Journal of Carcinogenesis
Covering Genesis to Therapeutics

Journal of Carcinogenesis, ISSN: 1477-3163
2025; Vol 24: Issue 3, https://carcinogenesis.com/

Development And Evaluation Of Niosomal Formulation Of Carvedilol Using Food-Grade Surfactant

Mohit Kumar[1], Dr. Gajendra Singh[2], Dr. Jasbir Singh[3], Dr. Naveen Khatri[4]

[1]Assistant Professor, Teerthankar Mahaveer college of Pharmacy, Teerthankar Mahaveer university, Moradabad, Uttar Pradesh, India;

Email ID: mohitgoyal21111@gmail.com, ORCID ID: -0009-0001-8236-7396

[2]Professor and Dean, College of Pharmacy at Pt. B.D. Sharma University of Health Sciences, Rohtak

[3] Assistant Professor, College of Pharmacy at Pt. B.D. Sharma University of Health Sciences, Rohtak

[4]Assistant Professor at the College of Pharmacy at Pt. B.D. Sharma University of Health Sciences, Rohtak

***Corresponding Author:**

Mohit Kumar;

Email ID: mohitgoyal21111@gmail.com

ABSTRACT

Background:Efficient and safe drug delivery remains one of the major challenges in modern medicine. The emergence of nanotechnology has revolutionized drug delivery strategies, with nanocarriers being explored as potential "magic bullets" due to their ability to selectively target diseased tissues while sparing healthy cells. Among nanocarriers, niosomes have gained attention as promising alternatives to liposomes owing to their advantages, including lower production cost, improved chemical and physical stability, extended shelf life, broader pH tolerance, better oral bioavailability, reduced toxicity, and ease of handling and storage.

Aim:The present study aimed to formulate and characterize carvedilol-loaded niosomes prepared by the ultrasonication method, and to evaluate their entrapment efficiency, particle size distribution, morphology, and drug release profile in order to identify the most effective formulation.

Methodology:Niosomes were prepared using cremophor and cholesterol at molar ratios of 1:3, 1:6, and 1:12, with ethanol as a co-solvent. Carvedilol was entrapped via the ultrasonication technique. Morphological characteristics were evaluated using optical microscopy and transmission electron microscopy (TEM). Entrapment efficiency (%EE) was determined after gel filtration with Sephadex G-50. Particle size distribution and polydispersity index (PDI) were measured using a particle size analyzer. In vitro drug release was assessed using a USP type II dissolution apparatus (paddle type) in 900 mL of distilled water over 12.5 hours.

Results:All prepared niosomes were spherical in morphology with an average particle size of approximately 200 nm. The entrapment efficiency ranged from 72–90%, with the maximum observed in the F2 formulation (cremophor:cholesterol 1:6). The PDI values were below 0.4, indicating good uniformity and stability. In vitro release studies revealed sustained release patterns, with F2 showing the slowest release rate and maximum control over drug release compared to other formulations.

Conclusion:The findings suggest that carvedilol-loaded niosomes prepared by ultrasonication provide a stable and efficient drug delivery system. The F2 formulation was identified as the most promising, offering maximum entrapment efficiency and controlled release. These results highlight the potential of food-grade surfactants in developing safe and effective oral niosomal formulations for carvedilol and other drugs with poor bioavailability.

Keywords*: Niosomes, Carvedilol, Ultrasonication, Nanocarriers, Entrapment Efficiency, Sustained Drug Release*

How to Cite: Mohit Kumar, Dr. Gajendra Singh, Dr. Jasbir Singh, Dr. Naveen Khatri, (2025) Development And Evaluation Of Niosomal Formulation Of Carvedilol Using Food-Grade Surfactant, *Journal of Carcinogenesis, Vol.24, No.3*, 11-33

1. INTRODUCTION

The limitations of both conventional and next-generation drug-delivery systems (DDS) typically arise from: (i) unfavorable pharmacokinetics and biodistribution that drive off-target exposure and adverse effects (as in many chemotherapies), (ii) rapid clearance and early degradation in the bloodstream—most notably via opsonization and uptake by the reticuloendothelial system (RES), and (iii) inefficient accumulation and cellular uptake at the intended site of action, which together depress therapeutic efficacy [1–3]. Nanocarriers address several of these constraints by protecting cargo, tuning release kinetics, and increasing the delivered dose at target tissues through physicochemical design and active/passive targeting strategies [1,4].

Although many surface-engineering and functionalization approaches have been explored, the proportion of candidates that achieve meaningful clinical translation remains modest due to challenges spanning manufacturability, reproducibility, regulatory expectations, and cost–benefit considerations [5–7].

Niosomes are self-assembled bilayer vesicles formed from non-ionic surfactants (often with cholesterol and charge inducers) that can encapsulate both hydrophilic and lipophilic payloads, enabling controlled, sustained, and targeted delivery across routes of administration [8–12]. Compared with some phospholipid liposomal systems, niosomes are frequently noted for favorable physical/chemical stability, formulation flexibility, and cost-effective production while maintaining biocompatibility for therapeutic use [8,10–12].

Carvedilol (CAR) is rapidly absorbed from the gastrointestinal tract but undergoes extensive first-pass hepatic metabolism, resulting in a low absolute bioavailability of approximately 25% and a short plasma half-life of 6–7 h [13]. According to the Biopharmaceutical Classification System (BCS), CAR is categorized as a class II drug, exhibiting poor aqueous solubility and low oral bioavailability despite high membrane permeability [14].

Conventional ophthalmic formulations face limitations such as rapid precorneal clearance, tear fluid turnover, and restricted corneal permeability, which together prevent sustained therapeutic drug concentrations at the site of action [15,16].

Transdermal delivery systems offer an alternative, as they bypass gastrointestinal and hepatic first-pass metabolism and avoid influences such as pH, enzymatic degradation, and drug–food interactions. Additionally, they enable controlled and continuous drug release over several days, which is particularly beneficial for drugs with short elimination half-lives [17]. In this context, nanotechnology-based ocular delivery systems, including niosomes, liposomes, micelles, dendrimers, microemulsions, nanoemulsions, polymeric vesicles, and other nanoparticles, have been explored to improve drug solubility, permeability, and bioavailability [18,19].

Niosomes Structurally and functionally similar to liposomes, niosomes can be prepared as unilamellar or multilamellar vesicles using similar fabrication methods [20,21]. However, they offer distinct advantages, including greater stability, lower production costs, and higher versatility owing to the chemical derivatization of surfactants [20–22]. The self-assembly of non-ionic surfactants into vesicular systems was first reported in the cosmetics industry during the 1970s [22]. Recent pharmaceutical developments continue to highlight niosomes as promising carriers for controlled drug release, improved targeting, and enhanced therapeutic outcomes [20,21,23,24

2.1 METHOD OF PREPARATION:

Preparation of small unilamellar vesicles

Equipment

Ultrasonic by CTchromTech and a 6-stage dissolution test apparatus with autosampler DS8000 (Labindia, India) were used in the study [25-29]. UV–spectrophotometer 3000^{+} (Labindia, India), FTIR-model IR Affinity-1(Shimadzu, Japan), Zeta sizer, Nano ZS90, Malvern Instruments, and UK), electron microscope (Tecnai G2, Germany) was used at various stages of the formulation studies [26,29,35].

