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SODIUM ALGINATE COATED NIOSOME: A NOVEL ORAL DELIVERY SYSTEM OF SIMVASTATIN FOR THE TREATMENT OF HYPERLIPIDEMIA

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ABSTRACT

Hyperlipidemia is a metabolic disorder characterized by abnormally elevated levels of lipids, including cholesterol and triglycerides, in the blood. It is considered as one of the major risk factors for the development of cardiovascular diseases, atherosclerosis, and stroke. Statins are the first-line drugs used for the management of hyperlipidemia. Simvastatin, a BCS Class II drug, is a potent HMG-CoA reductase inhibitor used to lower cholesterol levels. Despite its therapeutic efficacy, simvastatin possesses poor aqueous solubility and low oral bioavailability due to extensive first-pass metabolism, which limits its clinical application. To overcome these limitations, novel drug delivery systems have been explored to enhance the solubility and bioavailability of poorly soluble drugs. Among various approaches, vesicular drug delivery systems such as niosomes have gained significant attention due to their ability to encapsulate both hydrophilic and lipophilic drugs. Furthermore, surface modification of niosomes with mucoadhesive polymers can improve gastrointestinal residence time and provide controlled release. The aim of the present research work was to develop and characterize sodium alginate coated niosomes of simvastatin as an oral delivery system for the treatment of hyperlipidemia. Niosomes were prepared by thin film hydration technique using non-ionic surfactant Span 60 and tween 80 and cholesterol. The prepared niosomes were coated with sodium alginate. The developed formulations were evaluated for various parameters including particle size, polydispersity index, zeta potential, entrapment efficiency, surface morphology, drug-excipient compatibility studies by FTIR, and in-vitro drug release studies. The objective was to achieve sustained release of simvastatin and thereby improve its oral bioavailability for effective management of hyperlipidemia.

KEYWORDS: Simvastatin, Niosomes, Sodium alginate, Oral drug delivery, Hyperlipidemia, Sustained release.

INTRODUCTION

Hyperlipidemia is a major modifiable risk factor for cardiovascular diseases, including coronary artery disease, myocardial infarction, and stroke.[1] Statins are first-line pharmacological agents for the management of hyperlipidemia because they inhibit 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, thereby reducing cholesterol synthesis and low-density lipoprotein cholesterol levels.[2] Simvastatin is an effective statin; however, its poor aqueous solubility and extensive first-pass metabolism contribute to low and variable oral bioavailability, presenting challenges for effective oral drug delivery.[3] Therefore, formulation approaches capable of improving the solubility, protection, and controlled release of simvastatin are of considerable interest.

Niosomes are vesicular drug-delivery systems composed primarily of non-ionic surfactants and cholesterol and can accommodate poorly water-soluble drugs within their bilayer.[4,5] Their ability to improve drug solubilization and provide controlled release makes them attractive carriers for oral delivery. However, conventional niosomes may be affected by vesicular instability and rapid drug release under gastrointestinal conditions.[6] Surface modification with polymers such as sodium alginate may provide an additional protective and mucoadhesive layer. Sodium alginate is a biocompatible,

biodegradable polysaccharide with mucoadhesive properties and has been investigated extensively in oral drug-delivery systems. Alginate-based systems can provide prolonged gastrointestinal residence and modulate drug release, supporting their application in oral delivery.[7,8]

Although niosomes have been extensively investigated as carriers for poorly water-soluble drugs, the development and systematic evaluation of sodium alginate-coated simvastatin-loaded niosomes as an oral delivery platform remain comparatively limited. In particular, there is a need to investigate whether alginate coating can be incorporated into a simvastatin-loaded niosomal system while maintaining satisfactory entrapment, physicochemical characteristics, and controlled drug release. Therefore, the present study aimed to develop and optimize sodium alginate-coated simvastatin-loaded niosomes using the thin-film hydration method and to evaluate the optimized formulation for entrapment efficiency, drug content, particle size, polydispersity index, zeta potential, drug–excipient compatibility, in-vitro drug release, release kinetics, and short-term stability.

2. MATERIAL and METHODOLOGY

2.1 Materials

Simvastatin was received as a gift sample from Dhamtech India. Span 60, Tween 80, cholesterol, sodium alginate, chloroform, methanol, dialysis membrane, and other analytical-grade chemicals were procured from standard commercial suppliers and used without further purification. Double-distilled water was used throughout the study.

2.3 Preparation of Simvastatin-Loaded Niosomes

Simvastatin-loaded niosomes were prepared by the thin-film hydration method. Span 60, Tween 80, cholesterol, and simvastatin were dissolved in a chloroform: methanol mixture (8:2, v/v) in a round-bottom flask. The organic solvents were removed under reduced pressure using a rotary vacuum evaporator to obtain a thin lipid film on the inner wall of the flask.[9]

The dried film was hydrated with phosphate buffer (pH 7.4) at a temperature above the phase transition temperature of the surfactants under continuous rotation until complete hydration was achieved. The resulting niosomal dispersion was allowed to equilibrate and stored at 4°C until further characterization.[10]

2.4 Preparation of Sodium Alginate-Coated Niosomes

Sodium alginate was used as a coating polymer for all six batches of the prepared simvastatin-loaded niosomal formulations. A 0.2% w/v sodium alginate solution was prepared by gradually dispersing the required quantity of sodium alginate in purified water under continuous magnetic stirring. The dispersion was stirred until a homogeneous polymer solution was obtained and was then allowed to stand to remove entrapped air bubbles.

