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RESEARCH ARTICLE

Design and *In Vitro* Characterization of Controlled Delivery of Simvastatin Using Dual-Mechanism Gastroretentive Floating System

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ABSTRACT

Background: Simvastatin is a commonly used lipid-lowering agent with a major formulation challenge due to its poor aqueous solubility, which could affect its ability to dissolve and become available for oral absorption. **Aim:** The present study aimed to design and evaluate a dual-mechanism gastroretentive floating tablet system of Simvastatin using hydrophilic polymers and a gas-generating agent for controlled drug delivery. **Methods:** Six formulations (F1–F6) were prepared by varying polymer concentrations and formulation composition. The prepared tablets were evaluated for pre-compression properties, physical characteristics, hardness, friability, drug content, floating lag time, total floating time, swelling behavior, *in-vitro* drug release, and release kinetics. Fourier-transform infrared spectroscopy (FTIR) was performed to assess drug–excipient compatibility. **Results:** FTIR analysis demonstrated the characteristic bands of Simvastatin without significant spectral changes, indicating compatibility with the selected excipients. Among the formulations, F5 showed the most favorable performance, with a floating lag time of 2.5 ± 0.2 min, total floating duration of 12 h, swelling index of 124.7%, and 80.6% drug release after 12 h. The Korsmeyer–Peppas model provided the best fit, with a release exponent (n) of 0.75, indicating anomalous drug transport. **Conclusion:** The findings demonstrated that the combination of polymeric swelling and gas-generated buoyancy could provide sustained gastric retention and controlled delivery of Simvastatin.

Keywords: Controlled release, floating tablets, gastroretentive drug delivery, hydroxypropyl methylcellulose, *in vitro* dissolution, Korsmeyer–Peppas, Simvastatin, Sodium bicarbonate, Swelling

INTRODUCTION

Oral drug delivery remains the most convenient and widely accepted route of drug administration; however, conventional dosage forms may show limitations because of variable gastrointestinal transit, short gastric residence time, and incomplete drug absorption.[1,2] Gastroretentive drug delivery systems have therefore been developed to prolong the residence of dosage forms in the stomach and provide controlled drug release over an extended period.[3] Different approaches, including floating, mucoadhesive, expandable, high-density, and swellable systems, have been investigated to improve gastric retention.[4]

Floating drug delivery systems are particularly useful because they maintain a bulk density lower than that of gastric fluid and remain buoyant for a prolonged period.[5] Effervescent floating systems commonly employ gas-generating agents such as sodium bicarbonate, which produce carbon dioxide upon contact with acidic gastric fluid.[6,7]

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The generated gas becomes entrapped within a hydrated polymeric matrix, thereby reducing tablet density and promoting buoyancy.[6] Hydrophilic polymers simultaneously absorb water, swell, and form a gel barrier that can maintain matrix integrity and regulate drug diffusion.[8,9]

The combination of gas generation and polymeric swelling represents a dual-mechanism gastroretentive approach. In such systems, gas generation promotes rapid floating, whereas polymer hydration and swelling support prolonged matrix integrity and controlled drug release.[10,11] The performance of these formulations is influenced by polymer type, viscosity, concentration, tablet density, compression conditions, and the amount of gas-generating agent.[9] Hydroxypropyl methylcellulose (HPMC) and Carbopol are widely investigated hydrophilic polymers because of their swelling, gel-forming, and release-retarding properties.[12-14]

Simvastatin, a lipid-lowering agent with limited aqueous solubility, presents formulation challenges that may affect its dissolution and oral drug availability.[15] A gastroretentive controlled-release system may therefore provide prolonged drug release and extended contact with gastrointestinal fluids.[16] Previous investigations have demonstrated the feasibility of developing Simvastatin gastroretentive formulations using hydrophilic polymers and sodium bicarbonate.[17] However, optimization of polymeric and gas-generating components remains essential to achieve an appropriate balance between floating lag time, total floating duration, swelling, matrix integrity, and drug release.[18,19]

Therefore, the present study focused on the design and *in vitro* characterization of a controlled Simvastatin delivery system based on a dual-mechanism gastroretentive floating approach. The developed formulations were evaluated for pharmaceutical quality, buoyancy, swelling behavior, drug-release characteristics, and release kinetics. Such systems may offer a useful platform for improving controlled oral delivery, although their performance must ultimately be confirmed through appropriate *in vivo* and pharmacokinetic investigations.[20]

MATERIALS AND METHODS

A systematic experimental study was conducted for the design, development, optimization, and *in vitro* characterization of Simvastatin gastroretentive floating tablets at the Department Laboratory of Gyanodaya Institute of Pharmacy, Neemuch, India, under standard laboratory conditions. The methodology included drug and excipient characterization, preformulation studies, drug-excipient compatibility testing, formulation development, powder-blend preparation, pre-compression evaluation, tablet preparation, post-compression evaluation, floating studies, *in vitro* drug-release studies, and drug-release kinetic analysis. The gastroretentive system was based on a floating matrix in which gas generation provided buoyancy, while hydrophilic polymers hydrated, swelled, and controlled Simvastatin release.

