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Formulation, Optimization and Evaluation of Gastroretentive floating microsphere of Dexlansoprazole and Omeprazole

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ABSTRACT

Proton pump inhibitors (PPIs) such as Dexlansoprazole and Omeprazole are widely used for the management of gastric acid–related disorders; however, their short plasma half-life, pH-dependent stability, and limited gastric residence time reduce therapeutic efficacy. Gastroretentive floating microspheres provide improved drug delivery by extending gastric retention, enhancing absorption, and maintaining prolonged therapeutic concentrations. In this study, floating microspheres of Dexlansoprazole and Omeprazole were formulated using polymers including HPMC and Ethyl Cellulose by solvent evaporation technique. Optimization was carried out by evaluating particle size, buoyancy, drug entrapment efficiency, and in-vitro drug release. The optimized formulations exhibited high floating capacity (> 85%) and sustained drug release for over 12 h, suggesting improved gastroretentive behavior and potential enhancement in bioavailability.

KEYWORDS: Dexlansoprazole; Omeprazole; Gastroretentive Drug Delivery System; Floating Microspheres.

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INTRODUCTION

Proton pump inhibitors (PPIs) are extensively prescribed for gastroesophageal reflux disease (GERD), peptic ulcer, and related acid-peptic disorders due to their potent suppression of gastric acid secretion [1]. Among the PPIs, Dexlansoprazole, a dual-release formulation, and Omeprazole, a first-generation PPI, exhibit short elimination half-lives of approximately 1–2 hours [2]. Their therapeutic performance is further impacted by degradation in acidic gastric conditions and poor bioavailability [3,4]. Gastroretentive drug delivery systems (GRDDS) are designed to remain buoyant in the stomach for prolonged periods, allowing improved drug stability and site-specific absorption [5]. Floating microspheres represent a promising GRDDS owing to their low bulk density, enhanced surface area, and controlled drug release properties [6]. These microspheres improve gastric residence time, minimize dose frequency, and reduce systemic drug exposure-related adverse effects [7]. Dexlansoprazole and Omeprazole exhibit optimal absorption in the upper gastrointestinal tract; thus, floating systems can significantly enhance their therapeutic effects [3]. Fabrication using polymers such as hydroxypropyl methylcellulose (HPMC) and ethyl cellulose enables formation of hollow structures with excellent buoyancy and controlled release profiles [8,9]. Therefore, formulation and optimization of gastroretentive floating microspheres of Dexlansoprazole and Omeprazole could contribute toward improved treatment outcomes in acid-peptic diseases.

MATERIAL AND METHODS

Development of Gastroretentive Floating Microspheres

Floating microspheres were formulated by **ionic gelation technique** using combinations of HPMC, ethyl cellulose, and guar gum. Sodium alginate was dissolved in deionized water, while ethyl cellulose and HPMC were dissolved separately and mixed with the alginate solution. For guar gum–containing batches, guar gum was incorporated into the polymer mixture. The drug was dispersed uniformly into the resulting polymer matrix and stirred to obtain a homogeneous slurry. The dispersion was then dropped slowly through a 26G syringe needle into a calcium chloride solution (10% v/v glacial acetic acid), facilitating instantaneous cross-linking and microsphere formation. The microspheres were separated by filtration, air-dried for 8–10 hours, and stored in airtight vials for further analysis [6,7].

Optimization of Drug-Loaded Floating Microspheres

Dexlansoprazole (DXZ) and Omeprazole (OMZ) gastroretentive microspheres were optimized using **Central Composite Design (CCD)** via Design-Expert® version 13. Polymer concentrations—HPMC E5 (X1), ethyl cellulose (X2), and guar gum (X3)—were selected as independent variables, while percentage yield (R1) and drug entrapment efficiency (R2) served as dependent responses. Statistical validation using ANOVA and 3-dimensional response surface plots was conducted to identify the most favorable formulation composition demonstrating enhanced floating capability and entrapment efficiency.