The prepared simvastatin-loaded niosomal dispersions were subsequently added slowly to the sodium alginate solution under gentle continuous stirring. The niosome dispersion and sodium alginate solution were mixed at a 1:1 volume ratio. The resulting dispersion was stirred gently for 30–60 min at room temperature to facilitate the adsorption and formation of a uniform sodium alginate coating around the niosomal vesicles. The coated dispersions were then allowed to equilibrate for approximately 30 min at room temperature.[11]

2.5 Evaluation of Niosomal Formulations

2.5.1 Entrapment Efficiency

Entrapment efficiency was determined by the centrifugation method. Niosomal dispersions were centrifuged to separate free drug from entrapped drug. The supernatant containing unentrapped simvastatin was collected, diluted appropriately with phosphate buffer (pH 7.4), and analyzed using a UV–Visible spectrophotometer at the predetermined wavelength.[12]

Entrapment efficiency was calculated as

Entrapment efficiency (%) = [(Total drug − Free drug) / Total drug] × 100

2.5.2 Drug Content

Drug content was determined by disrupting the vesicles using a suitable solvent to release the encapsulated drug completely. The resulting solution was diluted with phosphate buffer (pH 7.4) and analyzed spectrophotometrically. Drug content was expressed as the percentage of actual drug content relative to the theoretical drug content.[13]

Drug Content (%) = (Actual drug content / Theoretical drug content) × 100

2.5.3 In Vitro Drug Release

Drug release was evaluated using the dialysis bag diffusion technique. A measured volume of the sodium alginate-coated simvastatin-loaded niosomal formulation was transferred into a pre-soaked dialysis membrane and immersed in 900 mL of phosphate-buffered saline (PBS, pH 6.8), maintained at 37 ± 0.5°C under continuous stirring at 50 rpm using a USP Type II (paddle) dissolution apparatus. At predetermined time intervals, 5 mL aliquots were withdrawn and replaced with an equal volume of fresh PBS (pH 6.8) to maintain sink conditions. The collected samples were analyzed using UV–Visible spectrophotometry at 238 nm, and the cumulative percentage drug release was calculated using the calibration curve of simvastatin prepared in PBS (pH 6.8).[14,15]

2.6 Characterization of the Optimized Formulation

2.6.1 Particle Size and Polydispersity Index

The mean particle size and polydispersity index (PDI) of the optimized formulation were measured by dynamic light scattering (DLS). Samples were diluted with filtered distilled water before analysis to minimize

multiple scattering effects. Measurements were performed at room temperature.[16]

2.6.2 Zeta Potential

The surface charge of the optimized formulation was determined using a zeta potential analyzer after appropriate dilution with deionized water. Measurements were performed in triplicate, and results were expressed as mean ± SD.[17]

2.6.3 Drug excipient compatibility Study

Drug–excipient compatibility was evaluated using Fourier Transform Infrared (FTIR) spectroscopy to investigate possible interactions between simvastatin and the excipients used in the preparation of sodium alginate-coated niosomes. The FTIR spectra of pure simvastatin (SIM), the and the optimized formulation were recorded using the KBr pellet method over the range of 4000–400 cm^{-1}. The obtained spectra were compared to identify any possible drug–excipient interactions.[18]

2.6.4 Drug Release Kinetics

The in vitro release data of the optimized formulation were fitted to zero-order, first-order, Higuchi, Korsmeyer–Peppas, and Hixson–Crowell kinetic models. The model exhibiting the highest coefficient of determination (R^2) was considered the best-fit model for describing the release mechanism.[19]

2.7 Stability Study

The optimized formulation was subjected to stability studies following ICH guidelines. Samples were stored at 4 ± 2°C, 25 ± 2°C/60% RH**,** and 40 ± 2°C/75% RH for one month. At predetermined intervals, the formulations were evaluated for changes in physical appearance, drug content, entrapment efficiency, particle size, zeta potential, and in vitro drug release.[20]

2.8 Statistical Analysis

All experiments were performed in triplicate, and results are expressed as mean ± standard deviation (SD). Statistical analysis was carried out using one-way analysis of variance (ANOVA) followed by Tukey's multiple comparison test. A value of $p < 0.05$ was considered statistically significant.

3. RESULTS AND DISCUSSION

3.1 Optimization of Simvastatin-Loaded Niosomes

Six simvastatin-loaded niosomal formulations (F1–F6) were initially prepared by varying the Span 60: Tween 80 ratio while maintaining constant amounts of cholesterol and simvastatin. The resulting niosomal dispersions were subsequently coated with 0.2% w/v sodium alginate to obtain six sodium alginate-coated niosomal formulations. All coated formulations produced homogeneous, milky-white dispersions without visible aggregation, sedimentation, or phase separation. The composition of the initial niosomal formulations is presented in Table 1.

Table 1: Composition of Simvastatin-Loaded Niosomal Formulations.

Formulation code	Span 60 (mg)	Tween 80 (mg)	Cholesterol (mg)	Drug (mg)	Total Surfactant: Cholesterol: Drug ratio	Solvent system (Chloroform: Methanol)
F1	100	100	100	100	2:1:1	8:2 (v/v)
F2	120	80	100	100	2:1:1	8:2 (v/v)
F3	140	60	100	100	2:1:1	8:2 (v/v)
F4	160	40	100	100	2:1:1	8:2 (v/v)
F5	180	20	100	100	2:1:1	8:2 (v/v)
F6	190	10	100	100	2:1:1	8:2 (v/v)

The prepared formulations were evaluated for entrapment efficiency, drug content, and cumulative drug release, which were selected as the critical quality attributes for optimization.