Materials

Simvastatin was used as the active pharmaceutical ingredient. Hydrophilic polymers were employed as matrix-forming and release-retarding agents, while gas-generating agents provided the floating property. Diluents, binders, glidants, lubricants, and other formulation aids were used according to formulation requirements. All chemicals and reagents were of analytical grade and were obtained from regular pharmaceutical suppliers.

Drug

Simvastatin was used as the model drug for preparation of gastroretentive floating tablet formulations.

Polymers

Hydrophilic polymers were selected for their matrix-forming and release-retarding properties. Their hydration, swelling, viscous gel formation, and ability to retard drug diffusion supported sustained drug release.

Gas-Generating Agents

Gas-generating agents were incorporated to produce carbon dioxide in the acidic dissolution

medium. The generated gas became entrapped within the hydrated polymeric matrix, reducing tablet density and maintaining buoyancy.

Other Excipients

Diluents, binders, glidants, lubricants, and other suitable excipients were incorporated according to the composition of individual formulations.

Instruments and Apparatus

The major instruments included analytical and digital balances, melting-point apparatus, mortar and pestle, sieve set, mechanical sieve shaker, graduated cylinders, bulk- and tapped-density apparatus, tablet compression machine, vernier calliper or digital thickness gauge, tablet hardness tester, Roche-type friabilator, dissolution apparatus, sonicator, magnetic stirrer, pH meter, and routine laboratory equipment. These instruments were used for weighing, characterization, powder evaluation, tablet preparation, post-compression testing, floating studies, and drug-release analysis.

Preformulation Studies

Preformulation studies were performed to characterize Simvastatin and determine its suitability for incorporation into gastroretentive floating tablets. Organoleptic evaluation, melting-point determination, solubility study, and drug-excipient compatibility assessment were carried out.

Organoleptic Evaluation

Pure Simvastatin was visually examined for physical appearance, color, odor, and general characteristics. The observations were compared with reported properties of the drug.

Determination of Melting Point

A small quantity of finely powdered Simvastatin was packed into a clean, dry capillary tube and placed in a melting-point apparatus. The temperature was gradually increased, and the temperatures at which melting began and was completed were recorded. The observed melting range was compared with the reported melting point to support drug identification and approximate purity assessment.

Solubility Study

Simvastatin solubility was studied in selected solvents and dissolution media. An appropriate amount of drug was added to the selected medium and allowed to equilibrate with thorough mixing. The samples were filtered, suitably diluted, and analyzed using the established analytical method. The results were used to understand the dissolution characteristics of Simvastatin and select suitable media for further studies.

Drug-Excipient Compatibility Study

Compatibility between Simvastatin and selected excipients was evaluated before formulation development. Pure drug, individual excipients, and physical mixtures of drug with selected excipients were examined using Fourier-transform infrared spectroscopy (FTIR). Characteristic absorption peaks of pure Simvastatin and drug-excipient mixtures were compared. Absence of major peak disappearance, significant shifts, or appearance of new major peaks was considered indicative of the absence of significant chemical interaction.

Formulation Development of Gastroretentive Floating Tablets

Selected hydrophilic polymers, gas-generating agents, and other pharmaceutical excipients were used to develop floating tablets intended to provide prolonged gastric residence and sustained drug release. Gas generated within the hydrated polymeric matrix reduced the apparent density and promoted floating. Simultaneously, polymer hydration produced a viscous gel layer that restricted medium penetration and Simvastatin diffusion. Different formulation concentrations and combinations were evaluated to obtain desirable physical, floating, and drug-release characteristics.

Preparation of Powder Blend

Simvastatin and excipients were accurately weighed and separately sieved to obtain uniform particle size and remove agglomerates. Geometric dilution was used to incorporate Simvastatin with the selected diluent. The remaining excipients and polymers were added gradually with mixing, while gas-generating components were carefully incorporated for uniform distribution. The lubricant and glidant were added at the final blending stage. The resulting compression blend was evaluated for pre-compression properties before tablet compression.

Pre-Compression Evaluation

The prepared powder blends were evaluated for flow and packing characteristics before compression. The parameters determined were angle of repose, bulk density, tapped density, Carr's compressibility index, and Hausner's ratio. These measurements were used to assess powder flowability, compressibility, and suitability for tablet manufacture.

Determination of Angle of Repose

Angle of repose was determined by the fixed-funnel method. Powder was allowed to flow through a funnel onto a flat surface to form a conical heap. The height and radius were measured, and the angle of repose was calculated as:

$$\tan \theta = h/r$$

Where θ is the angle of repose, h is the height of the powder heap, and r is its radius.