Table 1: List of independent variables selected in experimental design

S. No.	Independent variables	Level of variation		
		Low	Medium	High
1.	X1- HPMC E-5 (% w/v)	10	20	20
2.	X2- EC (% w/v)	5	12.5	20
3.	X3- Gaur gum (%w/v)	5	10	15

Table 2: List of response or dependent variables selected in experimental design

S. No.	Response or dependent variables	Units
1.	R1- Percentage Yield	%
2.	R2 -Entrapment Efficiency	%

Table 3: Central composite experimental design for Floating Microsphere

S. No.	Std. Run	Batch No.	Factor 1 A:HPMC %	Factor 2 B:Ethyl cellulose %	Factor 3 C:Gaur Gum %
1.	5	GFM-1	10	12.5	5
2.	8	GFM -2	30	12.5	15
3.	10	GFM -3	20	20	5
4.	11	GFM -4	20	5	15
5.	6	GFM -5	30	12.5	5
6.	3	GFM -6	10	20	10
7.	12	GFM -7	20	20	15
8.	14	GFM -8	20	12.5	10
9.	1	GFM -9	10	5	10
10.	15	GFM -10	20	12.5	10
11.	13	GFM -11	20	12.5	10
12.	9	GFM -12	20	5	5
13.	2	GFM -13	30	5	10
14.	7	GFM -14	10	12.5	15
15.	4	GFM -15	30	20	10

Evaluation Parameters of Gastroretentive Floating Microspheres (GFM)

The prepared Dexlansoprazole (DXZ) and Omeprazole (OMZ) loaded floating microspheres were evaluated as per standard procedure [8-10]

Particle size distribution, polydispersity index (PDI), and zeta potential of microspheres (10 mg/mL) were analyzed at 25 ± 0.5°C using a Zetasizer Nano ZS90 (Malvern Instruments Ltd., UK).

Percentage yield was calculated using actual recovered microsphere weight relative to total polymer–drug solids.
Drug entrapment was determined by extracting drug from 100 mg crushed microspheres in SGF (pH 1.2), filtering through a 0.45 µm membrane, and analyzing drug content at 240 nm via UV-spectrophotometer (Shimadzu 1900, Japan).
Degree of Swelling: **Microspheres (100 mg) were placed in SGF (pH 1.2) using USP Type I apparatus for 12 h at 37 ± 0.1°C.**

In-vitro Mucoadhesion**: Wash-off test was performed using goat gastric mucosa mounted on a slide in a USP disintegration apparatus. The percentage of microspheres adhered over 12 h was calculated.**
In-vitro Buoyancy & Floating Time**: Buoyancy was evaluated by dispersing 200 mg microspheres in SGF (0.02% Tween-80) and stirring at 100 rpm for 12 h.**

Floating efficiency: Floating time was recorded as total duration microspheres remained buoyant in 0.1N HCl.
In-vitro Drug Release: **Dissolution was performed using USP Type II (paddle) apparatus at 100 rpm in 900 mL SGF (pH 1.2, 37 ± 0.5°C) for 24 h. Samples (5 mL) were withdrawn at intervals, filtered (0.45 µm), and analyzed UV-spectrophotometrically at 240 nm, maintaining sink conditions.**

RESULTS AND DISCUSSION

The formulation of Dexlansoprazole (DXZ) and Omeprazole (OMZ) gastroretentive floating microspheres was optimized using a Central Composite Design (CCD) approach in Design-Expert® (Version 13). A total of 15 experimental runs were generated and performed in a randomized manner to minimize systematic error. The influence of selected formulation variables (independent factors) on the critical quality attributes (response variables) was systematically evaluated. Based on model selection criteria, a linear model was identified as the best-fit for both responses. Statistical significance and model adequacy were further confirmed using analysis of variance (ANOVA), which yielded acceptable values for R^2, adjusted R^2, predicted R^2, standard deviation, and coefficient of variation (%CV), indicating excellent model predictability and reliability. The quantitative effects of the independent variables on the formulation responses are summarized in Table 4. Results for evaluation parameters is given

in table 5 and release is given in table 6.

Table 4: Effect of independent variables on response variables

Batch No.	Independent variable			Response variables	
	X1 % w/v	X2 % w/v	X3 % w/v	R1	R2
GFM-1	10	12.5	5	78.49	78.25
GFM -2	30	12.5	15	85.32	84.66
GFM -3	20	20	5	66.11	80.05
GFM -4	20	5	15	88.62	92.46
GFM -5	30	12.5	5	82.53	82.56
GFM -6	10	20	10	66.92	76.22
GFM -7	20	20	15	76.10	84.88
GFM -8	20	12.5	10	79.28	81.74
GFM -9	10	5	10	76.22	82.35
GFM -10	20	12.5	10	79.10	81.74
GFM -11	20	12.5	10	79.31	81.74
GFM -12	20	5	5	84.46	85.88
GFM -13	30	5	10	84.27	90.88
GFM -14	10	12.5	15	62.35	78.55
GFM -15	30	20	10	68.18	76.88

