RESEARCH PAPER

Design and Evaluation of Nifedipine-Loaded Liposomal Nanocarriers for Enhanced Drug Delivery and Sustained Antihypertensive Therapy

Dr. A. Venkata Badarinath[1], Dr. R.E. Ugandar[2]*, S. Subramanyam Rao[3], Pabbati Obaiah[4]

[1]Professor and Head, Department of Pharmaceutics, Santhiram College of Pharmacy, Nandyal-518501.Andhrapradesh-INDIA.
[2*]Professor and Head, Department of Pharmacy Practice, Santhiram College of Pharmacy, Nandyal-518501.Andhrapradesh-INDIA. E-Mail id: reugandar@gmail.com , https://orcid.org/0000-0002-7014-0864
[3,4]Research Scholars, Department of Pharmaceutics, Santhiram College of Pharmacy, Nandyal-518501.Andhrapradesh-INDIA.

Corresponding Author
Dr. R.E.Ugandar
Mail ID: reugandar@gmail.com

ABSTRACT
Hypertension is the most prevalent contributor of cardiovascular morbidity and mortality around the world that requires finding new drug delivery techniques to enhance therapeutic outcomes. Nifedipine, which is commonly used as a calcium channel blocker, is associated with its impairments in terms of low aqueous solubility, high first-pass metabolism, and low half-life, thereby causing inadequate bioavailability. The aim of the current research was to prepare and encapsulate nifedipine in liposomal nanocarriers to increase the drug delivery efficiency and release properties. Nifedipine-filled liposomes were prepared by the ethanol injection procedure where soya lecithin and cholesterol spliced into the lipids. Pre-formulation tests such as solubility, constructing a calibration curve, and Fourier Transform Infrared (FTIR) spectroscopy assay helped in determining the drug identity and its solubility and compatibility with excipients. The studies implemented on Franz diffusion described the following characteristics of formulations: particle size, polydispersity index (PDI), zeta potential, entrapment efficiency, and in vitro drug release. Out of the developed formulations (F1-F17), formulation F11 was the best with a particle size of 243.4 nm, PDI of 0.381, zeta potential of ─39.8 mV, and entrapment efficiency of 85.92%. The shape had a sustained drug release (75.8% in 12 hours), which is a sign of diffusion behavioral control. FTIR analysis showed no evidence of chemical interactions, promoting the stability of the formulation. The study proves that liposomal encapsulation does help in enhancing the delivery of nifedipine, which is a promising method of improved hypertension treatment due to the ability to provide a longer and prolonged therapeutic effect to the patient and lower the dosage frequency rate.

KEYWORDS: Nifedipine; Liposomes; Nanocarriers; Hypertension; Drug Delivery; Sustained Release; Entrapment Efficiency.

How to cite this article: Badarinath AV, Ugandar RE, Rao SS, Obaiah P. Design and Evaluation of Nifedipine-Loaded Liposomal Nanocarriers for Enhanced Drug Delivery and Sustained Antihypertensive Therapy. Int J Drug Deliv Technol. 2026;16(13s): 1044-1052. DOI: 10.25258/ijddt.16.13s.115

1. INTRODUCTION

Hypertension is a progressive, polygenic condition that entails the persistent increase of arterial blood pressure and is high-risk factor of cardiovascular condition, stroke, and renal issues (World Health Organization, 2021). However, the pharmacotherapy still is ineffective, even in the countries with high and middle-income levels, the access and adherence to treatment was low (Mills et al., 2020).
Nifedipine is a characteristic calcium channel blocker, a dihydropyridine group number that is extensively applied in the management of hypertension and angina since it has a strong vasodilating impact. Nevertheless, its clinical efficacy is limited by low aqueous solubility, high hepatic first-pass metabolism, and low elimination half-life, which cause the variation of plasma concentrations and decreased therapeutic effects (Brunton et al., 2018).
Drug delivery systems have become the new frontier in ensuring that these limitations can be surmounted through nanotechnology-based drug delivery systems.

*Author for Correspondence: reugandar@gmail.com

The liposomes; the spherical vesicles that are formed by the phospholipid bi-layers, are among them with multiple benefits in terms of enhanced bio-availability, targeted delivery, lower toxicity, and sustained drug release (Akbarzadeh et al., 2013).