4. Evaluation of Different Batches of Sodium Alginate Coated Niosomes

4.1 Physical appearance

The prepared niosomal formulations (F1–F6) were visually evaluated immediately after preparation to assess their physical appearance. The formulations were examined for colour, appearance, homogeneity, phase separation, and overall physical stability. The observations are presented in Table 2.

Table 2: Physical Appearance of Prepared Niosomal Formulations.

Formulation Code	Color	Appearance	Observation
F1	Milky white	Slightly turbid	Stable dispersion
F2	Off-white	Turbid	Stable dispersion
F3	Milky white	Opalescent	stable and uniform dispersion
F4	White	Turbid	Stable dispersion

F5	White	Slightly turbid	Stable dispersion
F6	Milky white	Turbid	Stable dispersion

The physical appearance of the prepared niosomal formulations (F1–F6) was evaluated by visual observation. All formulations appeared homogeneous with no visible phase separation. F3 exhibited a uniform milky-white dispersion without visible aggregation or sedimentation. Based on its physical appearance, F3 was considered suitable for further evaluation.

4.2 Entrapment Efficiency

Entrapment efficiency is an important parameter reflecting the ability of niosomal vesicles to encapsulate the drug. As shown in Table 3, the entrapment efficiency of the prepared formulations ranged from 78.21 ± 0.45% to 93.05 ± 0.48%.

Table 3: % Entrapment Efficiency of Different Simvastatin-Loaded Niosomal Formulation.

Batch	F1	F2	F3	F4	F5	F6
% EE ±SD	78.12 ± 0.39	82.65 ± 0.35	**93.05 ± 0.48**	80.44 ± 0.42	84.88 ± 0.37	76.21 ± 0.45

±SD (n=3)

The optimized formulation (F3) exhibited the highest entrapment efficiency 93.05 ± 0.48% **(**n = 3**)**. The high entrapment efficiency may be attributed to the lipophilic nature of simvastatin and the optimized surfactant-to-cholesterol ratio, which enhanced membrane rigidity and minimized drug leakage.

The % EE of all formulations are graphically represented in Figure 1.

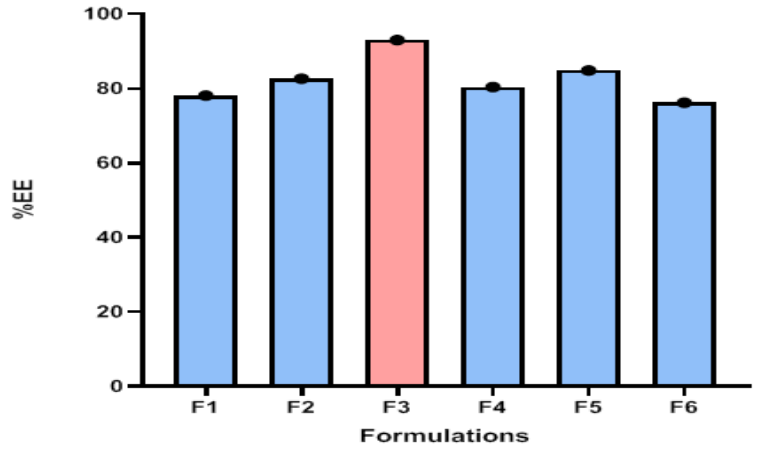

Fig. 1: % EE of Sodium Alginate Coated Simvastatin Loaded Niosomes.

Data are expressed as mean ± SD (n = 3). Statistical analysis was performed using one-way ANOVA followed by Tukey's multiple comparison test. Groups with different letters differ significantly (P < 0.05).

4.3 Drug Content

The drug content of the formulations was determined to assess drug loading efficiency and formulation uniformity. The results are summarized in Table 4 and figure 2.

Table 4. Drug Content of Simvastatin-Loaded Niosomal Formulations.

Batch	F1	F2	F3	F4	F5	F6
% Drug content ± SD	96.63 ± 0.42	97.41 ± 0.38	**98.02 ± 0.35**	96.09 ± 0.45	96.93 ± 0.40	95.27 ± 0.48

±SD (n=3)

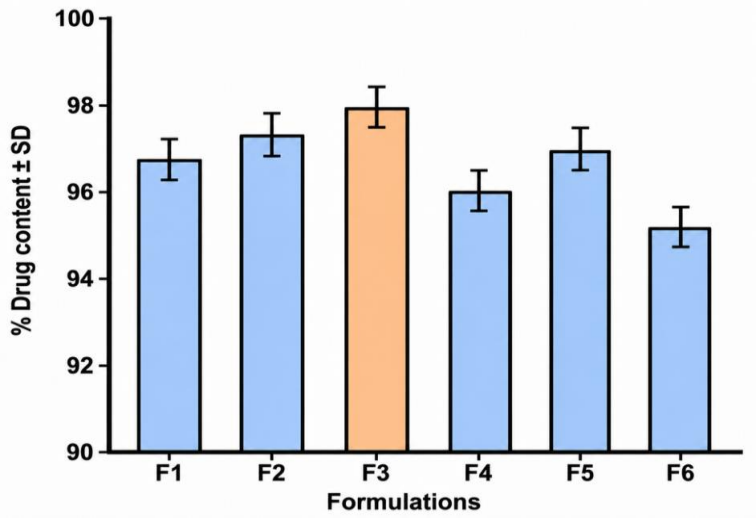

Fig. 2: % Drug Content of Different Batches.

