J Nanostruct 15(4): 2143-2151, Autumn 2025

RESEARCH PAPER

Development of Carvedilol-Encapsulated Liposomal Nanoparticles Using the Thin Film Hydration Method: A Design Expert®-Based Approach

Husain Saeed [1]*, ***Sarmad Al-Edresi*** [2]

[1] *Najaf Health Directorate, Alzahraa Teaching Hospital, Najaf, Iraq*

[2] *Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, University of Kufa, Najaf-52001, Iraq*

ARTICLE INFO

Article History:
Received 29 June 2025
Accepted 16 September 2025
Published 01 October 2025

Keywords:
Carvedilol
Liposomes
Thin-film hydration method

ABSTRACT

Liposomes are tiny spherical structures made from phospholipid bilayers that can encapsulate drugs with varying solubility profiles. Their unique ability to improve drug solubility, protect active compounds, and enable targeted delivery makes them valuable in pharmaceutical applications. This nanocarrier system is handy for enhancing the bioavailability of drugs like carvedilol, which have poor water solubility. Carvedilol is a non-selective beta-blocker commonly used to treat hypertension and heart failure. However, its poor water solubility limits its bioavailability and therapeutic effectiveness. Incorporating carvedilol into liposomal nanoparticles can improve its solubility and controlled release, potentially enhancing its clinical performance. This study aimed to prepare carvedilol-loaded liposomal nanoparticles using the hydration method and to apply Design Expert® software to choose the best formulation while minimising time and cost. The quantities of phospholipids and cholesterol were varied and considered as independent variables. In contrast, particle size, polydispersity index (PDI), entrapment efficiency, drug loading and zeta potential were considered as characterisation outcomes. The liposomes were prepared using the thin film hydration method. The particle size and polydispersity index (PDI) were analysed using the ABT-9000 Nano Laser particle Size analyser. The particle size ranged from 147-61 nm, with a homogeneous distribution indicated by a PDI of ≤ 0.1, and the zeta potential values of the liposomal formulations ranged from −0.3 mV to −12.4 mV. The entrapment efficiency (EE) and drug loading (DL) of the formulations ranged from 55.41% to 92.38% and from 6.52% to 13.58%, respectively, as determined using a Shimadzu UV–Visible spectrophotometer. Liposomes were successfully prepared using the film hydration method, followed by particle size reduction through extrusion. The selected formulation consisted of 24.5 mg DPPC, 15.5 mg HSPC, and 7.5 mg cholesterol.

How to cite this article
Saeed H., Al-Edresi S.. Development of Carvedilol-Encapsulated Liposomal Nanoparticles Using the Thin Film Hydration Method: A Design Expert®-Based Approach. J Nanostruct, 2025; 15(4):2143-2151. DOI: 10.22052/JNS.2025.04.054

* *Corresponding Author Email: husseins.alsarraf@student.uokufa.edu.iq*

INTRODUCTION

Carvedilol is a nonselective beta-adrenergic antagonist commonly prescribed for the chronic management of heart failure with reduced ejection fraction, hypertension, and impaired left ventricular function following myocardial infarction in clinically stable patients. Additionally, it is sometimes used off-label to treat stable angina, control atrial fibrillation, prevent oesophageal variceal bleeding in cirrhotic patients, and manage ventricular arrhythmias [1].

Carvedilol exhibits low oral bioavailability and is poorly soluble in water, which can result in frequent dosing and reduced patient adherence to long-term treatment [2]. Currently on the market, about 40% of medications are classified as poorly soluble in water. Furthermore, it's believed that roughly 70% of recently created medication candidates have poor solubility in water [3].

In order to get around this problem for weakly water-soluble APIs, several techniques have been developed, including liposomes, nanoemulsions, melt extrusion, salt creation, solid dispersions, nanostructured lipid carriers, and micellar systems [4]. In 1961, Alec D. Bangham, in England, developed the first artificial liposomes. He discovered that phospholipids spontaneously assemble into spherical structures when mixed with water, as each molecule possesses a water-soluble end and a water-insoluble end [5].

Liposomes are small, spherical vesicles composed of the same material as the cell membrane. The term 'liposome' originates from two Greek words: 'Lipos, meaning fat, and 'soma, meaning body. Phospholipid molecules can spontaneously self-assemble into a bilayer structure, forming these tiny vesicles [6]. Liposomes can encapsulate both lipophilic and hydrophilic drugs within their lipid bilayer and internal aqueous compartment, respectively [7]. Liposomes offer several advantages as oral drug carriers, such as excellent biocompatibility, the ability to encapsulate various drugs, adaptable membrane composition, modifiable surfaces, potentially enhanced permeability, and tunable pharmacokinetic profiles [8].

The present study aimed to formulate and optimise liposomal formulations using Design Expert® software to minimise both time and cost.