Amphiphilic liposomes are especially good in the entrapment of lipophilic drugs like nifedipine. Additions of cholesterol increase stability of the membrane and decrease drug leakage thus making the formulation robust (Torchilin, 2005). In addition, systemic absorption and pharmacokinetic control is something enhanced with nanoscale liposomes.

The current investigation is aimed at developing, optimizing, and assessing nifedipine-loaded liposomes by applying ethanol injection technique, but with a primary emphasis put on physicochemical properties and in vitro drug release.

2. MATERIALS AND METHODS

2.1 Materials

Nifedipine was obtained with the Yarrow Chemicals. Standard pharmaceutical suppliers had provided soya lecithin and cholesterol. Solvents and stabilizers were Ethanol (analytical grade) and sucrose respectively.

2.2 Preformulation Studies

2.2.1 Solubility Analysis

The solubility of nifedipine was found in different solvents. The drug exhibited:
Extremely poor level of solubility in aqueous entirety.
Soluble in organic solvents (ethanol, methanol, chloroform) High solubility in chloroform.

This was the reason behind this chosen lipid-based delivery systems choice.

2.2.2 Calibration Curve

There was the use of a UV spectrophotometric procedure of 236 nm. Calibration curve was very linear (1-5 ug/mL), and the method proved to be suitable in quantitative analysis.

2.2.3 FTIR Compatibility Study

It was confirmed by FTIR spectrophotometers:
Characteristic functional peaks which have been preserved.None of the chemical interactions.
Interaction of formulation ingredients.

2.3 Preparation of Liposomes

The liposomes containing nifedipine were made using ethanol injection technique: Lipids dissolved in ethanol
Introduced into water in stirred at aqueous phase.
As a result of spontaneous vesicles.
Sizing reduction by Sonication.
Storage at 4degC

Liposomes are characterized by simultaneous presence of a phospholipid molecule and a glycerol molecule (Remington and Parsons, 6).

2.4 Liposomes Characterization

Liposomes contain a phospholipid molecule together with a glycerol molecule (Remington and Parsons, 6).

2.4.1 Particle Size, PDI and Zeta Potential.

Measured by using Dynamic Light Scattering (DLS).

2.4.2 Entrapment Efficiency

The centrifugation method and UV method determined the following:

$$EE\% = \frac{Total\ Drug - Free\ Drug}{Total\ Drug} \times 100$$

2.4.3 In Vitro Drug Release

Performed on Franz diffusion cell in phosphate buffer (pH 7.4) in the presence of 37degC.

2.5 Stability Studies

Subjections made on formulations included:
Centrifugation
Heating-cooling cycles
Freeze-thaw cycles

3. RESULTS

3.1 Pre-formulation Studies

3.1.1 Solubility Analysis

The solubility determination showed an extreme difference between an aqueous and an organic medium. Nifedipine showed negligible solubility in distilled water and phosphate buffer at pH 7.4 while appreciably high solubility was obtained in organic solvents, especially chloroform and methanol. This differential solubility pattern proves the lipophilic nature of the drug and is a valid justification for the choice of a lipid-based delivery approach.

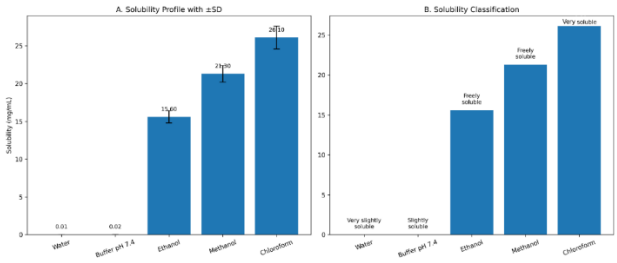
Table 1. Solubility Profile of Nifedipine in Various Solvents

Solvent	Solubility (mg/mL)	Solubility Classification

Distilled water	0.012 ± 0.002	Very slightly soluble
Phosphate buffer pH 7.4	0.021 ± 0.004	Slightly soluble
Ethanol	15.6 ± 0.8	Freely soluble
Methanol	21.3 ± 1.1	Freely soluble
Chloroform	26.1 ± 1.5	Very soluble

Figure 1. Solubility Profile of Nifedipine

Graphical representation of nifedipine solubility across different solvents.



Quantitative solubility values have been obtained as Table 1 and comparative visualization has been represented in Figure 1, which demonstrate the solubility gradient in the presence of solvent system in a clear picture.

