Journal of Molecular Science

Journal of Molecular Science
Volume 35 Issue 3, Year of Publication 2025, Page 870-880
DoI-10.004687/1000-9035.2025.119

Journal of Molecular Science

www.jmolecularsci.com ISSN:1000-9035

Formulation And Evalution Of Felodipine-Loaded Polymeric Nanosponges Using The Emulsion Solvent Diffussion Method

Lonkar Vidya G.[*1], Nagargoje Sanjay S.[2], Hapse Sandip A.[3]
[1]Research Scholar, Shubham University, Bhopal, Madhya Pradesh (MP)-462038
[2]Associate Professor, S.V.N.H.T. College of Pharmacy, Rahuri, Ahmednagar Maharashtra (MS)-413705
[3]Assistant Professor, Dr. V. V. P. F's College of Pharmacy, Vilad Ghat, Ahmednagar Maharashtra (MS)-414111

Article Information
Received: 06-09-2025
Revised: 24-09-2025
Accepted: 16-10-2025
Published: 25-11-2025

Keywords
Nanosponges, Felodipine, Drug delivery, Bioavailability enhancement, Sustained release.

ABSTRACT
Nanotechnology has revolutionized healthcare, particularly in targeted drug delivery systems, by enhancing solubility, stability, bioavailability, and controlled release profiles of therapeutic agents. Among various nanocarriers, nanosponges—porous, sponge-like structures—offer high drug loading and sustained release, making them ideal for hydrophobic drugs. This study focuses on the formulation and evaluation of felodipine-loaded nanosponges to overcome the drug's poor aqueous solubility and erratic oral bioavailability. Felodipine, a calcium channel blocker used in hypertension management, was incorporated into polymeric nanosponges via the emulsion solvent diffusion method using ethyl cellulose as the polymer and polyvinyl alcohol as the stabilizer.Twelve formulations (F1–F12) were prepared and assessed for production yield, particle size, polydispersity index (PDI), zeta potential, entrapment efficiency, and in vitro drug release. The optimized formulation, F9, exhibited a particle size of 186.6 nm, PDI of 0.140, zeta potential of +19.99 mV, and entrapment efficiency of 98.44%. SEM analysis confirmed spherical, porous morphology, while FTIR and DSC studies validated drug-polymer compatibility and thermal stability. In vitro dissolution studies revealed biphasic sustained release over 8 hours, with drug release kinetics best fitting the Korsmeyer–Peppas model (r^2 = 0.9932), indicating diffusion-controlled release.These findings underscore the potential of nanosponges as effective carriers for enhancing the solubility and bioavailability of poorly water-soluble drugs like felodipine, offering a promising strategy for improved therapeutic outcomes and patient compliance.

1. INTRODUCTION:

1.1 Nanotechnology in Drug Delivery:

Nanotechnology involves the manipulation of materials at the 1–100 nm scale, enabling transformative innovations across medicine, water purification, ICT, and materials engineering (1,2). In healthcare, it has revolutionized diagnostics and therapeutics by facilitating targeted, personalized, and efficient drug delivery systems (3,4). Approximately 13% of pharmaceutical products now incorporate nanotechnology-based carriers, particularly for biomolecules such as proteins and DNA. Nanomedicine, the clinical application of nanoscience, is instrumental in treating central nervous system, cardiovascular, respiratory, and oncological disorders by enhancing therapeutic efficacy and minimizing systemic toxicity (5,6). Nanocarriers—including solid lipid nanoparticles (SLNs), polymeric micelles, dendrimers, carbon nanotubes, magnetic and inorganic particles, and nanosponges—enable controlled release and improved bioavailability (8,9). These systems are increasingly applied in diagnostics, orthopedics, tissue engineering, neurodelivery, and dental care. Literature by Godge et al. (2024, RJPS) and others has emphasized the versatility of lipid-based and polymeric nanocarriers in overcoming solubility and permeability barriers, particularly for BCS Class II drugs (10-12).

1.2. Polymeric Nanosponges: Structure and Utility: Polymeric nanosponges are porous, cross-linked structures capable of encapsulating both hydrophilic and lipophilic drugs (3,8,9). Their three-dimensional architecture contains internal cavities for drug entrapment, while surface modifications allow site-specific targeting. These systems offer sustained release, microbial protection, toxin adsorption, reduced dosing frequency, and stability across diverse pH and temperature conditions.Nanosponges are particularly effective for poorly soluble antihypertensives such as Felodipine, a BCS Class II drug. They can be synthesized via cyclodextrin cross-linking, solvent evaporation, emulsion diffusion, and ultrasound-assisted techniques (9,14). Drug loading typically involves solvent evaporation or β-cyclodextrin dispersion, with formulation parameters influenced by drug properties, polymer type, temperature, and substitution degree. Characterization includes assessments of yield, solubility, thermal behavior (DSC/TGA), particle size, zeta potential, drug loading, crystallinity (XRD), chemical interactions (FTIR), and morphology (microscopy) (15,16) and others have demonstrated the potential of polymer nanocomposites and nanosuspension technologies in enhancing drug stability, releasing kinetics, and bioavailability (10,17,18). These findings support the rationale for using emulsion solvent diffusion to fabricate Felodipine-loaded nanosponges (13,19).

1.3 Hypertension and Nanotechnological Interventions:
Hypertension remains a major global health concern, often leading to stroke, myocardial infarction, and other cardiovascular complications. Conventional antihypertensive therapies are limited by poor solubility, extensive first-pass metabolism, and P-glycoprotein-mediated efflux, resulting in low bioavailability and frequent dosing. Nanotechnology addresses these limitations by encapsulating drugs in nanoparticles (~100 nm), enhancing absorption, bypassing metabolic barriers, and enabling targeted delivery (6,7,21).Surfactants such as Solutol HS 15 and Poloxamer 188 inhibit P-gp and CYP450 enzymes, further improving drug efficacy. Emerging therapies, including AT2 receptor agonists, PDE-5 inhibitors, and ACE2 modulators—benefit from nano-formulations that enhance solubility, permeability, and sustained release. Techniques such as mucoadhesion and permeation enhancement improve gastrointestinal absorption, while sub-100 nm, negatively charged particles favor lymphatic uptake.Stable emulsions like SMEDDS and SNEDDS have optimized the pharmacokinetics of drugs such as olmesartan, amlodipine, and felodipine. The integration of polymeric nanosponges into these platforms offers a promising strategy for personalized and long-acting antihypertensive therapy, as supported by recent reviews on nanosuspension and inclusion complex technologies (17,20).

2. MATERIALS AND METHODS:
2.1 Materials:
Felodipine, polyvinyl alcohol, and dichloromethane were obtained from Dhamtec Pharma and Consultant, Navi Mumbai. Ethyl cellulose was acquired from an authorized laboratory supplier, while methanol and distilled water were sourced from the Drug library of college.A variety of analytical and processing instruments were employed throughout the experimental procedures. Quantitative assessments were carried out using a Shimadzu electronic balance and a Jasco V-630 UV-Visible spectrophotometer. The formulation process incorporated equipment such as a magnetic stirrer, sonicator, magnetic shaking incubator, and centrifuge, all provided by Remi Instruments Ltd. Particle size and zeta potential analyses were performed using the Horiba Scientific SZ-100 particle size analyzer.

