Journal of Complementary Medicine Research, ISSN: 2146-8397 Vol. 16, No. 1, 2025 (pp.32-46)
RESEARCH ARTICLE WWW.JOCMR.COM

FORMULATION, OPTIMIZATION, AND EVALUATION OF GASTRO-RETENTIVE FLOATING DELIVERY SYSTEMS OF DEXLANSOPRAZOLE: IN-VITRO AND IN-VIVO CHARACTERIZATION FOR BIOAVAILABILITY ENHANCEMENT

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ABSTRACT

Dexlansoprazole, a proton pump inhibitor (PPI), is widely used in the treatment of gastroesophageal reflux disease (GERD) and peptic ulcers. However, its short biological half-life and pH-dependent solubility limit its therapeutic efficacy. A gastro-retentive floating drug delivery system (GRFDDS) can enhance gastric residence time, improve bioavailability, and ensure prolonged drug release. Dexlansoprazole-loaded floating tablets were prepared using hydrophilic polymers (HPMC K4M, HPMC K100M) and gas-generating agents (sodium bicarbonate, citric acid) via direct compression. A 3^2 factorial design was applied to optimize key formulation parameters. The prepared formulations were evaluated for pre-compression and post-compression characteristics, including hardness, swelling index, buoyancy lag time, and total floating duration. In-vitro drug release studies were performed in simulated gastric fluid (pH 1.2) for 12 hours. In-vivo pharmacokinetic studies were conducted in animal models to assess bioavailability enhancement.

The optimized formulation exhibited excellent buoyancy properties with a buoyancy lag time of <30 seconds and a total floating duration exceeding 12 hours. In-vitro dissolution studies showed sustained drug release, following non-Fickian diffusion kinetics. In-vivo pharmacokinetic evaluation revealed a significant increase in the bioavailability of dexlansoprazole compared to the conventional immediate-release formulation. The developed gastro-retentive floating delivery system of dexlansoprazole successfully prolonged gastric residence time and enhanced bioavailability. This novel formulation provides a promising strategy for improving the therapeutic efficacy of dexlansoprazole in GERD management. Further clinical studies are required to validate its potential benefits.

Keywords: Dexlansoprazole, Gastro-retentive floating drug delivery system, Factorial design, Bioavailability enhancement, In-vitro drug release, In-vivo pharmacokinetics.

1. INTRODUCTION

Gastroesophageal reflux disease (GERD) and peptic ulcers are prevalent gastrointestinal disorders that significantly impact patients' quality of life. Proton pump inhibitors (PPIs) such as dexlansoprazole are commonly prescribed for their potent acid suppression activity, providing symptomatic relief and promoting mucosal healing. Dexlansoprazole, an enantiomer of lansoprazole, offers dual delayed-release characteristics, leading to prolonged acid suppression. However, its therapeutic efficacy is limited by its short biological half-life (~1–1.5 hours) and pH-dependent solubility, which result in rapid drug elimination and reduced bioavailability.

Need for a Gastro-Retentive Floating Drug Delivery System

Oral drug delivery of PPIs faces significant challenges due to the acidic gastric environment and rapid gastric emptying. Conventional dosage forms often fail to maintain effective plasma drug concentrations, necessitating frequent dosing and leading to variability in therapeutic response. Gastro-retentive drug delivery systems (GRDDS) offer a potential solution by prolonging gastric residence time, ensuring controlled drug release, and enhancing drug bioavailability. Among various GRDDS approaches, floating drug delivery systems (FDDS) have gained considerable attention due to their ability to remain buoyant in the stomach for an extended duration without being affected by gastric emptying.

A floating drug delivery system for dexlansoprazole can:

- Improve gastric retention time and extend drug release.
- Enhance bioavailability by maintaining drug release in the acidic gastric environment.
- Reduce dosing frequency and improve patient compliance.

Advantages of Floating Drug Delivery Systems

Floating drug delivery systems employ low-density materials and gas-generating agents (e.g., sodium bicarbonate and citric acid) to maintain buoyancy in gastric fluid. The key advantages of FDDS include:

- Prolonged drug release: Enhances therapeutic effects and reduces dosing frequency.
- Improved absorption window: Facilitates better drug absorption in the upper gastrointestinal tract.
- Minimized drug degradation: Reduces exposure to alkaline intestinal pH, preventing premature drug degradation.

2. LITERATURE REVIEW

1. Gastro-Retentive Drug Delivery Systems (GRDDS)

Gastro-retentive drug delivery systems (GRDDS) have been widely explored to improve drug absorption in the upper gastrointestinal tract. These systems prolong gastric retention time, enhance drug solubility, and ensure controlled drug release. Various approaches for gastro-retention include floating drug delivery systems (FDDS), bioadhesive systems, expandable systems, and high-density systems (Patel & Patel, 2020). Among these, FDDS are the most commonly utilized due to their ability to remain buoyant in gastric fluid, preventing premature emptying (Streubel et al., 2006).

2. Floating Drug Delivery Systems (FDDS)

FDDS utilize low-density materials and gas-generating agents to maintain buoyancy in the stomach for an extended period. These systems are particularly beneficial for drugs that exhibit site-specific absorption in the stomach or upper small intestine. Floating formulations can be categorized into effervescent and non-effervescent systems. Effervescent FDDS employ gas-generating agents such as sodium bicarbonate and citric acid, which produce CO_2 in the presence of gastric fluid, leading to tablet expansion and buoyancy (Singh & Kim, 2000). Non-effervescent FDDS rely on swelling polymers such as hydroxypropyl methylcellulose (HPMC) and alginates to create a gel barrier, preventing gastric emptying (Tripathi et al., 2019).

