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Research Article

FORMULATION AND EVALUATION OF FLOATING DRUG DELIVERY SYSTEM OF REPAGLINIDE

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ABSTRACT

Objective: The present study's is to develop floating drug delivery system of repaglinide.

Methods: Moringa gum, Repaglinide, HPMC K100M, Sodium alginate, Calcium Carbonate, Sodium Citrate. The obtained formulation was evaluated for drug content, pH, *in vitro* gelling capacity, *in vitro* buoyancy studies, and *in vitro* dissolution studies.

Results and Discussion: All the total F1-F12 formulations showed pH ranging from 5.1 to 7.9, floating lag time of F1-F12 ranging from 5 s to 12 s with total floating time greater than 12 h, viscosity of F1-F12 ranging from 619 to 3856 cp, drug content of F1-F12 ranging from 31.2% to 93.1%, and percent drug release of F1-F12 ranging from 78.9% to 93.9%. Dissolution studies showed that F12 formulation-containing drug (30 mg) and polymer (4000 mg) showed 93.9% drug release in 12 h which is said to be optimized. Thus, the best formulation (F12) was subjected for a 3-month period of stability studies found to be stable and reported no significant change.

Conclusion: The study's goal is to develop and evaluate floating *in situ* gel forming solution of repaglinide with moringa gum as rate retardant polymer.

Keywords: Repaglinide, *Moringa oleifera* gum, HPMC K100M, Sodium alginate, Calcium carbonate, Sodium citrate.

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INTRODUCTION

Oral drug delivery: Oral administration of dosage forms is the most commonly used route of administration. Due to the potential advantages, it could provide such as an established delivery method. It is the most well-liked drug delivery method in the pharmaceutical sector due to its patient friendliness, practicality, economy, and lack of invasiveness. The drug enters the liver through the portal circulation after GI tract absorption [1]. Gastric retention drug delivery system: The oral controlled drug delivery method has made significant progress over the past 2 decades, but it has narrow success when it comes to medications with a poor oral bioavailability throughout the Gi tract. Bioavailability of drug from the digestive tract is a complicated process with many variables. The duration of contact with the small intestinal mucosa is widely acknowledged to be related to the level of drug absorbed by the intestines. Gastroretention contributes to the increased availability of novel therapeutic products with significant patient benefits. A sustained release formulation has several advantages over a sustained release drug administration system which endures in the stomach for a long time. Such absorption systems (for example, GRDDS) are crucial for drugs that break down in the gastrointestinal system, for drugs like aspirin, or for medications that should behave locally in the stomach, like certain enzymes. Stomach retention might improve bioavailability by increasing the solubility of drugs that are insoluble in the stomach because of their alkaline pH before being emptied. By regulating the release of medications that are best absorbed in the stomach, these systems can also assist when absorbed by the GIT, drugs with limited window of absorption, such as albuterol. FDDS or floating drug delivery system is a significantly simpler and rational method in creation of GRDs, both in terms of formulation and technology [2]. Introduction of *Moringa oleifera*: Moringa gum is an exudate extracted from *M. oleifera* stem or bark. It is white in color when freshly extracted. Its color turns reddish brown or maybe even light brown black in color after drying. When revealed to water, it swells and becomes viscous. Components of *M. oleifera*:

Fig. 1: *Moringa oleifera* gum

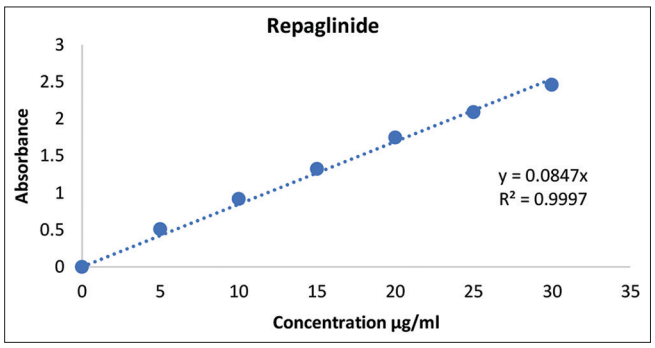


Fig. 2: Standard plot of repaglinide

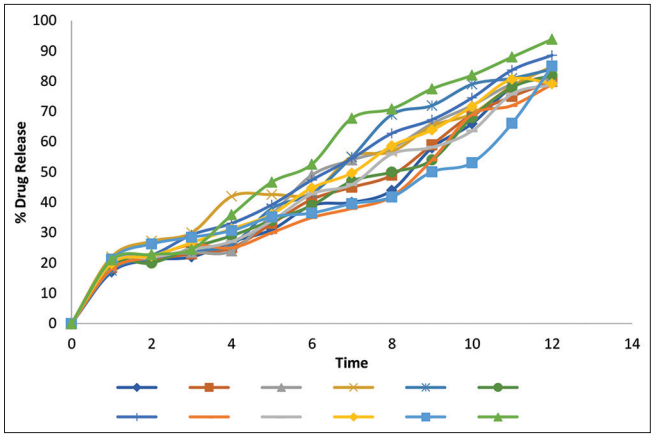


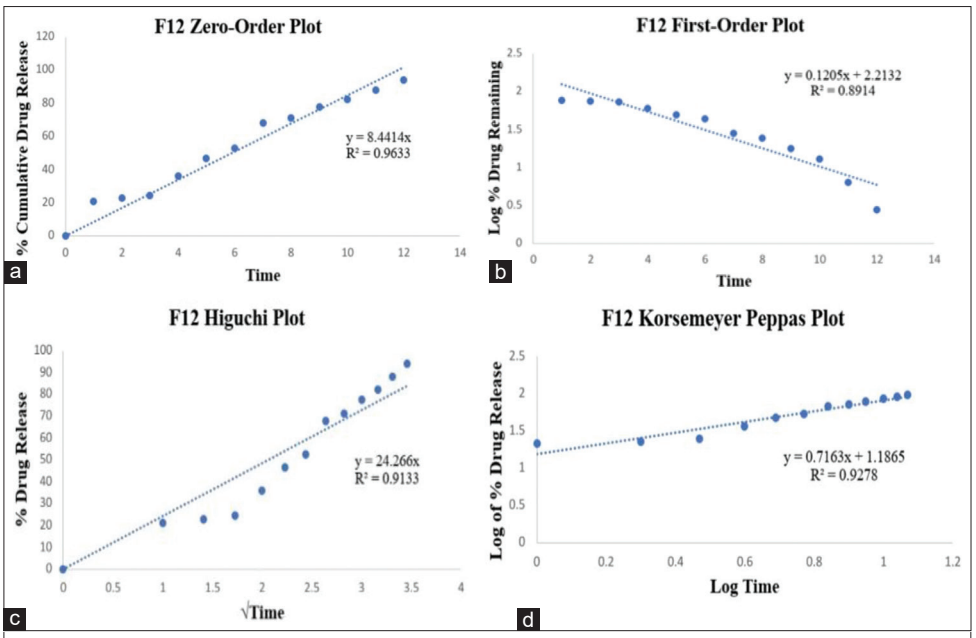
Fig. 3: Graphical representation of percent drug release of F1-F12 formulations

The gum's chemical components include glucose, rhamnose, galactose, glycolic acid, and arabinose [3] (Fig. 1).

Uses: Binder: It is used for the manufacturing of tablets and capsules for its binding properties. Film forming property: *M. oleifera* gum has been shown in studies to have huge potential for use in creating polymeric films for drug-delivery systems. Rate retardant: It is used for the manufacturing of tablets and capsules for its rate retardant property. Mucoadhesive: It is used for the manufacturing of tablets and capsules for its mucoadhesive property. Disintegrant: *M. oleifera* gum powder that has been isolated can be used as a disintegrant. When compared to a synthetic gum tablet, organic gum was found to disintegrate more quickly [4].

METHODS

Repaglinide (Lupin Pharmaceutical, Inc.), Moringa gum (MiracleTree Life Science, Tamil Nadu) HPMC K100M (S.D. Fine Chemicals), Sodium alginate (Colorcon Asia Pvt. Ltd, India), Calcium Carbonate (S.D. Fine Chemicals), Sodium Citrate (S.D. Fine Chemicals).