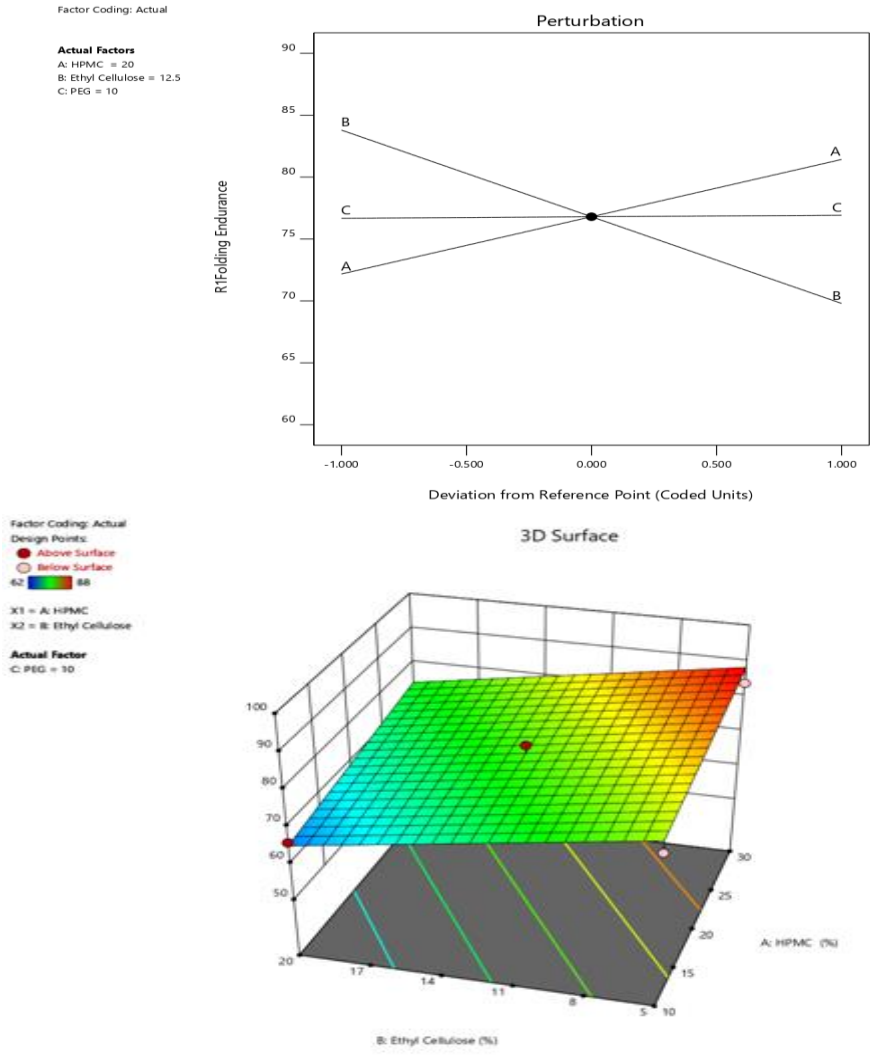

Fig. 1: 3D surface plot of GFM for percentage yield

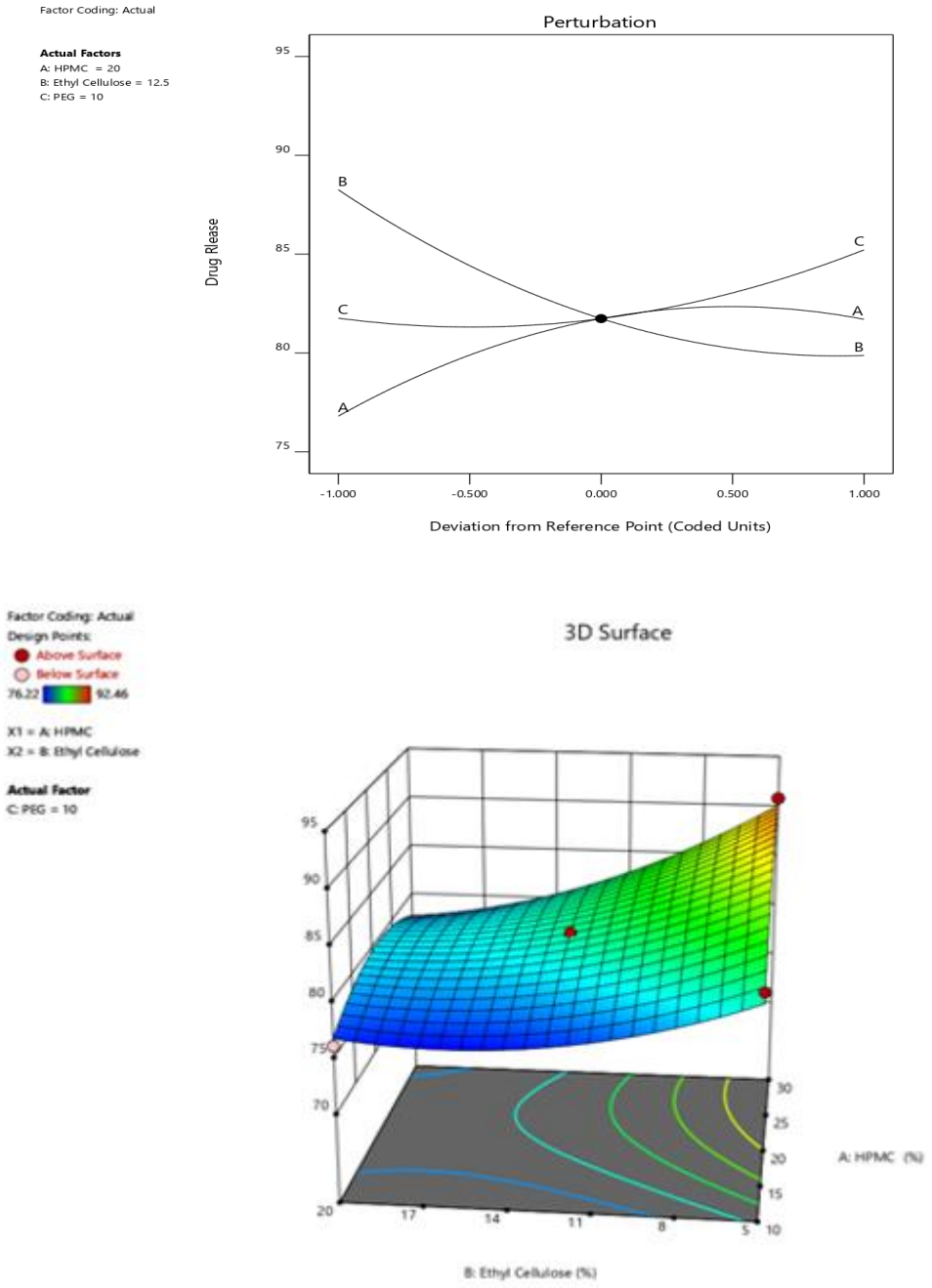

Fig. 2: 3D surface plot of GFM for Entrapment Efficiency

Table 5: Evaluation Parameters of Gastroretentive Floating Microsphere of Dexlansoprazole (DXZ) and Omeprazole (OMZ)

Formulation Code	Particle Size (µm)	PDI	Zeta Potential (mV)	% Yield	% EE	Degree of Swelling	% Mucoadhesiveness	% Floating	Floating Time (Hrs)
GFM-1	60.48±1.11	0.73±0.28	-34.26	78.49	78.25	0.64±1.10	69.10±2.11	70.43±2.17	13
GFM -2	53.29±1.18	0.71±0.39	-33.18	85.32	84.66	0.71±1.89	73.28±2.17	69.28±2.17	12
GFM -3	55.81±1.19	0.68±0.21	-34.10	66.11	80.05	0.82±1.45	80.46±2.29	73.46±2.18	13
GFM -4	50.13±1.15	0.72±0.22	-31.12	88.62	92.46	0.93±1.16	94.31±2.18	88.45±1.12	14
GFM -5	57.39±1.13	0.58±0.16	-30.42	82.53	82.56	0.91±1.18	87.14±1.17	82.39±2.04	16