3. Dexlansoprazole: Pharmacokinetics and Challenges

Dexlansoprazole is a proton pump inhibitor (PPI) used for treating gastroesophageal reflux disease (GERD) and peptic ulcers. It has a dual delayed-release mechanism, offering prolonged acid suppression. However, dexlansoprazole faces challenges such as a short biological half-life (~1–1.5 hours), pH-dependent solubility, and poor bioavailability due to rapid gastric emptying (Rouge et al., 1996). Enhancing gastric retention through an FDDS can provide sustained drug release and improve bioavailability.

4. Role of Polymers in Floating Tablets

Hydrophilic polymers such as HPMC K4M and HPMC K100M are widely used in FDDS to control drug release and enhance matrix swelling properties. The swelling mechanism allows water penetration, leading to polymer hydration and gel formation, which sustains drug release (Garg &

Sharma, 2003). The combination of polymers and gas-generating agents ensures prolonged floating behavior, reducing variability in drug absorption (Chawla et al., 2003).

5. Factorial Design for Formulation Optimization

Traditional formulation approaches involve trial-and-error methods, which are time-consuming and inefficient. Factorial design, a statistical optimization tool, allows for the systematic evaluation of multiple formulation parameters and their interactions. Box and Wilson (1951) introduced the concept of factorial design, which has been extensively applied in pharmaceutical research for optimizing drug delivery systems (Bansal & Bansal, 2021). In this study, a 3^2 factorial design was employed to optimize key formulation parameters, including polymer concentration and gas-generating agents, ensuring optimal buoyancy and sustained drug release.

6. In-Vitro and In-Vivo Characterization

The success of FDDS relies on rigorous in-vitro and in-vivo evaluations. In-vitro studies include buoyancy lag time, total floating duration, and drug release kinetics, which provide insights into formulation performance. In-vivo pharmacokinetic studies further validate bioavailability enhancement by comparing plasma drug concentration profiles (Klausner et al., 2003). Previous studies have demonstrated that gastro-retentive formulations of PPIs significantly improve drug absorption and prolong therapeutic effects (Rajinikanth & Mishra, 2008).

7. Clinical Implications and Future Perspectives

The development of an optimized gastro-retentive floating system for dexlansoprazole has significant clinical implications. By improving bioavailability and prolonging drug release, FDDS can enhance patient compliance and therapeutic outcomes in GERD management. Future studies should focus on clinical validation and long-term stability assessments to facilitate commercial translation (Ubaidulla et al., 2021).

The literature supports the potential of floating drug delivery systems for enhancing the bioavailability of dexlansoprazole. By leveraging hydrophilic polymers, gas-generating agents, and factorial design optimization, a novel FDDS can be developed to improve therapeutic efficacy. This study builds upon existing research to formulate and evaluate an optimized gastro-retentive system for dexlansoprazole, addressing key pharmacokinetic limitations.

3. METHODOLOGY

1. UV-visible spectrophotometric analysis of Dexlansoprazole: The diluent was prepared by mixing 0.1 N potassium hydroxide and methanol in a 40:60 v/v ratio. Subsequently, a sample stock solution (Sample Stock Solution 1) was prepared by dissolving 10.0 mg of Dexlansoprazole (DLS) in the diluent to achieve a concentration of 50 µg/mL. To prepare sample working solutions, 0.5 mL of Sample Stock Solution 1 was transferred into a 10 mL volumetric flask and diluted to the mark with the prepared diluent. The suitable wavelength for the determination of Dexlansoprazole in the diluent was identified by scanning the sample working solution over the range of 200-400 nm using a Shimadzu UV-160 double beam spectrophotometer. Finally, the analysis was performed using a Schimadzu UV-1800 double beam spectrophotometer equipped with UV probe software and 1 cm matched quartz cells at the identified suitable wavelength.

2. HPLC analysis of Dexlansoprazole: The analysis was conducted using a Waters HPLC system consisting of an Alliance 2695 separation module equipped with an auto injector and temperature controller for sample storage and column. The diluent was prepared by mixing 0.1 N potassium hydroxide and methanol in a 40:60 v/v ratio. A standard stock solution (500 µg/mL) was then prepared by dissolving 50 mg of Dexlansoprazole (DLS) in the diluent and making up the volume to 25 mL. Standard working solutions were prepared by diluting 5 mL aliquots of this stock solution to 10 mL with the diluent. For the sample solution, an equivalent of 50 mg of Dexlansoprazole was dissolved in 10 mL of diluent with sonication until the pellets dissolved completely. The solution was then diluted to 25 mL with the diluent and centrifuged. A 5 mL aliquot of the supernatant was further diluted to 10 mL with the diluent. Chromatographic separation was achieved on a Waters XBridge BEH Shield RP18 (250 x 4.6 mm, 5 µm) using a mobile phase consisting of 10 mM dibasic potassium phosphate buffer (pH adjusted to 7.21 with dilute orthophosphoric acid): Methanol: TEA (30:69:1 v/v/v) at a flow rate of 1 mL/min. The

injection volume was 10 µL, and detection was performed at 285 nm using a Schimadzu UV-1800 double beam spectrophotometer equipped with UV probe software. Data acquisition and analysis were performed using Empower 3 Software.