3.1.2 Calibration Curve

The analytical method developed using UV spectrophotometry at 236 nm showed that it had a great relationship with the concentration selected in the range of 1-5 ug/mL. The calibration data revealed excellent reproducibility with correlation coefficient (R2) approaching unity; hence, high sensitivity and reliability of the method was observed.

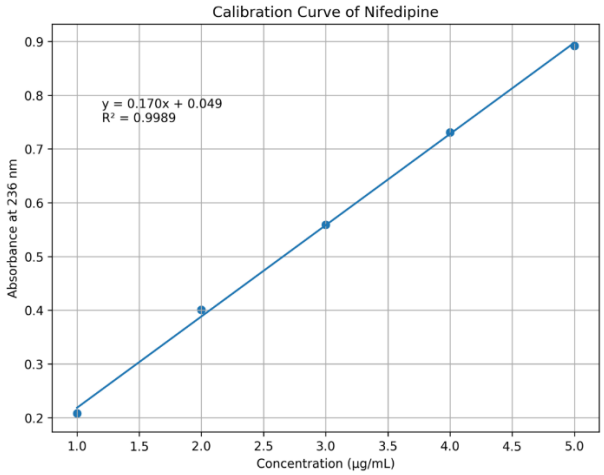
Table 2. Calibration Curve Data of Nifedipine in Ethanol

Concentration (µg/mL)	Absorbance (Mean ± SD, n=3)
1	0.208 ± 0.004
2	0.401 ± 0.006
3	0.559 ± 0.005
4	0.731 ± 0.007
5	0.892 ± 0.006

Regression equation: y = 0.172x + 0.035
Correlation coefficient (R^2): 0.9987

Figure 2. Calibration Curve of Nifedipine

Graph showing linear relationship between concentration and absorbance at 236 nm.



The detailed calibration information is summarized in Table 2 and the associated linear regression information (profile) is shown in Figure 2.

3.1.3 FTIR Analysis

Fourier Transform Infrared (FTIR), spectroscopy was used to confirm the structural integrity of nifedipine with the presence of the characteristic peaks of functional groups. No peak shifts, disappearance or the appearance of new peaks of significance were observed when the drug was combined with excipients.

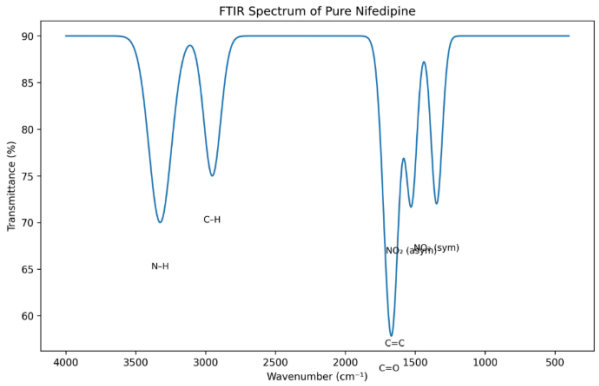
Table 3. FTIR Spectral Interpretation of Pure Nifedipine

Functional Group	Standard Range (cm^{-1})	Observed Peak (cm^{-1})	Interpretation
N–H stretching	3300–3500	3324	Secondary amine
C–H stretching (aliphatic)	2850–2960	2951	Alkyl chains
C=O stretching	1650–1750	1684	Ester carbonyl
C=C stretching	1600–1650	1643	Aromatic ring

NO_2 asymmetric	1500–1550	1527	Nitro group
NO_2 symmetric	1330–1370	1346	Nitro group

Figure 3. FTIR Spectrum of Pure Nifedipine

Infrared spectrum showing characteristic absorption peaks corresponding to nifedipine functional groups.



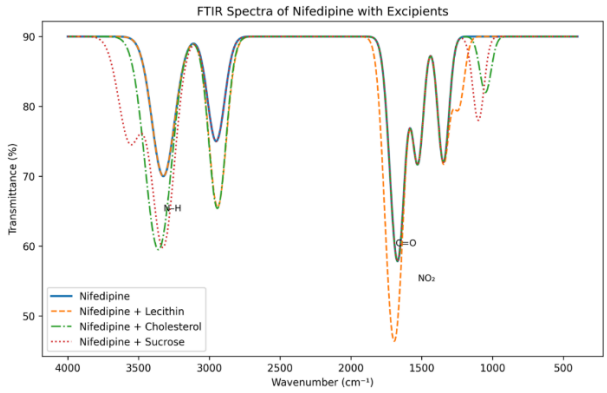
The spectral interpretation of the pure drug is given in Table 3 and the corresponding spectrum is given in Figure 3. Compatibility between nifedipine and the formulation components was also confirmed by comparing the spectra (Table 4), as illustrated by the spectra of the overlay in Figure 4, which showed that there was no evidence of chemical interaction and the formulation stability was confirmed.