GFM -6	54.46±1.10	0.59±0.13	-31.29	66.92	76.22	0.89±1.77	90.31±2.02	85.26±1.13	15

GFM -7	61.20±1.12	0.62±0.11	-35.21	76.10	84.88	0.88±1.34	68.43±2.48	66.12±1.66	15
GFM -8	60.16±1.19	0.68±0.18	-34.26	79.28	81.74	0.89±1.29	70.47±2.41	70.43±1.88	16
GFM -9	62.43±1.12	0.69±0.16	-32.18	76.22	82.35	0.66±1.81	89.44±1.89	83.10±2.10	12
GFM -10	63.26±1.10	0.63±0.38	-30.28	79.10	81.74	0.66±1.27	67.26±2.10	80.49±2.17	12
GFM -11	54.19±1.07	0.66±0.16	-34.15	79.31	81.74	0.83±1.23	74.19±2.11	76.39±2.42	13
GFM -12	56.16±1.16	0.71±0.18	-33.10	84.46	85.88	0.87±1.19	84.72±2.28	78.42±1.32	13
GFM -13	60.27±1.03	0.72±0.27	-36.25	84.27	90.88	0.84±1.37	86.11±2.09	81.43±2.04	14
GFM -14	58.46±1.02	0.65±0.20	-33.18	62.35	78.55	0.90±1.10	90.15±2.05	80.46±2.20	15
GFM -15	61.47±1.12	0.69±0.27	-34.27	68.18	76.88	0.85±1.35	88.29±2.19	84.39±2.33	16
Optimized	51.29±1.11	0.71±0.13	-30.5	84.78	92.48	0.92±1.36	93.29±2.71	88.10±1.18	14