Development and Optimization of Dexlansoprazole-Loaded Gastroretentive Floating Microspheres using Central Composite Design (CCD)

Preparation of floating microspheres: Floating microspheres of dexlansoprazole were prepared using the ionotropic gelation method, for optimal results. Initially, sodium alginate was dispersed in distilled water using a magnetic stirrer at 60 °C. Concurrently, polymeric dispersions were prepared independently at room temperature with a magnetic stirrer. Once the sodium alginate dispersion was ready, both dispersions were thoroughly mixed for about 10 minutes at 1000 rpm using a magnetic stirrer. An accurately weighed amount of dexlansoprazole (DLS) was then uniformly mixed into the polymeric compositions and agitated for 1 hour with the aid of a mechanical stirrer at approximately 1000 rpm. The required amount of sodium bicarbonate was added to the solution with continuous stirring. The resulting solution was gently added dropwise through an 18-gauge needle into a 10% w/v calcium chloride solution. To obtain appropriately rounded microspheres, the excess microspheres were allowed to soak in the calcium chloride solution for around 3 hours. The formed microspheres were kept suspended in the calcium chloride solution for an additional hour to improve their mechanical strength. Finally, the microspheres were collected using the decantation process, washed with purified water, and air-dried evenly at 45 °C for about 12 hours. This approach ensures the production of robust and uniformly sized dexlansoprazole floating microspheres.

Optimization of formulation by Central composite design: The DLS-loaded microsphere was optimized using Design Expert 12.1.1. (State-Ease Inc., Minneapolis, MN). Three independent factors were considered: sodium alginate concentration (A), Concentration of PLGA (B), cross-linking duration in hours (C), the additional impact of these individual variables on observed responses (drug release, mucoadhesion, entrapment efficiency, and particle size). Table 1 depicts the optimization design with the three components and 3 levels. Twenty different runs have been undertaken, and the responses for each run were documented. The composition with the optimal outcomes was chosen for future research.

Table Optimization Desing of DLS Microspheres

Independent variables	**Levels**		
	Low (-1)	**Medium (0)**	**High (+1)**
Qty of Sodium alginate in mg (X_1)	300	450	600
Conc. of PLGA in % (X_2)	5%	7.5%	10%
Cross-linking time in h (X_3)	2.0	3.5	5
Dependent variables or Response factors			
% Drug release (Y_1)			
% Mucoadhesion (Y_2)			
% Entrapment efficiency (Y_3)			
Particle size in µM			

Table Composition of different runs of mucoadhesive microspheres of DLS as per CCD

Std	**Run**	**Qty of Sodium alginate in mg (X_1)**	**Conc. of PLGA in % (X_2)**	**Cross linking time in h (X_3)**
19	1	450	7.5	3.5
9	2	197.731	7.5	3.5

7	3	300	10	5
4	4	600	10	2
16	5	450	7.5	3.5
6	6	600	5	5
15	7	450	7.5	3.5
11	8	450	3.295	3.5
20	9	450	7.5	3.5
14	10	450	7.5	6.022
12	11	450	11.704	3.5
18	12	450	7.5	3.5
2	13	600	5	2
8	14	600	10	5
5	15	300	5	5
13	16	450	7.5	0.977
1	17	300	5	2
3	18	300	10	2
17	19	450	7.5	3.5
10	20	702.268	7.5	3.5

Characterization of mucoadhesive microspheres of DLS

Particle size analysis: The particle size of the produced DLS-loaded microspheres was estimated using optical microscopy. An Olympus BX53 optical microscope was used for this purpose. For each batch, over 300 microspheres were placed on a glass slide, and their dimensions were randomly measured after calibrating the eyepiece micrometer with a stage micrometer.

Percentage yield: The percentage yield of dried mucoadhesive DLS loaded microspheres was calculated by dividing the weight of the dried microspheres by the combined weight of the pure drug and polymers used in the formulation, and then multiplying by 100.

% yield = Weight of dried mucoadhesive microspheres X 100 / Weight of pure drug and polymers.

Drug entrapment efficiency: Entrapment efficacy was determined by dissolving approximately 25 mg of microspheres in 100 mL of pH 7.3 phosphate buffer. The solution was then allowed to stand for 24 hr and filtered through Whatman filter paper. The DLS content in the filtrate was measured using HPLC at its maximum absorbance wavelength (λ_{max}) of 285 nm. The entrapment efficiency was then calculated using the below equation.

% Entrapment efficiency = Actual drug content * 100 / Theoretical drug content

Loose surface crystal study: The proportion of drug present on the surface of the drug-loaded microspheres was determined using loose surface crystal analysis. This involved agitating 100 mg of DLS-loaded microspheres in 20 mL of pH 7.4 phosphate buffer for 5 minutes, followed by filtration through a 0.45 μm membrane filter. The total drug content, including both surface-bound and encapsulated drugs, was then estimated using spectrophotometric analysis.

FT-IR analysis: Fourier-transform infrared spectroscopy (FT-IR) analysis was performed on the developed DLS-loaded microspheres to evaluate potential interactions between dexlansoprazole and the polymers. This technique is a valuable tool for identifying functional groups within a sample. FT-IR spectra were obtained for pure enalapril maleate, the PLGA polymer, and the optimized microsphere formulation. Each sample was prepared by mixing with ethanol and dichloromethane, followed by trituration in a glass mortar and placement in the sample holder. By comparing the spectra of the microspheres to those of the pure drug and polymer, the presence of

key functional groups was confirmed, aiding in the characterization of the microsphere formulation.