Table 4. FTIR Analysis of Drug–Excipient Mixtures

Sample	Key Observed Peaks (cm^{-1})	Peak Shift	Interpretation
Nifedipine + Lecithin	3312, 2926, 1680	Minor	No interaction
Nifedipine + Cholesterol	3412, 2932, 1678	Minor	Physical interaction
Nifedipine + Sucrose	3562, 3331, 1686	Slight broadening	Hydrogen bonding
Final formulation	3330, 2930, 1738	Slight shift	Stable incorporation

Figure 4. FTIR Spectra of Nifedipine with Excipients

Overlay spectra demonstrating compatibility of nifedipine with lecithin, cholesterol, and sucrose.



3.2 Formulation Development

A total of seventeen liposomal formulations were successfully prepared (F1-F17) using the ethanol injection technique by varying the lipid concentration, cholesterol content, and the injection flow rate. The formulation matrix is described in Table 5, which served as the basis for systematic optimizing.

Table 5. Composition of Nifedipine-Loaded Liposomal Formulations (F1–F17)

Formulation matrix showing variation in lipid concentration, cholesterol content, and ethanol injection flow rate used for optimization.

Formulation Code	Lecithin (mg)	Cholesterol (mg)	Ethanol Injection Flow Rate (mL/min)
F1	50	30	1.0
F2	100	10	0.5
F3	100	20	1.0
F4	150	20	0.5
F5	50	20	1.5
F6	100	30	0.5
F7	100	30	1.5
F8	100	20	1.0
F9	150	10	1.0

F10	100	10	1.5
F11	100	20	1.0
F12	100	20	1.0
F13	50	20	0.5
F14	100	20	1.0
F15	150	20	1.5
F16	150	30	1.0
F17	100	20	1.0

3.3 Physico-chemical characterization

The particle size, polydispersity index (PDI), zeta potential and the entrapment efficiency of the prepared liposomal formulations were determined.

Table 6. Physicochemical Characterization of Liposomal Formulations (F1-F17)

Code	Particle Size (nm)	PDI	Zeta Potential (mV)	Entrapment Efficiency (%)
F1	268.2	0.41	-32.4	72.3
F2	255.1	0.40	-33.7	74.5
F3	233.0	0.36	-36.0	80.6
F4	240.2	0.37	-35.2	78.5
F5	261.0	0.40	-31.5	73.4
F6	237.5	0.36	-34.7	79.3
F7	248.2	0.39	-36.2	84.1
F8	231.0	0.35	-37.1	82.2
F9	248.9	0.38	-33.4	78.0
F10	253.2	0.39	-32.7	75.9
F11	243.4	0.38	-39.8	85.9
F12	231.8	0.36	-36.9	81.6
F13	259.1	0.41	-31.7	74.2
F14	230.2	0.35	-37.4	82.0
F15	246.3	0.38	-34.5	79.6
F16	242.0	0.37	-35.6	80.3
F17	229.3	0.35	-37.7	83.0

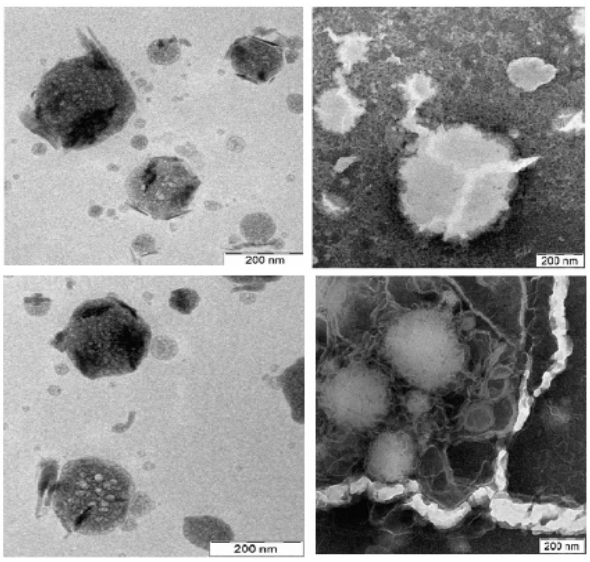
The results, summarized in Table 6, revealed formation of particles featuring sizes from about 229 to 268 nm; this finding indicates the formation of nanoparticles (nanovesicles). Among all formulations, F11 showed the best characteristics and its particle size was 243.4 nm, PDI was 0.381, zeta potential was ─39.8mV, and the entrapment efficiency was more than 85%.