Kinetic data of F12 formulation

Formulation	Zero order	First order	Higuchi plot (R^2)	Korsmeyer-Peppas (R^2)	n value
F12	0.9633	0.8914	0.9133	0.9278	0.802381

Fig. 4: (a) Zero-order plot for optimized F12 formulation, (b) first-order plot for optimized F12 formulation, (c) Higuchi plot for optimized F12 formulation, (d) Korsmeyer-Peppas for optimized F12 formulation

Table 1: Formulations table

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Drug	30	30	30	30	30	30	30	30	30	30	30	30
Moringa gum	300	500	1000	1000	1500	1750	2000	2500	3250	3250	4000	4000
Sodium alginate	600	600	600	600	600	600	600	600	600	600	600	600
HPMC K100 M	15	15	15	150	15	115	15	15	45	115	15	150
Sodium citrate	150	150	150	150	150	150	150	150	150	150	150	150
Calcium carbonate	150	150	150	150	150	150	150	150	150	150	150	150
Distilled water	Make up to 30 mL	Make up to 30 mL	Make up to 30 mL	Make up to 30 mL	Make up to 30 mL	Make up to 30 mL	Make up to 30 mL	Make up to 30 mL	Make up to 30 mL	Make up to 30 mL	Make up to 30 mL	Make up to 30 mL

Preparation of floating *in situ* gel forming solution

The appropriate amount of sodium alginate, HPMC K100M, Moringa gum, and sodium citrate were dissolved in sufficient amount of distilled water and stirred for 20 min on the mechanical stirrer for complete swelling of polymers. Drug solution containing 30 mg of the drug in 1 ml of ethanol was slowly added to 20 ml of polymer solution with continuous stirring on the mechanical stirrer for 15 min. Specified concentrations of sodium citrate and $CaCO_3$ were prepared in distilled water and add to the polymer solution while stirring, continue stirring for 10 min, and finally, make up the volume up to 30 ml with distilled water (Table 1).

RESULTS AND DISCUSSION

Analytical method development

Calibration curve of repaglinide was developed in pH 0.1 NHCL and a graph was plotted with concentration on X axis and absorbance on Y axis. The absorbance was determined using UV spectrophotometer at 297 nm. The method was validated for linearity (R=0.9997). The standard graph followed Beer–Lambert's law, i.e., as concentration increases absorbance also increases as mentioned in the below Table 2 and Fig. 2.

Formulation development and evaluation

The prepared gel solution was evaluated for pH, drug content, *in vitro* buoyancy studies, *in vitro* gelling capacity, viscosity, and dissolution studies.

Table 2: Calibration table for repaglinide

Concentration (µg/mL)	Absorbance at 297 nm
5	0.508±0.01
10	0.918±0.001
15	1.322±0.008
20	1.748±0.004
25	2.091±0.005
30	2.462±0.007

- Determination of pH.: According to the table, the pH of all the formulations (F1–F12) was found to be between pH 5.1 and 7.9 [5].
- *In vitro* buoyancy studies: *In vitro* buoyancy studies were observed for all the formulations from F1-F12 showed greater than 12 h.

Floating lag time was observed for all formulations (F1–F12) which was found in range of 5 sec – 12 s [6].

- *In vitro* gelling capacity: Gelling studies were carried out using 0.1N HCl (pH 1.2), and the obtained data were represented in Table 3. Formulations F1, F3, and F6 showed gelation after a few minutes and dispersed quickly, Formulations F2, F5, F8, and F11 showed gelation immediate and remain for few hours, and Formulations F4, F7, F9, F10, and F12 showed gelation immediately and lasts for a long time [7].
- Drug content: The % drug content was ranged from 30% to 90%. Formulations F4, F7, F11, and F12 have showed greater than 90% of drug content. As the Moringa gum concentration increased, the formulation showed increased drug content [8].
- Viscosity of *in situ* gelling solutions: The viscosity of all the formulations was found in the range of 619–3,856 cp. F4, F7, F9, F10, F11, and F12 showed viscosity 1838–3856 as they contain high amount of Moringa gum. It is sufficient to maintain good consistency. All the values are within the acceptable limit [9].
- *In vitro* dissolution studies: The *in vitro* drug release study of repaglinide for the all formulations was carried and dissolution data are represented in Table 4. Formulations F2, F3, F1, F6, F5, F4, F11, and F7 released 80%, 81%, 82%, 82%, 84%, 84.9%, 85%, and 88.6% in 12 h of dissolution. Formulation F12 released 93.9% in 12 h of dissolution, respectively [10] Fig. 3.