MATERIALS AND METHODS

Materials

Carvedilol was purchased from Shanghai Aladdin Biochemical Technology Co., Ltd. (Shanghi, china). 1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC) was purchased from Shanghai CarbonBond Chemical Co., Ltd. (Shanghai, China). Hydrogenated soy phosphatidylcholine (HSPC) was purchased from JYOUKI Pharmaceutical CO., Ltd. (Fushun, China). Isopore™ Polycarbonate (PC) Membrane Filters with a pore size of 100 nm were purchased from Merck Millipore Ltd. (Cork, Ireland).

Methods

Preparation of carvedilol liposomes

This research involved the preparation of

Table 1. Various formulations of carvedilol-loaded liposomes.

Formula	DPPC (mg)	HSPC (mg)	Cholesterol (mg)
F1	45	45	2
F2	45	15	8
F3	15	45	2
F4	15	45	2
F5	15	15	8
F6	45	45	8
F7	45	45	8
F8	30	30	5
F9	15	15	8
F10	45	15	8
F11	15	15	2
F12	15	15	2
F13	15	45	8
F14	45	45	2
F15	15	45	8
F16	45	15	2
F17	45	15	2

liposomes through the thin-layer hydration method using a Heidolph rotary evaporator [9]. For the preparation of liposome formulations, various quantities of phospholipids (DPPC, HSPC) and cholesterol were used, as shown in Table 1. In a round-bottom flask, all lipids and the hydrophobic medication are dissolved in 2:3 methanol and chloroform mixture [10]. The organic solvent was then removed using a rotary evaporator operated under reduced pressure at a temperature above the lipid transition temperature, until a thin film was formed [11].

The film was then hydrated by adding 10ml of phosphate buffer. The flask was once again circulated on the rotary flask evaporator without vacuum above the phospholipid transition temperature until a white, milky suspension was achieved in order to disperse the film in the solution [7]. In order to decrease the liposomes' size further, the dispersion was repeatedly extruded 10 times through a polycarbonate membrane with a pore size of 100 nm.

Characterisation of carvedilol liposomes

Measurement of particle size, polydispersity index

Particle size and polydispersity index of liposomes were determined by the dynamic light scattering method by using ABT-9000 Nano Laser Particle Size Analyser. In essence, PDI shows how the sizes of populations are distributed throughout a sample. A PDI of 0.3 or less is regarded as appropriate in drug delivery applications utilising lipid-based carriers, such as liposome and nanoliposome formulations, and denotes a uniform population of phospholipid vesicles [12].

Measurement of zeta potential

Zeta potential of liposome formulations was measured using a Zetasizer (Malvern Panalytical, UK). After diluting each sample with distilled water to the appropriate concentration, analysis was carried out at 25 ºC with a detection angle of 90 ºC [13].

The charges that are present on the liposome surface are known as the zeta potential. All liposomes in the formulation must have a charge on their surface, as this prevents particle coagulation [14]. This charge causes the liposome particles to repel one another, preventing coagulation [15]. It is necessary to have a zeta potential value that falls between +30 and -30mV. These ranges stop liposomal particles from aggregating [6].

Entrapment Efficiency and Drug Loading

The entrapment efficiency and drug loading were determined by separating non-encapsulated carvedilol from the liposomal suspension by centrifugation [16]. A 2 ml of liposome suspension was centrifuged at 13000 rpm for 30 min at 4 °C.

The supernatant was removed, and liposomes were disrupted with methanol to release the entrapped drug. The quantity of the drug was measured by using UV spectroscopy at 285 nm [17]. The EE and LC were measured using Eqs. 1 and 2.

$$\text{Entrapment efficiency} = \frac{\text{Entrapped drug(mg)}}{\text{Total drug added(mg)}} \times 100 \quad (1)$$

$$\text{Loading efficiency} = \frac{\text{Weight of entrapped drug(mg)}}{\text{Weight of liposome(mg)}} \times 100 \quad (2)$$

In vitro drug release

The *in vitro* release of carvedilol-loaded liposomes was evaluated using the dialysis bag diffusion method. A dialysis membrane with a molecular weight cutoff of 14,000 Da was pre-soaked in phosphate buffer (pH 6.8) for 24 hours prior to use to ensure complete wetting and removal of any preservatives. The release study was performed in phosphate buffer (pH 6.8) containing 0.1% Tween 80, maintained at 37 ± 0.5 °C under constant magnetic stirring at 100 rpm [3]. A 2 mL aliquot of the liposomal dispersion, equivalent to 2 mg of carvedilol, was placed into the dialysis bag, and the open end was securely tied with a thread before immersion in the release medium. At predetermined time intervals (1, 2, 3, 4, 5, 6, 7, 8, and 14 hours), 5 ml of the release medium was withdrawn and replaced with an equal volume of fresh medium to maintain sink conditions [18]. The amount of carvedilol released was quantified using UV–visible spectrophotometry.

Fourier transform infrared spectroscopy

Several FTIR spectra were obtained using an FTIR spectrophotometer (Shimadzu, Japan) for pure carvedilol powder, a physical mixture, blank liposomal nanoparticles (without drug), and the carvedilol-loaded liposomal formulation [19]. For each measurement, the sample was thoroughly mixed with potassium bromide (KBr) powder and subsequently compressed into a disc containing approximately 2% (w/w) of the sample. The

spectra were recorded over the range of 4000–600 cm^{-1} with a resolution of 4 cm^{-1} [20].