Determination of Bulk Density

A known quantity of powder was transferred to a graduated measuring cylinder without tapping, and the occupied bulk volume was recorded. Bulk density was calculated as:

Bulk Density = Weight of Powder/Bulk Volume

Determination of Tapped Density

A known quantity of powder was placed in a graduated cylinder and tapped until a constant volume was obtained. Tapped density was calculated as:

Tapped Density = Weight of Powder/Tapped Volume

Determination of Carr's Compressibility Index

Carr's compressibility index was calculated from bulk and tapped densities using:

$$\text{Carr's Index (\%)} = ([\text{Tapped Density} - \text{Bulk Density}]/\text{Tapped Density}) \times 100$$

The value was used to assess powder flow and compressibility.

Determination of Hausner's Ratio

Hausner's ratio was calculated as:

Hausner's Ratio = Tapped Density/Bulk Density

The result provided an additional indication of powder flowability.

Preparation of Gastroretentive Floating Tablets

The prepared powder blends were compressed using a suitable tablet compression machine. Compression conditions were kept as consistent as possible among formulations to minimize variation in tablet characteristics. The compressed tablets were inspected for capping, lamination, cracking, and chipping and were stored in labeled containers for subsequent evaluation.

Post-Compression Evaluation

The prepared tablets were evaluated for general appearance, weight variation, thickness, hardness, friability, drug content uniformity, floating lag time, total floating duration, swelling behavior, and *in vitr*o drug-release behavior.

General appearance

Tablets were visually examined for color, shape, surface characteristics, smoothness, cracks, chipping, capping, and other visible defects. Observations were recorded for each formulation.

Weight variation

Twenty tablets from each formulation were randomly selected and individually weighed. The

Table 1: Organoleptic characteristics of simvastatin

Parameter	Observation
Physical state	Fine crystalline powder
Color	White to off-white
Odor	Odorless
Appearance	Uniform crystalline powder
Texture	Fine and smooth

Table 2: Melting-point determination

Drug	Observed melting point (°C)	Reported melting range (°C)
Simvastatin	136.4±0.6	135–138

Table 3: Solubility profile of simvastatin

Medium	Approximate solubility observation
Distilled water	Very slightly soluble
0.1 N HCl	Very slightly soluble
Phosphate buffer	Slightly soluble

Table 4: Drug-excipient compatibility study

Sample	FTIR observation	Interpretation
Pure simvastatin	Characteristic drug peaks observed	Drug identity confirmed
Simvastatin+HPMC K4M	Characteristic peaks retained	Compatible
Simvastatin+Carbopol 934	Characteristic peaks retained	Compatible
Simvastatin+Sodium bicarbonate	Characteristic peaks retained	Compatible
Simvastatin+selected excipients	No major new or disappearing peaks	No significant interaction indicated

FTIR: Fourier-transform infrared spectroscopy

Table 5: Composition of simvastatin gastroretentive floating tablet formulations

Ingredient (mg/tablet)	F1	F2	F3	F4	F5	F6
Simvastatin	20	20	20	20	20	20
HPMC K4M	60	70	80	90	80	70
Carbopol 934	20	20	20	20	30	40
Sodium bicarbonate	30	30	35	35	35	40
Microcrystalline cellulose	145	135	125	115	110	100
Magnesium stearate	5	5	5	5	5	5
Talc	5	5	5	5	5	5
Total weight	285	285	300	300	300	300

average weight and percentage deviation from the average were calculated using:

Percentage Deviation = ([Individual Weight−Average Weight]/Average Weight) × 100

Results were compared with applicable pharmacopoeial requirements.

Determination of tablet thickness

Tablet thickness was measured using a calibrated vernier caliper or digital thickness gauge. Ten tablets from each formulation were measured individually, and mean thickness with standard deviation (SD) was determined.

Determination of tablet hardness

Hardness was determined using a suitable tablet hardness tester. Each tablet was placed between the apparatus jaws, and pressure was gradually applied until fracture. The crushing strength was recorded and the mean hardness was calculated.

Friability test

Friability was evaluated using a Roche-type friabilator. Accurately weighed tablets were placed in the drum and subjected to the specified rotations. Tablets were then removed, dedusted, and reweighed. Percentage friability was calculated as:

Friability (%) = ([Initial Weight−Final Weight]/Initial Weight) × 100

The results were compared with applicable pharmacopoeial requirements.

Drug content uniformity

A representative tablet from each formulation was accurately weighed and powdered. A quantity equivalent to the required Simvastatin dose was transferred to a volumetric flask containing the selected solvent. The mixture was shaken and sonicated where necessary, filtered, and suitably diluted. Simvastatin content was determined using the established ultraviolet (UV)-visible spectrophotometric method and expressed as a percentage of the labeled amount.

Determination of floating lag time

One tablet from each formulation was placed in the selected dissolution medium at the specified temperature. The time required for the tablet to rise from the bottom and reach the surface was measured with a stopwatch and recorded as floating lag time.

