Advances in Bioresearch
Adv. Biores., Vol 15 (4) July 2024: 38-49
©2024 Society of Education, India
Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.15.4.3849

Advances in Bioresearch

ORIGINAL ARTICLE

Formulation Development and *In vitro* Evaluation of Lovastatin Nanosponges by Emulsion Solvent Evaporation Method

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ABSTRACT

The present investigation was undertaken to prepare nanosponges of Lovastatin to achieve improved drug release. Eudragit RS100, Polyvinyl alcohol (PVA) was used as a polymer; Acetone was used as the solvent. Prepared nanosponges were evaluated for particle size, zeta potential, entrapment efficiency and in vitro drug release. Optical microscopy was used to determine the particle size of the nanosponge, and it was observed that the nanosponges were uniform in size. The average particle size of all formulations ranges from 312.2 nm to 420.2 nm. The entrapment efficiency of formulation F1 was found to be 79.12%, formulation F2 was found to be 82.48%, formulation F3 was found to be 80.54%, formulation F4 was found to be 85.16%, formulation F5 was found to be 78.02%, and formulation F6 was found to be 79.24%, formulation F7 was found to be 73.84%, formulation F8 was found to be 74.88%, and F9 was found to be 72.12 %. F8 shows a high entrapment efficiency of 85.16 % among all the formulations. Hence, Lovastatin loading into nanosponges using the emulsion solvent evaporation process thus successfully boosted and controlled the drug release.

Keywords: *Lovastatin, Nanosponges, Polyvinyl alcohol, Acetone, Eudragit RS100*

Received 24.02.2024 Revised 20.03.2024 Accepted 22.05.2024

How to cite this article:
Magharla D D, Vankayala D S, Anilkumar V, Yanamadala M A. Formulation Development and *In vitro* Evaluation of Lovastatin Nanosponges by Emulsion Solvent Evaporation Method. Adv. Biores. Vol 15 [4] July 2024. 38-49

INTRODUCTION

Nanosponges are made of microscopic particles with a few nanometres-wide cavities in which a large variety of substances can be encapsulated. These particles can carry both lipophilic and hydrophilic substances, thereby improving the solubility of poorly water-soluble molecules. The studies conducted in this field prove that the tiny mesh-like structures called nanosponges may revolutionise the treatment of many diseases, and early trials suggest this technology is up to five times more effective at delivering drugs for breast cancer than conventional methods [1]. The nanosponge is about the size of a virus with a 'backbone' (a scaffold structure) of naturally degradable polyester. They 'cross-link' polyester segments to form a spherical shape with many pockets (or cavities) where drugs can be encapsulated. Polyester is biodegradable, which means that when it breaks down in the body, the drug can be released on a known schedule [2].

Lovastatin is a statin medication used primarily to lower cholesterol levels and prevent cardiovascular disease. It operates by inhibiting the enzyme HMG-CoA reductase, which is a key enzyme in the biosynthesis of cholesterol in the liver. This inhibition leads to reduced levels of cholesterol within the body, particularly low-density lipoprotein (LDL) cholesterol, often referred to as "bad" cholesterol due to its association with an increased risk of cardiovascular events. [3,4]

MATERIAL AND METHODS

Materials

Pharma Life Research Lab, India, provided lovastatin as a gift sample. Eudragit RS100, Polyvinyl alcohol, Acetone, Dichloromethane, span 80, Tween 80, Trichloro citrate, and Distilled water were Purchased from B.M.R. Chemicals, Hyderabad. All other ingredients used were analytical grade.

Pre-formulation studies

Solubility studies

Several solvents, such as pure water, 0.1 N HCL, 6.8 pH buffers, and organic solvents, including ethanol and methanol, were used to investigate the solubility of lovastatin. An excess of the medication was added to various beakers containing varying solvents to conduct the solubility investigations. For a full day, the mixes were shaken to guarantee consistent intervals. Whatman grade no. 41 filter paper was used to filter the solutions. Spectrophotometry was utilised to examine the solutions. [5]

Determination of absorption maximum (λmax):

The wavelength at which maximum radiation absorption occurs is referred to as λmax. The λmax value is distinct for each substance and valuable for substance identification. Establishing the absorption maxima of the studied substance is crucial for precise analytical work. Most drugs absorb radiation in the ultraviolet region (190-390nm) due to their aromatic nature or the presence of double bonds.

The 10mg of Lovastatin was precisely measured and dissolved in 10 ml of methanol in a clean 10 ml volumetric flask. The volume was adjusted to 10ml using the same solution, resulting in stock Solution-I with a 1000µg/ml concentration. 1ml was pipetted out from stock Solution-I into a 10ml volumetric flask. A stock solution-II was prepared by adding methanol buffer to the volume of 10ml, resulting in a concentration of 100µg/ml. 1ml was pipetted out from stock solution-II into a 10ml volumetric flask. The volume was adjusted to 10ml using methanol buffer to achieve a 10µg/ml concentration. The solution was scanned in a UV-visible double-beam spectrophotometer at 200-400nm to determine the absorption maximum (λ-max). [6-9]

Construction of calibration curve:

The 10mg Lovastatin was dissolved in methanol and placed in a clean 10-volumetric flask. The volume was adjusted to 10ml using a 6.8 pH buffer, resulting in a 1000µg/ml concentration. The solution was prepared by pipetting 1ml from the standard solution into a 10-volumetric flask. Methanol was then added to make the volume up to 10ml, resulting in a 100µg/ml concentration. The stock solution was divided into aliquots of varying volumes, ranging from 0.2 to 1.2 ml. Each aliquot was then transferred to a separate 10ml volumetric flask, and the solution was diluted with methanol buffer to reach a final volume of 10ml. This resulted in concentrations of 2, 4, 6, 8, 10, and 12µg/ml, respectively. The absorbance measurement for each solution was taken at a wavelength of 234nm. [10,11]

Drug excipient compatibility study

Fourier transform–infrared spectroscopy (FT-IR) was used to observe the drug and excipient compatibility. The FT-IR spectra obtained from Bruker FT-IR Germany (Alpha T) investigated potential interactions between the pure drug and the excipients in the solid state. The potassium bromide pellets were prepared on a KBr press by grinding the solid powder sample with a large quantity of KBr in a mortar. The finely ground powder was then placed into a stainless steel die and compressed between polished steel anvils at approximately 8t/in2 pressure. The spectra were recorded across wave numbers from 4000 to 400 cm^{-1}. [12]