2.2 Preparation of Nanosponges
1. Organic Phase Preparation
Ethyl cellulose and felodipine were carefully weighed and dissolved in dichloromethane to produce a unique organic phase. This ensured the drug's complete solubilization within the polymeric matrix, promoting constant nanosponge formation. To guarantee homogeneity, the solution was gently shaken before processing.

2. Aqueous Phase Preparation
Dispersing polyvinyl alcohol (PVA) in distilled water and heating it to 80 °C while stirring continuously produced a clear, uniform solution. During emulsification, PVA was utilized as a stabilizing agent, and the high temperature aided in its full dissolution. The solution was allowed to cool to room temperature before being utilized.

3. Emulsification and Stirring
The produced organic phase was constantly agitated with magnetic stirring at 1200 RPM as the aqueous phase was progressively combined with it dropwise. To encourage solvent dispersion and the formation of nanosponge by phase separation and polymer crosslinking, the process was run for two and a half hours. A uniform, milky-looking colloidal dispersion was the end result.

4. Collection and Washing
The produced nanosponges were extracted from the dispersion by filtering them via Whatman filter paper. The collected nanosponges were again washed with distilled water to remove any residual surfactant, solvent, or unreacted chemicals. By reducing potential

toxicity, this purification step ensured product quality.

5. Drying
The purified nanosponges were dried in a hot air oven at 40 °C for 24 hours in order to remove any last traces of moisture and solvent. The gentle drying conditions prevented agglomeration and preserved the size of the nanosponge. The dry powder that was created was stored in an airtight container for further characterization.

2.3 Screening of different polymeric carriers by preparing various batches of nanosponges
Various polymeric carriers, including Eudragit S100, Eudragit L100, and Ethyl Cellulose (EC), together with stabilizers such polyvinyl alcohol (PVA) and Kolliphor P188, were used to create empty nanosponges. Dichloromethane (DCM) was used as the organic solvent. By altering the kind and concentration of the carrier polymer while keeping the solvent and stabilizer ratios constant, twelve formulations (F1–F12) were created. The produced nanosponges were assessed for particle size distribution, dispersion behaviour, and visual qualities. Ethyl cellulose-containing formulations showed a narrow polydispersity index (PDI < 0.3), particle sizes ranging from 150 to 1000 nm, and high homogeneity, smooth surface, and lack of phase separation. On the other hand, formulations made with Eudragit polymers had bigger particles (>1000 nm) and poor dispersion, suggesting that the nanosponge production was not complete. As a result, ethyl cellulose-based nanosponges were found to be the best since they produced homogeneous, spherical, and nanosized particles that were appropriate for additional optimization and drug loading research.

Table No. 2.1 . Formulation of different batches of nanosponges

Material	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Eudragit S100 (mg)	150	200	250	300	_	_	_	_	_	_	_	_
Eudragit L100 (mg)	_	_	_	_	150	200	250	300	_	_	_	_
Ethyl Cellulose (EC) (mg)	–	–	–	–	–	–	–	–	50	100	150	200
Polyvinyl Alcohol (PVA) (w/v)	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	–	–	–	–
Dichloromethane (DCM) (ml)	20	20	20	20	20	20	20	20	20	20	20	20
Kolliphor P188 (w/v)	–	–	–	–	–	–	–	–	0.5%	0.5%	0.5%	0.5%
Distilled Water (ml)	100	100	100	100	100	100	100	100	100	100	100	100

Formulation of felodipine nanosponges by emulsion solvent diffusion method:
Felodipine-loaded nanosponges were prepared using the emulsion solvent diffusion method, employing ethyl cellulose as the polymer. The dispersed phase was formulated by dissolving a specified amount of Felodipine and polymer in 30 mL of dichloromethane. Separately, the aqueous phase was prepared by dissolving polyvinyl alcohol in 100 mL of distilled water and heating the solution to 80 °C with continuous stirring. The dispersed phase was then added dropwise into the aqueous phase under magnetic stirring at 1200 rpm for approximately 2.5 hours. The resulting nanosponges were collected by filtration, dried in an oven at 40 °C for 24 hours, and stored in a vacuum desiccator to eliminate residual solvent.

Table No. 2.2 Formulation of different batches of Drug Loaded Nanosponges

Sr. No.	Ingredients	Formulations											
		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1.	Felodipine (Mg)	100	100	100	100	100	100	100	100	100	100	100	100
2.	Ethyl Cellulose (Mg)	50	100	150	300	200	150	50	300	300	300	150	150
3.	Poly Vinyl Alcohol (mg)	100	150	200	400	300	400	100	200	400	100	200	200
4.	Dichloromet hane (ml)	30	30	30	30	30	30	30	30	30	30	30	30
5.	Kolliphor P188(w/v)	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5 %	0.5 %	0.5%	0.5 %	0.5%	0.5%
6.	Distilled Water (ml)	100	100	100	100	100	100	100	100	100	100	100	100

2.4 Characterization Techniques
1. The estimation of the maximum absorbance (λmax)
Using a blank solution of phosphate buffer pH 6.8, the standard stock solution was scanned in the UV spectrophotometer between 200 and 400 nm. The highest felodipine absorption levels were measured at 234 and 360 nm, and they were compared to the highest levels of the reference samples specified in the Indian Pharmacopoeia.

1. Physical Characteristics:
To verify conformity with established specifications, the drug's appearance, color, and odor were assessed. The capillary method was used to determine the melting point, which offers information about the

Journal of Molecular Science
Volume 35 Issue 3, Year of Publication 2025, Page 870-880
DoI-10.004687/1000-9035.2025.119

compound's identity and purity. Impurities or degradation products may be present if the reported melting range is not followed. Before formulation, the felodipine sample's stability and validity were first confirmed by these observations. Consequently, the evaluation created a baseline for future formulation and analysis research.

3. Solubility Test:

The solubility profile of felodipine was examined in several solvents, such as methanol, water, dichloromethane, and chloroform. To find the best solvent solution for developing formulations and loading drugs into nanosponges, this assessment was essential. Due to felodipine's weak water solubility, finding a solvent with the right solubility improves medication dispersion and encapsulation effectiveness. The solubility trends that were observed offered crucial direction for the selection of polymeric materials and preparation methods that would improve the drug's bioavailability in its final dosage form.

4. Fourier Transform Infrared (FTIR) Spectroscopy:

Fourier Transform Infrared (FTIR) Spectroscopy: This technique was used to examine the chemical compatibility of felodipine with the chosen polymers. To find any possible shifts, peaks that would suggest chemical interactions, or peaks that might disappear or form, the spectra were compared. It was proven that there was no substantial chemical bonding between the medicine and excipients during formulation because there were no notable alterations in the dstinctive peaks. This outcome confirmed the stability and compatibility of the ingredients employed in the preparation while guaranteeing the structural integrity of felodipine within the nanosponges.

5. Percentage Yield:

The practical weight of the final product was compared to the theoretical weight of each ingredient employed in the formulation to determine the prepared nanosponges' percentage yield. The effectiveness and repeatability of the preparation procedure are reflected in this metric. A high yield shows low material loss during synthesis, filtration, and drying processes, proving process improvement. On the other hand, a lower yield can indicate inefficiencies in the process or incomplete polymerization. To guarantee the nanosponge formulation's scalability and cost-effectiveness, it is imperative to assess the yield percentage.