Dissolution kinetics of final formulation

Repaglinide's drug release mechanism was identified by the use of zero order, first order, Higuchi's model, and Korsmeyer-Peppas model. Respective plots of F12 Formulation are shown in below Fig. 4.

Table 3: Evaluation studies

Batch	pH	Viscosity (centipoise)	Floating lag time (s)	Total floating time (h)	Gelling capacity	Drug content (%)
F1	5.1	619	12	>12	+	31.2
F2	5.5	688	9	>12	++	38.7
F3	5.3	799	11	>12	+	37.8
F4	7.3	1838	7	>12	+++	90
F5	6.2	828	7	>12	++	41.4
F6	6.5	962	5	>12	+	42
F7	7.8	2567	9	>12	+++	91.6
F8	6.3	931	8	>12	++	43.5
F9	7.6	2242	9	>12	+++	86.3
F10	6.8	1141	10	>12	+++	76.25
F11	7.5	2830	7	>12	++	91
F12	7.9	3856	8	>12	+++	93.1

Table 4: Dissolution studies

Time (h)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)	F7 (%)	F8 (%)	F9 (%)	F10 (%)	F11 (%)	F12 (%)
1	17	18.5	19	22	17.5	19.5	20.7	18	20.1	19.8	21.2	21
2	21	21.2	22	27.2	21.5	20	22.6	22	21.8	22.3	26.3	22.8
3	22	23	23.5	30	24	25	29.3	26	24.4	26.7	28.5	24.5
4	27	25	24	42	26	29	33.1	25	27.1	31.3	30.7	35.9
5	31	33	36	42.6	38	34	39.2	30	33.9	36.1	35.2	46.7
6	39	41	49	43	43	39	47.4	35	42.8	44.8	36.5	52.6
7	40	45	54	55.1	55	47	54.5	38	45.9	49.7	39.6	67.8
8	44	49	58	56.8	69	50	62.8	42	56	58.7	41.8	70.9
9	58	59	66	65.2	72	54	67.3	54	58.2	63.9	50.1	77.5
10	66	69	72	69.3	79	68	74.5	69	63.6	71.7	53.1	82
11	78	75	79	78.5	81	78	83.7	72	75.8	80.7	66.1	88
12	82	80	81	84.9	84	82	88.6	79	78.9	79.2	85	93.9

CONCLUSION

The study's goal is to develop and evaluate floating *in situ* gel forming solution of repaglinide with Moringa gum as rate retardant polymer. Formulations of F1-F12 were prepared using Moringa gum and HPMC K100M polymer. The prepared formulations was evaluated for pH, *in vitro* buoyancy studies, *in vitro* gelling capacity, viscosity, drug content, and dissolution studies. Concentration of polymers showed great impact on the as the level of the drug is released, the polymer increased, the release of the drug increased. Increased gel viscosity and the development of a gel layer with an extended diffusion path were both caused by an increase in the polymer proportion. Later on, as more fluid penetrated, the viscous gel layer of Moringa gum expanded significantly and served as an effective barrier for drug diffusion. The investigation shows that Moringa gum, HPMC K100M at suitable concentration can be used effectively to modify the release rates. Polymer forms a gel layer upon contact with HCL from which the drug is released slowly. As the drug is more soluble in acidic pH, it will be readily absorbed from stomach. Calcium carbonate is used as gas-generating agent which reacts with HCL. As a result, it leads to the evolution of CO_2 gas because of which the gel will float. For the formulation F12, the pH was 7.9, the floating lag time was 8 s, and the floating time was observed more than >12 h. Viscosity was 3856 cp, drug content was 93.1%, and drug release was 93.9%. The repaglinide gastroretentive drug delivery system's designed formulations showed zero-order release kinetics, and the drug release method used non-Fickian diffusion for F12 formulation. Stability tests on an improved formulation F12 denote that, after three months of storage, there have been no significant modifications to the drug content or dissolution parameter values. The polymer used forms a gel-like layer where the drug is slowly diffused into the systemic circulation. This study indicates suitability of Moringa gum, HPMC K100M in the development of a gastroretentive drug delivery system. Hence, the aim of preparing repaglinide gastroretentive drug is successfully achieved and established.

AUTHOR'S CONTRIBUTIONS

All the authors have equally contributed.

CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

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