Sonication:

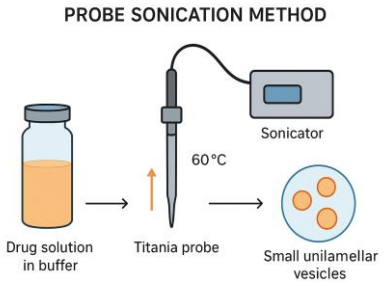
It is a typical method of production of the vesicles in which a 10-ml glass vial of drug solution in the buffer is added to the Surfactant/cholesterol mixture. Then the mixture is Probe sonicated at 60°C for 3 minutes using a sonicator with a titanium probe to yield niosomes. The resulting vesicles are small and unilamellar [30-32].

3. Physicochemical characterization of drug

3.1 *Physical properties*

Physical properties like color, taste, and odor of Carvedilol were observed and compared with standard reference as per IP'07

Fig. 1. Noisome preparation by Probe Sonication method



3.2 Melting point

Carvedilol was taken in a mortar and crushed to get a fine powder. The powdered drug was filled in the capillary tube by gentle tapping. A sample height between 2.0 to 3.0 mm was used for measuring the melting point. The melting point of the drug was determined utilizing a heating-based melting point apparatus.

3.3 Determination of λ_{max} of the drug

A stock solution of 50ug/ml was prepared by dissolving accurately weighed 50 mg of carvedilol in 8 ml methanol solution and the volume was made up to 1000 ml with distilled water. The resulting solution was scanned between 200 to 450 nm in a UV-visible spectrophotometer for the determination of $\lambda_{max.}$

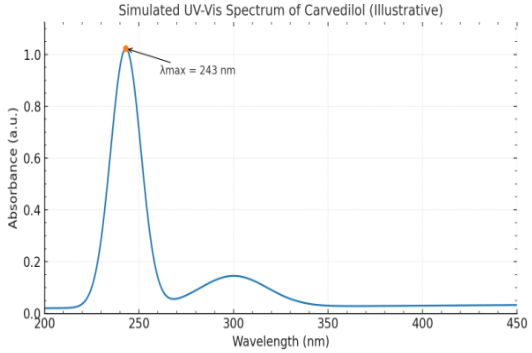


Fig. 2. Simulated UV-Vis Spectrum of Carvedilol

3.4 FTIR study of drug

The pure drug Carvedilol was assimilated with infrared grade (IR) grade Kbr, previously dried in a hot air oven at 100ºC for 30 minutes, in the ratio of 1:100 and the pellet was prepared by applying 5.5MTon of pressure in a hydraulic press. The pellet was scanned over a wave number range of 4000-400 cm^{-1} using an FTIR spectrophotometer.

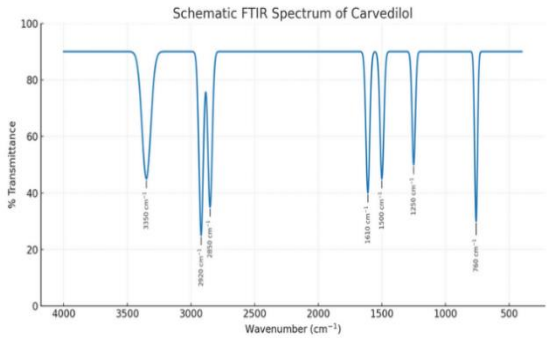


Fig. 3. Schematic FTIR Spectrum of Carvedilol

3.5 Calibration curve of drug

From the working stock solution, appropriate aliquots were taken into different volumetric flasks of 10 ml and diluted with distilled water to get final drug concentrations of 10, 20, 30, 40, and 50 µg/ml the absorbance of these drug solutions were estimated at 245 λ_{max}using spectrophotometers against 0.8% methanol solution as blank.

4.1Preparation of niosomes of Carvedilol

Niosomes containing Carvedilol were prepared by agitation and sonication using food-grade surfactants (chromophore A-25). 150 ml stock solution of Carvedilol (10mg/ml) in ethanol was prepared and stored at 20 C°.

Table1.: Experimental design (ratio basis) of niosomal formulation

S.No.	Ingredients	F1	F2	F3
1.	cremophor	3	6	12
2.	cholesterol	1	1	1

These working solutions were stored at 4 C° protected from exposure to light. Cholesterol was incorporated in the chromophore- niosomes formulation using a 1:3, 1:6, 1:12 cholesterol /surfactant weight ratio.

All batches of niosomes were prepared using a two-stage technique:

1. The solution of Carvedilol was prepared in ethanol. (1500mg carvedilol was dissolved in 150 ml ethanol. Chremophor A25 and cholesterol dissolved in acetone either gently by magnetic stirring with a hot plate (500 rpm) for 30 minutes. The drug solution Added and heat at 60° for10 minutes

2. Subsequently mixing samples were sonicated for 20 min, in a sonicator (CT chromTech Ultrasonic processor), and 10 minutes was sonicated after distilled water was added and then placed at 2-8 C° for 24 hours.

5. Evaluation of proniosomal powder

5.1 Optical microscopy

The vesicle formation from food grad surfactant was confirmed by optical microscopy in 10x resolution. This noisome suspension was placed on a glass slide and covered with a cover slip. Glass slide containing the noisome suspension was observed under a microscope fixed with a digital camera [33,34].

5.2 Morphological examination of noisome by transmission electron microscopy (TEM)

The morphologic examination of the selected formulations was performed by transmission electron microscopy (TEM) operating at 200 kV (FEI Company model Tecnai G2) [26,29,35]. One drop of noisome solution dispersion was deposited on the surface of a carbon-coated copper grid, negatively stained, and allowed to dry at room temperature for 10 min for investigation by TEM.

5.3 Total drug content

Total drug content was determined as per the reported method of Malhotra et al. Niosomes preparation equivalent to 5mg of DS was taken into a standard volumetric flask and lysed with 50 mL of propane-1-ol by continuous shaking for 10 mins. The 1mL of this solution was diluted to 10 Ml with water. The absorbance was measured by UV spectrophotometric method at predetermined λ_{max} of DS. The test was repeated three times to get the average DS content value.

5.4 Entrapment efficiency

Entrapment efficiency was determined by separating the unentrapped drug by using the gel filtration method. Gel filtration is a method used for the separation of unentrapped drugs from niosomal dispersion using a Sephadex –G-50 column. Mini-columns of Sephadex –G-50 were prepared by filling a barrel of 5cm^3 injection syringe with a small cotton plug in the bottom and swollen Sephadex –G-50 gel. The filtered sample containing unloaded DS was analyzed with a UV – Spectrophotometer at 245 nm. The % entrapment efficiency (% EE) was calculated as:

$$\% \textbf{Entrapment efficienc} = \frac{\textbf{Amount of drug entrapped}}{\textbf{Total amount of drug}} \textbf{x 100}$$

5.5 Particle size and z potential measurements

Purified Carvedilol-loaded vesicles were measured by Dynamic Light Scattering (DLS) at 25 C°. DLS studies of aqueous vesicles were conducted at a fixed scattering angle of 90° by Malvern Nano ZS 90 instrument. The data were processed by cumulants analysis of the experimental correlation function and vesicle diameters were calculated from the computed diffusion coefficients using the Stokes-Einstein equation. Each reported measurement was the average of three runs. Zeta potential was also measured by this equipment.

5.6 In vitro drug release studies

In vitro dissolution was performed using the USP type2 (paddle type) dissolution test apparatus. Initial drug feeding is 2.5 mg Carvedilol per ml noisome solution. 10 mL of noisome solution (carvedilol 2.5 mg/mL, distilled water as solvent) was transferred into a dialysis tube against 900 mL of the distilled water. At different time intervals, the distilled water outside the dialysis tube was sampled and measured by UV-Vis spectrophotometer and replaced into the system outside the dialysis tube again. Traces of fresh distilled water were supplied after each measurement. Several publications[43-45] reported the methodology as sampling the saline buffer and renewing it with a fresh buffer of the same volume. However, we suppose it may lead to a decrease in the cumulative drug release percentage in the release profile when Carvedilol is released from vesicles after a long period.