6. SEM Analysis:

Scanning electron microscopy (SEM) was used to analyse the surface morphology and structural features of the created nanosponges. A spherical or nearly spherical shape with a uniformly smooth surface texture was visible in the micrographs. This homogeneity in morphology indicates appropriate cross-linking between polymer chains and successful drug encapsulation in the nanosponge matrix. Good mechanical integrity is also indicated by the lack of surface fissures or imperfections, which is preferable for stable drug release behavior and storage stability.

7. Particle Size:

After being dispersed in an appropriate medium, the average particle size of the produced nanosponges was determined using Dynamic Light Scattering (DLS). A restricted size distribution within the nanometer range was validated by the research, suggesting that the nanosponge production process was successful. A smaller particle size increases the surface area, which improves the bioavailability and rate of drug dissolution. Another important factor in guaranteeing repeatable drug release kinetics is particle size homogeneity. The selected preparation technique is confirmed to be suitable for producing nanoscale drug carriers by these results.

8. Zeta Potential:

The surface charge and electrostatic stability of the nanosponge suspension were ascertained using zeta potential analysis. To prevent aggregation and guarantee colloidal stability, a high enough positive or negative zeta potential value indicates strong repulsive forces between particles. Stable surface characteristics are essential for preserving dispersion uniformity and shelf life, and the observed zeta potential values verified this. This characteristic also sheds light on possible interactions that can occur between the administered nanocarriers and biological membranes.

9. Entrapment Efficiency:

Using UV-visible spectrophotometry, the amount of unentrapped felodipine in the supernatant following centrifugation was measured to assess the drug entrapment efficiency of the nanosponge formulation. The percentage of medication that was successfully incorporated into the polymeric matrix in relation to the total amount employed is represented by this measure. A high entrapment efficiency boosts the formulation's therapeutic potential by indicating strong drug–polymer interactions and efficient drug loading. The outcomes validated the appropriateness of the chosen polymers and preparation technique in attaining the best possible encapsulation.

$$\%\ Percentage\ entrapment = \frac{Entrapped\ drug\ (mg)}{Total\ drug\ added\ (mg)} \times 100$$

10. In Vitro Release:

The amount of unentrapped felodipine that remained in the supernatant after centrifugation was measured using UV-visible spectrophotometry to determine the drug entrapment efficiency of the nanosponge formulation. This measure displays the percentage of drug that was successfully incorporated into the

Journal of Molecular Science
Journal of Molecular Science
Volume 35 Issue 3, Year of Publication 2025, Page 870-880
DoI-10.004687/1000-9035.2025.119

polymeric matrix in relation to the total amount used. A high entrapment efficiency indicates powerful drug–polymer interactions and effective drug loading, increasing the formulation's potential for therapeutic usage. The results confirmed that the selected polymers and preparation method were suitable for achieving the optimal encapsulation.

11. Release Kinetics:

To clarify the drug release mechanism, the in vitro release data were further examined using mathematical models such the zero-order, first-order, Higuchi, and Korsmeyer–Peppas equations. According to the best-fitting model, felodipine was released from the nanosponges via a sustained, diffusion-controlled process. This suggests that the total release process is controlled by drug diffusion across the polymeric network. Predicting formulation performance, maximizing polymer composition, and customizing release characteristics for intended therapeutic results are all made easier with an understanding of kinetic behavior.

3. RESULTS AND DISCUSSION:

A significant influence of carrier type on nanosponge properties was found in the comparative analysis of formulations F1–F12 (Table no.2.1). Turbid dispersions with evident aggregation and a wide particle size distribution (1150–1700 nm) were produced by formulations using Eudragit S100 and L100 (F1–F8), indicating poor compatibility between the polymer and the dichloromethane system. On the other hand, formulations based on ethyl cellulose (F9–F12) generated transparent dispersions with distinct spherical nanosponges that had great homogeneity (PDI < 0.3) and mean particle sizes ranging from 150 to 1000 nm. The hydrophobic and semi-permeable properties of ethyl cellulose, which promoted stable nanosponge matrix formation and effective solvent diffusion during emulsification, are responsible for the enhanced performance of EC-based systems. Furthermore, the stabilizing effect of Kolliphor P188 improved emulsion stability and inhibited particle coalescence during solvent evaporation. Superior physicochemical properties of the resultant EC-based nanosponges supported the choice of ethyl cellulose as the best carrier polymer for further formulation development and drug inclusion.

3.1 Physical Characteristics:

Felodipine's physical and organoleptic characteristics were assessed. The drug had the appearance of an amorphous, light-yellow powder that was odorless, as described in the literature. Thiele's tube method confirmed its identification and purity by determining that its melting point was 142 °C, which is within the specified range of 141 to 145 °C. These results suggest that the medication was genuine and devoid of significant contaminants that might compromise the effectiveness of the formulation.

Table No. 3.1 Melting point of Felodipine

Sr. No.	Method	Observed M.P.	Standard M.P
1.	Thieles Tube	142 °C	141-145 °C

3.2 Solubility:

Felodipine is insoluble in water, but soluble in ethanol, dichloromethane, and DMSO, according to solubility testing. Because felodipine is poorly soluble in water, formulations based on nanosponge are required to improve dissolution and bioavailability. Given the drug's established Class II nature according to the Biopharmaceutics Classification System (BCS)— low solubility but high permeability—these results, given in Table No. 3.2., call for formulation techniques that enhance the drug's solubility profile.

Table No. 3.2 Solubility test for Felodipine in different solvents

Sr. No	**Solvent**	**Soluble**	**Sparing Soluble**	**Insoluble**
1.	Ethanol	+	-	-
2.	Dichloromethane	+	-	-
3.	DMSO	+	-	-
4.	Water	-	-	+

3.3 Selection of Wavelength:

The π–π* electronic transitions of Felodipine's aromatic and conjugated systems were represented by the strong peaks in its UV absorption spectra at 234 nm and 360 nm. Because of its distinct and sharp peak, 360 nm was chosen as the analytical wavelength for the ensuing investigations. For the quantitative investigation of felodipine in nanosponge formulations, this wavelength offered the best sensitivity and repeatability. The absorption peak obtained is shown in Figure No. 3.1.

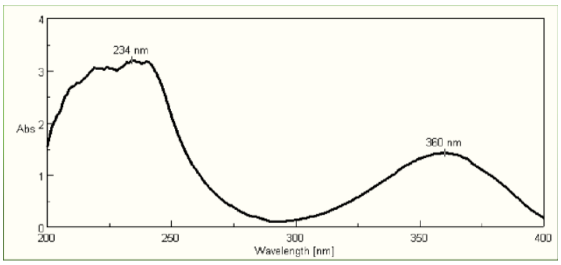

Figure No. 3.1 Ultra-Violet (UV) absorption spectra of Felodipine

3.4 Construction of calibration curve of Felodipine

A calibration curve with a correlation coefficient ($r2$ = 0.998) that was built in the concentration range of 2–10 µg/mL at 360 nm showed good linearity (Table No. 3.3). The developed UV spectrophotometric method's accuracy in quantifying felodipine in future formulation studies is demonstrated by the straight-line relationship, which validates conformity with Beer-Lambert's law within the measured range.

