: The optimized formulation was found to be F6 which released 98.3% of drug in 8 h *in vitro*, while the buoyancy time was 3.5 min. Formulations containing psyllium husk, sodium bicarbonate and HPMC K100M in combination can be a promising for gastroretentive drug delivery systems.

Key words: Buoyancy time, floating tablets, korsemeyer, liquorice extract

INTRODUCTION

Oral controlled release dosage forms have been developed over the past three decades due to their considerable therapeutic advantages such as ease of administration, patient compliance, and flexibility in formulation. However, this approach has several physiological difficulties such as inability to restrain and locate the controlled drug delivery system within the desired region of the gastrointestinal tract (GIT) due to variable gastric emptying and motility. Gastroretentive dosage form can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility of drugs that are less soluble in a high pH environment. The types of gastroretentive dosage forms are floating drug systems – effervescent and non

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effervescent systems.[1] Liquorice consists of dried peeled or unpeeled roots and stolons of *Glycyrrhiza glabra* Linn belonging to the family Fabaceae.[2] It has been reported that liquorice is effective in gastric ulcer treatment[3] and glycyrrhetinic acid, the aglycone of glycyrrhizin, has an anti-inflammatory and antiulcer effect.[4] Liquorice can raise the concentration of prostaglandins in the digestive system that promote mucus secretion from the stomach; it was also reported that liquorice prolongs the life span of surface cells in the stomach and has an antipepsin effect.[5] It has also been reported that *Helicobacter pylori* shows susceptibility to liquorice extract.[6]

MATERIALS AND METHOD

Materials

The roots and rhizomes of the plant Glycyrrhiza glabra were purchased from local market in Bramhapuri.dist Chandrapur India. HPMC K100M was obtained from Samar chemicals India. Psyllium husk was purchased from a local market in Bramahpuri India. Sodium bicarbonate was obtained from Samar chemicals india. Talc and magnesium stearate were obtained from Samar chemicals.. Magnesium stearate was obtained from Modern Chemical Corporation. All chemicals used were of analytical and pharmaceutical grade.

Method

Preparation and standardization of aqueous extract from liquorice root.

The powdered liquorice root was extracted with distilled water containing ammonia. The extraction temperature was maintained at 90°C with constant shaking. The extract was filtered and concentrated to get a thick paste. The amount of glycyrrhetinic acid in the extract was determined by HPTLC.[7]

Sample preparation.

Two hundred and fifty milligrams of the extract was refluxed with 50 mL 1N HCl for 4 h. It was cooled to room temperature and it was extracted with (20 × 5) mL chloroform. The combined chloroform extract was washed with water and filtered. It was evaporated at temperature of 30°C and the residue was dissolved in chloroform: methanol (1:1) and the volume was made upto 25 mL.

Formulation of tablets.

In the present study, all the tablets were formulated by direct compression technique using polymer like HPMC K100M and other ingredients like psyllium
husk, magnesium stearate, talc, and sodium bicarbonate. All ingredients were passed through sieve no # 80 and weighed accurately on electronic balance. The extract, HPMC K100M, sodium bicarbonate, and psyllium husk were mixed properly in a mortar and pestle to get a uniform tablet blend. Finally talc and magnesium stearate were mixed with the blend. The tablet blend was then weighed individually according to the formula and compressed into tablets using single

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punch tableting machine (Cadmach, Ahmedabad). The different formulations were labeled F1–F5 and their formulae are given in Table 1..

Table 1: Composition of floating tablet formulations

Ingredients	F1	F2	F3	F4	F5
Liquorice extract	250	250	250	250	250
Psyllium husk	75	100	125	100	100
HPMC k-100M	50	50	50	40	50
Sodium Bicarbonate	100	100	100	100	90
Magnesium stearate	5	05	05	05	05
talc	20	20	20	20	20

Evaluation Parameter of floting tablet

The prepared floating tablets were evaluated for diameter and thickness using Vernier calipers. The hardness of the tablets was evaluated using a Monsanto hardness tester. The friability was determined in a Roche friabilitor. Twenty tablets from each formulation were weighed and their average weight was determined

Buoyancy Time.