Data are expressed as mean ± standard deviation (SD) (n = 3). Statistical analysis was performed using one-way analysis of variance (ANOVA) followed by Tukey's multiple comparisons test. Groups with different letters are significantly different ($P < 0.05$).

The drug content of all the formulation batches was determined using UV-Visible spectrophotometer at λmax of Simvastatin. The % drug content was found to be in the range of 95.2 ± 0.8% to 98.02 ± 0.35%. Among all the batches, formulation batch F3 showed the highest drug content of 98.02 ± 0.35%.

4.4 In Vitro study

4.4.1 Preparation of calibration curve of simvastatin in PBS pH 6.8

A calibration curve of simvastatin was prepared in phosphate-buffered saline (PBS, pH 6.8) for the quantitative estimation of simvastatin during the in-vitro drug release study. Different concentrations of simvastatin were prepared in PBS (pH 6.8), and their absorbance was measured using a UV-Visible spectrophotometer at 238 nm. The obtained absorbance values were plotted against the corresponding concentrations to obtain the calibration curve.

Table 5: Concentration and Absorbance Data for the Calibration Curve in PBS 6.8.

Concentration (µg/mL)	Absorbance
2	0.201
4	0.397
6	0.592
8	0.787
10	0.964

The graph is represented below

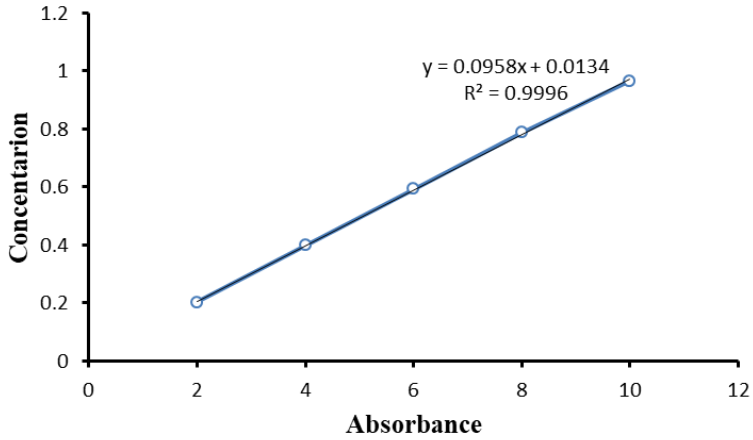

Fig. 3: Calibration Curve of Simvastatin in PBS 6.8.

The calibration curve exhibited excellent linearity over the concentration range of 2–10 µg/mL, with the regression equation y = 0.0958x − 0.0134 and a correlation coefficient (R^2 = 0.9996). The high correlation coefficient indicates that the method obeyed Beer–Lambert's law within the selected concentration range and is suitable for the quantitative estimation of simvastatin in PBS (pH 6.8). Therefore, this calibration curve was used to calculate the cumulative percentage drug release during the dissolution study.

4.4.2 In Vitro Drug Release Study

The in vitro release profiles of simvastatin from sodium alginate-coated niosomes were evaluated over 12 h using the dialysis bag diffusion method. The cumulative drug release profiles are presented in Table 6 and Figure 4.

Table 6: In Vitro Drug Release Profile of Simvastatin-Loaded Niosomal Formulations.

Time (h)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	11.82 ± 0.42	13.54 ± 0.38	17.20 ± 0.51	11.40 ± 0.35	12.91 ± 0.44	14.48 ± 0.47
2	21.15 ± 0.68	23.48 ± 0.72	30.15 ± 0.59	20.33 ± 0.65	22.70 ± 0.58	23.91 ± 0.71
4	36.84 ± 0.91	39.25 ± 0.88	49.80 ± 0.95	36.05 ± 0.84	38.23 ± 0.90	40.67 ± 0.87
6	49.63 ± 1.12	53.32 ± 1.05	66.90 ± 1.18	48.78 ± 1.08	52.11 ± 1.15	54.38 ± 1.10
12	72.98 ± 1.34	76.75 ± 1.28	**94.08 ± 1.14**	72.20 ± 1.30	75.68 ± 1.36	78.28 ± 1.25

±SD (n=3

Graphical representation of drug release profile of F1-F6:

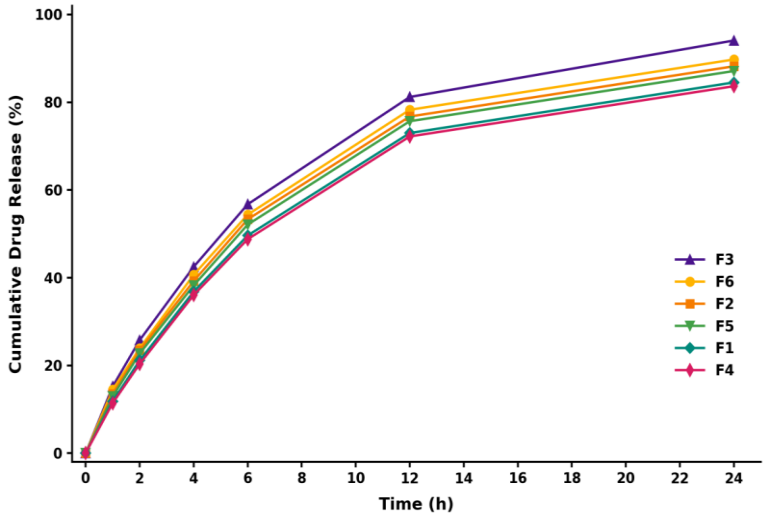

Fig. 4: In-Vitro Drug Release Profile of Sodium Alginate Coated Simvastatin Loaded Niosomes.