Preparation of Nanosponges

Dissolve lovastatin, Eudragit RS100, and polyvinyl alcohol (PVA) in acetone. Add dichloromethane to the above solution slowly under stirring until a clear solution is obtained. Prepare a solution of Span 80 and Tween 80 in distilled water. Add the lovastatin nanosponge solution dropwise to the surfactant solution under constant stirring. Stir the solution for an additional 2 hours to ensure complete drug encapsulation within the nanosponges. Evaporate the solvent under reduced pressure to obtain a nanosponge dispersion. Wash the nanosponges with distilled water to remove any unentrapped drug. Dry the nanosponges at room temperature under vacuum. Add triethyl citrate to the dried nanosponges and mix well to enhance flexibility and drug release [13,14]

Table 1: Formulation table of Lovastatin nanosponges with different ratios (F1 to F9)

Ingredient	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)
Lovastatin	50	75	100	50	75	100	50	75	100
Eudragit RS100	150	150	150	200	200	200	250	250	250
Polyvinyl alcohol (PVA)	50	50	50	50	50	50	50	50	50
Acetone (mL)	10	10	10	10	10	10	10	10	10
Dichloromethane (mL)	10	10	10	10	10	10	10	10	10
Span 80	100	100	100	100	100	100	100	100	100
Tween 80	50	50	50	50	50	50	50	50	50
Triethyl citrate	20	20	20	20	20	20	20	20	20
Distilled water (mL)	100	100	100	100	100	100	100	100	100

Evaluation parameters of Nanosponges [15-17]

Drug content uniformity

The weight equivalent of 10mg of Lovastatin was dissolved in a 10 ml isotonic solution and left overnight. The dilutions underwent filtration and were subsequently analyzed using UV to determine their content uniformity. The absorbance of the formulations was measured using a UV-Vis spectrophotometer with a one cm cell. The instrument was calibrated to the wavelength (nm) for drug analysis. The drug content in each formulation was determined by analyzing the absorbance values of known standard solutions.

Entrapment efficiency

The Nanosponges suspension containing 1mg of Lovastatin weight equivalent was carefully analyzed by dissolving the sample in 10ml of distilled water. 10ml of the clear layer of the dissolved drug is taken after the drug is dissolved. The drug concentration in the water phase was measured using a UV-spectrophotometric method at 255nm (U.V Spectrophotometer, systronics). Another nanoparticulate sample was used for the repeated test. The drug concentration in the suspension was determined through centrifugation at 500rpm for 5 minutes, followed by measuring the drug concentration in the clear supernatant layer using the UV-spectrophotometric method. The concentration of the drug is determined using a calibration curve. Calculating the drug content within the particles involved subtracting the drug amount in the aqueous phase from the total drug amount in the nanoparticle suspension. The drug's entrapment efficiency (%) is calculated using the following equation.

$$\% \text{ of Drug entrapment} = \frac{\text{Mass of drug in Nanosponges}}{\text{The mass of drug used in the formulation}} \times 100$$

Scanning electron microscopy

The morphological features of prepared Nanosponges are observed by scanning electron microscopy at different magnifications.

Particle size and shape

The Nanosponges' particle size was measured using the Horibo scientific nanoparticle SZ100 particle size analyzer. The measurement involved diluting 100µl of the formulation with the appropriate volume of PBS pH 6.8 and then determining the vesicle diameter and zeta potential. A scan was conducted on the sample to determine its particle size.

Release Kinetics of the Optimized Formulations

To study the in vitro release kinetics of the optimised formulation, data obtained from dissolution study were plotted in various kinetics models. Different kinetic models such as zero order (cumulative amount of drug released vs. time), first order (log cumulative percentage of drug remaining vs. time), Higuchi model (cumulative percentage of drug released vs. square root of time), Korsmeyer-Peppas model (Log Cumulative per cent drug release versus log time) and Hixson Crowell model (cube root of cumulative percentage of drug remaining vs. time) were applied to interpret the drug release kinetics from the formulations. The best-fit model was decided based on the highest regression values for correlation coefficients for formulations.

RESULTS AND DISCUSSION

Solubility

Solubility studies of Lovastatin: Solubility of Lovastatin pure drug in Water, Ethanol, Methanol,0.1 N HCl, pH 6.8 Buffer was studied. It was found to be 0.0019mg/ml in distilled water,3.3 mg/ml in Ethanol,44 mg/ml in methanol,0.042 mg/ml in 0.1N HCL, 0.005 mg/ml in Phosphate buffer pH 6.8.

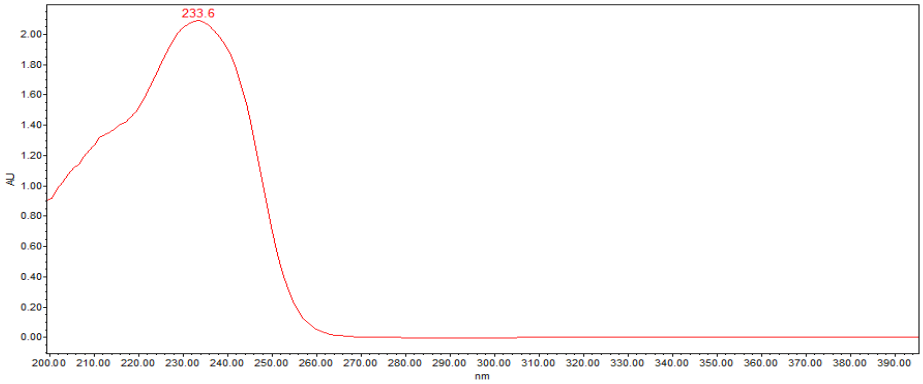
Table 2: Solubility studies of Lovastatin

Buffer/Solvent	Solubility (mg/mL) at 25℃	Description
Water	0.0019	Very low solubility, typical for hydrophobic drugs
Ethanol	3.3	Good solubility, suitable for various formulations
Methanol	44	Very high solubility,
0.1 N HCl	0.042	Increased solubility in acidic conditions
pH 6.8 Buffer	0.005	Slightly higher than in water, low solubility

From the above-obtained solubility studies, we can say the drug's solubility is higher in the 6.8 pH phosphate buffer than in the other buffers. In organic solvents, the solubility was found more in Ethanol than in methanol.