The time taken for dosage form to emerge on surface of medium called floating lag time (FLT) or buoyancy lag time (BLT). Floating behavior studies were performed in a USP type II (paddle) apparatus at speed 100 rpm in 900 mL 0.1N HCl at 37 ± 0.2°C to mimic *in vivo* conditions. FLT was determined on the basis of visual inspection.[8]

In vitro dissolution studies.

The *in vitro* dissolution studies were carried out using USP type I (basket) apparatus. The dissolution medium was 900 mL 0.1N HCl. The dissolution medium was kept in thermostatically controlled water bath, maintained at 37±0.5°C. The tablet was placed into the basket. The speed of rotation was kept at 100 rpm. At different time intervals, 5 mL of sample was withdrawn and dissolution medium was kept constant throughout by replacing with equal volume 5 mL of dissolution medium. The aliquots were extracted with 30 mL of
chloroform and the chloroform fraction was analyzed spectrophotometrically at 251 nm against blank chloroform for drug release. The study was performed in triplicate. A plot of cumulative % drug release versus time in hours was plotted.[8]

RESULTS

Evaluation of formulated tablets.

The diameter of all formulations was in the range 11.166–11.933 mm; thickness was in the range 4.02–4.086 mm. The hardness ranged from 3.1 to 3.5 kg/cm2. All formulations passed the USP requirements for friability and uniformity of weight [Table 2].

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Table 2: Evaluation of formulated tablets

Formulation	Diameter (mm)	Thickne (mm)	Hardness (kg/cm²)	Fribility (%)	Uniformity of weight (mg)	Drug content (%)	Buoyancy Time(min)
F1	11.16	4.02	3.13	0.85	500.4	97.27	5.0
F2	11.53	4.06	3.10	0.86	525.3	98.02	4.5
F3	11.93	4.08	3.40	0.72	550.6	98.27	4.0
F4	11.30	4.03	3.36	0.71	515.2	99.61	4.0
F5	11.73	4.04	3.46	0.81	515.2	96.10	3.5

Buoyancy time.

The buoyancy time of formulations are shown in Table 2. FLT of all formulations was found to be less than 5 min. The carbon dioxide generated from sodium bicarbonate upon contact with the acidic medium will remain entrapped in the gellified layer of the swollen polymer (hydrocolloids). This produces an upward motion of the dosage form and maintains its buoyancy.[12,13] The FLT may be explained as a result of the time required for dissolution medium to penetrate the tablet matrix and develop the swollen layer for entrapment of CO2 generated *in situ*. The tablet mass decreased progressively due to liberation of CO2 and release of drug from the matrix. On the other hand, as solvent front penetrated the glassy polymer layer, the swelling of HPMC K100 M caused an increase in volume of the tablet. The combined effect is a net reduction in density of the tablets, which prolongs the duration of floatation beyond 8 h.

In vitro drug release.

In this work, we have carried out *in vitro* drug studies in 0.1N HCl as the dissolution medium to study the drug release of the tablet formulations. Effect of different concentrations of psyllium husk on *in vitro* release was as shown in Figure 1. As the concentration of psyllium husk increased from 75 (F1) to 125 mg (F3) per tablet, the percent cumulative drug release decreased from 98.29 ± 0.86% (F1) to 96.1 ± 0.634% (F2). The percent
cumulative drug release for (F3) was 99.8 ± 0.965% after 8 h. The slow release of the drug could have attributed to the gelling properties of psyllium husk.