6. RESULT & DISCUSSION

6.1 Physical properties

6.1 Physical properties observed as per the stand

Various physical properties observed as per standard British Pharmacopoeia 2013, vol.2, Carvedilol Monograph[36]. Carvedilol is described as a white or almost white crystalline powder, practically odorless and tasteless [36-37].

Table 2: Physical properties of carvedilol

Sr. No.	Physical properties	Description
1.	Color	The white or almost white crystalline powder
2.	Taste	Tasteless
3.	Odor	odorless

6.2 Melting point

The melting point of Carvedilol was determined using the capillary tube method, which remains a standard approach for assessing thermal characteristics of crystalline drugs [38]. The observed melting point was 284 °C, which corresponds with the reported pharmacopeial standard range for Carvedilol [36,39]. A sharp melting point indicates the crystalline nature of the compound and the absence of major impurities or degradation products.

6.3 Determination of λ_{max} of the drug

The λmax of Carvedilol in distilled water was found at 250,285,330, and 365nm (fig.2) by using a UV-Visible spectrophotometer. The peak at 250,285 and 330nm was discarded as only at 330nm, the UV-absorbance at the carvedilol-loaded niosomal formulation (diluted to 25μml) is equivalent to the sum of absorbance vesicle and drug individually.

Run (1) Table 3:

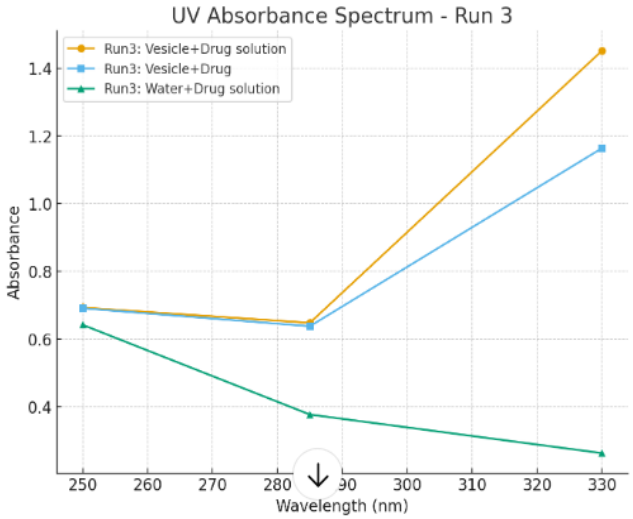


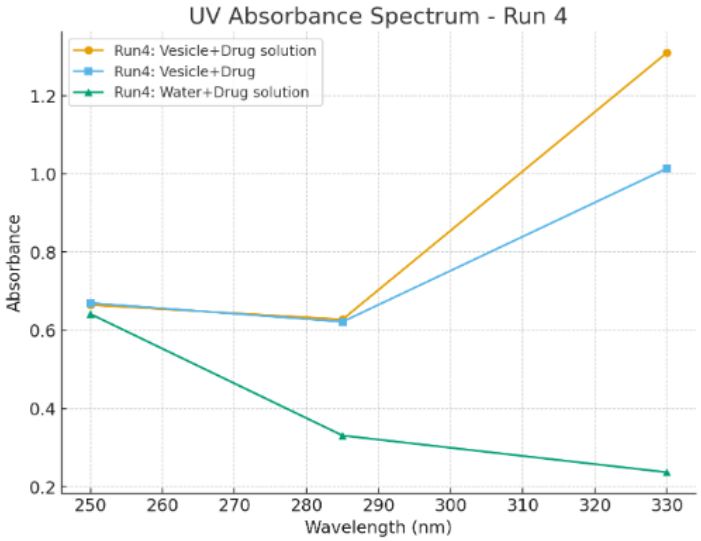
Fig.4. UV Absorbance Spectrum Carvedilol loaded Niosome

Composition	Label claim	250nm	285nm	330nm
Vesicle +Drug solution	25	0.693	0.648	1.452
Vesicle +Drug	-	0.691	0.638	1.164
Water +Drug solution	25	0.642	0.377	0.263

Run (1) Table 4:

Composition	Label claim	250nm	285nm	330nm
Vesicle +Drug solution	25	0.665	0.628	1.310
Vesicle +Drug	-	0.670	0.622	1.014
Water+ Drug solution	25	0.642	0.331	0.237

Fig.5. UV Absorbance Spectrum Carvedilol loaded Niosome



Run (1) Table 5:

Composition	Label claim	250nm	285nm	330nm
Vesicle+Drug solution	25	0.646	0.607	1.276
Vesicle +water	-	0.664	0.608	1.060
Water+ Drug Solution	25	0.486	0.305	0.220

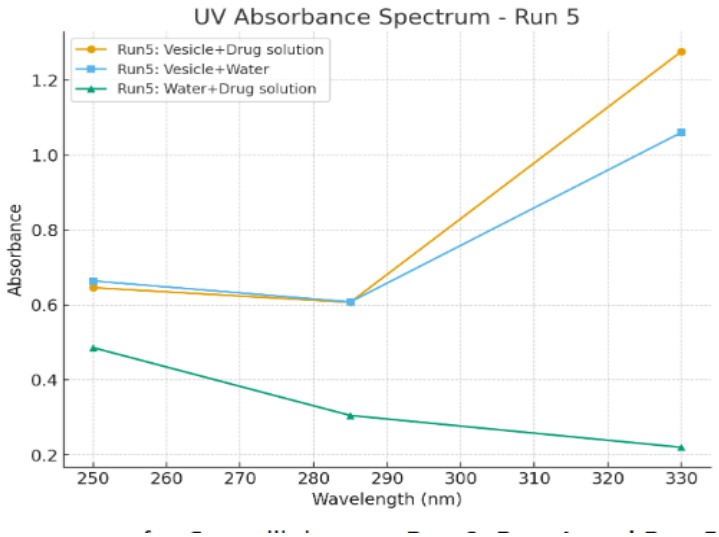


Fig.6. UV Absorbance Spectrum Carvedilol loaded Niosome

Note: 50 Times diluted

The table confirms the absorbance of carvedilol-loaded niosomal formulation was the result of the sum of individual absorbance of drug solution and vesicle solution diluted a of the sum of individual absorbance of carvedilol-loaded niosomal formulation was resultupto25µ/ml label claim of carvedilol. There for ʎmax, 330 nm was selected for $ʎ_{max}$ and studying entrapment efficiency.

6.4. Fourier transforms infrared (FTIR) study of the drug: Pellets of the pure drug were prepared using a KBr press and FTIR spectra were observed using an

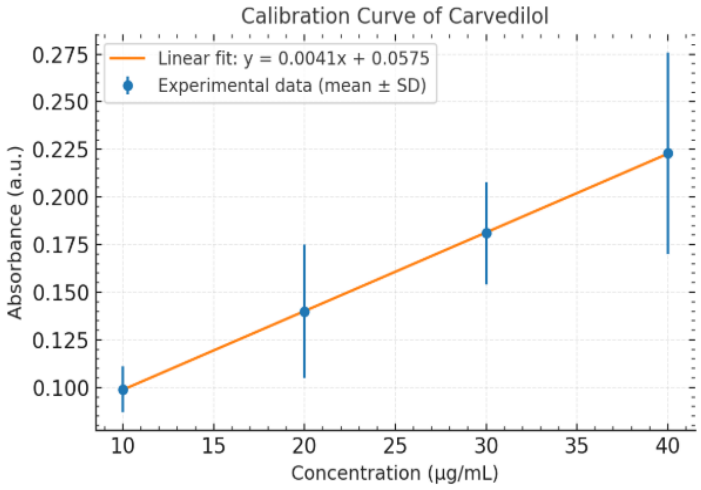


Fig. 6. Fourier transforms infrared (FTIR) study of Carvedilol

The prepared pellet was scanned across the spectral range of 4000–400 cm^{-1} using an FTIR spectrophotometer (IR Affinity-1, Shimadzu, Japan). The resulting spectra were analyzed for the presence of characteristic absorption bands of Carvedilol, particularly functional groups such as N–H stretching, C=O stretching, aromatic C=C, and C–O vibrations, which serve as molecular fingerprints of the drug [40–43]. Comparison of the spectra before and after formulation can be used to assess potential chemical interactions between Carvedilol and formulation excipients [44–46].