Data are expressed as mean ± SD (n = 3). Statistical analysis was performed using one-way ANOVA followed by Tukey's multiple comparison test. Different letters indicate statistically significant differences between formulations **(P < 0.0001**).

All formulations exhibited a biphasic release pattern characterized by an initial burst release followed by sustained drug release. The initial release may be attributed to the diffusion of drug adsorbed on or near the vesicle surface, whereas the subsequent sustained phase resulted from gradual diffusion of the encapsulated drug through the niosomal bilayer and sodium alginate coating. Among the formulations, F3 demonstrated the highest cumulative drug release (94.08 ± 1.14%) after 12 h. The superior release behavior of F3 may be attributed to its optimized surfactant composition, which produced vesicles with improved membrane integrity and controlled drug diffusion. The sodium alginate coating further contributed to sustained release by acting as an additional diffusion barrier, thereby prolonging drug release throughout the study period.

Based on its superior entrapment efficiency, high drug content, and sustained release characteristics, formulation F3 was selected as the optimized formulation for further characterization.

4.5 Characterization of the Optimized Formulation

4.5.1 Particle Size and Polydispersity Index

Particle size plays a significant role in determining the stability, cellular uptake, and oral absorption of nanocarrier systems. Dynamic light scattering analysis revealed that the optimized formulation possessed a mean particle size of 228.6 ± 2.5 nm with a polydispersity index (PDI) of 0.232 ± 0.01 (Figure 5)

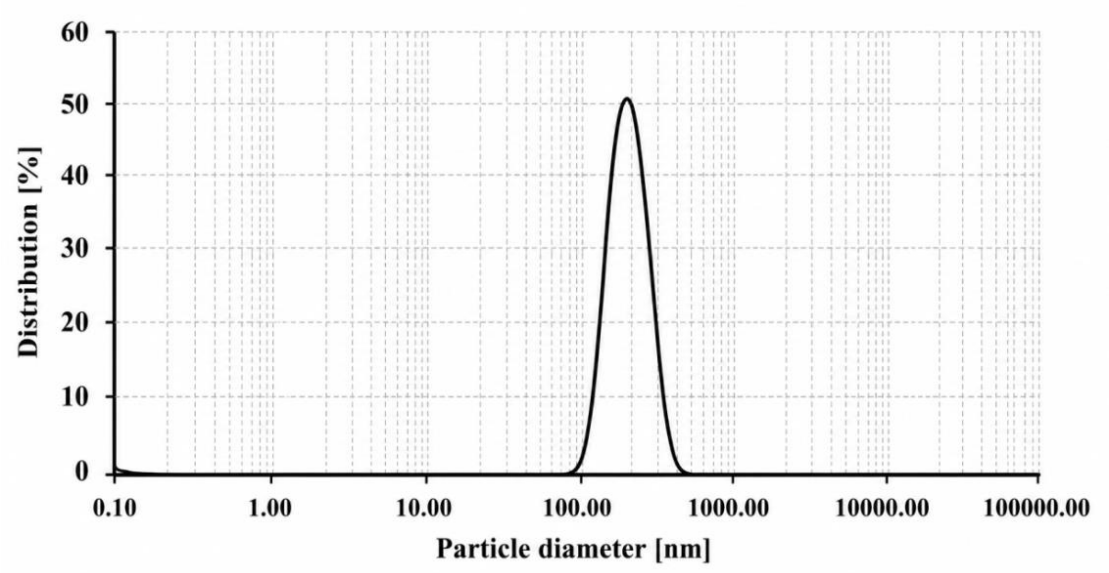

Fig.5 Particle size Distribution of Sodium Alginate Coated Simvastatin Loaded Niosomes.

The particle size obtained is considered suitable for oral nanocarrier systems and may facilitate improved intestinal uptake. The low PDI value (<0.3) indicates a narrow and homogeneous particle size distribution, suggesting successful formulation and uniform vesicle formation.

4.5.2 Zeta Potential

The surface charge of colloidal systems influences their physical stability by preventing particle aggregation through electrostatic repulsion. The optimized formulation exhibited a zeta potential of −36.0 ± 1.1 mV (Figure 6)**.**

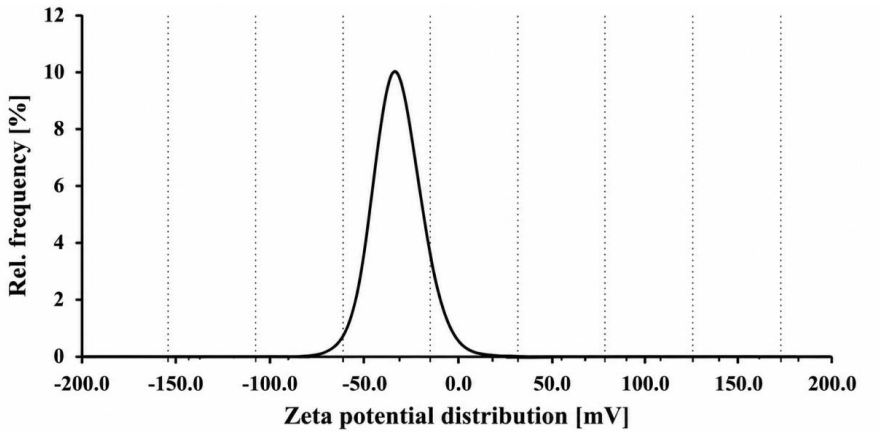

Fig. 6: Zeta Potential Distribution of Sodium Alginate Coated Simvastatin Loaded Niosomes.