Journal of Molecular Science
Journal of Molecular Science
Volume 35 Issue 3, Year of Publication 2025, Page 870-880
DoI-10.004687/1000-9035.2025.119

Table no. 3.3 Concentration and absorbance values for estimation of Felodipine

Sl. No	Concentration (µg/ml)	Absorbance at 360 nm
1.	0	0
2.	2	0.0394±0.12
3.	4	0.0799±0.21
4.	6	0.1182±0.34
5.	8	0.1576±0.42
6.	10	0.1970±017

*n=3

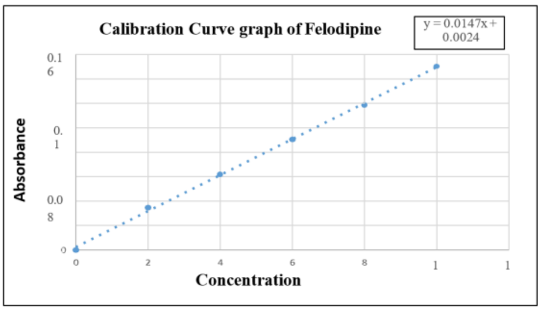

Figure No. 3.2 Calibration Curve graph of Felodipine API

3.5 Compatibility Studies:

a. FTIR Analysis:

The presence of functional groups and component compatibility were confirmed by the FTIR spectra of Felodipine (Figure No. 3.3), PVA, and Ethyl Cellulose, which displayed distinctive peaks for O–H (3375–3483 cm⁻¹), C–H (2982 cm⁻¹), C=O (1695 cm⁻¹), and C–O–C (1273 cm⁻¹), as well as 1193.72 cm⁻¹ (in-plane = C–H bending) and 724.139 cm⁻¹ (C–H rocking) functional groups that don't significantly change their peaks or vanish. The stability of the nanosponge system is ensured by the absence of new peaks, which verify the chemical compatibility and lack of interactions between the drug and polymers during formulation.

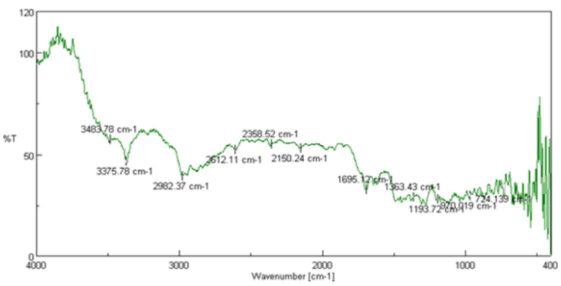

Figure No. 3.3 FTIR analysis of the physical mixture containing Felodipine, PVA, and Ethyl Cellulose

b. DSC Studies:

The improved nanosponge formulation's DSC thermogram (Figure No. 3.4) showed a distinct endothermic peak at 46.85 °C, which is the melting point of felodipine inside the polymeric matrix. A partially amorphous or solid-solution condition that is conducive to better dissolution is suggested by the decrease and broadening of the peak intensity in comparison to the pure drug, which show successful drug encapsulation and molecular dispersion inside the nanosponge network.

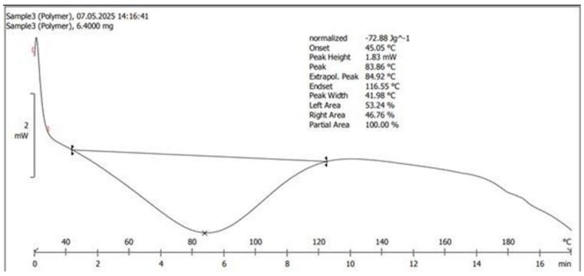

Figure No. 3.4: DSC Thermogram of Nanosponges (Batch F 2).

3.6 Percentage Yield

Felodipine nanosponges' percentage yield ranged from 78.63% to 98.15% (Table No. 3.4) for each formulation (F1–F12). Perhaps because of the effective emulsification procedure and the optimum polymer-to-drug ratio, formulation F9 (Figure No. 3.5) had the greatest yield (98.15%). The consistently high yield across batches suggests low material loss throughout the solvent diffusion and recovery processes and good repeatability.

Table No. 3.4 Percentage yield of Felodipine nanosponges

Sr. No	Formulation code	Percentage yield (%)
1.	F1	86.5±0.22
2.	F2	93.21±0.13
3.	F3	87.29±0.24
4.	F4	91.1±0.41
5.	F5	93.97±0.36
6.	F6	85.7±0.33
7.	F7	83.44±0.58
8.	F8	79.89±0.61
9.	F9	98.15±0.15
10.	F10	91.45±0.37
11.	F11	89.08±0.60
12.	F12	78.63±0.11

*n=3

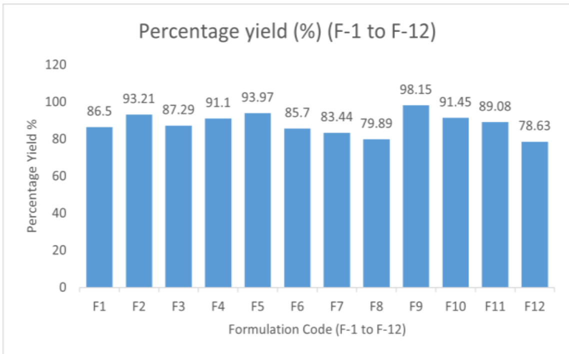

Figure No. 3.5 Percentage yield analysis of Felodipine nanosponges

3.7 Surface Morphology (SEM):

The spherical, distinct, evenly formed felodipine nanosponges with a smooth exterior and porous interior structure were identified by SEM analysis. Within the polymer matrix, the observed morphology facilitates effective drug entrapment and solvent diffusion. Well-formed nanosponges with surface properties that allow for regulated drug release and

Journal of Molecular Science
Journal of Molecular Science
Volume 35 Issue 3, Year of Publication 2025, Page 870-880
DoI-10.004687/1000-9035.2025.119

improved dissolution are indicated. (Figure No.3.6)

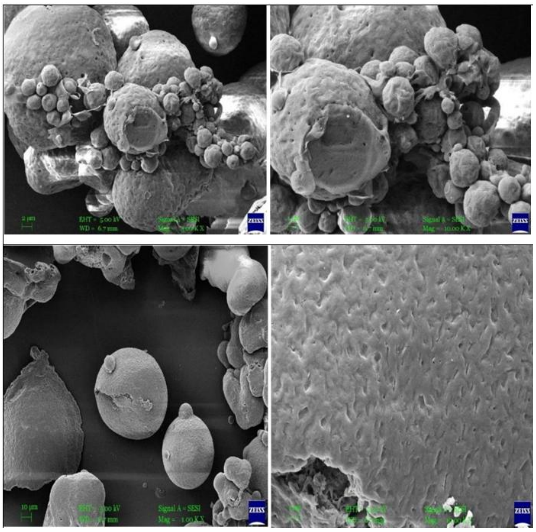

Figure No. 3.6 SEM images of F-9 formulation

3.8 Particle Size Analysis & Polydispersity Index (PDI):

The formulation composition and polymer content of felodipine nanosponges affected their mean particle size, which varied from 186.6 nm (F9) to 1000.6 nm (F7). Formulation F9 had the smallest size of all (186.6 nm) and the lowest PDI of 0.140, suggesting a uniformly small size distribution (Table No,3.5). On the other hand, greater particle size and heterogeneity were caused by higher polymer concentrations (e.g., F6–F7). These findings emphasize how important it is to optimize

polymer ratios in order to attain the desired uniformity at the nanoscale. Particle Size analysis and PDI of formulation is depicted in the following Figure No.3.7 to Figure 3.10.