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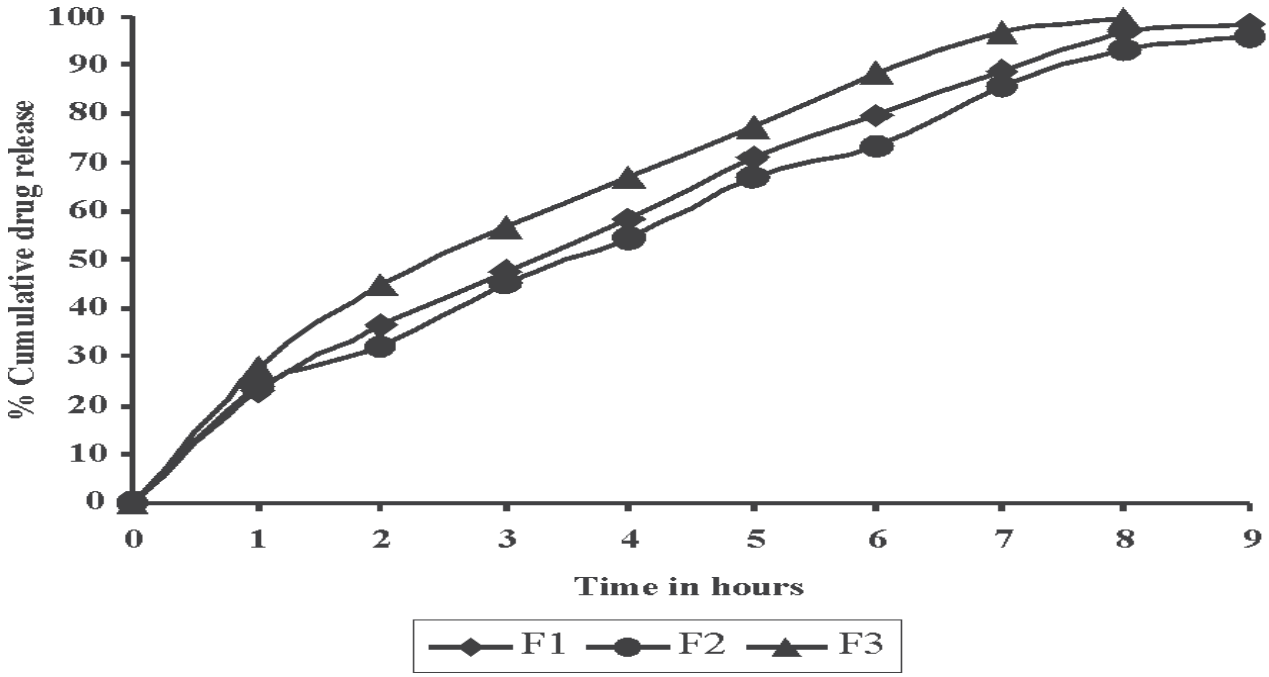

Figure 1: Comparative drug release profile of tablet formulations F1,F2 and F3

Effect of different concentrations of HPMC K100M on in *vitro* release was as shown in Figure 2. As the concentration of HPMC K100M was increased from 40 (F4) to 60 mg (F5), drug release decreased from 97.5± 0.696% to 97.3 ± 0.408%. This might be due to the increased polymer concentration which could have increased the diffusion path length for the drug, which could have retarded the drug release.