Determination of absorption maximum (λmax)

The determination of Lovastatin λ-max was done in a 6.8 pH phosphate buffer for an accurate quantitative assessment of the drug dissolution rate.



Wave length - 234 nm

Fig. 1: λ-max in 6.8 phosphate buffer

The maximum absorbance of the Lovastatin in pH 6.8 buffer was found to be 234nm, as shown in Fig 1. Hence, the wavelength of 234nm was selected for the analysis of the drug in dissolution media.

Calibration curve

The linearity was found to be in the range of 2- 12µg/ml. The regression value was closer to 1 indicating the method obeyed Beer-lambert's law

Table 3: Calibration curve Results of Lovastatin

Concentration(µg/ml)	Absorbance
0	0
2	0.136
4	0.251
6	0.369
8	0.480
10	0.581
12	0.682

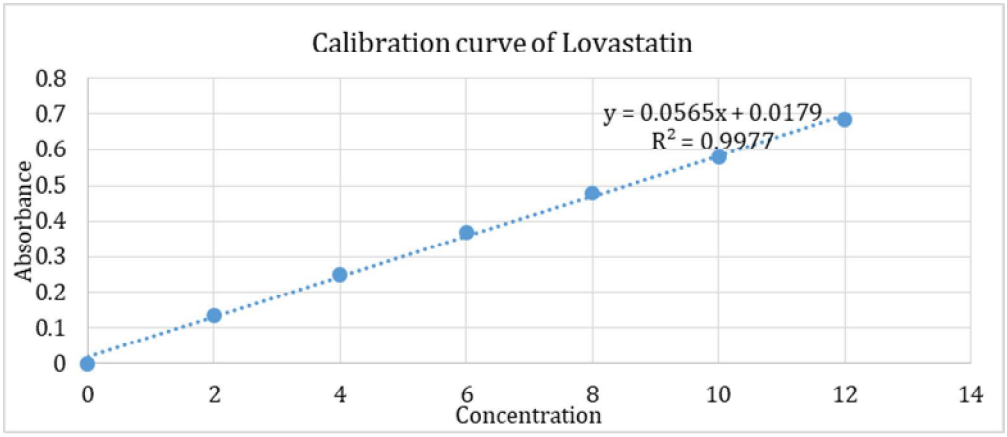


Fig.2: Calibration Curve of Lovastatin in 6.8 pH phosphate buffer

Drug excipient compatibility

Drug and excipient compatibility was confirmed by comparing spectra of FT-IR analysis of Pure drug with that of various excipients used in the formulation

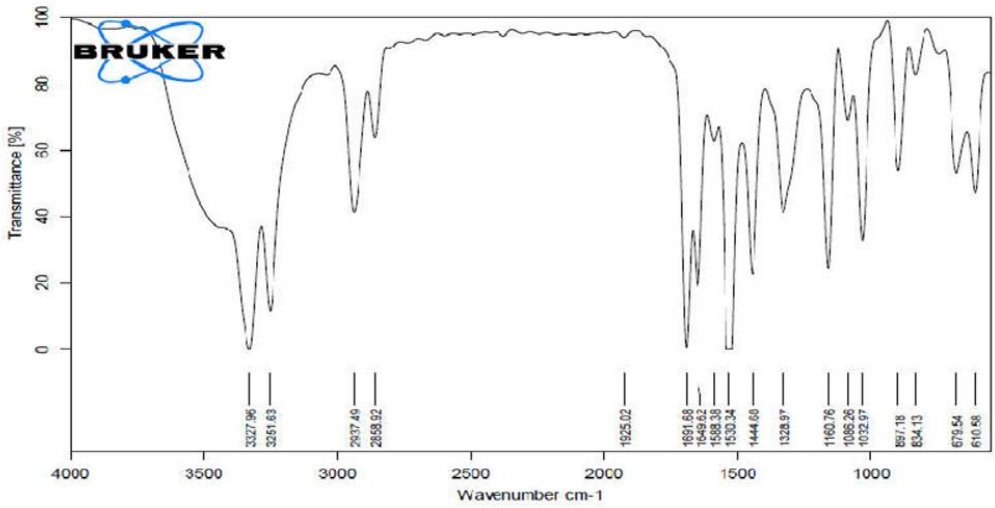


Fig.3: FTIR Spectra of Pure Drug

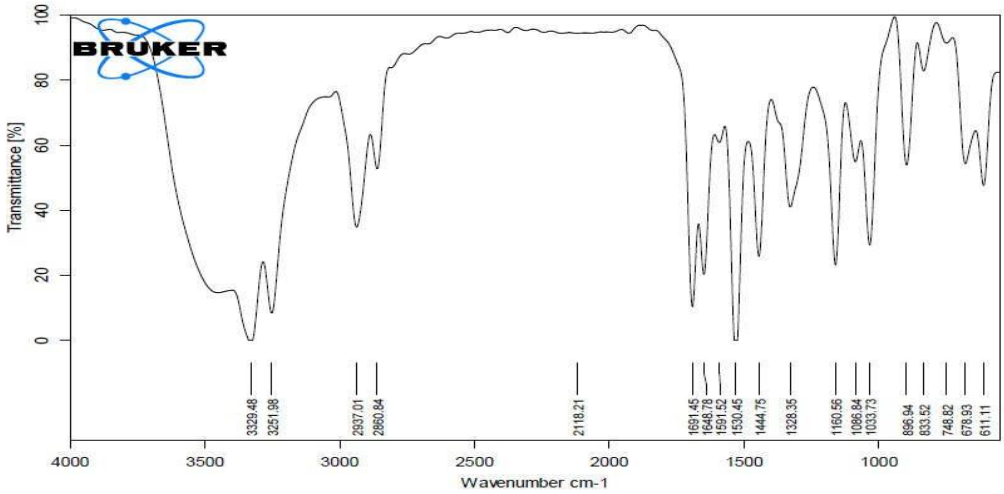


Fig.4: FTIR Spectra of Optimized Formulation

Particle size analysis of Nanosponges

Optical microscopy was used to determine the particle size of the nanosponge, and it was observed that the nanosponges were uniform in size. The average particle size of all formulations ranges from 312.2 nm to 420.2 nm. This range increases as the concentration of polymer increases. However, it was observed that after reaching a certain concentration, the particle size decreased as the ratio of drug to polymer

increased. The reason for this could be that in a high drug to polymer ratio, there is a relatively smaller amount of polymer available per nanosponge. When the drug-polymer ratio is high, there is a decrease in the amount of polymer surrounding the drug. This results in a reduction in the thickness of the polymer wall, leading to the formation of nanosponges with smaller sizes. The particle size analysis reveals that the particle size of the formulation varies depending on the concentration of the polymer drug ratio.