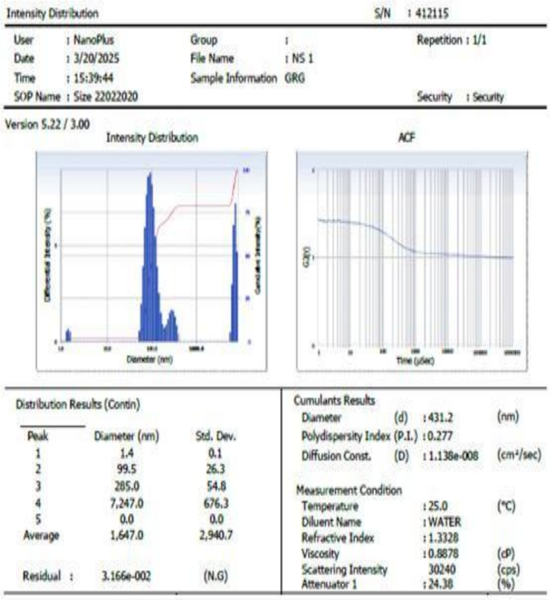

Figure No. 3.7 Particle Size and PDI of Nanosponges (F-1)

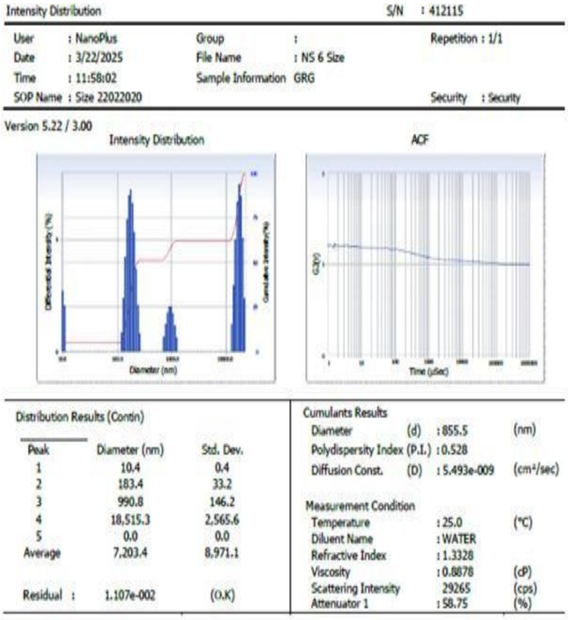

Figure No. 3.8: Particle Size and PDI of Nanosponges (F-6)

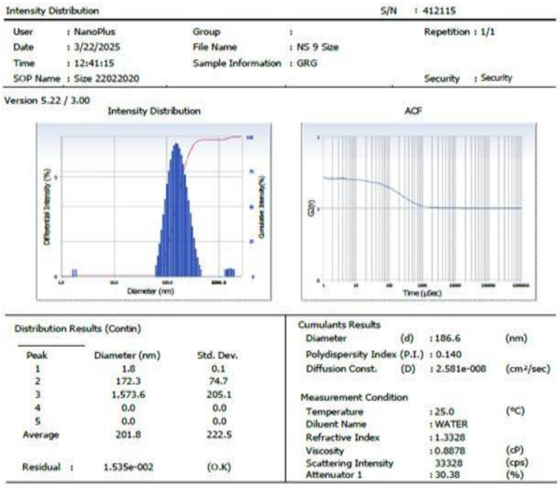

Figure No. 3.9 Particle Size and PDI of Nanosponges (F-9)

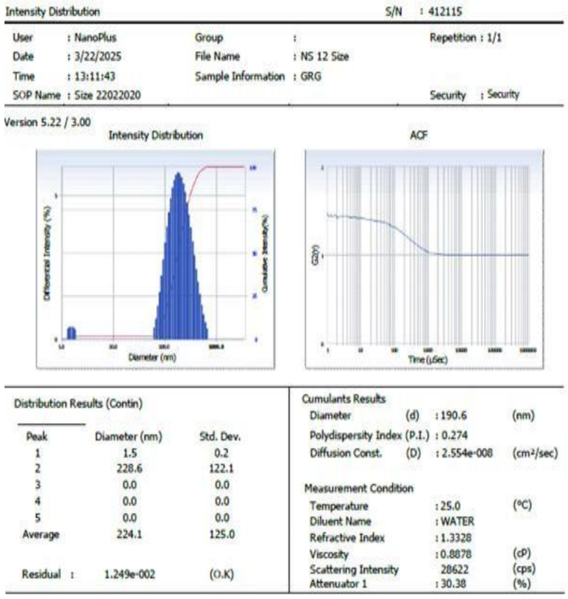

Figure No. 3.10: Particle Size and PDI of Nanosponges (F- 12)

Journal of Molecular Science
Journal of Molecular Science
Volume 35 Issue 3, Year of Publication 2025, Page 870-880
DoI-10.004687/1000-9035.2025.119

3.9 Zeta Potential:

Zeta potential experiments revealed values that varied depending on the combination of the polymer and stabilizer, ranging from –17.65 mV to +19.99 mV across formulations. Particle aggregation was less likely with Formulation F9's improved electrostatic stability and potential of +19.99 mV. Moderate zeta potential values imply that polymer chain steric stabilization also plays a role in the stability of nanosponge dispersion. Zeta potential distribution of formulation F-1 to F-12 is depicted in Figure No. 3.11 to 3.14.

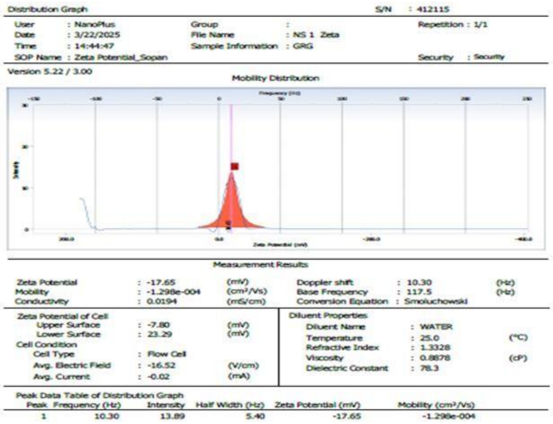

Figure No. 3.11 Zeta Potential of Nanosponges (F-1)

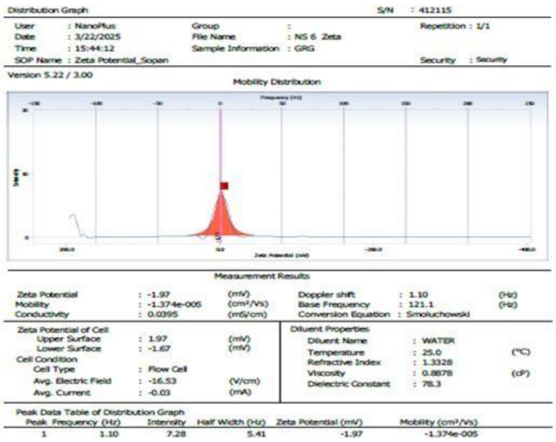

Figure No. 3.12: Zeta Potential of Nanosponges (F-6)