A zeta potential greater than ±30 mV is generally considered indicative of good colloidal stability. The observed negative surface charge is primarily attributed to the presence of sodium alginate on the vesicle surface and suggests that the optimized formulation possesses sufficient electrostatic repulsion to minimize aggregation during storage.

4.4.3 Drug Excipient Compatibility Study

The compatibility between simvastatin and the formulation excipients was investigated using FTIR spectroscopy. The characteristic absorption peaks of pure simvastatin were retained in the optimized formulation with only minor shifts in peak positions (Table 7, Figures 7 and 8)**.**

Table 7: Characteristic FTIR Peaks of Pure Simvastatin and Optimized Formulation.

Functional group	Pure Simvastatin (cm^{-1})	Optimized formulation (cm^{-1})	Interpretation
O–H stretching	3545	3326	Broad O–H stretching retained
C–H stretching	2956, 2874	2920, 2850	Aliphatic C–H stretching retained
C=O stretching	1704	1731	Ester carbonyl retained with slight shift
C=C stretching	1635	1603	Slight shift due to formulation matrix
CH_2/CH_3 bending	1462, 1380	1416	Retained
C–O stretching	1268, 1062	1243, 1122, 1031	Characteristic C–O bands retained

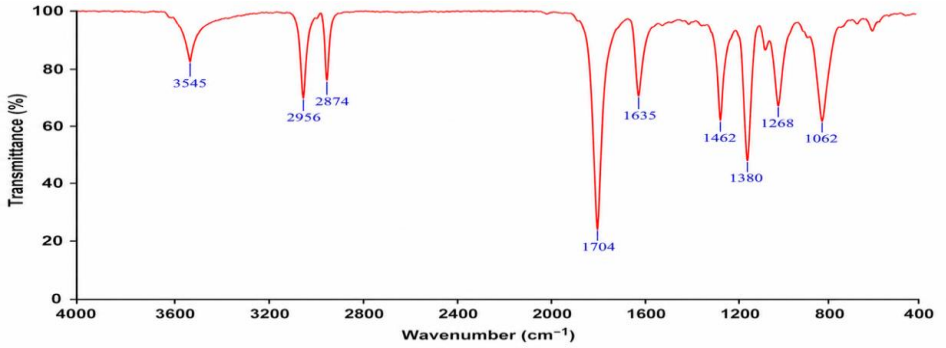

Fig. 7: FTIR Spectrum of Simvastatin.

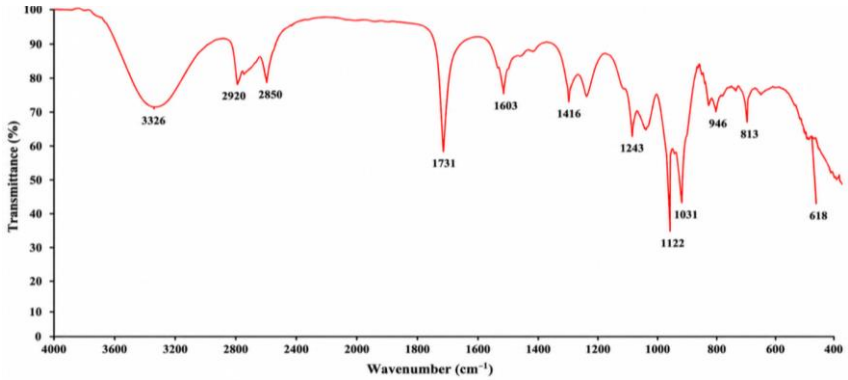

Fig. 8: FTIR Spectrum of Sodium Alginate Coated Niosomes.

The absence of newly formed peaks or disappearance of characteristic functional group peaks indicates that no significant chemical interaction occurred between simvastatin and the formulation excipients during the preparation process. The minor spectral shifts observed are likely due to physical encapsulation and intermolecular interactions within the vesicular matrix.

4.4.5 Drug Release Kinetics

The in vitro drug release data of the optimized formulation (F3) were fitted to various kinetic models, including zero-order, first-order, Higuchi, and Korsmeyer–Peppas models, to determine the drug release kinetics and elucidate the underlying release mechanism. The kinetic parameters obtained from the analysis are presented in Table8, and the corresponding kinetic plots are shown in Figures 9-12.

Table 8: Release kinetics of optimized formulation F3.

Zero order		First order		Higuchi model		Korsmeyer-peppas model	
R^2	K_0	R^2	K_1	R^2	K_h	R^2	n
0.8266	3.689	0.6754	0.0287	0.9687	20.881	0.9998	0.734

The in vitro drug-release data were evaluated using zero-order, first-order, Higuchi, and Korsmeyer–Peppas kinetic models. The Korsmeyer–Peppas model showed the highest R^2 value (0.9998), indicating the best fit to the release data. The n value of 0.734 suggests an anomalous (non-Fickian) release mechanism, indicating that drug release occurs through a combination of diffusion and polymer relaxation/swelling. The Korsmeyer–Peppas model provided the better fit.

The kinetic plots of the optimized formulation (F3) are shown in following figs.