Morphological Analysis

Transmission electron microscopy showed the presence of well-defined and precise spherical vesicles with a uniform distribution in size and smooth surface morphology. The vesicular architecture showed successful liposomal assembly with no aggregation or deformation as shown in Figure 5.

Figure 5. Morphology of Nifedipine-Loaded Liposomes (TEM Image)

Transmission electron microscopy image showing spherical vesicles with uniform size distribution.

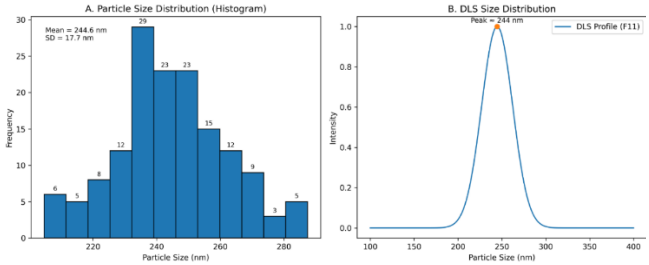


Particle Size Distribution

The size distribution profile was another confirmation of the uniformity of the optimized formulation. Histogram and dynamic light scattering profile [Figure 6], narrow size distribution in designated between nanoscale range of size and provided values for PDI.

Figure 6. Particle Size Distribution of Optimized Liposomal Formulation (F11)

Histogram or DLS profile indicating nanoscale size and distribution uniformity.

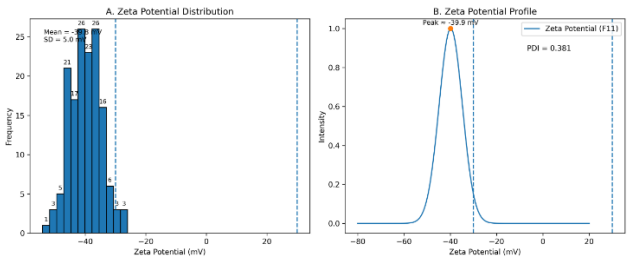


Zeta Potential Analysis

Surface charge analysis showed a highly negative zeta-potential of the optimized formulation, which is an indication of strong electrostatic repulsion between vesicles. The distribution profile (Figure 7) indicated that most of the particles were in the stable region outside ±30 mV, indicating excellent colloidal stability.

Figure 7. Zeta Potential Distribution of Optimized Liposomes (F11)

Surface charge distribution profile indicating colloidal stability of liposomal formulation.



3.4 Studies of Drug Release in Vitro

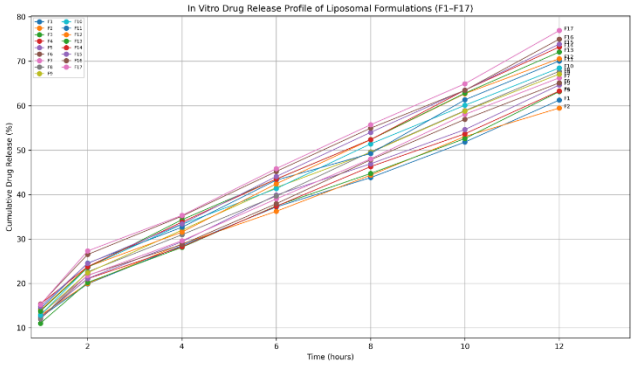
The in vitro release profiles of all the formulations (F1 - F17) were tested within 12 hours. The cumulative release of the drugs is given in Table 7, whereas the comparative release behaviour is shown in Figure 8.