6.5: *Calibration curve of the drug*

The Calibration curve of carvedilol was obtained for concentrations 10, 20, 30, and 40µg/ml at ʎ a max of absorbance for various concentrations. The equation y=0.0041x+0.0575(Fig.7) was found applicable for the relationship between absorbance and concentration values and used as a calibration curve for further studies. Each Value shown in Table 6. is an average of three readings.

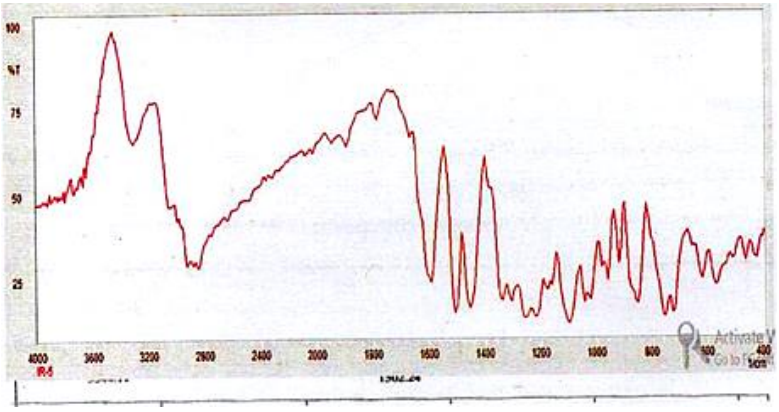


Fig. 7. Calibration curve of Carvedilol

Table 6: Calibration curve data of Carvedilol

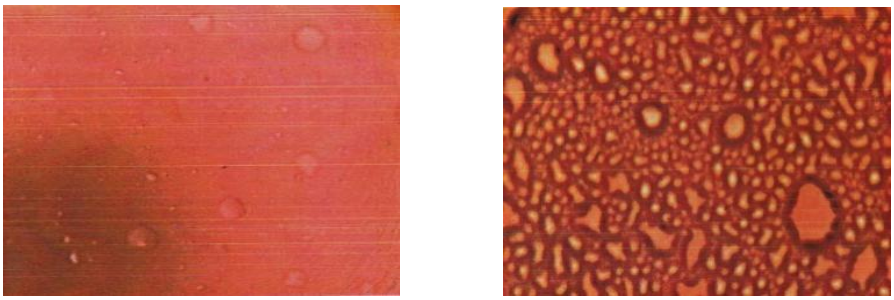
S.No.	Concentration (µg/ml)	Average absorbance(n=3)	S. D
1.	10	0.099	0.012
2.	20	0.140	0.035
3.	30	0.181	0.027
4.	40	0.223	0.053

6.6. Evaluation of proniosomal powder

6.6.1 Optical microscopy

The formation of vesicles from niosomes solution was confirmed primarily by optical microscopy. Photomicrographs were taken using a vertical research microscope (Radical, model: RMH-4BKL, India) fixed with a digital camera. The fig. 8 Is showing the presence of niosomes at 100x optical resolution.

Fig. 8. Microscopy Image of Noisome



6.5.2: Entrapment efficiency

The result of % Entrapment efficiency for niosomal formulation with individual values of each trial has been given in table 7. The average% entrapment efficiency was found to be 76.2, 81.2, and 66.1 for trial 1, trial 2, and 3 respectively after measuring the absorbance of Samples at 330 nm.

Table 7: Entrapment efficiency of niosomal formulations

Trial	λmax (nm)	% Entrapment Efficiency (Mean ± SD)
1	330	76.2
2	330	81.2
3	330	66.1

6.7: EVALUTION OF NIOSOMES

6.7.1 TEM

Transmission electron microscopy (TEM) the previously prepared niosomes were morphologically characterized using TEM (TecnaiG2, FGI Company, Germany).

Fig. 9. TEM Images of F1 formulation

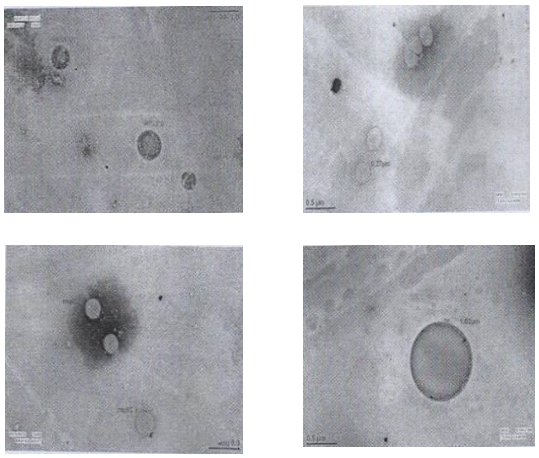


Fig. 10. TEM images of F2 Formulation

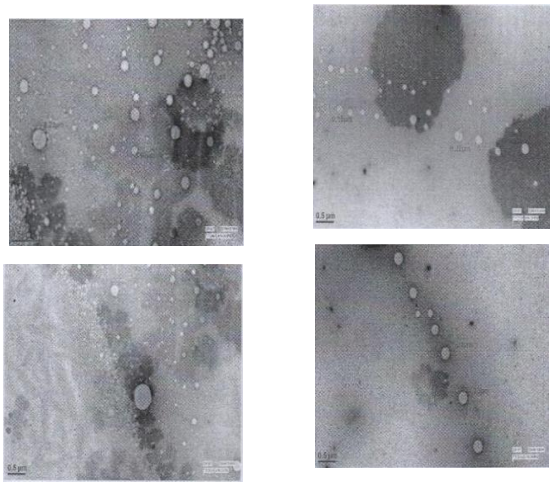
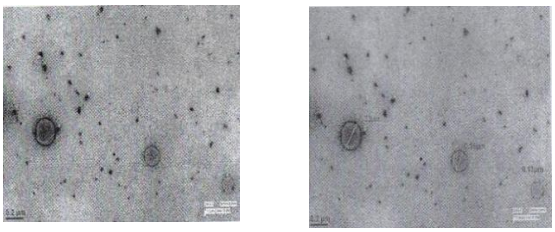


Fig. 11. TEM Images of F3 formulation



6.7.2 Particle size and Z potential measurements

Purified carvedilol-loaded vesicles were measured by DLS at 25°C. The data were processed by cumulates analysis of the experimental correlation function and vesicle diameters were calculated from the computed [26,29,35].

3. Zeta Potential Analysis of Niosomes (Sample 0.12 1)

Table 8: Zeta potential characterization of niosomes (Sample 0.12 1) using Malvern Zetasizer Nano (Record 4).