Powder Characteristics:

Angle of repose: The flowability of the microspheres was assessed by determining the angle of repose (α). This was achieved using the fixed funnel method, where a funnel was positioned with minimal clearance between its tip and the growing pile of microspheres. A pre-weighed quantity of microspheres was allowed to flow freely through the funnel onto a flat surface. The height (h) and radius (r) of the resulting conical pile were measured, and the angle of repose was calculated using the following equation:

$$\alpha = \tan^{-1} (h/r)$$

Where α = angle of repose, h = height, and r = radius of a heap of microspheres

Bulk Density: Bulk density was determined by carefully transferring a known mass of microspheres into a 100 mL graduated cylinder. The initial volume, representing the bulk volume (which includes both the true volume of the microspheres and the inter-particle void space), was recorded. The cylinder was then tapped gently until the volume stabilized, representing the tapped volume. Bulk density was calculated using below equation.

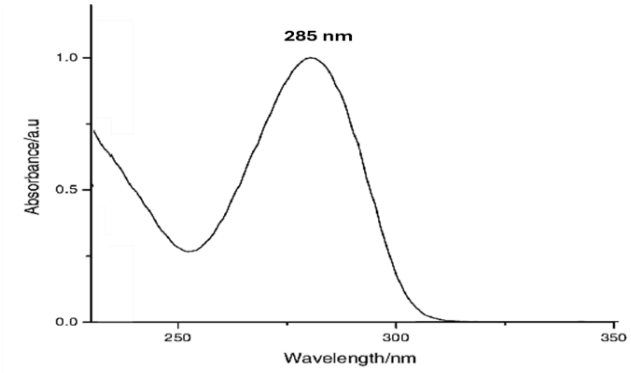
Bulk Density = (Mass of microspheres) / (Bulk volume)

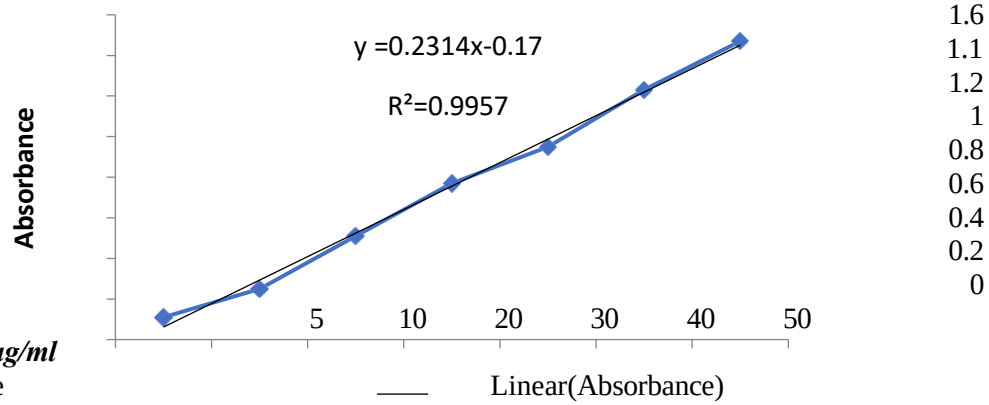
Tapped Density: Tapped density was determined by placing a known volume of microspheres into a graduated cylinder and tapping the cylinder 100 times using a bulk density apparatus. The minimum volume achieved after tapping was recorded as the tapped volume. Tapped density was then calculated using below equation.

Bulk Density = (Mass of microspheres) / (Tapped volume)

4. RESULTS

UV-VisibleSpectrophotometricanalysisofDexlansoprazole





FigureUVspectrophotometricabsorptionscanofDLS(1a)andLinearityofDLSat240 nm of

absorbance (1b).

Table:UVspectrometricabsorbanceofDLS

Conc.ofDLSinµg/ml	Absorption@ 285 nm
2.5	0.11
5	0.25
10	0.51
20	0.77
30	0.95
40	1.23
50	1.47

1. HPLCanalysisofDexlansoprazole

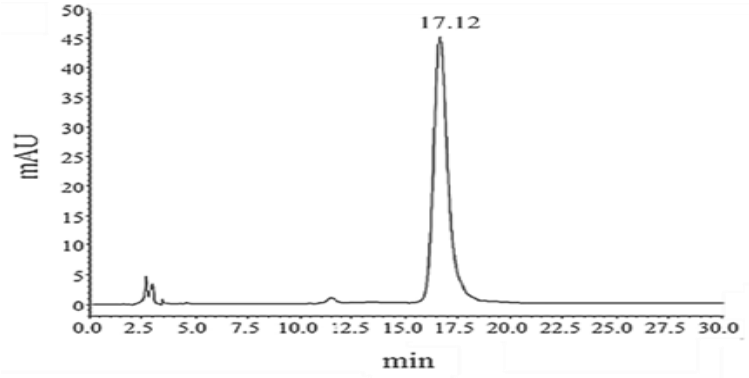
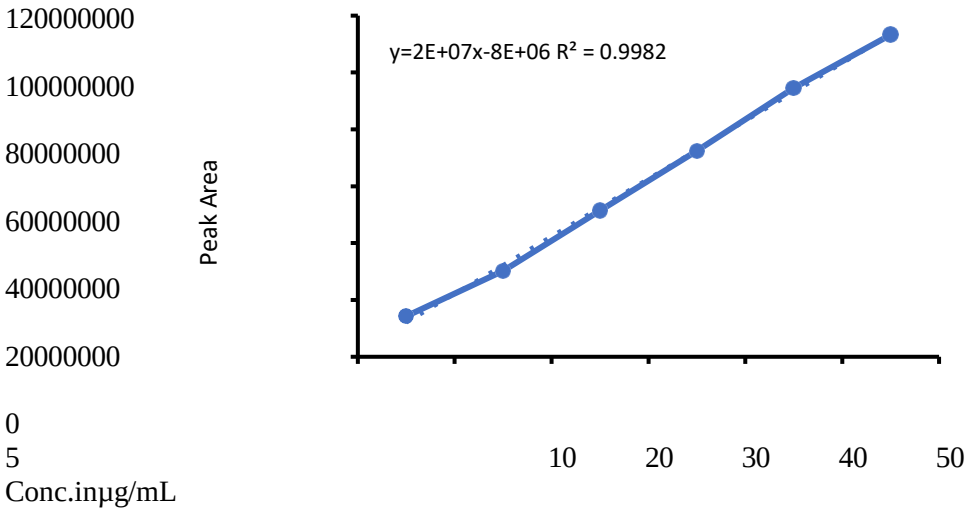