Table 9: Particle size of Nanosponges

S.NO	Formulation code	Particle size (nm)
1	F1	315.2
2	F2	258.3
3	F3	315.3
4	F4	420.2
5	F5	300.3
6	F6	325.5
7	F7	378.6
8	F8	315.3
9	F9	312.1

Morphology determination by scanning electron microscopy (SEM)

The sample was placed in an evacuated chamber and scanned in a controlled pattern by an electron beam. Interaction of the electron beam with the specimen produces a variety of physical phenomena that, when detected, are used to form images and provide elemental information about the specimens. It was observed that the nanosponges were spherical, and uniform with no drug crystals on the surface. The shape of the nanosponges affects the surface area and surface area per unit weight of spherical nanosponges. The irregular shape of the particles may affect dissolution rate present in dissolution environment.

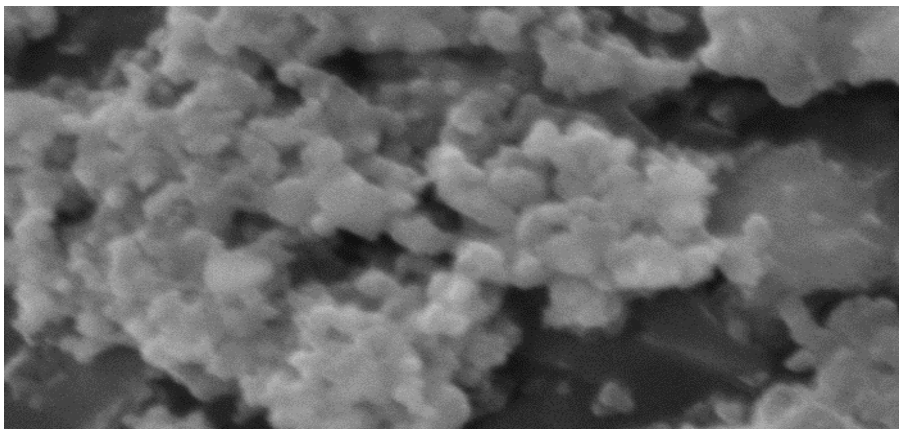
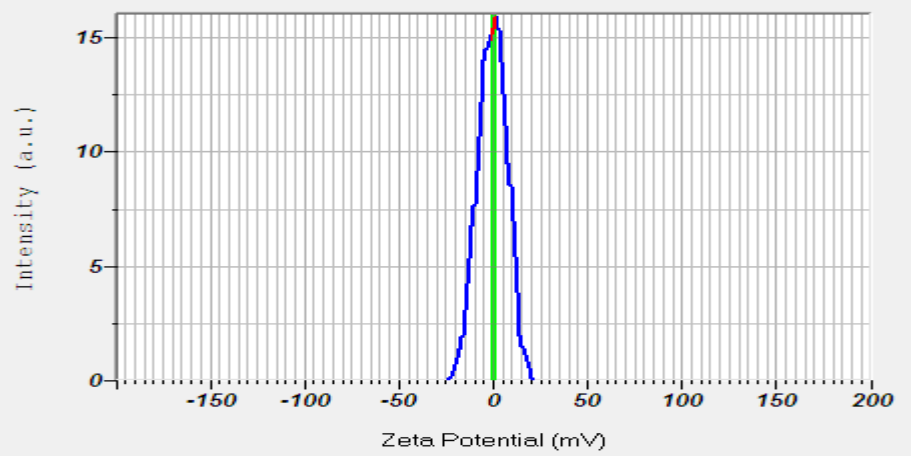


Fig.5: SEM of Nanosponges optimized formulation (F4)



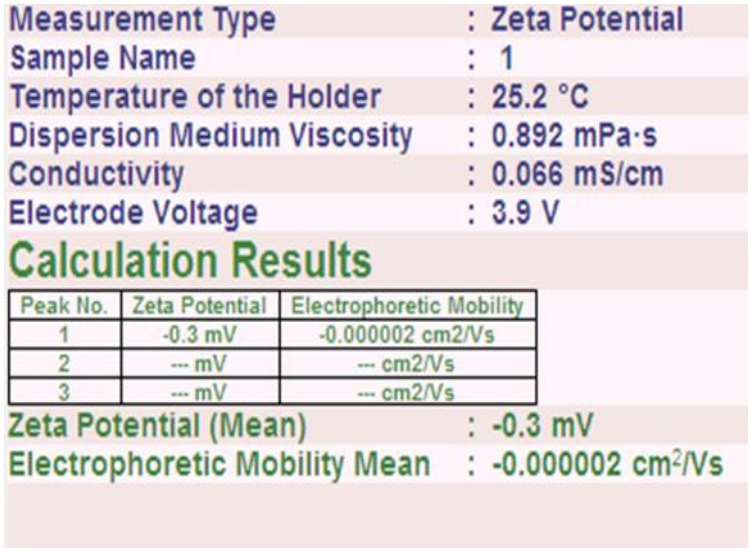


Fig.6: Zeta Potential of Lovastatin

Entrapment efficiency

The entrapment efficiency of formulation F1 was found to be 79.12%, formulation F2 was found to be 82.48%, formulation F3 was found to be 80.54%, formulation F4 was found to be 85.16%, formulation F5 was found to be 78.02%, and formulation F6 was found to be 79.24%, formulation F7 was found to be 73.84%, formulation F8 was found to be 74.88%, and F9 was found to be 72.12 %. Among all the formulations, F8 shows high entrapment efficiency of 85.16 %.