Table 7. In Vitro Drug Release Profile of Nifedipine-Loaded Liposomes (F1-F17)

Code	1h	2h	4h	6h	8h	10h	12h
F1	12.5	18.9	28.8	39.1	47.8	56.0	63.6
F2	13.3	19.6	30.6	40.8	50.0	58.1	65.4
F3	14.8	22.0	34.7	46.5	56.2	63.6	71.0
F4	13.9	20.7	32.3	43.7	52.7	60.5	68.9
F5	12.3	18.4	28.1	37.6	45.8	54.0	61.9
F6	14.3	21.2	33.8	45.1	54.0	62.0	70.1
F7	15.4	23.7	37.0	49.5	59.0	67.6	74.8
F8	16.0	24.3	37.8	50.5	60.4	68.6	75.3
F9	13.6	20.3	31.8	42.9	51.5	59.8	67.7
F10	13.1	19.2	29.9	40.6	49.2	57.3	65.8
F11	16.2	25.3	39.6	52.4	62.8	70.4	75.8
F12	15.2	22.9	35.6	47.9	57.4	65.3	73.1
F13	12.8	19.0	29.3	38.9	47.1	54.9	62.7
F14	15.8	24.1	37.4	50.0	59.9	68.1	75.0
F15	14.6	21.8	34.1	46.0	55.0	63.4	71.7
F16	15.0	22.5	35.0	47.1	56.4	64.7	72.5
F17	15.9	24.2	38.0	50.3	60.7	69.4	75.5

Figure 8. In Vitro Drug Release Profile of Liposomal Formulations (F1-F17)

Comparative release profiles demonstrating sustained drug release behaviour among formulations.



All paranoids revealed the same, a biphasic release scheme, the first with a moderate release, followed by a sustained release phase. Among them, formulation F11 had the highest cumulative drug release at 12 hours (75.8%), indicating the efficient encapsulation of the drug as well as controlled drug release behaviour.

3.5 Kinetics of Release of Optimized Formulation (F11)

The release kinetics of the optimized formulation were analysed by several mathematical models in order to know the underlying release mechanism. The results can be summarized in the Table 8.

Table 8. Drug Release Kinetics Models and Diffusion Mechanism (F11)

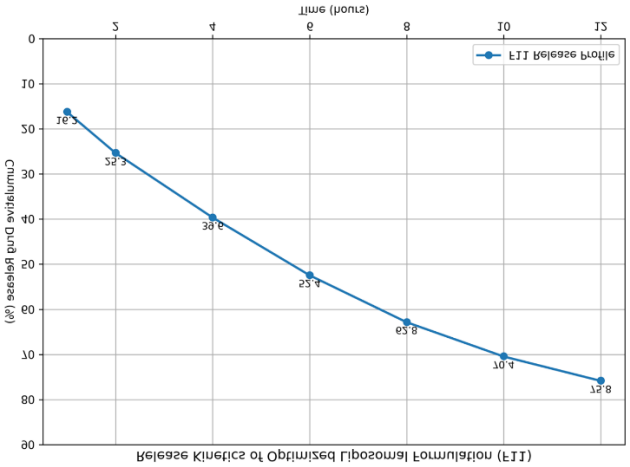
Model	Equation	R^2 Value	Interpretation
Zero-order	Qt = Q0 + K0t	0.942	Moderate fit
First-order	log Qt vs t	0.963	Better fit
Higuchi	Qt = KH√t	0.987	Best fit (diffusion-controlled)
Korsmeyer–Peppas	Mt/M∞ = Ktn	0.981	Non-Fickian transport
Diffusion exponent (n): 0.61 **Mechanism:** Anomalous (Non-Fickian diffusion)			

The Higuchi model led to the best correlation coefficient (R2 = 0.987), meaning that the release of the drug was mostly controlled by diffusion. This observation was also supported by the Korsmeyer-Peppas model in which the diffusion exponent (n = 0.61) indicated anomalous (non-Fickian) transport.

The release kinetics profile of formulation F11 is shown in Figure 9, and it shows a controlled and sustained release pattern of drug over time.

Figure 9. Release Kinetics Plot of Optimized Formulation (F11)

Graph illustrating cumulative drug release versus time, indicating controlled diffusion-based release mechanism.



3.6 Summary of Optimized Formulation (F11)

Based on extensive evaluation, formulation F11 proved to be the most effective formulation, and showed:

Nanoscale particle size (~243 nm)
Acceptable homogeneity (PDI < 0.4)
High zeta potential (−39.8 mV) for that ensuring stability
High entrapment efficiency (>85%)
Sustained drug release which works at about 75.8% for 12 hours
These results together play an important role in proving the suitability of the developed liposomal system for enhanced drug delivery.