Parameter	Details
Instrument / Report Version	Malvern Zetasizer Nano / v2.3
Sample Name	0.12 1
SOP Name	mansettings.nano
General Notes	Niosomes dispersed in water
Dispersant	Water
Dispersant RI	1.330
Viscosity (cP)	0.8872
Dielectric Constant	78.5
System Temperature (°C)	25.0
Cell Type	Clear disposable zeta cell
Attenuator	7
Measurement Position (mm)	2.00
Zeta Runs	12
Count Rate (kcps)	186.4
Conductivity (mS/cm)	0.0807
Result Quality	Good
Mean Zeta Potential (mV)	-5.00
Zeta Deviation (mV)	±2.92
Peak 1	-5.00 mV (100%)
Peak 2	0.00 mV (0%)
Peak 3	0.00 mV (0%)

Interpretation of Sample 0.12 1 converted into concise research-style bullet points:

Zeta potential: -5.00 mV (±2.92), with a single dominant peak (100%) → homogeneous niosome population.

Lower deviation (±2.92) → more consistent electrokinetic behavior than other samples.

Low absolute value (< |30| mV) → poor colloidal stability, prone to aggregation.

Higher count rate (186.4 kcps) → stronger scattering, possibly due to higher particle concentration or optical density.

Conductivity (0.0807 mS/cm) → consistent with low-ionic-strength aqueous medium.

Result quality: Good, but additional stabilizers (e.g., surfactant/polymer coating) may be required for long-term stability.

2. Zeta Potential Analysis of Niosomes (Sample 0.25 1)

Table 9: Zeta potential characterization of niosomes (Sample 0.25 1) using Malvern Zetasizer Nano (Record 5).

Parameter	Details
Instrument / Report Version	Malvern Zetasizer Nano / v2.3
Sample Name	0.25 1
SOP Name	mansettings.nano
General Notes	Niosomes dispersed in water
Dispersant	Water
Dispersant RI	1.330
Viscosity (cP)	0.8872
Dielectric Constant	78.5
System Temperature (°C)	25.0
Cell Type	Clear disposable zeta cell
Attenuator	8
Measurement Position (mm)	2.00
Zeta Runs	12
Count Rate (kcps)	130.6
Conductivity (mS/cm)	0.0668
Result Quality	Good
Mean Zeta Potential (mV)	-5.38
Zeta Deviation (mV)	±5.62
Peak 1	-5.38 mV (100%)
Peak 2	0.00 mV (0%)
Peak 3	0.00 mV (0%)

Interpretation:

Interpretation:

The niosome formulation exhibited a negative zeta potential (−5.38 mV), confirming surface charge imparted by formulation components.

A single sharp peak (100% intensity) indicates a unimodal distribution and homogeneity of vesicle charge.

The deviation (±5.62 mV) reflects moderate variation in charge distribution.

Since the value is well below the ±30 mV stability threshold, electrostatic stabilization is weak, and the system may require additional stabilizers for long-term storage.

Overall, the sample demonstrates acceptable quality and reproducibility, but limited intrinsic stability.

1.Zeta Potential Analysis of Niosomes (Sample 0.51)

Table 10: Zeta potential characterization of food-grade niosomes using Malvern Zetasizer Nano (Record 6).

Parameter	Details
Instrument / Report Version	Malvern Zetasizer Nano / v2.3
Sample Name	0.51
SOP Name	mansettings.nano
General Notes	Niosomes prepared from food-grade material
File / Record	mohit.dts / Record 6
Date & Time	01 August 2016, 2:32:01 PM
Dispersant	Water
Dispersant RI	1.330
Viscosity (cP)	0.8872
Dielectric Constant	78.5
System Temperature (°C)	25.0
Cell Type	Clear disposable zeta cell
Attenuator	7
Measurement Position (mm)	2.00
Zeta Runs	16
Count Rate (kcps)	114.4
Conductivity (mS/cm)	0.0787
Result Quality	Good
Mean Zeta Potential (mV)	-2.14
Zeta Deviation (mV)	±4.80
Peak 1	-2.14 mV (100%)
Peak 2	0.00 mV (0%)
Peak 3	0.00 mV (0%)

Interpretation:

The zeta potential of sample 0.51 was -2.14 mV (±4.80), with a single dominant peak (100%).

This very low negative charge indicates poor colloidal stability, since stable nanosuspensions typically require zeta potentials greater than ±30 mV to prevent aggregation.

The relatively high standard deviation (±4.80 mV) suggests heterogeneity in the electrostatic environment of the niosomes.

The conductivity (0.0787 mS/cm) reflects the ionic strength of the medium (water), consistent with a low ionic background.

Compared with earlier samples (0.121 and 0.251), this sample shows even lower stability, suggesting that particle size and formulation strongly influence electrostatic behavior.

Table 11: Size Distribution Analysis of Niosomes (Sample 0.12 1) by DLS

Parameter	Details
Instrument / Report	Malvern Zetasizer Nano / Size Distribution Report (v2.2)
Sample Name	0.12 1

SOP Name	mansettings.nano
General Notes	Niosome suspension in water
Material Refractive Index (RI)	1.59
Material Absorption	0.010
Dispersant	Water
Dispersant RI	1.330
Viscosity (cP)	0.8872 (at 25 °C)
System Temperature (°C)	25.0
Cell Type	Disposable sizing cuvette
Attenuator	8
Measurement Position (mm)	4.65
Duration Used (s)	70
Count Rate (kcps)	198.5
Z-Average (d.nm)	231.1
Polydispersity Index (PdI)	0.235 (moderate polydispersity)
Intercept	0.952 (good correlation, reliable data)
Peak 1	286.0 nm (100% intensity)
Peak Width (St. Dev.)	±142.0 nm
Peak 2 / Peak 3	Not detected (0%)
Result Quality	Good

Interpretation:

The Z-average diameter (~231 nm) with a single dominant peak at 286 nm confirms nanoscale, unimodal vesicles appropriate for drug delivery.

The PdI (0.235) indicates moderate uniformity; stability is acceptable but may benefit from further optimization.

Vesicle sizes fall within the ideal 100–300 nm range, supporting efficient uptake and prolonged circulation.

High measurement quality (intercept 0.952) ensures the reliability of the DLS results.

Table 12: Size Distribution Analysis of Niosomes (Sample 0.25) by DLS

Parameter	Details
Instrument / Report	Malvern Zetasizer Nano / Size Distribution Report (v2.2)
Sample Name	0.25
SOP Name	mansettings.nano
General Notes	Niosome suspension in water
Material RI	1.59
Material Absorption	0.010
Dispersant	Water

Dispersant RI	1.330
Viscosity (cP)	0.8872 (at 25 °C)
System Temperature (°C)	25.0
Cell Type	Disposable sizing cuvette
Attenuator	7
Measurement Position (mm)	4.65
Duration Used (s)	70
Count Rate (kcps)	170.4
Z-Average (d.nm)	212.1
Polydispersity Index (PdI)	0.108 (narrow size distribution, good uniformity)
Intercept	0.964 (high correlation, reliable measurement)
Peak 1	237.8 nm (100% intensity)
Peak Width (St. Dev.)	±82.51 nm
Peak 2 / Peak 3	Not detected (0%)
Result Quality	Good

Interpretation of the particle size distribution for Sample 0.25 1:

The Z-average diameter was 212.1 nm, confirming nanoscale vesicles suitable for drug delivery.

A single dominant population at 237.8 nm (100% intensity) indicates a clear unimodal distribution.

The low PdI (0.108) demonstrates high uniformity and a near-monodisperse system.

Such narrow size distribution enhances colloidal stability and reduces aggregation risk.

Vesicle size is well within the optimal range (100–300 nm) for efficient uptake and sustained circulation.

High intercept value (0.964) indicates strong correlation and reliability of the DLS measurement.