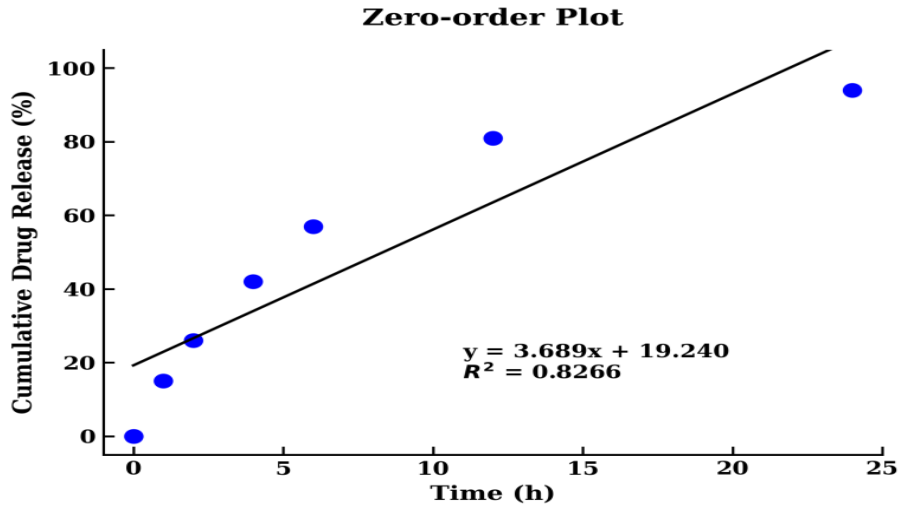

Fig. 9: Zero Order Plot of F3.

The zero-order kinetic model showed an R^2 value of 0.8266 with a K_0 value of 3.689, indicating a relatively good correlation between cumulative drug release and time. However, the lower R^2 value compared with the other kinetic models suggests that the drug-release profile was not best described by zero-order kinetics.

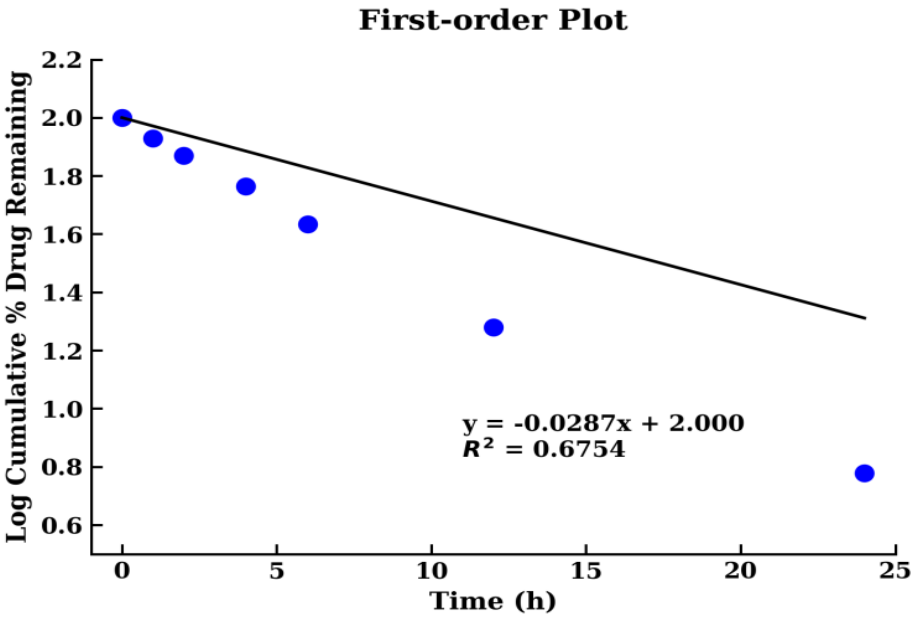

Fig. 10: First order plot of F3.

The model exhibited an R^2 value of 0.6754, with a calculated first-order rate constant (K_1) of 0.0287. The relatively lower R^2 value indicated that the first-order model provided a comparatively weaker fit to the observed drug release data.

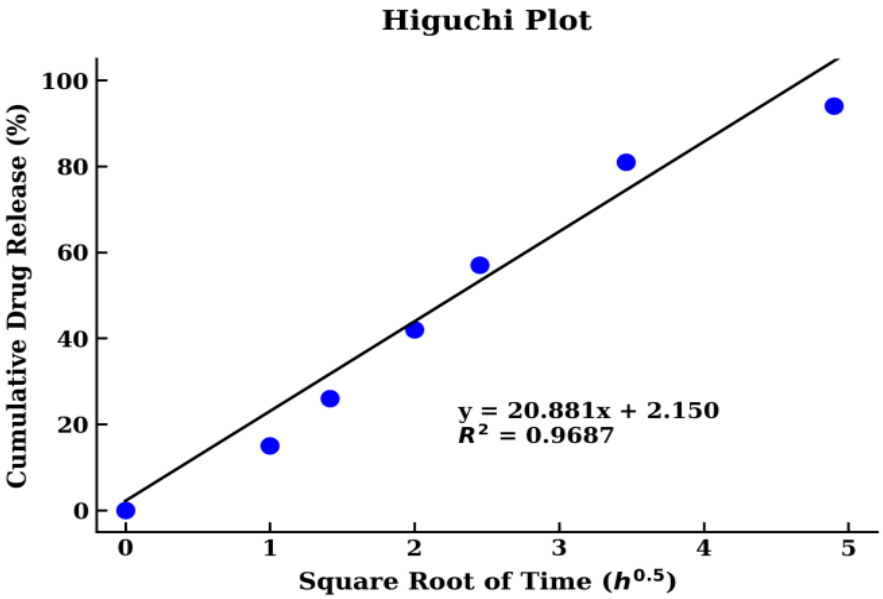

Fig. 11: Higuchi Plot of F3.