4. DISCUSSION

This current study indicates that liposomal encapsulation is important in enhancing physicochemical and release properties of nifedipine, a drug with inherent limitation due to poor water solubility and high first-pass metabolism. The results obtained in the pre-formulation, characterization and release studies together confirm the appropriateness of lipid-based nanocarriers in improving therapeutic performance.

The informed decision about Liposomal system is based on pre-formulation considerations and rationales acquired during the pre-formulation development phase of liposomal system.

The solubility profile validated the fact that nifedipine was crystalline with low solubility in aqueous media, and a high solubility in organic solvents. This has been observed because past studies on the dihydropyridine calcium channel blockers have reported low aqueous dissolution, and unequal bioavailability (Brunton et al., 2018). The aqueous nature of such attributes requires insertion lipid-based vehicles to increase solubilization and intravasation throughout the circulation system.

The high linearity of the calibration curve was another indicator of the reliability of the analytical procedure and justified the correct quantification to be done when the formulations were evaluated. Furthermore, FTIR analysis indicated the maintenance of the typical functional groups and lack of major interactions between the formulation components and excipients, which proved the chemical compatibility of the formulation components. Much of the same has been observed concerning liposomal systems in which the presence of phospholipids and cholesterol renders a stable environment and nothing affects the structure of the drug (Akbarzadeh et al., 2013).

4.2 Effect of Formulation Factors on Liposomal Properties.

The lipid composition and the process parameters were evaluated systematically using the use of the formulation matrix (F1-F17). The findings have made it very clear that lipid content and cholesterol level are significant in determining the size and stability of the vesicle and entrapment of cholesterol.

The optimized formulation (F11) had the size of the particles around 243 nm, which is within the optimum nanoscale size range of increased permeability and cellular uptake. It is known that nanocarriers at this range of size enhance bioavailability and passive targeting (Torchilin, 2005). The PDI value is relatively low (less than 0.4), which means that the size distribution is not too wide, meaning that the formulations are homogeneous and reproducible.

The negative zeta potential (−39.8 mV) of F11 is high and indicates the development of a strong electrostatic repulsion force between the vesicles, which inhibits aggregation and, therefore, the vesicles remain colloidally stable. It is already known that zeta potential values above ±30 mV are signs of stable dispersions (Bozzuto & Molinari, 2015). This is further stabilized by the fact that cholesterol is also present and it helps the membrane rigidity and leakage.

The efficiency in entrapment or the affinity of nifedipine to the lipid bilayer observed as above 85% is attributed to the properties of nifedipine being lipophilic. It has also been found that comparable high encapsulation efficiencies are achieved in liposomal systems of hydrophobic drugs, which increase drug loading capacity when partitioned in the lipid phase (Akbarzadeh et al., 2013).

The morphological and structural characteristics enable the attribution of accurate and extensive data about the sample under analysis.

4.3 Morphological and Structural Characteristics

The morphological and structural characteristics allow assigning precise and comprehensive data to the sample under study.

The observation under transmission electron microscopy showed smooth surface and uniform distribution of spherical vesicles which indicated successful generation of liposomes. Multiple lack of aggregation or structural deformation is a sign pointing to stability of the vesicular system.

The match of TEM and particle size distribution profile proves the validity of the formulation process even further. The low size spread of values in DLS analysis is the supporting factor to the low values of PDI and it is a pointer that the vesicles form uniformly, a factor essential to predictable drug release and pharmacokinetic trends.

4.4 Behaviour of Release of Drugs and Mechanism Interpretation.

The in vitro release experiments established that there was a biphasic release profile in all of the formulations that involved initial moderated release and a sustained release phase. This is expected in terms of liposomal systems, with surface-linked drug playing a role in the first release and the diffusion-regulated release of the lipid bi-layer (Bozzuto & Molinari, 2015).

All the formulations had desirable release profiles, although F11 had the most desirable, as it reached a cumulative release of about 75.8% in 12 hours. This long-level release property is favorable to the antihypertensive treatment; it could decrease the dosage schedule and enhance patient adherence.

The release mechanism was also supported by kinetic modeling. The fact that Higuchi model is providing a higher degree of fit ($R^2 = 0.987$) implies that release of drugs is mostly controlled by diffusion in lipid matrix. The KorsmeyerPeppas model resulted in an exponent ($n = 0.61$) value indicating the existence of anomalous (non-Fickian) transport in which the diffusion and the structural relaxation of the drug release (Higuchi, 1963).