Figure HPLCquantificationofDLS chromatogram

TableLinearitystudiesofDLSusingHPLCchromatographyanalysis

Concentration (µg/mL)	**PeakArea(arbitrary units)**
5	14256981
10	30225698
20	51374895
30	72448951
40	94558789
50	113265895



FigureLinearityofDLSanalyzedusingHPLCchromatographyoveraconcentrationrange of 5 to 50 µg/mL.

DevelopmentandOptimizationofDexlansoprazole-LoadedGastroretentiveFloating Microspheres using Central Composite Design (CCD)

Preparationoffloatingmicrospheres

TableOptimizationDesingofDLSMicrospheres

Independentvariables	**Levels**		
	Low(-1)	**Medium(0)**	**High(+1)**
QtyofSodium alginatein mg (X1)	300	450	600
Conc.ofPLGAin% (X2)	5%	7.5%	10%
Cross-linkingtimeinh(X3)	2.0	3.5	5
DependentvariablesorResponse factors			
%Drugrelease (Y1)			
%Mucoadhesion(Y2)			
%Entrapmentefficiency(Y3)			
ParticlesizeinμM (Y4)			

TableCompositionofdifferentrunsofmucoadhesivemicrospheresof DLSasperCCD

Std	**Run**	**QtyofSodiumalginate in mg (X1)**	**Conc.ofPLGA in % (X2)**	**Crosslinkingtime in h (X3)**
19	1	450	7.5	3.5
9	2	197.731	7.5	3.5
7	3	300	10	5
4	4	600	10	2
16	5	450	7.5	3.5
6	6	600	5	5
15	7	450	7.5	3.5
11	8	450	3.295	3.5
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18	12	450	7.5	3.5
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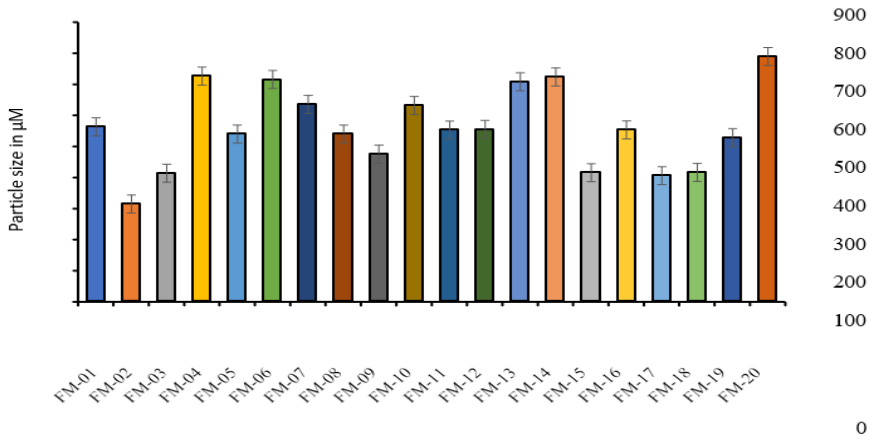
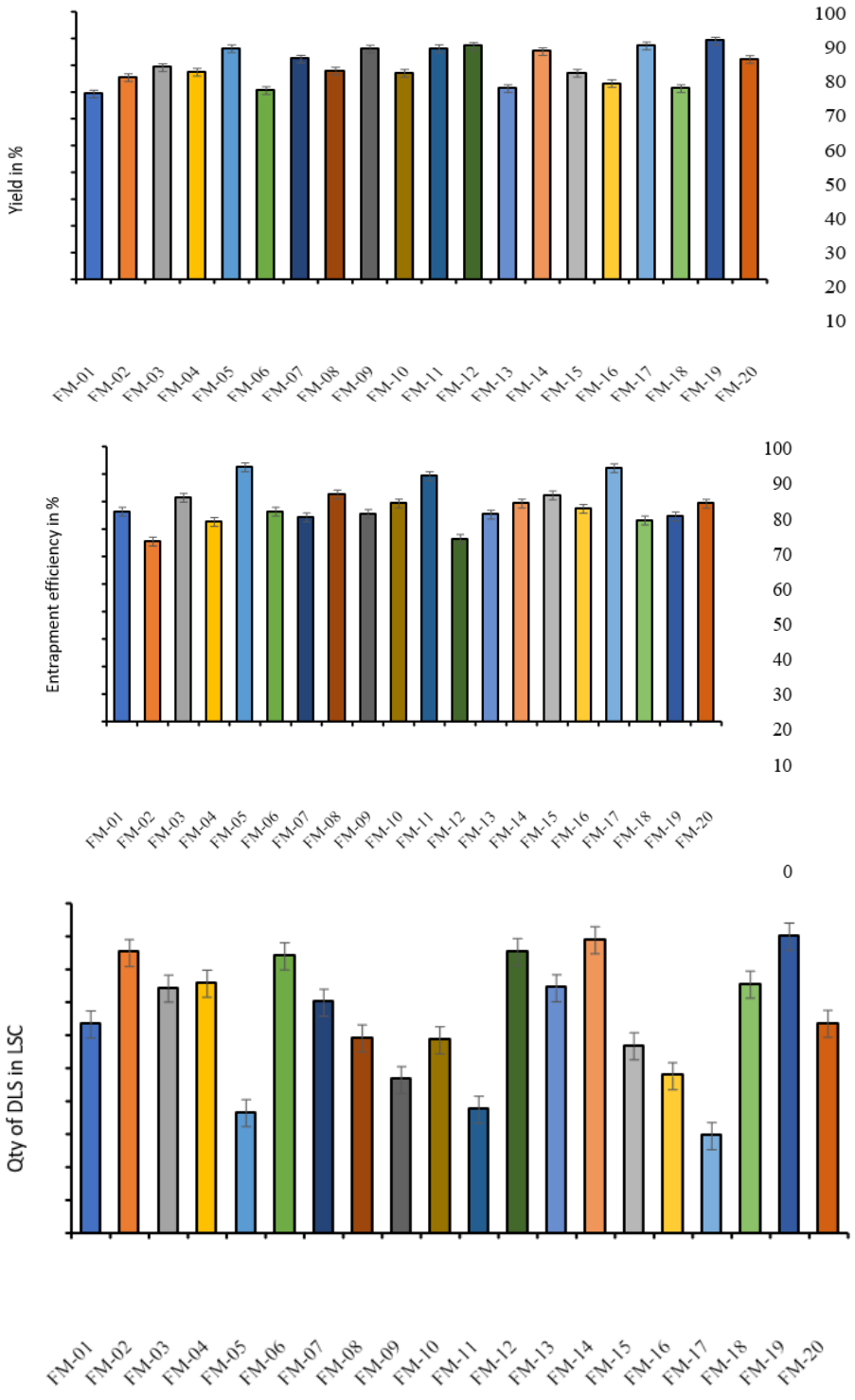
8	14	600	10	5
5	15	300	5	5
13	16	450	7.5	0.977