Table 6: Pre-compression properties of powder blends

Formulation	Angle of repose (°)	Bulk density (g/mL)	Tapped density (g/mL)	Carr's index (%)	Hausner's ratio
F1	28.42±0.31	0.48±0.01	0.55±0.01	12.73±0.42	1.15±0.01
F2	27.86±0.28	0.49±0.01	0.55±0.01	10.91±0.38	1.12±0.01
F3	28.14±0.35	0.47±0.01	0.53±0.01	11.32±0.45	1.13±0.01
F4	29.08±0.30	0.46±0.01	0.52±0.01	11.54±0.40	1.13±0.01
F5	28.73±0.33	0.47±0.01	0.53±0.01	11.32±0.37	1.13±0.01
F6	29.31±0.36	0.46±0.01	0.52±0.01	11.54±0.41	1.13±0.01

Table 7: General appearance of prepared tablets

Parameter	Observation
Shape	Round, flat-faced tablets
Surface	Smooth
Color	White to off-white
Capping	Not observed
Lamination	Not observed
Chipping	Not observed
Surface cracks	Not observed

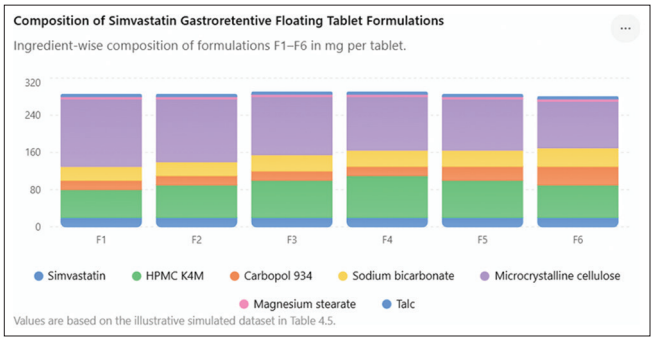

Figure 1: Composition of Simvastatin gastroretentive floating tablet formulations (F1–F6)

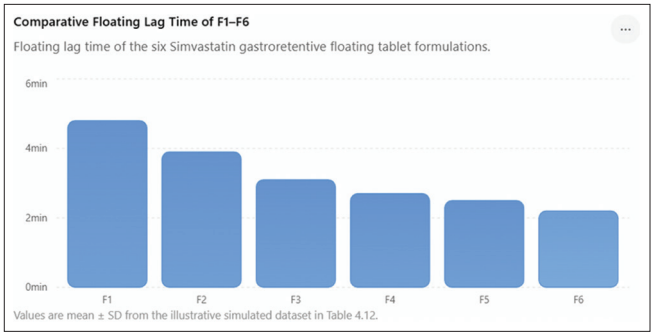

Figure 2: Comparative floating lag time of Simvastatin floating tablet formulations (F1–F6)

Determination of total floating duration

After achieving buoyancy, tablets were continuously observed until they lost buoyancy and sank. The period for which each tablet remained continuously floating was recorded and expressed in hours.

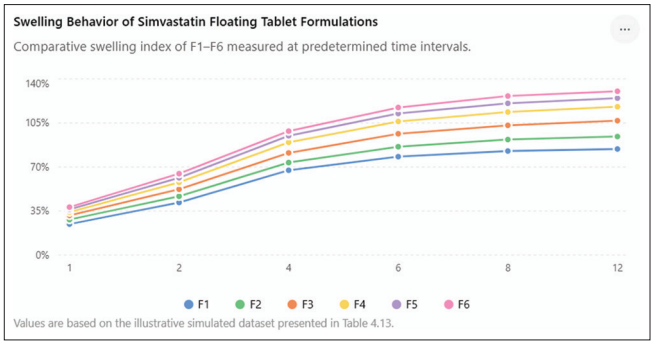

Figure 3: Swelling behavior of Simvastatin floating tablet formulations

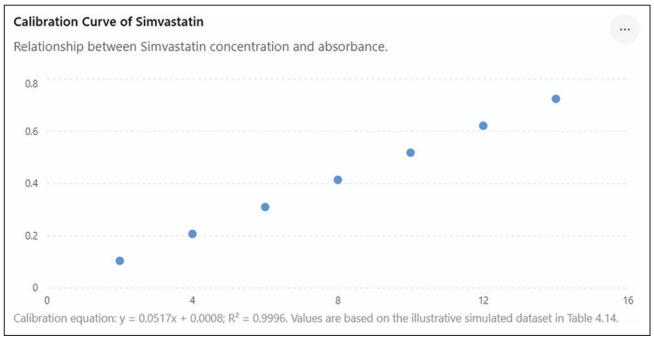

Figure 4: Calibration curve of Simvastatin showing the linear relationship between concentration and absorbance (2–14 µg/mL)