In vitro dissolution studies of prepared nanosponges:

Table 10: Percentage of drug release of Nanosponges formulations

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	37.62	26.25	6.89	22.18	17.24	8.52	31.52	35.28	9.12
2	53.04	35.50	10.16	34.41	24.21	18.26	52.85	42.12	12.71
3	60.78	44.49	18.87	43.39	30.62	26.12	60.84	50.16	26.63
4	71.82	52.02	24.05	55.58	37.48	32.86	72.22	58.06	38.12
5	79.94	63.30	29.57	67.70	43.18	40.84	80.84	67.82	44.68
6	85.92	74.39	35.06	71.80	49.22	49.88	88.12	79.68	50.54
7	92.96	85.50	40.89	79.18	56.47	56.26	94.86	87.24	62.24
8	98.12	92.26	49.48	83.32	62.82	64.12	98.84	96.12	73.26
9		97.70	52.87	89.75	78.54	70.18		99.56	78.12
10			60.40	94.40	84.16	77.94			83.36
11			67.11	97.22	92.94	82.18			87.90
12			75.26	99.26		86.92			92.14

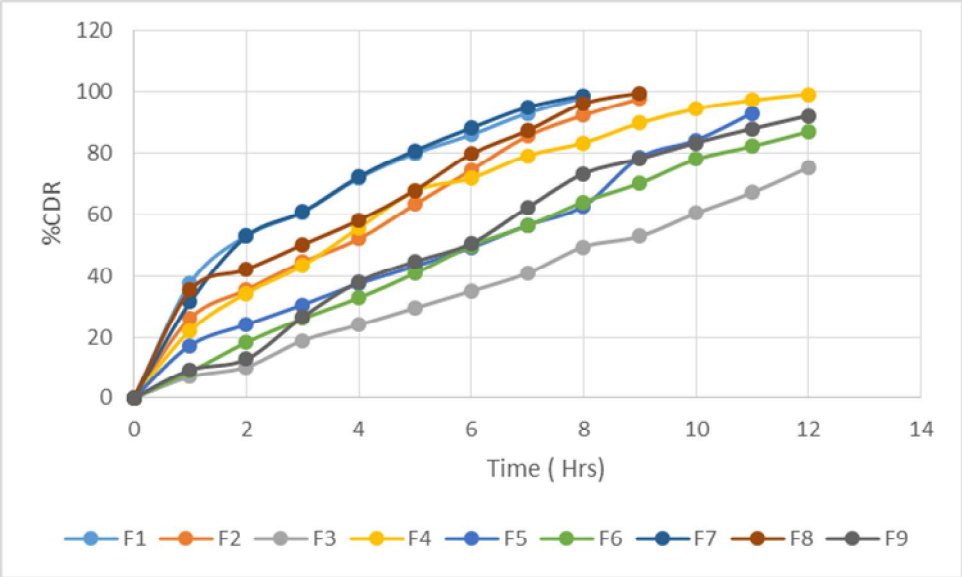


Fig.7: Percentage of drug release graph of formulations F1-F9

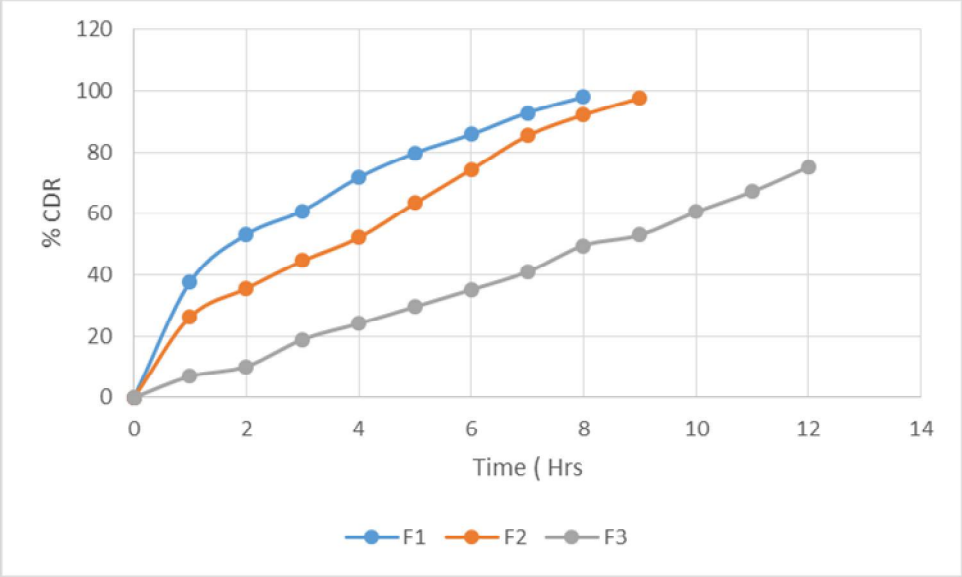


Fig.8: Percentage of drug release graph of formulations F1-F3

The table you provided shows the drug release profile of Lovastatin from three different formulations (F1, F2, F3) over a time span of up to 12 hours. Each formulation releases the drug at different rates over time. Initially, all formulations start with 0% release. Over the first hour, F1 releases the most drug at 37.62%, followed by F2 at 26.25%, and F3 at 6.89%. This trend continues with F1 consistently showing the highest release rate at each time point, followed by F2, and then F3, indicating that F1 has the fastest release rate and F3 the slowest. By the end of the observed period, F1 almost reaches complete release (98.12%), F2 approaches full release but slightly slower (97.70%), and F3, despite having the slowest release rate, shows a steady increase, ending at 75.26%. This data suggests that the formulation components or ratios impact the release kinetics of Lovastatin, with F1 being the most rapidly releasing formulation.