Table 6: % Drug Release of Gastroretentive Floating Microsphere of Dexlansoprazole (DXZ) and Omeprazole (OMZ)

Time (Hrs)	Formulation Code	
	GFM-4	Optimized
0	0	0
2	5.02	5.48
4	18.25	20.19
6	30.89	33.22
8	34.28	35.18
10	39.42	42.18
12	44.28	46.20
14	50.45	52.38
16	57.28	58.11
18	60.11	62.17
20	69.26	70.42
22	84.29	86.19
24	93.46	95.21

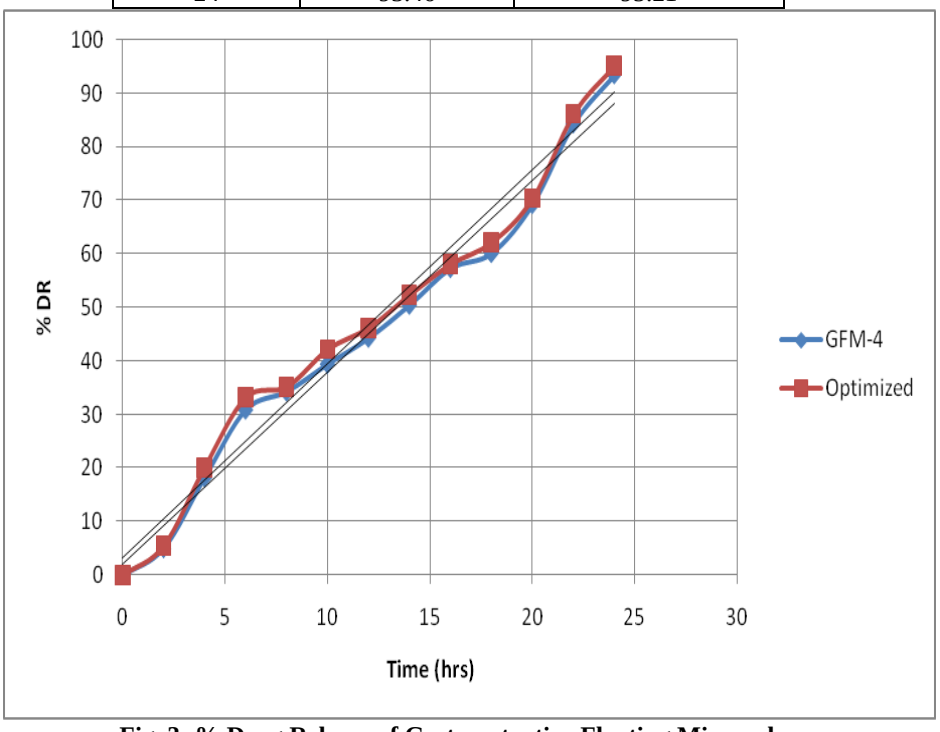

Fig. 3: % Drug Release of Gastroretentive Floating Microsphere

CONCLUSION

The present research successfully demonstrated the formulation, optimization, and evaluation of gastroretentive floating microspheres of Dexlansoprazole (DXZ) and Omeprazole (OMZ) to enhance gastric residence time and improve therapeutic efficacy in acid-related disorders. The floating microspheres were efficiently prepared using a polymer-based solvent evaporation technique, followed by systematic optimization through Central Composite Design (CCD). The optimized formulations showed desirable physicochemical characteristics, including appropriate particle size, high percentage yield, satisfactory entrapment efficiency, and excellent micromeritic properties. In vitro buoyancy and swelling studies confirmed prolonged gastric retention, while mucoadhesive behavior supported enhanced adherence to gastric mucosa, contributing to sustained localization in the stomach. The in vitro drug release profile demonstrated extended drug release for more than 24 hours, conforming to controlled-release kinetics suitable for once-daily administration. Collectively, the outcomes indicate that the developed gastroretentive floating microspheres of DXZ and OMZ offer a promising platform for improving drug bioavailability, reducing dosing frequency, and potentially enhancing patient compliance in the management of gastroesophageal reflux disease and peptic ulcer-related complications.Further in vivo studies and clinical translation are warranted to validate the therapeutic potential and long-term safety of the optimized formulations.

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