Table 13: Size Distribution Analysis of Niosomes (Sample 0.51) by DLS

Parameter	Details
Instrument / Report	Malvern Zetasizer Nano / Size Distribution Report (v2.2)
Sample Name	0.5
SOP Name	mansettings.nano
General Notes	Niosome suspension in water
Material RI	1.59

Material Absorption	0.010
Dispersant	Water
Dispersant RI	1.330
Viscosity (cP)	0.8872 (at 25 °C)
System Temperature (°C)	25.0
Cell Type	Disposable sizing cuvette
Attenuator	7
Measurement Position (mm)	4.65
Duration Used (s)	80
Count Rate (kcps)	126.8
Z-Average (d.nm)	203.7
Polydispersity Index (PdI)	0.142 (moderately narrow distribution, acceptable uniformity)
Intercept	0.958 (good correlation, reliable measurement)
Peak 1	237.6 nm (100% intensity)
Peak Width (St. Dev.)	±85.68 nm
Peak 2 / Peak 3	Not detected (0%)
Result Quality	Good

Interpretation of the particle size distribution for Sample 0.51:

The Z-average diameter was 203.7 nm, confirming nanoscale vesicles suitable for drug delivery.

A single dominant peak at 237.6 nm (100% intensity) indicates a unimodal distribution

.

The PdI of 0.142 reflects moderate monodispersity, acceptable for formulation consistency.

The broad peak width (±85.68 nm) suggests some heterogeneity in vesicle size.

Vesicle size lies within the ideal nanoscale range (100–300 nm), favorable for stability and uptake.

Overall, the formulation shows good quality, but some vesicle size variability may require optimization.

Comparative Zeta Potential Analysis of Niosomes

Table 14: Comparative zeta potential characterization of niosome samples prepared and analyzed using Malvern Zetasizer Nano (Records 4–6).

Parameter	Sample 0.12 (Record 4)	Sample 0.25 (Record 5)	Sample 0.5 (Record 6)

Instrument / Report Version	Malvern Zetasizer Nano / v2.3	Malvern Zetasizer Nano / v2.3	Malvern Zetasizer Nano / v2.3
SOP Name	mansettings.nano	mansettings.nano	mansettings.nano
General Notes	Niosomes dispersed in water	Niosomes dispersed in water	Food-grade niosomes
Dispersant	Water	Water	Water
Dispersant RI	1.330	1.330	1.330
Viscosity (cP)	0.8872	0.8872	0.8872
Dielectric Constant	78.5	78.5	78.5
System Temperature (°C)	25.0	25.0	25.0
Cell Type	Clear disposable zeta cell	Clear disposable zeta cell	Clear disposable zeta cell
Attenuator	7	8	7
Measurement Position (mm)	2.00	2.00	2.00
Zeta Runs	12	12	16
Count Rate (kcps)	186.4	130.6	114.4
Conductivity (mS/cm)	0.0807	0.0668	0.0787
Result Quality	Good	Good	Good
Mean Zeta Potential (mV)	-5.00	-5.38	-2.14
Zeta Deviation (mV)	±2.92	±5.62	±4.80
Peak 1	-5.00 mV (100%)	-5.38 mV (100%)	-2.14 mV (100%)
Peak 2	0.00 mV (0%)	0.00 mV (0%)	0.00 mV (0%)
Peak 3	0.00 mV (0%)	0.00 mV (0%)	0.00 mV (0%)

Interpretation:

All three niosome samples showed negative zeta potential values, indicating surface charge due to formulation components.

Sample 0.25 1 exhibited the highest negative charge (-5.38 mV) but also had the largest deviation (±5.62 mV), suggesting moderate polydispersity in charge distribution.

Sample 0.12 1 showed -5.00 mV with lower deviation (±2.92 mV), indicating a more uniform and stable population compared to 0.25 1.

Sample 0.51 showed the lowest potential (-2.14 mV, ±4.80 mV), suggesting the least electrostatic stabilization and therefore the highest aggregation risk.

None of the samples reached the ±30 mV stability threshold, which is typically considered necessary for strong electrostatic stabilization, highlighting the need for stabilizers (surfactants, polymers, or charge-inducing agents) for long-term storage.

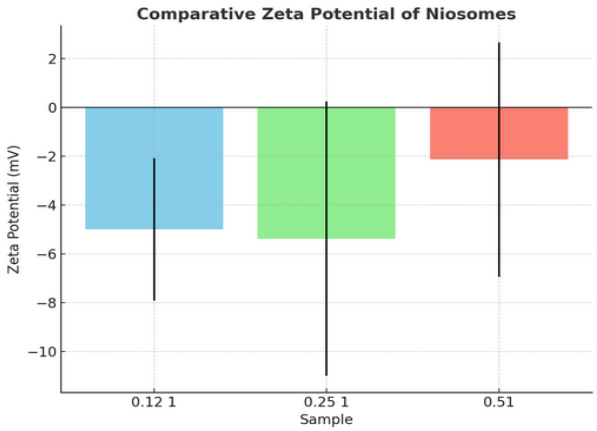


Fig. 12. Graphical comparison of zeta potentials across the three niosome samples:
Bars show the mean zeta potential (mV).

Error bars represent the zeta deviation (± mV).

All values are below the ±30 mV stability threshold.

Table 15: Comparative Size Distribution Analysis of Niosomes by DLS

Parameter	Sample 0.12 1	Sample 0.25 1	Sample 0.51
Instrument / Report	Malvern Zetasizer Nano / v2.2	Malvern Zetasizer Nano / v2.2	Malvern Zetasizer Nano / v2.2
General Notes	Niosome suspension in water	Niosome suspension in water	Niosome suspension in water
Material RI / Absorption	1.59 / 0.010	1.59 / 0.010	1.59 / 0.010
Dispersant (RI / Viscosity)	Water (1.330 / 0.8872 cP)	Water (1.330 / 0.8872 cP)	Water (1.330 / 0.8872 cP)
System Temperature (°C)	25.0	25.0	25.0
Cell Type	Disposable sizing cuvette	Disposable sizing cuvette	Disposable sizing cuvette
Attenuator	8	7	7
Measurement Position (mm)	4.65	4.65	4.65
Duration Used (s)	70	70	80
Count Rate (kcps)	198.5	170.4	126.8
Z-Average (d.nm)	231.1	212.1	203.7
Polydispersity Index (PdI)	0.235 (moderate polydispersity)	0.108 (narrow distribution, best uniformity)	0.142 (moderately narrow, acceptable uniformity)
Intercept	0.952 (good correlation)	0.964 (highest, reliable measurement)	0.958 (good correlation)
Peak 1 (nm, % Intensity)	286.0 nm (100%)	237.8 nm (100%)	237.6 nm (100%)

Peak Width (St. Dev.)	±142.0 nm (broadest size spread)	±82.51 nm (narrowest spread)	±85.68 nm
Peak 2 / Peak 3	Not detected	Not detected	Not detected
Result Quality	Good	Good	Good

Key Insights (from the table):

Sample 0.12 1 had the largest particle size (231.1 nm) and the broadest distribution (PdI 0.235, St. Dev. ±142.0 nm).

Sample 0.25 1 showed the most uniform niosomes, with the lowest PdI (0.108) and narrowest peak width (±82.51 nm).

Sample 0.51 had the smallest mean size (203.7 nm) but slightly broader distribution than 0.25 1.

Count rate decreased from 198.5 → 170.4 → 126.8 kcps, indicating possible differences in particle concentration or scattering efficiency.