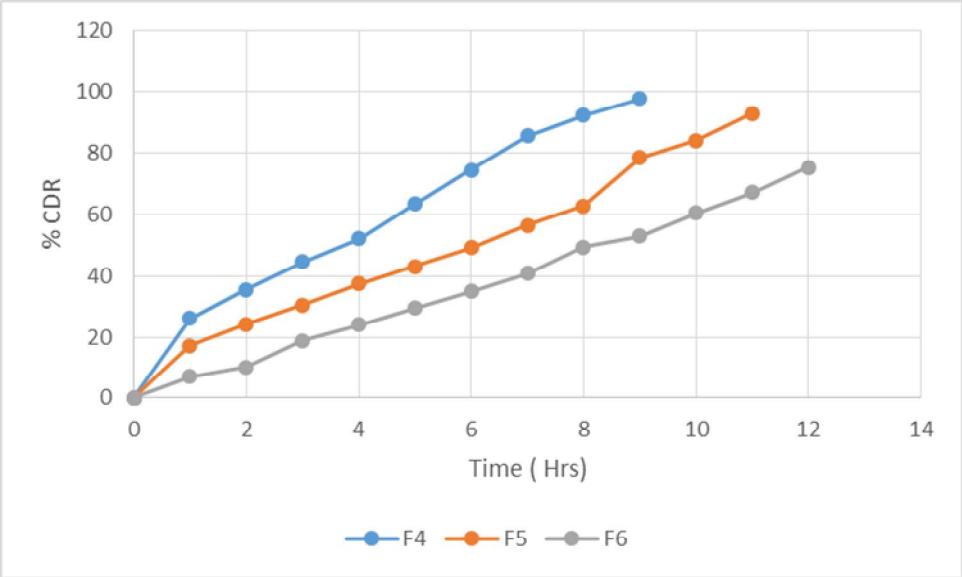


Fig.9: Percentage of drug release graph of formulations F4-F6

The table shows the drug release profiles for three different formulations (F4, F5, F6) of Lovastatin over a 12-hour period. Initially, all formulations start with zero release at time zero. As time progresses, each formulation releases Lovastatin at varying rates. F4 exhibits the fastest release rate, closely followed by F5, and F6 shows the slowest release among them. By the first hour, F4 releases 22.18% of the drug, compared to F5's 17.24% and F6's 8.52%. This trend of F4 leading in drug release continues throughout the 12-hour period. By the end of the study, F4 reaches nearly complete drug release at 99.26%, while F5 approaches this level but is not listed at the 12-hour mark, and F6 releases 86.92% of the drug. The data indicate that the composition or the method of formulation affects the rate at which Lovastatin is released, with F4 designed for the quickest release.

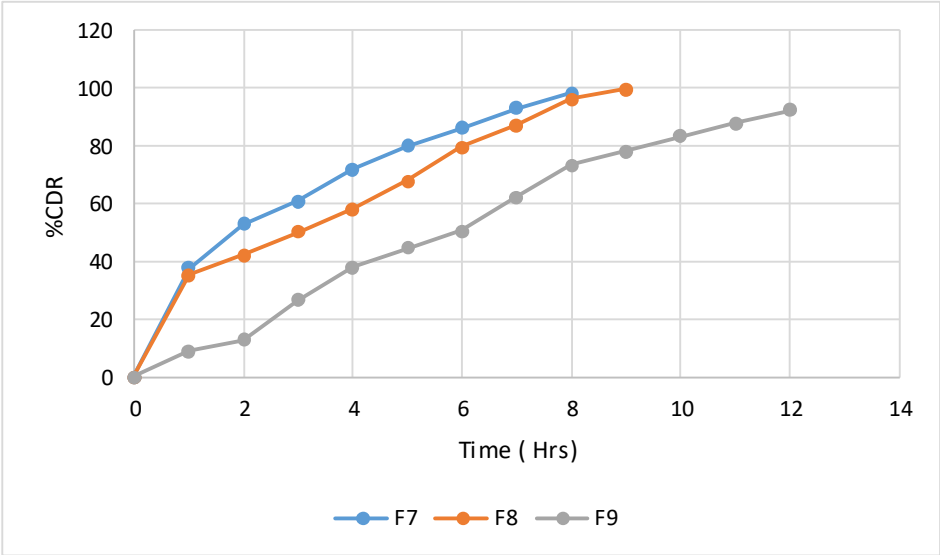


Fig.10: Percentage of drug release graph of formulations F7-F9

The table displays the drug release profiles from three different formulations of Lovastatin (F7, F8, F9) over a 12-hour period. Each formulation starts with zero release at the beginning (0 hours). Over time, F7 shows a fairly rapid and consistent release rate, reaching near complete release at 98.84% by the 8th hour and maintaining this level with minimal increase thereafter. F8 also demonstrates a steady increase in release, albeit slightly slower than F7 initially, but eventually achieves a high level of release at 99.56% by the 9th hour. F9, in contrast, starts with the slowest release and continues at a slower pace throughout the 12 hours, achieving only 92.14% release by the end of the period. This suggests that F9 has the most controlled and extended release profile of the three, while F7 and F8 release the drug more quickly, which might be due to differences in the composition or manufacturing processes of the formulations.