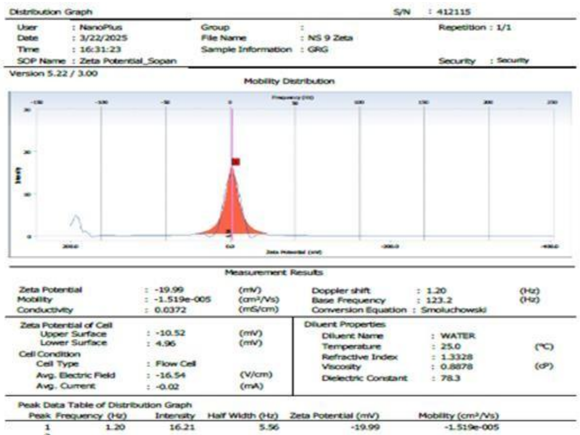

Figure No. 3.13 Zeta Potential of Nanosponges (F-9)

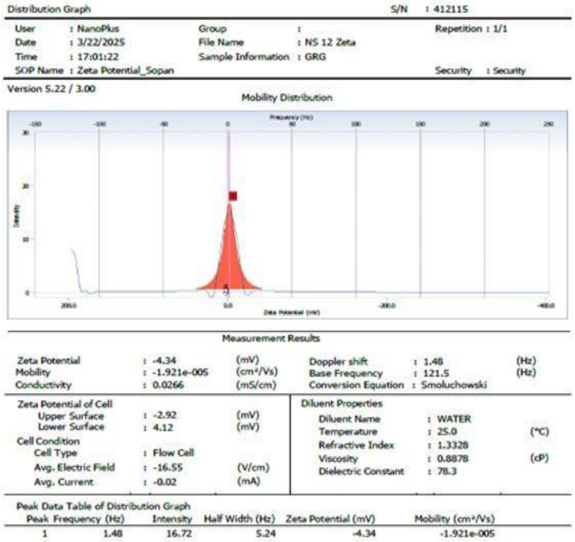

Figure No. 3.14: Zeta Potential of Nanosponges (F-12)

Table No. 3.5 List of particle size, polydispersity index, zeta potential of all batches.

Sr no	Batch name	Particle size(nm)	Polydispersity index (PDI)	Zeta potential
1	**F-1**	431.2	0.277	-17.65
2	**F-2**	251.6	0.302	-5.25
3	**F-3**	262.2	0.458	-1.93
4	**F-4**	259.6	0.191	-1.94
5	**F-5**	250.7	0.283	-0.46
6	**F-6**	855.5	0.528	-1.97
7	**F-7**	1000.6	0.460	-1.63
8	**F-8**	346.0	0.345	-1.96
9	**F-9**	186.6	0.140	19.99
10	**F-10**	254.6	0.192	5.91
11	**F-11**	200.8	0.216	3.63
12	**F-12**	190.6	0.274	-4.34

1.2 Entrapment Efficiency:

The entrapment efficiency of polymeric nanosponges loaded with felodipine varied from 85.29% (F7) to 98.44% (F9), as indicated in Figure 3.15 and Table 3.6. The formulation with the highest entrapment efficiency, F9, demonstrated the best polymer-to-drug ratio and successful encapsulation within the nanosponge matrix. The variance in entrapment efficiency among formulations could be explained by variations in the type, concentration, and diffusion rate of polymers during the emulsification process. In general, formulations with a balanced polymer composition (such as F2, F8, and F9) demonstrated better drug retention, indicating that effective pore formation and cross-linking improve the drug-holding ability of nanosponges.

Table No. 3.6 Entrapment Efficiency of polymeric nanosponges formulations

Sr. No	Formulation Code	Entrapment Efficiency (%)
1.	F1	95.55±012
2.	F2	97.33±0.31
3.	F3	92.19±0.23
4.	F4	93.90±0.37

Journal of Molecular Science
Journal of Molecular Science
Volume 35 Issue 3, Year of Publication 2025, Page 870-880
DoI-10.004687/1000-9035.2025.119

5.	F5	91.21±0.42
6.	F6	87.96±0.19
7.	F7	85.29±0.36
8.	F8	95.47±0.27
9.	F9	98.44±0.62
10.	F10	91.23±0.24
11.	F11	90.04±0.52
12.	F12	88.30±0.45

*n=3

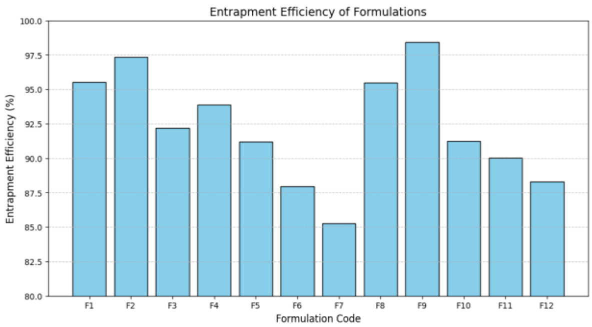

Figure No. 3.15 Entrapment Efficiency of polymeric nanosponges formulations

1.3 *In-Vitro* Release:

According to Table 3.7 and Figure 3.16, the in-vitro release profiles of Felodipine nanosponges (F1–F12) revealed a consistent drug release pattern over an 8-hour period. The formulations F2 and F9 demonstrated the most effective drug diffusion from the nanosponge matrix, with cumulative releases of 97.45% and 98.87%, respectively, outperforming all others. The polymer content, entrapment efficiency, and particle size all affected the release rate; formulations with a high entrapment (98.44%) and a smaller particle size (F9, 186.6 nm) produced the most regulated and comprehensive release.

Table No. 3.7 *In vitro* drug release profile of Felodipine nanosponges (F1-F12)

Sr. No	Time (hr)	Cumulative percentage drug release (%)											
		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	0	0	0	0	0	0	0	0	0	0	0	0	0
2	1	23.18±0.12	47.55±0.11	33.78±0.15	37.33±0.24	30.21 ±0.18	21.44 ±0.21	20.12 ±0.32	20.80 ±0.34	25.36 ±0.11	31.42 ±0.22	37.33 ±0.23	30.21 ±0.19
3	2	30.21±0.25	56.25±0.23	46.84±0.17	49.78±0.23	40.78 ±0.23	32.87 ±0.32	31.07 ±0.43	31.68 ±0.61	30.38 ±0.12	43.50 ±0.31	49.78 ±0.43	40.78 ±0.21
4	3	39.98±0.32	64.19±0.32	57.21±0.26	60.08±0.34	46.55 ±0.26	43.74 ±0.45	41.1± 0.32	37.61 ±0.42	41.85 ±0.32	55.01 ±0.19	60.08 ±0.54	46.55 ±0.26
5	4	47.87±0.16	71.85±0.42	67.88±0.31	63.12±0.32	54.98 ±0.29	51.20 ±0.52	49.60 ±0.54	48.43 ±0.52	52.30 ±0.23	63.8± 0.17	63.12 ±0.42	54.98 ±0.29
6	5	52.54±0.52	79.64±0.34	71.94±0.23	78.54±0.43	61.52 ±0.22	62.56 ±0.21	61.05 ±0.21	59.58 ±0.22	63.19 ±0.34	73.49 ±0.23	78.54 ±0.47	61.52 ±0.42
7	6	58.45±0.23	87.14±0.32	79.56±0.34	85.48±0.23	70.87 ±0.45	71.32 ±0.23	69.80 ±0.81	63.19 ±0.44	75.29 ±0.23	80.78 ±0.62	85.48 ±0.19	70.87 ±0.82
8	7	63.87±0.54	95.06±0.43	86.41±0.21	89.47±0.12	78.21 ±0.34	79.12 ±0.53	75.64 ±0.72	69.78 ±0.32	83.27 ±0.54	87.56 ±0.18	89.47 ±0.11	78.21 ±0.11
9	8	81.98±0.21	97.45±0.22	90.07±0.29	90.78±0.16	91.72 ±0.33	88.74 ±0.62	85.23 ±0.46	72.66 ±0.12	98.87 ±0.34	91.71 ±0.27	90.78 ±0.18	91.72 ±0.28