The Higuchi model showed an R^2 value of 0.9687 with a Higuchi constant (K_h) of 20.881. The high R^2 value indicates a strong correlation between cumulative drug release and the square root of time, suggesting that diffusion is an important contributing mechanism in the drug-release process.

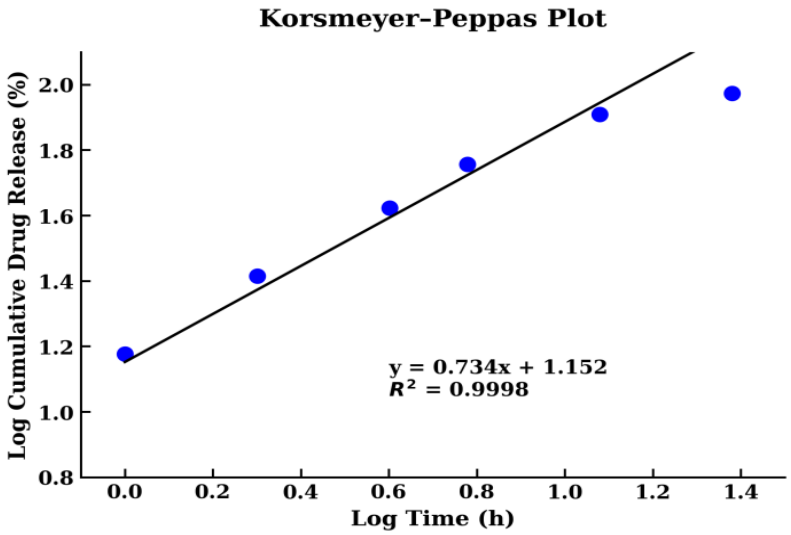

Fig. 12: Korsmeyer-Peppas plot of F3.

The Korsmeyer–Peppas model showed the highest R^2 value of 0.9998, indicating an excellent fit to the experimental drug-release data. The release exponent (n) was found to be 0.734, suggesting an anomalous/non-Fickian release.

4.4.6 Stability Studies

The optimized formulation was evaluated for stability under refrigerated, room temperature, and accelerated storage conditions for one month. The results are summarized in Table 9.

Table 9: Stability Study of Optimized Formulation (F3).

Parameter	Time	4 ± 2°C (Refrigerated)	25 ± 2°C(Room Temperature)	40 ± 2°C/ 75 ± 5% RH(Accelerated)
Physical appearance	0 Day	Milky/opalescent dispersion	Milky/opalescent dispersion	Milky/opalescent dispersion
	30 Days	No visible change	No visible change	Slight aggregation
Drug content (%)	0 Day	98.02 ± 0.35	98.02 ± 0.35	98.02 ± 0.35

	30 Days	97.78 ± 0.39	97.46 ± 0.44	95.92 ± 0.58
Entrapment efficiency (%)	0 Day	93.05 ± 0.48	93.05 ± 0.48	93.05 ± 0.48
	30 Days	91.61 ± 0.52	90.94 ± 0.61	88.82 ± 0.75

The stability of the optimized formulation was evaluated under refrigerated, room temperature, and accelerated storage conditions for 30 days. The formulation remained clear under refrigerated and room temperature conditions, whereas slight aggregation was observed under accelerated conditions after 30 days. Drug content and entrapment efficiency showed a slight decrease with increasing temperature; however, the formulation retained acceptable stability throughout the study period.

5. CONCLUSION

The present study successfully developed sodium alginate-coated simvastatin-loaded niosomes using the thin-film hydration technique and evaluated their physicochemical characteristics, in-vitro drug release, release kinetics, and short-term stability. Among the investigated formulations, F3 exhibited the highest entrapment efficiency (93.05 ± 0.48%) and drug content (98.02 ± 0.35%), along with a favorable 12-h drug-release profile (94.08 ± 1.14%). The optimized formulation showed a mean particle size of 228.6 ± 2.5 nm, a PDI of 0.232 ± 0.01, and a zeta potential of −36.0 ± 1.1 mV, indicating a relatively uniform nanosized dispersion with good electrostatic stability. FTIR analysis showed retention of the characteristic functional groups of simvastatin without the appearance of major new peaks, suggesting the absence of significant chemical interactions with the formulation components.

The release profile of the optimized formulation was best fitted to the the Korsmeyer–Peppas model R^2 value of 0.9998. The release exponent (n) was found to be 0.734, suggesting an anomalous/non-Fickian release mechanism, in which drug diffusion occurs in combination with polymer relaxation/swelling. Short-term stability evaluation demonstrated better stability under refrigerated and room-temperature conditions, whereas slight aggregation and greater changes in drug content and entrapment efficiency were observed under accelerated conditions. Overall, the findings suggest that sodium alginate-coated niosomes have potential as an oral delivery approach for simvastatin by providing high drug entrapment and prolonged in-vitro drug release. However, the potential improvement in oral bioavailability and therapeutic efficacy cannot be established from the present in-vitro study alone. Further in-vivo pharmacokinetic, pharmacodynamic, gastrointestinal-retention, and long-term stability studies are required to establish the clinical potential of the developed formulation.

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