Kinetics Analysis for F4

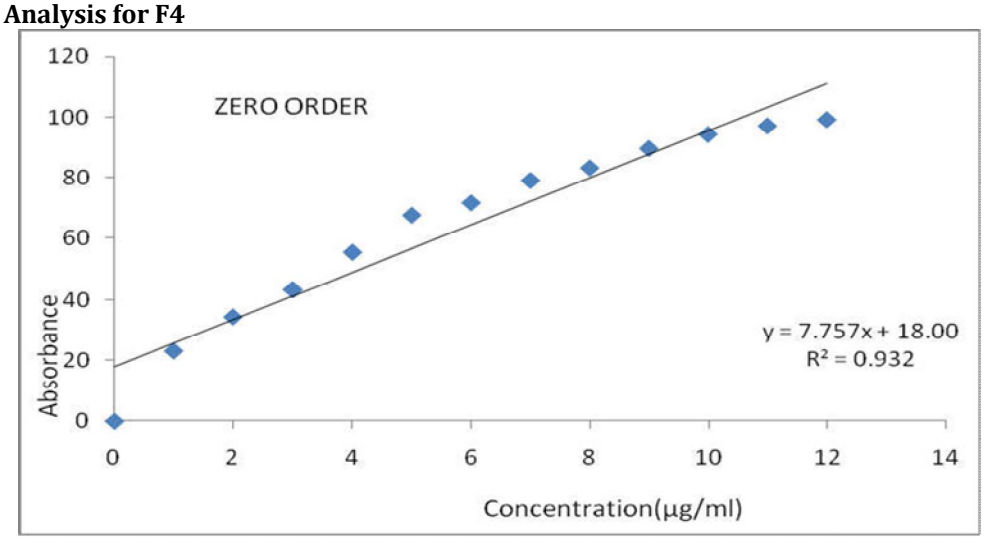


Fig.11: Zero Order Plot for F4

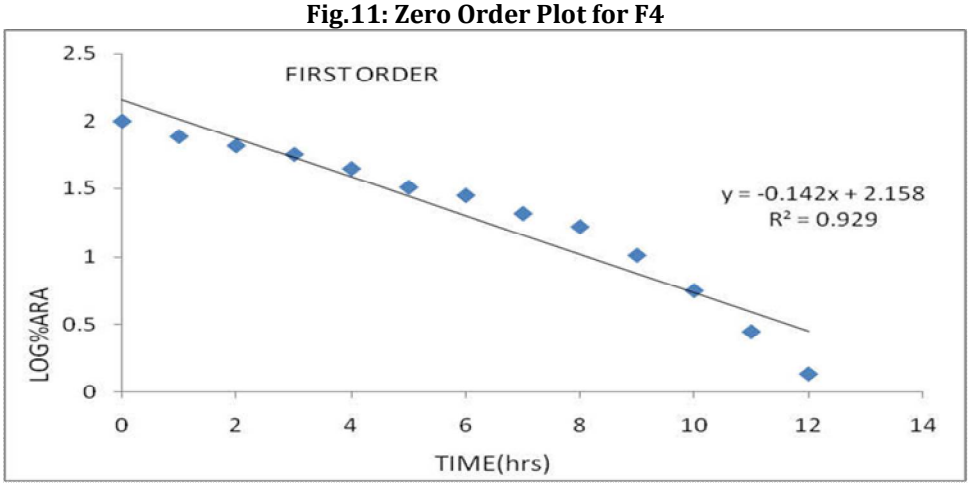


Fig.12: First Order Plot for F4

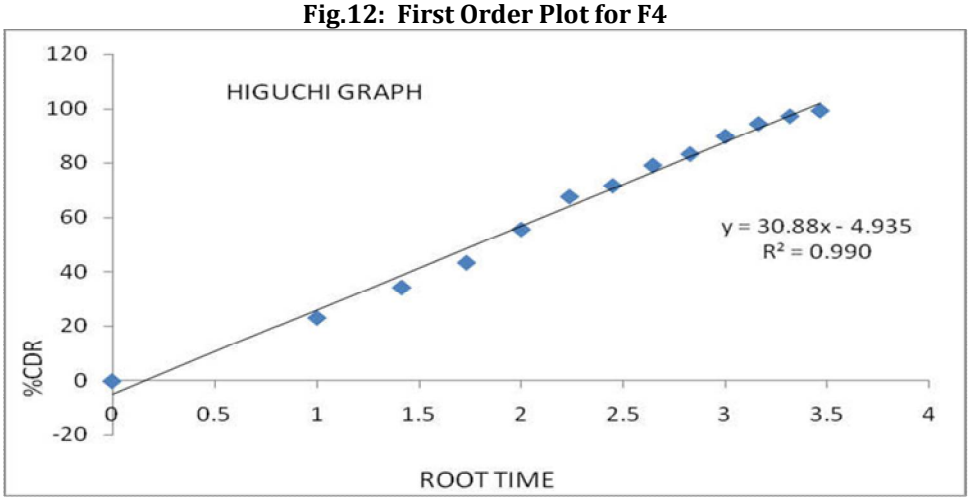


Fig.13: Higuchi graph for F4

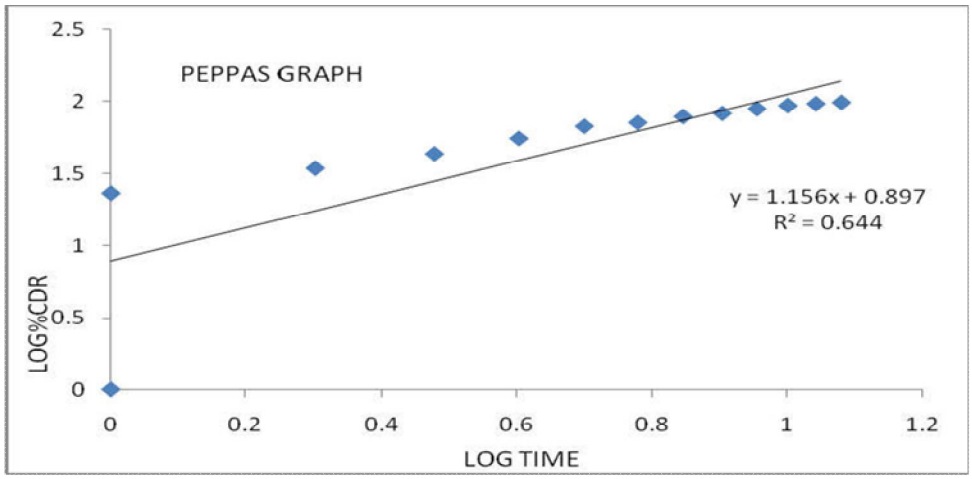


Fig.14: Peppas graph for F4

Drug release kinetics of F4 formulation

Table 11: Drug release kinetics of F4 formulation

S.NO	Zero order	First order	Higuchi	Peppas
Code	R^2	R^2	R^2	R^2
F4	0.932	0.929	0.990	0.664

With a coefficient of determination (R2) values of 0.932, 0.929, 0.990, and 0.664 for Zero order, first order, Higuchi, and Korsmeyer Peppas, respectively, the formulation F4 exhibits high levels of accuracy. A steady drug release rate via diffusion was shown by the data's high linearity with the Zero order. The data was fitted into the Korsmeyer Peppas equation to validate this diffusion process, and the optimized formulation also revealed a linear connection with an n value of 1.156. The value of n indicates the transport mechanism for Super case II. The Higuchi model accurately represented the improved formulation's release kinetics, showing a zero-order drug release with a super case II transport mechanism.