*n=3

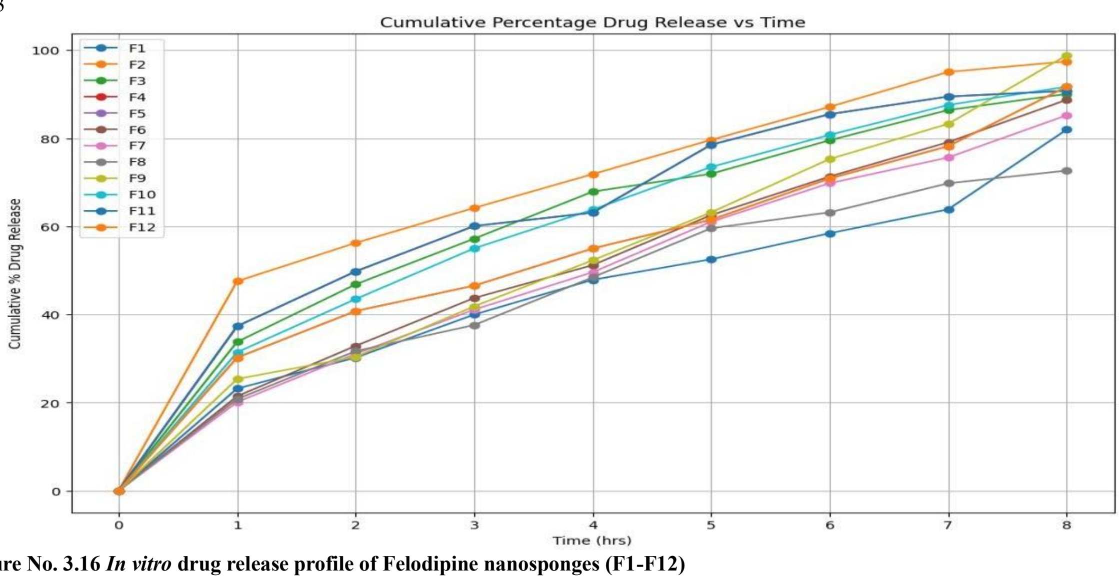

Figure No. 3.16 *In vitro* drug release profile of Felodipine nanosponges (F1-F12)

Journal of Molecular Science
Volume 35 Issue 3, Year of Publication 2025, Page 870-880
DoI-10.004687/1000-9035.2025.119

3.12. Release Kinetics:

A non-Fickian (anomalous) diffusion mechanism, in which both diffusion and erosion regulate drug release, is suggested by the release kinetics of the improved F9 formulation (Figure No.3.17,Table 3.8), which fit the Korsmeyer–Peppas model the best (R2 = 0.9932). Overall, the studies show that Felodipine release is efficiently modulated by nanosponge formulations, allowing for consistent and long-lasting drug delivery. The combined findings (Table 3.9) show that F9 is the best batch for additional pharmacokinetic analysis because to its higher physicochemical stability, encapsulation effectiveness, and controlled release profile.

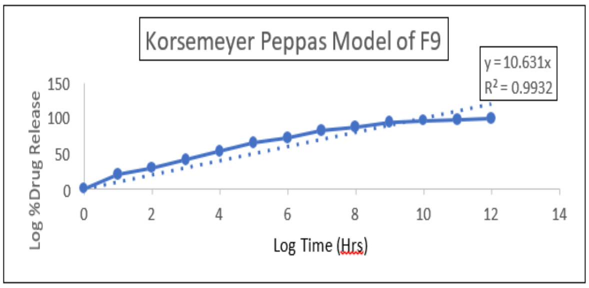

Figure No. 3.17: Drug release Kinetics of F-9 optimized Formulation.

Table No. no. 3.8 Kinetics Release of F-9 optimized Formulation

Models	Zero order	First Order	Higuchi	Korsemeyer Peppas (Best fit model)	Hixcon Crowel
R^2 Value	0.9343	0.9481	0.9672	**0.9932**	0.9227

2. Summary of Characterization and Optimization

The optimized batch with the best physicochemical and functional characteristics was Formulation F9, according to the thorough analysis of all twelve formulations (F1–F12). It demonstrated exceptional homogeneity and nanoscale stability by having the lowest PDI (0.140), the smallest particle size (186.6 nm), and the highest percentage yield (98.15%). The entrapment efficiency (98.44%) and drug release (98.87%) verified effective drug loading and sustained release behavior, whereas the zeta potential of +19.99 mV demonstrated good electrostatic stabilization. F9 is the best formulation for additional in vivo and pharmacokinetic studies because of these combined properties, which show that it offers the best balance between stability, encapsulation, and controlled release.

Table No. no. 3.9 Summary of characterization results of felodipine nanosponges formulations (F1-F12)

Formulation Code	Percentage yield (%)		Particle size(nm)	Polydispersity index (PDI)	Zeta potential	Entrapment Efficiency	*In vitro* drug release
F-1	86.5±0.22		431.2	0.277	-17.65	95.55	81.98±0.21
F-2	93.21±0.13		251.6	0.302	-5.25	97.33	97.45±0.22
F-3	87.29±0.24		262.2	0.458	-1.93	92.19	90.07±0.29
F-4	91.1±0.41		259.6	0.191	-1.94	93.90	90.78±0.16
F-5	93.97±0.36		250.7	0.283	-0.46	91.21	91.72±0.33
F-6	85.7±0.33		855.5	0.528	-1.97	87.96	88.74±0.62
F-7	83.44±0.58		1000.6	0.460	-1.63	85.29	85.23±0.46
F-8	79.89±0.61		346.0	0.345	-1.96	95.47	72.66±0.12
F-9	98.15±0.15		186.6	0.140	19.99	98.44	98.87±0.34
F-10	91.45±0.37		254.6	0.192	5.91	91.23	91.71±0.27
F-11	89.08±0.60		200.8	0.216	3.63	90.04	90.78±0.18
F-12	78.63±0.11		190.6	0.274	-4.34	88.30	91.72±0.28

*n=3

5. CONCLUSION:

As the best formulation for long-term drug distribution, formulation F-9 of felodipine nanosponges showed excellent physicochemical and biopharmaceutical qualities based on thorough preformulation and characterization experiments. The choice was based on a thorough analysis of the key factors affecting the performance of nanosponges, including particle size, polydispersity index (PDI), zeta potential, entrapment efficiency, and in vitro drug release kinetics.