1	17	300	5	2
3	18	300	10	2
17	19	450	7.5	3.5
10	20	702.268	7.5	3.5

CharacterizationofmucoadhesivemicrospheresofDLS Table 3. Particle size, % yield, EE in %, and Qty of LSC in %

Formulation Code	PSinμm	% yield	EEin %	Qtyof LSCin %
FM-01	563.22±16.4	69.32±5.31	76.35±5.22	6.35 ±0.58
FM-02	314.56±12.3	75.48±6.34	65.36±5.78	8.52 ±0.71
FM-03	413.84±11.7	79.23±5.89	81.47±6.32	7.44 ±0.69
FM-04	726.47±15.7	77.51±6.14	72.58±5.12	7.59 ±0.58
FM-05	539.72±12.4	86.32±5.87	92.64±4.98	3.66 ±0.32
FM-06	715.72±13.6	70.63±6.34	76.35±6.23	8.42 ±0.94
FM-07	635.47±14.5	82.45±7.21	74.28±7.24	7.01 ±0.68
FM-08	539.71±17.1	77.92±6.59	82.69±6.23	5.93 ±0.57
FM-09	475.20±12.9	86.21±5.48	75.54±7.12	4.66 ±0.29
FM-10	632.10±13.7	77.12±7.21	79.31±5.89	5.87 ±0.49
FM-11	552.65±11.6	86.36±6.59	89.42±6.33	3.76 ±0.31
FM-12	554.87±13.7	87.24±7.35	66.35±5.48	8.55 ±0.74
FM-13	708.43±14.5	71.36±6.32	75.24±6.23	7.45 ±0.85
FM-14	723.84±13.2	85.27±6.98	79.31±4.78	8.91 ±0.92
FM-15	415.36±11.7	77.13±4.87	82.34±6.39	5.69 ±0.63
FM-16	553.21±15.3	73.24±7.13	77.39±5.88	4.78 ±0.55
FM-17	405.82±12.4	87.41±6.98	92.33±6.91	2.96 ±0.34
FM-18	416.35±13.7	71.36±6.22	73.12±7.14	7.56 ±0.66
FM-19	528.36±11.3	89.23±7.14	74.63±6.35	9.02 ±0.81
FM-20	789.42±15.9	82.31±6.98	79.24±7.44	6.37 ±0.77