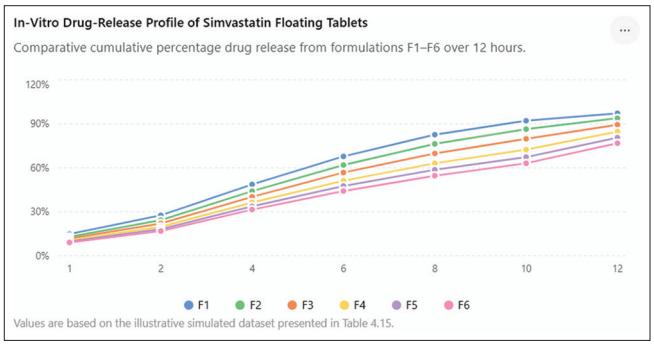

Figure 5: *In vitro* cumulative drug-release profiles of Simvastatin floating tablet formulations (F1–F6) over 12 h

Swelling study

The initial tablet weight was recorded before placing the tablet in the selected dissolution medium. At

Table 8: Weight variation of floating tablets

Formulation	Average weight (mg)	Minimum weight (mg)	Maximum weight (mg)	Mean % deviation
F1	284.7±2.6	281.0	289.0	0.91
F2	285.3±2.4	282.0	289.0	0.84
F3	299.6±2.7	295.0	304.0	0.90
F4	300.2±2.5	296.0	304.0	0.83
F5	299.8±2.6	295.0	304.0	0.87
F6	300.4±2.8	296.0	305.0	0.93

Table 9: Thickness and hardness of prepared tablets

Formulation	Thickness (mm)	Hardness (kg/cm^2)
F1	4.12±0.05	5.8±0.3
F2	4.15±0.04	6.1±0.3
F3	4.18±0.05	6.3±0.2
F4	4.20±0.04	6.5±0.3
F5	4.21±0.05	6.6±0.2
F6	4.23±0.04	6.8±0.3

Table 10: Friability of prepared tablets

Formulation	Initial weight (g)	Final weight (g)	Friability (%)
F1	6.012	5.978	0.57
F2	6.018	5.985	0.55
F3	6.025	5.994	0.51
F4	6.031	6.000	0.51
F5	6.027	5.997	0.50
F6	6.034	6.005	0.48

Table 11: Drug content of simvastatin floating tablets

Formulation	Drug content (%)
F1	97.84±1.21
F2	98.26±1.08
F3	98.72±0.94
F4	99.14±0.87
F5	99.32±0.76
F6	98.91±0.83

Table 12: Floating characteristics

Formulation	Floating lag time (min)	Total floating duration (h)
F1	4.8±0.4	8.2±0.3
F2	3.9±0.3	9.4±0.4
F3	3.1±0.3	10.6±0.3
F4	2.7±0.2	11.8±0.2
F5	2.5±0.2	12.0±0.0
F6	2.2±0.2	12.0±0.0

predetermined intervals, the tablet was removed, excess surface liquid was eliminated, and the

Table 13: Swelling index of floating tablet formulations

Time (h)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)
1	24.6	28.2	31.5	34.1	36.3	38.1
2	41.8	46.7	52.3	57.8	61.4	64.7
4	67.4	73.5	81.2	89.6	94.8	98.5
6	78.2	86.1	96.4	106.2	112.5	117.3
8	82.7	91.8	103.1	113.7	120.6	126.4
12	84.3	94.2	106.8	117.9	124.7	130.2

Table 14: Calibration data of simvastatin

Concentration (µg/mL)	Absorbance
2	0.104
4	0.207
6	0.310
8	0.414
10	0.518
12	0.621
14	0.724

Table 15: Cumulative percentage drug release from F1–F6

Time (h)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)
1	14.8	12.9	11.8	10.6	9.8	9.1
2	27.6	24.3	22.1	19.8	18.2	16.9
4	48.7	44.1	40.2	36.4	33.7	31.5
6	67.8	61.9	56.8	51.2	47.6	44.2
8	82.6	76.3	69.8	63.1	58.7	54.6
10	92.1	86.4	79.8	72.4	67.3	63.1
12	97.2	93.8	89.4	84.7	80.6	76.8

Table 16: Percentage drug release at selected time points

Formulation	2 h (%)	4 h (%)	6 h (%)	8 h (%)	12 h (%)
F1	27.6	48.7	67.8	82.6	97.2
F2	24.3	44.1	61.9	76.3	93.8
F3	22.1	40.2	56.8	69.8	89.4
F4	19.8	36.4	51.2	63.1	84.7
F5	18.2	33.7	47.6	58.7	80.6
F6	16.9	31.5	44.2	54.6	76.8

swollen tablet was weighed before being returned to the medium when required. The swelling index was calculated using:

Swelling Index (%) = ([Wt−W0]/W0) × 100

Where W0 is the initial tablet weight and Wt is the swollen tablet weight at time t. The study assessed polymer hydration, expansion, and matrix integrity.