Its purity and identity were confirmed by the melting point of Felodipine, a light yellow, odorless, amorphous powder, which was 142 °C, within the acceptable range of 141 to 145 °C. Felodipine is soluble in ethanol, dichloromethane, and DMSO, but insoluble in water, according to solubility profile. This suggests that a solubilizing carrier system is required to increase the drug's bioavailability. Quantitative estimation was done using dual absorption maxima at 234 nm and 360 nm that were found by UV spectrophotometric investigation. The calibration curve confirmed compliance with Beer-Lambert's law with high linearity (r2 = 0.998) throughout 3–15 µg/mL.The retention of distinctive peaks from FTIR compatibility tests demonstrated that there were no chemical interactions between felodipine and the excipients (PVA and ethyl cellulose). The nanosponges formulation's DSC thermograms showed a distinct endothermic peak at 46.85 °C, signifying both good drug uptake and thermal stability.Out of all the batches, F-9 had the best particle size (186.6 nm), which is good for increasing cellular absorption and dissolution rate. Its PDI score of 0.140 indicates a very homogeneous particle dispersion, which is necessary for stable and repeatable medication release. A zeta potential of

Journal of Molecular Science
Volume 35 Issue 3, Year of Publication 2025, Page 870-880
DoI-10.004687/1000-9035.2025.119

+19.99 mV indicates that there is high electrostatic repulsion between the particles, which promotes colloidal stability and less aggregation.With the maximum entrapment efficiency of 98.44%, F-9 demonstrated efficient drug loading within the polymeric matrix. Long-lasting therapeutic effects and little medication waste are guaranteed by this high encapsulation efficiency. Compared to all other formulations, in vitro release experiments showed a total drug release of 98.87% over 8 hours. This sustained release profile fits the intended pharmacokinetic goals by showing regulated drug diffusion from the nanosponges matrix.The performance of F-9 was further supported by release kinetics modeling. With a r2 value of 0.9932, the drug release was consistent with the Korsmeyer-Peppas model, indicating a diffusion- controlled mechanism. The robustness of the formulation design was confirmed by the fact that this model fit the release data the best when compared to zero-order, first-order, Higuchi, and Hixson-Crowell models.Ultimately, formulation F-9 proved to be the best option for delivering felodipine using nanosponges technology due to its ideal particle size, homogeneity, stability, drug loading, and prolonged release behavior. Its performance across analytical and kinetic parameters validates its potential for further development in advanced drug delivery systems aimed at improving the bioavailability and therapeutic efficacy of poorly soluble drugs like Felodipine.

6. Future Perspectives:

Future research should concentrate on pharmacokinetic and pharmacodynamic studies conducted in vivo to demonstrate bioavailability increase and correlate in vitro performance with biological efficacy. Translating this nanosponge system into a clinically feasible dosage form also requires stability testing in accordance with ICH criteria and scale-up feasibility evaluations. The therapeutic use of these nanosponges may be further increased by incorporating them into transdermal patches or oral sustained-release tablets. The successful creation of felodipine nanosponges promotes the adaptability of nanosponge technology as a cutting-edge and effective drug delivery system and creates new opportunities for creating other medications that are poorly soluble in water.

7. REFERENCES:

1. Sahoo SK, Parhi P, Sahoo SK. Nanotech approaches to drug delivery and imaging. Nanomedicine. 2007; 3: 20–31.
2. Debjit B, et al. Role of nanotechnology in novel drug delivery systems. J Pharm Sci Tech. 2009; 1(1): 20–35.
3. Shiwangi S, Monika K. Nanosponges as emerging carriers for drug delivery. J Pharm Sci. 2022; 13(1): 55–62.
4. Vauthier C, Lesieur S, Legrand P, Bochot A, Gref R, Raatjes W, Barratt G. Influence of polymer behaviour in organic solution on the production of polylactide nanoparticles by nanoprecipitation. Int J Pharm tech. 2007; 344: 33–43.
5. Sahoo SK, Labhasetwar V. Nanotech approaches to drug delivery and imaging. Nanomedicine. 2007; 8(24): 1–9.
6. Mishra B, Patel BB, Tiwari S. Colloidal nanocarriers: a review on formulation technology, types and applications toward targeted drug delivery. Nanomed Nanotech Biomed. 2010; 6: 9–24.
7. Parhi P, Mohanty C, Sahoo SK. Nanotechnology-based combinational drug delivery: an emerging approach for cancer therapy. Drug Discov Today. 2012; Sep; 17(17-18): 1044-52.
8. Bhowmik H, Venkatesh DN, Kuila A, Kumar KHH. Nanosponges: A Review. J Pharm Sci. 2018; 10(4).
9. Subramanian S, Singireddy A, Krishnamoorthy K, Rajappan M. Nanosponges: A novel class of drug delivery system – Review. J Pharm Pharmaceut Sci. 2012;15(1):103–111.
10. Godge GR, Panchal U, Gade S, Sumbe R, Pawar G, Ranshur V. Pharmaceutical formulation using polymer nanocomposites. Int J Res Sci Innov. 2025;12(4):1497–1526.
11. Godge GR, Randhawan BB, Shaikh AB, Bharat SC, Raskar MA, Hiremath SN. Formulation perspective and applications of solid lipid nanoparticles for drug delivery: A review. RGUHS J Pharm Sci. 2024;14(1):1–10.
12. Penjuri SCB, Ravouru N, Damineni S, Sailakshmi BNS, Poreddy SR. Formulation and evaluation of Lansoprazole loaded nanosponges. Turk J Pharm Sci. 2016;13(3):304–310.
13. Godge GR, Zarekar SB, Padale PJ. Nanosuspension technologies: An innovative approach in drug delivery of sparingly soluble drugs. Int J Creat Res Thoughts. 2021;9(7):409–420.
14. Godge GR, Garje MA, Dode AB, Tarkase KN. Nanosuspension technology for delivery of poorly soluble drugs and its applications: A review. Int J Pharm Sci Nanotech. 2020;13(4):4965–4978.
15. Godge GR, Hiremath SN. An investigation into the characteristics of natural polysaccharide: Polymer Metoprolol Succinate tablets for colonic drug delivery. Mahidol Univ J Pharm Sci. 2014;41(2):7–21.
16. Godge GR, Hiremath SN. Development and evaluation of colon targeted drug delivery system by using natural polysaccharides/polymers. Dhaka Univ J Pharm Sci. 2014;13(1):105–113.
17. Hiremath S, Godge G. Preparation and in vitro evaluation of inclusion complexes of Nelfinavir with chemically modified β-cyclodextrins. Dhaka Univ J Pharm Sci. 2012;11(2):107–116.
18. Chemate SZ, Godge GR, Pawa KK, Rupnar KA. Preparation and evaluation of hollow calcium pectinate beads for floating-pulsatile drug delivery. Turk J Pharm Sci. 2016;13(1):91–102.
19. Godge GR, Hiremath SN, Panchal US, Sumbe RR, Pawar GS, Raskar MA, Bharat SC. An overview of nanocochleates for improving oral absorption using a phospholipid-based drug delivery system. Bioequiv Bioavailab Int J. 2024;8(2):000237.
20. Hedley M, Ishikawa T, Watanabe Y, Takayama K, et al. Effect of hydroxypropylmethylcellulose (HPMC) on the release profiles and bioavailability of a poorly water-soluble drug. Int J Pharm. 2000;202:173–8.
21. Sanap DS, Godge GR. Recent Trends in Medicated Chewing Gum Technology: A Review on History, Formulation Strategies and Characterization. Int. J. Pharm. Sci. Rev. Res. 2019; 59(2):72-85.