CONCLUSION

The Nanosponges of Lovastatin were prepared using the solvent evaporation method. Eudragit RS100, Polyvinyl alcohol (PVA) was used as a polymer; Acetone was used as the solvent. The prepared nanosponges were evaluated for various parameters, revealing intriguing results regarding the efficient preparation of the nanosponge. F4 outperforms the other eight formulations with its superior results. Solubility studies of Lovastatin: Solubility of Lovastatin pure drug in Water, Ethanol, Methanol, 0.1 N HCl, pH 6.8 Buffer was studied. It was found to be 0.0019mg/ml in distilled water, 3.3 mg/ml in Ethanol, 44 mg/ml in methanol, 0.042 mg/ml in 0.1N HCL, 0.005 mg/ml in Phosphate buffer pH 6.8. Optical microscopy was used to determine the particle size of the nanosponge, and it was observed that the nanosponges were uniform in size. The average particle size of all formulations ranges from 312.2 nm to 420.2 nm. The entrapment efficiency of formulation F1 was found to be 79.12%, formulation F2 was found to be 82.48%, formulation F3 was found to be 80.54%, formulation F4 was found to be 85.16%, formulation F5 was found to be 78.02%, and formulation F6 was found to be 79.24%, formulation F7 was found to be 73.84%, formulation F8 was found to be 74.88%, and F9 was found to be 72.12 %. Among all the formulations, F8 shows high entrapment efficiency of 85.16 %.

REFERENCES

1. Targe BM, Moreshwar P, Patil, Amol C, Jahagirdar, Baliram D. (2015). Nanosponges - An Emerging Drug Delivery System. International Journal Of Institutional Pharmacy and Life Sciences;5(6):ISSN 2249-6807.
2. Sri KV, Santhoshini G, Sankar DR, Niharika K. (2018). Formulation and Evaluation of Rutin Loaded Nanosponges. Asian Journal of Research in Pharmaceutical Sciences;8(1):21-24.
3. Gupta A, Sehgal V, Mehan S. (2011). Hyperlipidemia: An Updated Review.International Journal of Biopharmaceutical and Toxicological Research ;1(1):81-89.
4. Lovastatin - DrugBank [Internet]. Drugbank.ca. 2019
5. Suparna S, Mannur, Karishma K, Majik, Vinayak S, Mastiholimath et al. (2016). Development and Evaluation of Liquid and Solid Self-Microemulsifying Drug Delivery System of Lovastatin. Asian Journal of Pharmaceutics ;10 (1):22-34.

6. Srinivas P, Sreeja K. (2013). Formulation and Evaluation of Voriconazole Loaded Nanosponges for Oral and Topical Delivery. International Journal of Drug Development and Research;5(1):55-69.
7. Malpani A, Raju SA, Hiremath SN. (2009). Improved Dissolution Characteristics of Lovastain By Inclusion in B-CD AND Hp B-CD. Research J. Pharm. and Tech;2 (1):110-113.
8. Vinodh S, Mannur, Karishma K. Majik, Vinayak S. Mastiholimath. (2015). Formulation and Comparative Studies of Lovastatin Loaded Polymeric Nanoparticle Prepared By Ionic Gelation and Solvent Evaporation Technique. International Journal of Pharm Tech Research:6(11):4796- 4803.
9. Reddy KTK, Haque MA. (2024). LC-MS/MS Bioanalytical Procedure for Atrasentan in Human Plasma: Method Development and Validation. International Journal of Pharmaceutical Quality Assurance.15(2):605-610
10. Papinaboina Venkata Rao, Chinnakadoori Sanjeeva Reddy, Ravi Kumar Marram, Dantu Durga Rao, (2012). Simultaneous Determination Of Omeprazole And Domperidone In Capsules And *In Vitro* Dissolution Studies By Using Stability Indicating UPLC, Journal of liquid chromatography & related technologies, 35 (16), 2322-2332.
11. Niroja Vadagam, Sharath Babu Haridasyam, Muvvala Venkatanarayana, Narasimha S. Lakka, Sanjeeva R. Chinnakadoori, (2023). Separation and quantitative estimation of stereo-selective enantiomers of montelukast in pharmaceutical drug substance and tablets dosage forms by using stability-indicating normal phase-HPLC method, Chirality, 35(12), 952-965.
12. Niroja Vadagam, Sharath Babu Haridasyam, Muvvala Venkatanarayana, Narasimha S Lakka, Sanjeeva R Chinnakadoori, (2023). Separation and quantitation of valacyclovir enantiomers using stability-indicating chiral liquid chromatography method with a chiral stationary phase of amylose tris-(3,5-dimethylphenylcarbamate), Separation Science Plus, 6(12), 2300145.
13. Narasimha S Lakka, Chandrasekar Kuppan, Niroja Vadagam, Poornima Ravinathan, Kalyani Chepuri, Sanjeeva R Chinnakadoori, (2023). Molecular docking, in-vitro anticancer evaluation and ADME profiling of 7-Oxo Midostaurin, Journal of Molecular Structure, 1293, 136159.
14. Niroja Vadagam, Sharath Babu Haridasyam, Muvvala Venkatanarayana, Narasimha S Lakka, Sanjeeva R Chinnakadoori, (2024). Separation and simultaneous estimation of enantiomers and Diastereomers of muscarinic receptor antagonist Solifenacin using stability-indicating Normal-phase HPLC technique with chiral stationary phase amylose tris-(3,5-dimethylphenylcarbamate), Chirality, 36(2), e23632.
15. Mohan Pasham, Sharath Babu Haridasyam, Niroja Vadagam, NVVD Praveen Boppy, Sanjeeva R Chinnakadoori, Narasimha S Lakka, (2024). Separation and quantification of organic-related impurities of beta-adrenergic receptor blocking agent propranolol in pharmaceutical solid dosage forms: Impurity profiling using stability-indicating HPLC method, 7(1), 2300159.
16. N. V. V. D. Praveen Boppy, Sharath Babu Haridasyam, Niroja Vadagam, Muvvala Venkatanarayana, Sanjeeva R. Chinnakadoori, Narasimha S. Lakka, (2024). Separation and quantification of organic-related impurities of anti-histamine drug hydroxyzine in pharmaceutical dosage forms using stability-indicating high-performance liquid chromatography, liquid chromatography-mass spectrometry, and high-resolution mass spectrometry techniques, Separation Science Plus, 2300157.
17. Basavaraj K, Nanjwade, Ganesh K, Derkar, Hiren M, Bechra et al. (2011). Design and Characterization of Nanocrystals of Lovastatin for Solubility and Dissolution Enhancement. Nanomedicineand Nanotechnology ;2(2):1- 7
18. Kothule KU, Kesharwani P, Gidwani SK, Paraag. (2010). Development and Characterization of Chitosan Nanoparticles and Improvement of Oral Bioavailability of Poorly Water-Soluble Acyclovir. Research J. Pharm. and Tech. 3(4): 1241-1245