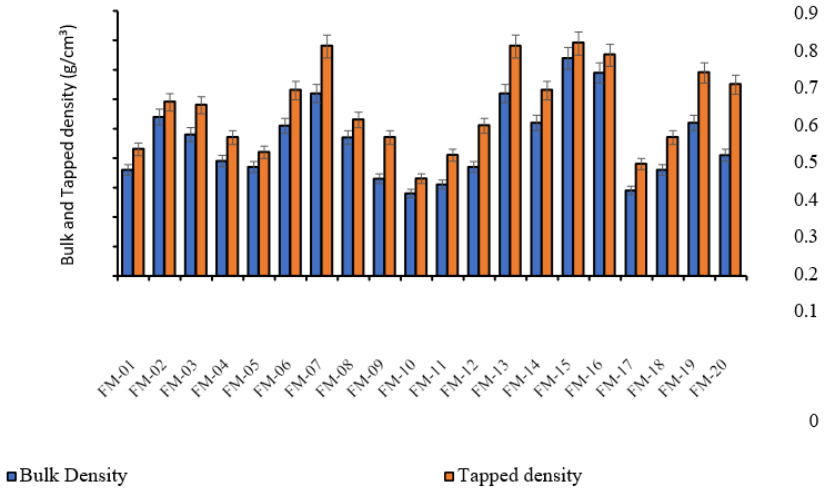


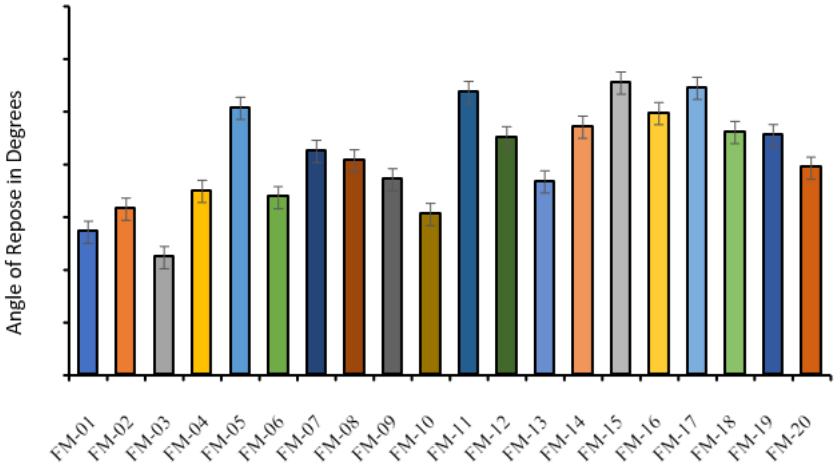
FigureCharacterizationpropertiesofDLSloadedmicrospheressuchasParticlesize(a),% yield (b), % Entrapment efficiency (C), Qty of DLS in Loose surface crystals (d). Data are presented asmean ±standarddeviation(SD)oftriplicateexperiments.Statisticalsignificance was determined using one-way ANOVA.

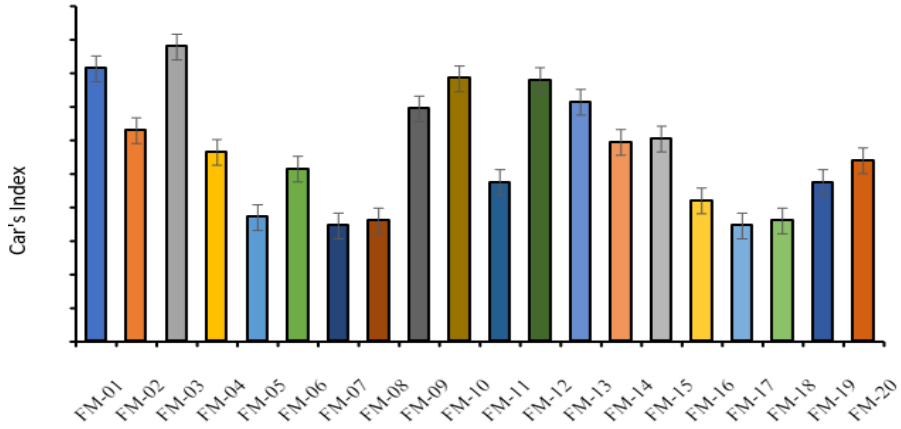
Micrometricproperties

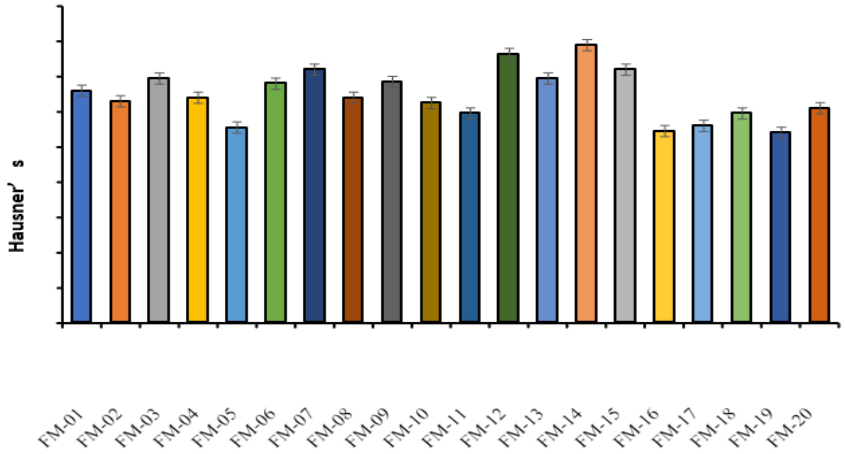
Table(Angle of repose,Bulkdensity, Tappeddensity,Compressibilityindex, Hausner's ratio)