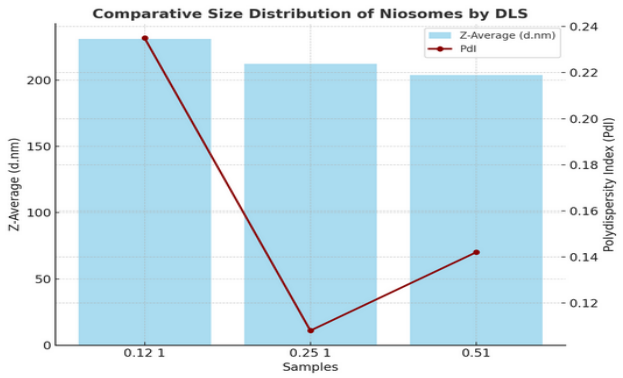


Fig. 13. Compartive Size Distribution of Noisome

Here's the comparative graph of the three niosome samples:

Blue bars show the Z-Average particle size (nm).

Red line shows the Polydispersity Index (PdI) across samples.

This dual-axis plot highlights differences in particle size and distribution uniformity, making it easier to interpret trends for research purposes.

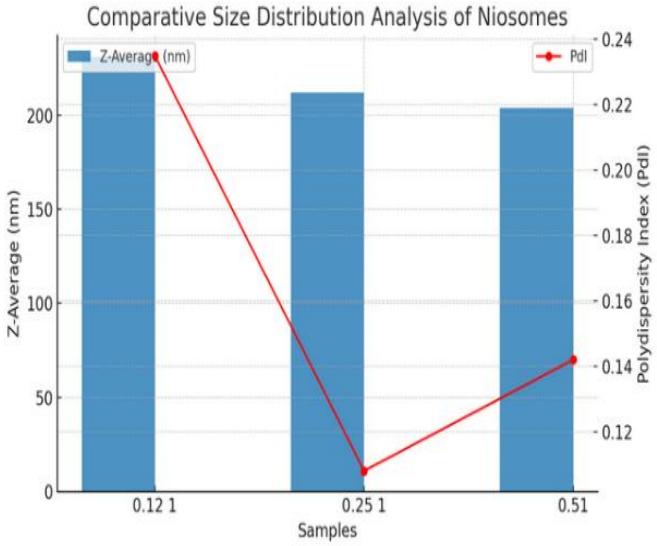


Fig. 14. Graphical comparison of Z-Average and PdI across the three niosome samples:

Bars (blue): Represent the Z-Average particle size (nm).

Line with red markers: Represents the Polydispersity Index (PdI).

6.8 In vitro drug release studies

The in vitro carvedilol release was performed in a USP type2 (Paddle type) dissolution test apparatus in distilled water. The volume of the freshwater outside the analysis tube is 900ml. considering the relatively short time interval for renewing the freshwater (30min), 900ml fresh water was considered enough in our experiment. The table shows the UV absorbance % release from placebo vesicle and carvedilol-loaded niosomal formulation.

Table 16: % Carvedilol release data from niosomal solution in distilled water

Time(min)	% Release of F1	% Release of F2	% Release of F3
0	0	0	0
30	13.56	1.85	2.94
90	14.38	2.45	5.90
210	17.67	4.67	10.79
330	18.36	7.25	18.10
510	19.50	10.87	23.49
750	23.45	18.6	33.2
1440	23.8	18.8	33.9

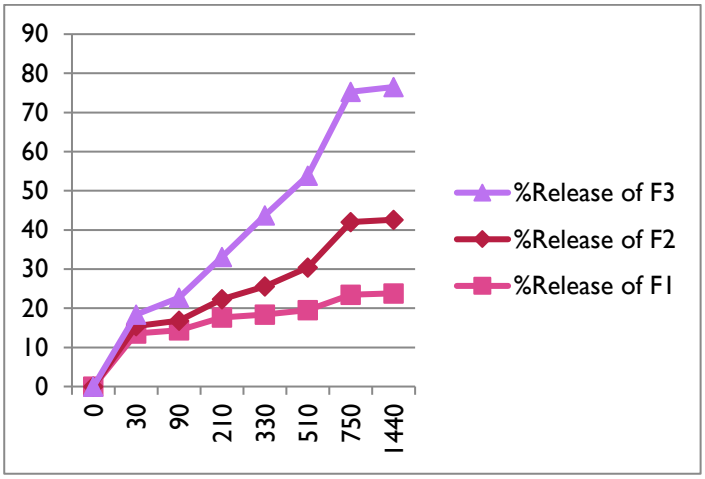


Fig. 15. Carvedilol release profiles from noisome formulations

6.9 Conclusion

Carvedilol-loaded niosomes made up of a simple combination of cremophor and cholesterol lie in the nano-range and can efficiently entrap lipophilic drugs. The entrapped was released at the slowest release rate which is supposed to be tunable

by the addition of other permeation-enhancing agents. Therefore, the food grade surfactants can provide a suitable alternative for orally consumable niosomal formulations.

All formulations exhibited negative zeta potentials, but none achieved the ±30 mV stability threshold.

F2 (Sample 0.25 1) showed optimal particle size (212.1 nm), narrowest distribution (PdI 0.108), and acceptable zeta potential (−5.38 mV), indicating good uniformity and moderate stability.

F1 (Sample 0.12 1) had larger, less uniform vesicles with poor size distribution.

F3 (Sample 0.51) achieved the highest drug release (33.9% at 24 h) but showed weak electrostatic stability (−2.14 mV), suggesting risk of aggregation and leakage.

FTIR confirmed no drug–excipient incompatibility across all formulations.

Overall, F2 is the most promising formulation, offering a balance between stability, uniformity, and controlled release, making it suitable for further development

REFERENCES

[1] Salvioni R, Rizzuto MA, Bertolini JA, Pandolfi L, Colombo M, Prosperi D. Thirty Years of Cancer Nanomedicine: Success, Frustration, and Hope. Cancers (Basel). 2019;11(12):1855. (Nanocarrier protection, targeting, PK/BD overview). PMC

[2] Wilhelm S, Tavares AJ, Dai Q, et al. Analysis of nanoparticle delivery to tumours. Nat Rev Mater. 2016;1:16014. (Factors governing PK/BD and tumour delivery). PMC

[3] Danaei M, Dehghankhold M, Ataei S, et al. Impact of particle size and polydispersity index on the clinical applications of lipidic nanocarrier systems. Pharmaceutics. 2018;10(2):57. (Barriers incl. RES/clearance; delivery inefficiencies). SpringerOpen

[4] Yang H, Zheng X, Liu X, et al. Transformative Impact of Nanocarrier-Mediated Drug Delivery. Small Sci. 2024;4(7):2300213. (Cargo protection, enhanced dose to target, design strategies). Wiley Online Library

[5] Ventola CL. Progress in Nanomedicine: Approved and Investigational Nanodrugs. P T. 2017;42(12):742–755. (Snapshot of approvals & the small fraction reaching clinic). PMC

[6] Shi J, Kantoff PW, Wooster R, Farokhzad OC. Cancer nanomedicine: progress, challenges and opportunities. Nat Rev Cancer. 2017;17(1):20–37. (Translational hurdles; limited clinical impact to date). Nature

[7] Lammers T, Ferrari M. Cancer nanomedicine toward clinical translation: Obstacles and opportunities. Med (N Y). 2022;3(7):467–471. (Contemporary view of low translation rates and causes). Cell

[8] Moghassemi S, Hadjizadeh A. Niosomes as nanoscale drug delivery systems: an updated review. J Control Release. 2014;185:22–36. (Definition; composition; advantages vs liposomes). ScienceDirect

[9] Abdelkader H, Alani AWH, Alany RG. Recent advances in non-ionic surfactant vesicles (niosomes): self-assembly, fabrication, characterization, drug delivery applications and limitations. Drug Deliv. 2014;21(2):87–100. (Self-assembly; hydrophilic/lipophilic loading; applications). PMC

[10] Muzzalupo R, Tavano L. Niosomes in nanotechnology: Paving the way to targeted drug delivery. Pharmaceutics. 2023;15(2):223. (Formulation flexibility; stability; targeting). MDPI

[11] Dodi G, Hritcu D, Popa MI. Niosome preparation techniques and structure—An illustrated review. Pharmaceutics. 2024;16(7):1183. (Structure; ability to encapsulate hydrophilic/lipophilic/amphiphilic drugs). PMC

[12] Balakrishnan P, Shanmugam S, Lee WS, et al. Formulation and in vitro assessment of niosome-encapsulated docetaxel for cancer therapy. Int J Pharm. 2009;373(1-2):39–48. (Demonstrates stability advantages and delivery performance).