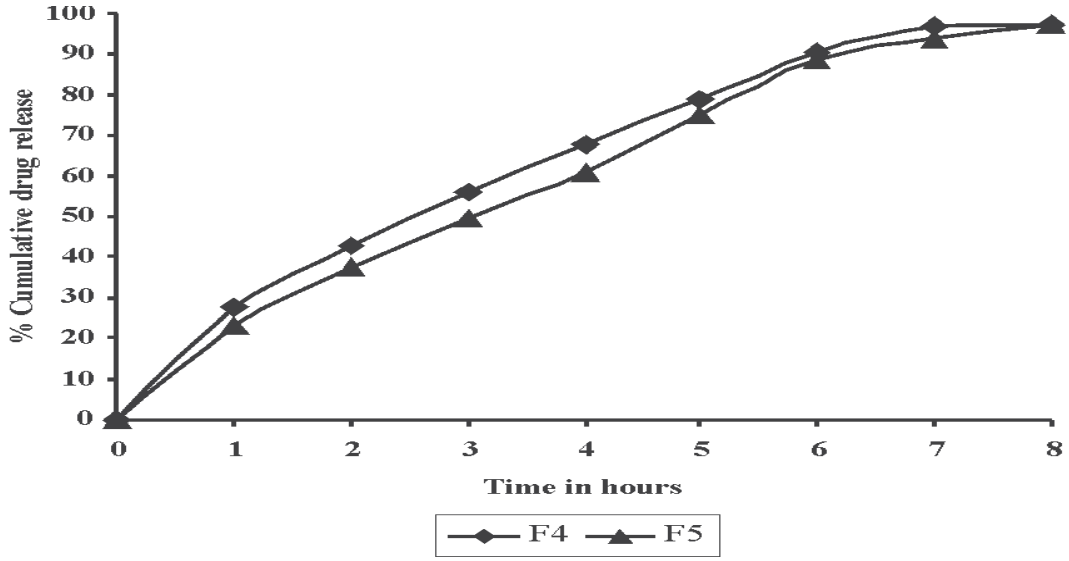

Figure 2: Comparative drug release profile of tablet formulations F4 and F5

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The effect of sodium bicarbonate on *in vitro* drug was shown in Figure 3. In such systems, sodium bicarbonate acts as a gas-generating agent. It generates gas when it comes into contact with an acidic environment of the stomach. This gas entraps into the matrix of watersoluble polymers and the formulation floats in an acidic environment of the stomach. As the concentration was increased from 90 (F6) to 110 mg (F7) per tablet, the drug release was decreased from 98.3 ± 0.935% to 93.6 ± 0.706%. Sodium bicarbonate being alkaline in nature creates an alkaline microenvironment around the tablet,which decreased the drug release from the tablet.

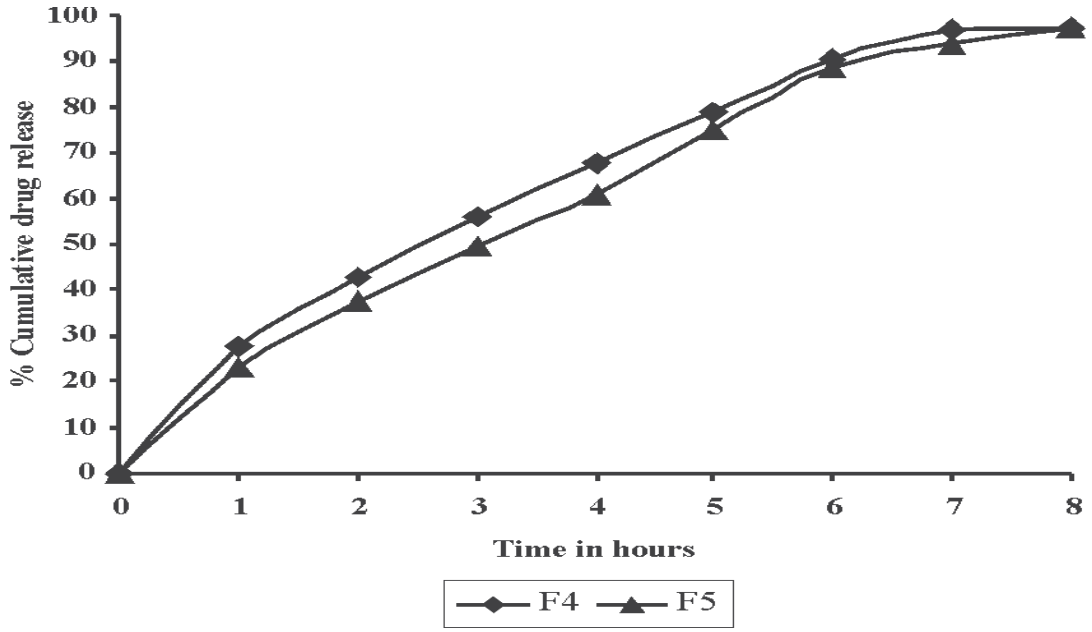

Figure 2: Comparative drug release profile of tablet formulations F4 and F5

CONCLUSION

Floating tablets of liquorice extract using psyllium husk, HPMC K100M, talc, sodium bicarbonate, and magnesium stearate were prepared. Formulated tablets were within acceptable limits for various physicochemical evaluations for tablets like tablet dimensions, hardness, uniformity of weight, friability, buoyancy time, and *in vitro* drug release. *In vitro* dissolution studies for the floating tablets were carried out in 0.1N HCl at 37 °C. About 93–99% of the drug was released in 8 h. Formulation F4 showed good floating behavior along with better-controlled drug release in comparison to other prepared formulations. We can conclude that psyllium husk, sodium bicarbonate and HPMC K100M in combination can be promising polymers for gastroretentive drug delivery systems. Floating tablets of aqueous extract of liquorice can be formulated as an approach to increase gastric residence time, thereby improving its bioavailability. The results indicate a promising potential of aqueous extract of liquorice floating tablets as an alternative to the conventional dosage form.

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