Code	Angleof repose	Bulk Density	Tapped density	Compressibility index	Hausner'sratio
FM-01	13.6 ±1.1	0.36 ±0.02	0.43 ±0.02	16.3 ±1.1	1.32 ±0.12
FM-02	15.8 ±1.6	0.54 ±0.04	0.59 ±0.04	12.6 ±0.6	1.26 ±0.17
FM-03	11.2 ±0.9	0.48 ±0.03	0.58 ±0.03	17.6 ±1.4	1.39 ±0.13
FM-04	17.5 ±1.2	0.39 ±0.02	0.47 ±0.05	11.3 ±1.5	1.28 ±0.15
FM-05	25.4 ±1.9	0.37 ±0.04	0.42 ±0.03	7.4 ±0.8	1.11 ±0.19
FM-06	16.9 ±1.7	0.51 ±0.02	0.63 ±0.02	10.3 ±1.1	1.36 ±0.12
FM-07	21.3 ±2.3	0.62 ±0.05	0.78 ±0.04	6.9 ±0.7	1.44 ±0.17
FM-08	20.4 ±1.5	0.47 ±0.03	0.53 ±0.05	7.2 ±0.8	1.28 ±0.15
FM-09	18.6 ±1.2	0.33 ±0.04	0.47 ±0.03	13.9 ±1.1	1.37 ±0.11
FM-10	15.3 ±1.6	0.28 ±0.03	0.33 ±0.02	15.7 ±1.4	1.25 ±0.18
FM-11	26.9 ±2.3	0.31 ±0.02	0.41 ±0.03	9.5 ±0.8	1.19 ±0.12
FM-12	22.6 ±2.1	0.37 ±0.04	0.51 ±0.05	15.6 ±1.2	1.53 ±0.14
FM-13	18.4 ±1.7	0.62 ±0.05	0.78 ±0.04	14.3 ±1.3	1.39 ±0.19
FM-14	23.6 ±2.1	0.52 ±0.06	0.63 ±0.05	11.9 ±1.5	1.58 ±0.15
FM-15	27.8 ±1.6	0.74 ±0.04	0.79 ±0.04	12.1 ±1.1	1.44 ±0.16
FM-16	24.9 ±1.3	0.69 ±0.05	0.75 ±0.03	8.4 ±0.9	1.09 ±0.11
FM-17	27.3 ±2.2	0.29 ±0.03	0.38 ±0.02	6.9 ±0.5	1.12 ±0.13
FM-18	23.1 ±2.7	0.36 ±0.02	0.47 ±0.05	7.2 ±0.8	1.19 ±0.18
FM-19	22.8 ±2.1	0.52 ±0.04	0.69 ±0.05	9.5 ±0.87	1.08 ±0.14
FM-20	19.7 ±1.3	0.41 ±0.03	0.65 ±0.04	10.8 ±1.12	1.22 ±0.17


Bulk and Tapped density (g/cm³)
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
FM-01 FM-02 FM-03 FM-04 FM-05 FM-06 FM-07 FM-08 FM-09 FM-10 FM-11 FM-12 FM-13 FM-14 FM-15 FM-16 FM-17 FM-18 FM-19 FM-20
Bulk Density
Tapped density


Angle of Repose in Degrees
FM-01 FM-02 FM-03 FM-04 FM-05 FM-06 FM-07 FM-08 FM-09 FM-10 FM-11 FM-12 FM-13 FM-14 FM-15 FM-16 FM-17 FM-18 FM-19 FM-20


Car's Index
FM-01 FM-02 FM-03 FM-04 FM-05 FM-06 FM-07 FM-08 FM-09 FM-10 FM-11 FM-12 FM-13 FM-14 FM-15 FM-16 FM-17 FM-18 FM-19 FM-20



FigureCharacterizationpropertiesofDLS-loadedmicrospheressuchasAngleofrepose(a), Bulkandtappeddensity(b),Carsindex(C),Hausner'sratio(d).Dataarepresentedasmean± standarddeviation(SD)oftriplicateexperiments.Statisticalsignificancewasdeterminedusing one-wayANOVA.

CONCLUSION

This study successfully formulated and optimized a gastro-retentive floating drug delivery system (GRFDDS) of dexlansoprazole using a factorial design approach. The optimized formulation demonstrated excellent buoyancy properties, with a minimal buoyancy lag time and prolonged floating duration, ensuring extended gastric retention. In-vitro dissolution studies confirmed a sustained drug release profile, which follows non-Fickian diffusion kinetics, providing a controlled and prolonged therapeutic effect.

In-vivo pharmacokinetic studies revealed a significant improvement in the bioavailability of dexlansoprazole compared to conventional immediate-release formulations. The enhanced gastric retention and sustained drug release contributed to prolonged plasma drug levels, reducing fluctuations in drug concentration and improving overall therapeutic efficacy.

The application of factorial design proved to be an efficient and systematic approach for optimizing formulation parameters, minimizing experimental runs, and achieving desired performance characteristics. The developed gastro-retentive floating system offers a promising strategy for improving dexlansoprazole therapy, particularly in the management of gastroesophageal reflux disease (GERD) and peptic ulcers.

Future studies should focus on clinical evaluation to validate the efficacy and safety of the optimized formulation in human subjects. Additionally, long-term stability assessments and scalability studies are essential for potential commercial translation. This research contributes to the advancement of gastro-retentive drug delivery technologies, offering a novel approach to enhancing the therapeutic outcomes of acid-suppressing agents.

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