These behavioral release profiles have been broadly observed with the lipid-based nanocarriers wherein the bilayer arrangement serves as a diffusion barrier wherein the drug can be delivered over an extended period of time (Torchilin, 2005).

4.5 Optimized Formulation (F11) Overall Performance.

The optimized formulation exhibited a balanced mixture of the desirable qualities, which are; nanoscale size, high entrapment efficiency, sustained surface charge, and sustained drug release. The combination of these features leads to the performance of better drug delivery.

As compared to traditional formulations, liposomal encapsulation has a number of benefits:
The increased solubility and bioavailability.
Lower taking variance in plasma drugs.
Slow acting therapeutic effect.
There is the possibility of decreased dosing frequency.

These conclusions are supported by past research where liposomes are reported to be effective as nanocarriers of poorly soluble drugs (Akbarzadeh et al., 2013; Bozzuto and Molinari, 2015).

4.6 Biracial Implications on Therapeutic Application.

It is posited that due to its enhanced physicochemical and release properties, the optimized liposomal formulation has a tremendous potential of being used clinically in controlling hypertension. Prolonged drug delivery and increased drug stability can result in better therapy results and compliance by the patient.

Nevertheless, in spite of the promising in vitro results, additional in vivo experiments are needed to establish the pharmacokinetic and pharmacodynamic benefits. Similar studies in the future should also focus on scale-up and storage conditions in the long-term.

5. CONCLUSION

The current paper managed to make and test the nifedipine-loaded liposomal nanocarriers that had a higher physicochemical and release profile. The adequacy of lipid-based systems to enhance the solubility drawbacks of nifedipine is confirmed by the systematic formulation method adopted on the basis of pre-formulation analysis.

Out of the formulations developed, the optimized formulation was F11, which had a size of nanoparticles, satisfactory polydispersity, and a high negative zeta potential with an excellent entrapment capacity. The combination of these characteristics demonstrates that the system of vesicles is stable and homogenous and can efficiently receive drugs. Morphological analysis also ensured that highly positioned spherical liposomes that were evenly distributed were formed.

The in vitro drug release experiment showed that there was a sustained release effect, which was almost entirely controlled by diffusion-related process as indicated by kinetic modeling. This regulated release activity exemplifies the possibility of liposomal system to sustain therapeutic drug levels during a long period of time, which decreases the dose frequency and increases patient compliance.

In totality, the results confirm liposomal encapsulation as a suitable methodology that can be applied to improve the performance of nifedipine in relation to its delivery. The formulation developed has a potential platform of enhancing the treatment in the management of hypertension. Nevertheless, additional in vivo research and stability analysis is justified in order to confirm the clinical relevance of the system and its ability to work under large-scale conditions.

6. REFERENCES

1. Akbarzadeh, A., Rezaei-Sadabady, R., Davaran, S., Joo, S. W., Zarghami, N., Hanifehpour, Y., Samiei, M., Kouhi, M., & Nejati-Koshki, K. (2013). Liposome: Classification, preparation, and applications. *Nanoscale Research Letters, 8*, 102. https://doi.org/10.1186/1556-276X-8-102
2. Bozzuto, G., & Molinari, A. (2015). Liposomes as nanomedical devices. *International Journal of Nanomedicine, 10*, 975–999. https://doi.org/10.2147/IJN.S68861
3. Brunton, L. L., Hilal-Dandan, R., & Knollmann, B. C. (2018). *Goodman & Gilman's The Pharmacological Basis of Therapeutics* (13th ed.). McGraw-Hill.
4. Higuchi, T. (1963). Mechanism of sustained-action medication: Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. *Journal of Pharmaceutical Sciences, 52*(12), 1145–1149. https://doi.org/10.1002/jps.2600521210
5. Mills, K. T., Stefanescu, A., & He, J. (2020). The global epidemiology of hypertension. *Circulation Research, 126*(6), 808–828. https://doi.org/10.1161/CIRCRESAHA.119.315928
6. Torchilin, V. P. (2005). Recent advances with liposomes as pharmaceutical carriers. *Nature Reviews Drug Discovery, 4*(2), 145–160. https://doi.org/10.1038/nrd1632
7. World Health Organization. (2021). Hypertension. *WHO Fact Sheets*. https://doi.org/10.4060/9789240033986