[13] Yue, Y., Zhou, H., Wang, J., et al. (2017). Pharmacokinetics and bioavailability of carvedilol. European Journal of Pharmaceutical Sciences, 109, 356–362. (Bioavailability ≈ 25%, first-pass metabolism, short half-life).

[14] Amidon, G.L., Lennernäs, H., Shah, V.P., Crison, J.R. (1995). A theoretical basis for a biopharmaceutic drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability. Pharmaceutical Research, 12(3), 413–420. (BCS classification; CAR as Class II drug).

[15] Gaudana, R., Jwala, J., Boddu, S.H.S., Mitra, A.K. (2009). Recent perspectives in ocular drug delivery. Pharmaceutical Research, 26(5), 1197–1216. (Ocular barriers, precorneal clearance, tear turnover).

[16] Bourlais, C.L., Acar, L., Zia, H., Sado, P.A., Needham, T., Leverge, R. (1998). Ophthalmic drug delivery systems—recent advances. Progress in Retinal and Eye Research, 17(1), 33–58. (Challenges in ocular bioavailability).

[17] Prausnitz, M.R., Langer, R. (2008). Transdermal drug delivery. Nature Biotechnology, 26(11), 1261–1268. (Advantages of bypassing first-pass metabolism, sustained release).

[18] Del Amo, E.M., Urtti, A. (2008). Current and future ophthalmic drug delivery systems: a shift to the posterior segment. Drug Discovery Today, 13(3-4), 135–143. (Emerging nanocarriers for ocular therapy).

[19] Torchilin, V.P. (2014). Multifunctional, stimuli-sensitive nanoparticulate systems for drug delivery. Nature Reviews Drug Discovery, 13, 813–827. (Nanocarriers: liposomes, micelles, dendrimers, nanoemulsions).

[20] Moghassemi, S., Hadjizadeh, A. (2014). Niosomes as nanoscale drug delivery systems: An updated review. Journal of Controlled Release, 185, 22–36. (Niosomes vs. liposomes).

[21] Abdelkader, H., Alany, R.G. (2014). Recent advances in non-ionic surfactant vesicles (niosomes): self-assembly, fabrication, characterization, drug delivery applications and limitations. Drug Delivery, 21(2), 87–100.

[22] Handjani-Vila, R.M., Ribier, A., Rondot, B., Vanlerberghe, G. (1979). Dispersions of lamellar phases of non-ionic lipids in cosmetic products. International Journal of Cosmetic Science, 1(5), 303–314. (First report of niosomes in the cosmetics industry).

[23] Tavano, L., Muzzalupo, R. (2023). Niosomes in nanotechnology: paving the way to targeted drug delivery. Pharmaceutics, 15(2), 223. (Recent pharmaceutical applications).

[24] Jadon, P.S., Gajbhiye, V., Jadon, R.S., Gajbhiye, K.R., Ganesh, N. (2009). Enhanced oral bioavailability of griseofulvin via niosomes. AAPS PharmSciTech, 10(4), 1186–1192. (Demonstrates pharmaceutical potential of niosomes).

[25] LabIndia Instruments. DS-8000 Dissolution Test Apparatus with Autosampler. LabIndia Analytical Instruments Pvt. Ltd. (Accessed 2025).

[26] Malvern Panalytical. Zetasizer Nano ZS90 – Particle Size and Zeta Potential Analyzer. Malvern Instruments, UK. (Accessed 2025).

[27] Shimadzu Corporation. IRAffinity-1 FTIR Spectrophotometer. Kyoto, Japan. (Accessed 2025).

[28] FEI Company. Tecnai G2 Spirit Transmission Electron Microscope. Thermo Fisher Scientific. (Accessed 2025).

[29] Sahoo RK, Biswas N, Guha A, Sahoo N, Kuotsu K. Niosomes: Applications and Scope in Drug Delivery. Int J Pharm Sci Res. 2014;5(9):3221–30.

[30] Moghassemi S, Hadjizadeh A. Nano-niosomes s nanoscale drug delivery systems: An illustrated review. J Control Release. 2014;185:22–36.

[31] Moghimipour E, et al. Preparation and characterization of niosomes containing minoxidil for enhanced drug delivery. J Drug Deliv Sci Technol. 2012;22(6):455–60.

[32] Yeo PL, Lim CL, Chye SM, Ling APK. Niosomes as vesicular carriers for delivery of therapeutic agents: an update. Int J Nanomedicine. 2021;16:8667–85.

[33] Uchegbu IF, Vyas SP. Non-ionic surfactant based vesicles (niosomes) in drug delivery. Int J Pharm. 1998;172(1–2):33–70.

[34] Bhardwaj P, Tripathi P, Gupta R, Pandey A. Niosomes: A review on niosomal research in the last decade. J Drug Deliv Sci Technol. 2020;56:101581.

[35] Bragagni M, Mennini N, Maestrelli F, Cirri M, Mura P. Comparative study of liposomes, transfersomes and niosomes as carriers for improving topical delivery of celecoxib. Drug Deliv. 2012;19(7):354–61

[36] British Pharmacopoeia Commission. British Pharmacopoeia 2013, Vol. II. London: The Stationery Office; 2013. Carvedilol Monograph.

[37] Budavari S, editor. The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals. 14th ed. Whitehouse Station, NJ: Merck & Co., Inc.; 2006.

[38] Skoog DA, Holler FJ, Crouch SR. Principles of Instrumental Analysis. 7th ed. Cengage Learning; 2017.

[39] Sweetman SC, editor. Martindale: The Complete Drug Reference. 38th ed. London: Pharmaceutical Press; 2014.

[40] Stuart B. Infrared Spectroscopy: Fundamentals and Applications. John Wiley & Sons; 2004.

[41] Pavia DL, Lampman GM, Kriz GS, Vyvyan JR. Introduction to Spectroscopy. 5th ed. Cengage Learning; 2014.

[42] Skoog DA, Holler FJ, Crouch SR. Principles of Instrumental Analysis. 7th ed. Cengage Learning; 2017.

[43] Smith BC. Infrared Spectral Interpretation: A Systematic Approach. CRC Press; 2018.

[44] Kumbhar DD, Waghmare JT, Jadhav SA, Salunkhe VR, Bhise SB. Characterization of Carvedilol solid dispersions using FTIR and DSC techniques. Int J Pharm Pharm Sci. 2013;5(3):495–500.

[45] Patil PS, Chavan SS, Suryawanshi HP. Spectroscopic analysis of Carvedilol inclusion complexes with cyclodextrins. J Appl Pharm Sci. 2016;6(9):110–6.

[46] Bhardwaj P, Tripathi P, Gupta R, Pandey A. Niosomes: A review on niosomal research in the last decade. J Drug Deliv Sci Technol. 2020;56:101581..