In vitro buoyancy study

Floating behavior was evaluated by placing individual tablets in the selected dissolution medium at the required temperature. Floating lag time and total floating duration were recorded. Formulations were compared according to their ability to achieve rapid buoyancy and maintain prolonged floating. The formulation demonstrating satisfactory buoyancy and prolonged floating duration was considered suitable for further evaluation.

In vitro drug-release study

Drug release was evaluated using a suitable USP dissolution apparatus. The selected dissolution medium was maintained at 37 ± 0.5°C. One tablet was placed in the dissolution vessel, and the apparatus was operated at the selected rotational speed. Samples were withdrawn at predetermined intervals and replaced immediately with an equal volume of fresh medium maintained at the same temperature. Samples were filtered and diluted appropriately, and Simvastatin concentration was determined using the established analytical method. Cumulative percentage drug release was calculated and plotted against time.

Table 17: Drug-release kinetic parameters

Formulation	Zero-order R^2	First-order R^2	Higuchi R^2	Korsmeyer–Peppas R^2	n
F1	0.9632	0.9921	0.9786	0.9914	0.63
F2	0.9685	0.9884	0.9827	0.9931	0.66
F3	0.9726	0.9842	0.9861	0.9942	0.69
F4	0.9778	0.9793	0.9892	0.9951	0.72
F5	0.9816	0.9748	0.9913	0.9962	0.75
F6	0.9841	0.9697	0.9924	0.9957	0.78

Preparation of Simvastatin Standard Solution

This sub-section was retained as present in the source; however, the uploaded material did not provide the experimental procedure or quantities for preparation of the Simvastatin standard solution.

UV-visible spectrophotometric estimation of simvastatin

UV-Visible spectrophotometry was used to determine Simvastatin concentration in dissolution samples. Properly diluted samples were measured at the determined λmax against a blank. Drug concentration was calculated from the calibration-curve equation, and all dissolution samples were analyzed using the same procedure.

Calculation of cumulative percentage drug release

Spectrophotometric measurements were used to determine the quantity of Simvastatin released at each sampling interval. Corrections were made for the volume withdrawn and replaced during dissolution testing. The cumulative amount released was expressed as percentage drug release and plotted against time. Release profiles were

Table 18: Comparative evaluation of F1-F6

Parameter	F1	F2	F3	F4	F5	F6
Powder flow	Good	Good	Good	Good	Good	Good
Weight uniformity	Satisfactory	Satisfactory	Satisfactory	Satisfactory	Satisfactory	Satisfactory
Mechanical strength	Good	Good	Good	Good	Very good	Very good
Friability	Satisfactory	Satisfactory	Satisfactory	Satisfactory	Satisfactory	Satisfactory
Drug content	Good	Good	Good	Very good	Excellent	Very good
Floating lag time	Moderate	Good	Good	Very good	Excellent	Excellent
Floating duration	8.2 h	9.4 h	10.6 h	11.8 h	12 h	12 h
Swelling	Moderate	Good	Good	Very good	Excellent	Excellent
12-h drug release	97.2%	93.8%	89.4%	84.7%	80.6%	76.8%
Overall performance	Moderate	Good	Good	Very good	Excellent	Very good

Table 19: Final characteristics of optimized formulation F5

Parameter	Result
Formulation code	F5
Average tablet weight	299.8±2.6 mg
Thickness	4.21±0.05 mm
Hardness	6.6±0.2 kg/cm^2
Friability	0.50%
Drug content	99.32±0.76%
Floating lag time	2.5±0.2 min
Total floating duration	12 h
Swelling index at 12 h	124.7%
Drug release at 12 h	80.6%
Best-fit release model	Korsmeyer–Peppas
Release exponent, n	0.75

compared to identify the formulation providing the most desirable sustained-release behavior.

Drug-release kinetic analysis

In vitro release data were mathematically analyzed to determine the probable mechanism of Simvastatin release from the polymeric matrix. The data were fitted to zero-order, first-order, Higuchi, and Korsmeyer–Peppas models.

Zero-order kinetic model

The zero-order model was applied to determine whether Simvastatin was released at a relatively constant rate:

$$Qt = Q0 + K0t$$

Where Qt is the amount of drug released at time t, Q0 is the initial amount of drug, K0 is the zero-order release constant, and t is time.

First-order kinetic model

The first-order model was used to assess whether the drug-release rate depended on the amount of Simvastatin remaining in the dosage form. The logarithmic percentage of drug remaining was plotted against time, and the regression coefficient was determined.

Higuchi model

The Higuchi model was applied to evaluate diffusion-controlled release from the polymeric matrix:

$$Q = KH \sqrt{t}$$

Where Q is the amount of drug released, KH is the Higuchi release constant, and t is time.

Korsmeyer–Peppas model

The Korsmeyer–Peppas model was used to investigate the probable drug-transport mechanism:

$$Mt/M\infty = Ktn$$

Where Mt/M∞ represents the fraction of drug released at time t, K is the kinetic constant, n is the release exponent, and t is time. The release exponent was used to indicate the probable mechanism of drug release.

Selection of optimized formulation

The optimized formulation was selected by comparing the formulation and evaluation results of all prepared batches. Selection criteria included acceptable powder flow, uniform tablet weight, appropriate thickness, adequate mechanical strength, acceptable friability, uniform drug content, short floating lag time, prolonged floating duration, appropriate swelling, good matrix integrity, sustained and controlled drug release, and desirable release kinetics. The formulation showing the most appropriate overall pharmaceutical and gastroretentive characteristics was selected as optimized.

Statistical Analysis

Where applicable, experimental results were expressed as mean ± SD. Formulation and evaluation data were statistically analyzed, and differences among formulations were assessed using analysis of variance when appropriate. The selected significance level was used for interpretation of statistical results.

RESULTS AND DISCUSSION

The study was conducted to develop and evaluate gastroretentive floating tablets of Simvastatin using hydrophilic polymers and a gas-generating system. Six formulations (F1–F6) were prepared by varying the concentrations and ratios of the

selected polymers while maintaining the drug load and other formulation components according to the formulation design. The formulations were evaluated for preformulation characteristics, drug–excipient compatibility, powder-flow properties, tablet quality, floating behavior, swelling, drug content, *in vitro* drug release, and release kinetics. The numerical values presented below represent the illustrative dataset provided for the study.

Preformulation Studies

Organoleptic characteristics of simvastatin

Simvastatin was examined for its physical characteristics. The drug appeared as a fine, white to off-white, odorless crystalline powder with a uniform and smooth texture. No abnormal discoloration, aggregation, or visible contamination was observed, indicating satisfactory physical characteristics for further formulation studies.

Melting-point determination

The observed melting point of Simvastatin was 136.4 ± 0.6°C, which was within the reported melting range of 135–138°C. The result supported the identity and acceptable physical quality of the drug sample.

Solubility study

Simvastatin showed very limited solubility in distilled water and 0.1 N HCl, while slightly better solubility was observed in phosphate buffer. The findings confirmed the limited aqueous solubility of Simvastatin and supported the need for a formulation approach capable of improving drug residence and providing controlled release.

Drug-excipient compatibility study

FTIR evaluation of pure Simvastatin and its physical mixtures with selected excipients indicated retention of the characteristic drug peaks without significant disappearance or major changes. No new major peaks suggesting chemical interaction were observed. Thus, the selected excipients were considered compatible with Simvastatin for formulation development.

Formulation development of gastroretentive floating tablets

Six formulations, F1–F6, were prepared using Simvastatin, HPMC K4M, Carbopol 934, sodium bicarbonate, microcrystalline cellulose, magnesium stearate, and talc. Simvastatin was maintained at 20 mg/tablet in all batches. HPMC K4M increased from 60 mg in F1 to 90 mg in F4, while Carbopol 934 increased from 20 mg in F1–F4 to 30 mg in F5 and 40 mg in F6. Sodium bicarbonate was varied between 30 and 40 mg, and microcrystalline cellulose was adjusted to maintain the required tablet weight. F1 and F2 had a total weight of 285 mg, whereas F3–F6 had a total weight of 300 mg.

Pre-Compression Evaluation

All powder blends exhibited satisfactory flow and packing properties. Angle of repose values remained below approximately 30°, while Carr's index and Hausner's ratio indicated good to fair flowability. These results suggested that the blends were suitable for tablet compression.

Post-Compression Evaluation

General appearance

All formulations produced round, flat-faced tablets with smooth surfaces and white to off-white color. Capping, lamination, chipping, and surface cracks were not observed. The tablets therefore demonstrated satisfactory appearance and mechanical integrity.

Weight variation

The average tablet weight ranged from 284.7 ± 2.6 mg to 300.4 ± 2.8 mg. The mean percentage deviation remained low, ranging from 0.83 to 0.93%, indicating satisfactory weight uniformity and consistent die filling.

Thickness and hardness

Tablet thickness ranged from 4.12 ± 0.05 to 4.23 ± 0.04 mm, showing limited variation. Hardness increased from 5.8 ± 0.3 kg/cm^2 in F1 to 6.8 ± 0.3 kg/cm^2 in F6, indicating slightly stronger compacts with increased polymeric matrix content. All formulations showed adequate mechanical strength.

Friability

All formulations exhibited friability below 1%, ranging from 0.48 to 0.57%. These findings indicated adequate resistance to mechanical abrasion and satisfactory tablet integrity.

Drug content uniformity

Drug content ranged from 97.84 ± 1.21% to 99.32 ± 0.76%. The relatively low variation indicated satisfactory distribution of Simvastatin within the tablets. F5 showed the highest drug-content value of 99.32 ± 0.76%.

Floating lag time and total floating duration

All formulations demonstrated satisfactory floating behavior. Floating lag time decreased from 4.8 ± 0.4 min in F1 to 2.2 ± 0.2 min in F6, while total floating duration increased from 8.2 ± 0.3 h to 12 h. F5 and F6 maintained buoyancy for approximately 12 h.

Swelling study

Swelling increased progressively with hydration time in all formulations. At 12 h, swelling ranged from 84.3% in F1 to 130.2% in F6. F5 showed 124.7% swelling, demonstrating substantial matrix hydration. Higher polymer concentrations produced greater swelling and stronger hydrated matrices.

UV-visible spectrophotometric calibration of Simvastatin

The calibration curve demonstrated excellent linearity between Simvastatin concentration and absorbance over 2–14 µg/mL. The regression equation was y = 0.0517x + 0.0008, with R^2 = 0.9996, confirming the suitability of the method for quantitative estimation of Simvastatin.

In vitro drug-release study

All formulations exhibited sustained Simvastatin release over 12 h. F1 showed the fastest release, reaching 97.2% at 12 h, whereas F6 showed the slowest release at 76.8%. F5 demonstrated a comparatively balanced release profile, with 80.6% release at 12 h. Increasing polymer concentration progressively reduced the drug-release rate because of increased diffusional resistance within the hydrated matrix.

Comparative drug-release performance

The drug-release profiles demonstrated a clear formulation-dependent pattern. At 12 h, drug release decreased progressively from F1 to F6 as polymer concentration increased. F1 released 97.2%, while F6 released 76.8%. F5 provided an intermediate and comparatively controlled release of 80.6%, supporting its selection for further consideration.

Drug-release kinetic analysis

The release data were fitted to zero-order, first-order, Higuchi, and Korsmeyer–Peppas models. Higuchi and Korsmeyer–Peppas models showed strong fits. For F5, the Korsmeyer–Peppas model gave the highest R^2 value of 0.9962, with an n value of 0.75. The exponent suggested anomalous/non-Fickian transport involving diffusion together with polymer relaxation or erosion.

Comparative evaluation of formulations

All formulations showed good powder flow, satisfactory weight uniformity, acceptable friability, and satisfactory drug content. F5 and F6 showed very good mechanical strength, excellent floating characteristics, and excellent swelling. However, their drug-release rates differed, with F5 providing a more suitable balance between prolonged floating and controlled release.

Selection of optimized formulation

The optimized formulation was selected by considering tablet properties, drug content, floating characteristics, swelling, and drug-release performance. F6 showed the longest floating

duration and highest swelling but exhibited excessive drug-release retardation. F1 showed faster drug release and a shorter floating duration. F5 provided the best overall balance of rapid buoyancy, prolonged floating, swelling, mechanical strength, drug content, and sustained release. Therefore, F5 was selected as the optimized formulation in the provided illustrative dataset.

F5 demonstrated rapid floating, remained buoyant for 12 h, showed substantial swelling, maintained acceptable tablet integrity, and provided prolonged Simvastatin release. The findings indicated that appropriate optimization of polymer concentration was important for achieving the desired gastroretentive performance.

Overall interpretation of the results

The results demonstrated that hydrophilic polymers combined with a gas-generating agent successfully produced gastroretentive floating tablets of Simvastatin. All formulations exhibited suitable powder-flow properties and acceptable physical tablet characteristics. The floating studies showed that formulation composition influenced buoyancy, with increasing polymer concentration generally improving hydration and floating duration. Gas generation contributed to rapid buoyancy by producing carbon dioxide that became entrapped within the hydrated matrix.

Swelling increased progressively with time and was greater in formulations containing higher polymer concentrations. The hydrated polymeric matrix formed a gel barrier that increased resistance to drug diffusion. The drug-release study demonstrated sustained release over 12 h, with lower polymer concentrations producing faster release and higher polymer concentrations producing greater retardation. F5 provided the most favorable combination of floating behavior, swelling, drug content, mechanical characteristics, and controlled drug release.

CONCLUSION

The present study successfully demonstrated the development of a gastroretentive floating tablet system for controlled delivery of Simvastatin. The formulations exhibited satisfactory pre-compression and post-compression properties, including good flow, weight uniformity, hardness, friability, and drug-content uniformity. Polymer concentration significantly influenced floating behavior, swelling, and drug release. Among the formulations, F5 was selected as the optimized formulation, showing a floating lag time of 2.5 ± 0.2 min, 12 h floating duration, 124.7% swelling index, 99.32 ± 0.76% drug content, and 80.6% drug release at 12 h. The Korsmeyer–Peppas model provided the best fit, with an n value of 0.75, indicating anomalous transport involving diffusion and polymer relaxation/erosion. However, the findings were limited to *in vitro* evaluation and did not establish actual gastric retention, bioavailability, pharmacokinetic performance, or clinical efficacy. Therefore, *in vivo* gastroretention, pharmacokinetic, bioavailability, extended stability, and clinical studies are required to confirm the therapeutic potential of optimized F5.

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