Statistical analysis

A full factorial design was employed using Design-Expert® software version 13 (Stat-Ease Inc., USA) to systematically investigate the influence of three independent variables -DPPC, HSPC, and cholesterol on the physicochemical properties of carvedilol-loaded liposomes [21]. The factorial design enabled the evaluation of both the individual effects of each variable and interaction effects between them on key responses, including particle size, polydispersity index (PDI), entrapment efficiency (EE), drug loading (DL), and zeta potential [22]. Statistical significance was assessed using analysis of variance (ANOVA), and model adequacy was evaluated through diagnostic plots such as Pareto charts and response surface plots. This approach facilitated the identification of an optimal formulation by maximising desirability, ensuring efficient and cost-effective development of a stable liposomal system.

RESULT AND DISCUSSION

Particle size and PDI

The influence of formulation variables A-DPPC, B-HSPC and C-Cholesteryl on the particle size of carvedilol-loaded liposomes was analysed using a Pareto chart, as shown in Fig. 1. The chart revealed that HSPC had the most significant positive effect on particle size, followed by DPPC and cholesterol [23]. This indicates that increasing their concentrations leads to larger vesicle sizes. Interaction terms such as AB, AC, and BC showed minor effects and were statistically insignificant compared to the main effects.

HSPC is a saturated phospholipid with a high phase transition temperature and tight lipid packing, leading to increased membrane rigidity and particle size. The observed increase in liposome particle size with increased concentrations of DPPC and cholesterol is consistent with the findings reported by Lopez-Pinto *et al*. (2005) and Kumar *et al*. (2010), who also demonstrated that increases in DPPC and cholesterol contribute to increased membrane rigidity and particle size [10, 24].

All formulations exhibited polydispersity index (PDI) values below 0.1, indicating a uniform and monodisperse particle distribution. The use of extrusion contributed significantly to achieving these low PDI values across all formulations. These results are consistent with the findings of Kuntsche *et al*. (2010), who demonstrated that extrusion effectively produces monodisperse liposomal formulations by reducing particle size [25].

Entrapment Efficiency and Drug Loading

The composition of phospholipids and cholesterol significantly influenced the entrapment efficiency of carvedilol-loaded liposomes. The combination of DPPC and HSPC exhibited the

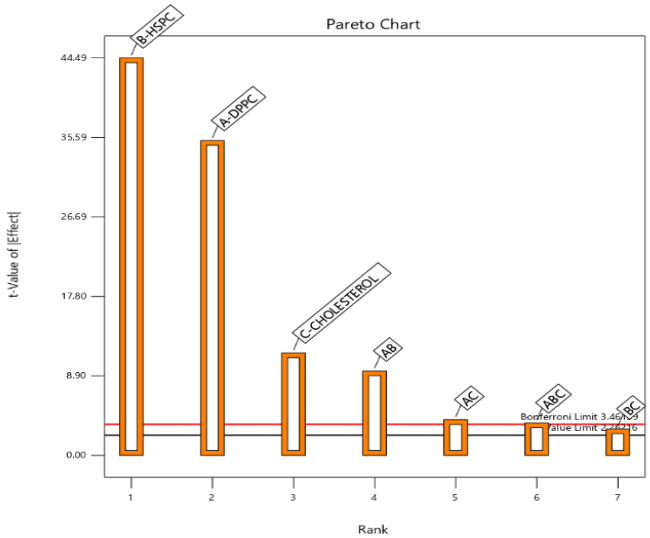

Fig. 1. Pareto chart showing the effects of DPPC, HSPC, and cholesterol on the particle size of carvedilol-loaded liposomes.

strongest, most potent positive effect on drug entrapment, suggesting a synergistic interaction between the two saturated phospholipids. Increasing the concentration of cholesterol also contributed positively, likely due to its role in enhancing bilayer stability and reducing membrane permeability [22].

This finding agrees with the results reported by El-Nesr *et al*. (2010), who observed that increasing the cholesterol content in liposomal formulations significantly improved the entrapment efficiency of fluconazole, attributing the effect to the reduced membrane fluidity and increased rigidity of the lipid bilayer, which minimises drug leakage [26]. Individually, DPPC had a greater impact on entrapment efficiency compared to HSPC, likely due to differences in lipid bilayer properties and specific interactions with carvedilol. This observation is consistent with findings reported by Najlah *et al*. (2018), where DPPC-based liposomes achieved 35–92% paclitaxel (PX) entrapment, compared to 25–60% with HSPC-based formulations [27].

In addition to entrapment efficiency, drug loading (DL) is another key parameter in evaluating liposomal formulations [28]. While EE reflects the proportion of drug successfully encapsulated relative to the total amount used, DL indicates the amount of drug loaded per unit weight of lipid, which is critical for determining dosing efficiency and excipient burden. An increased drug-to-lipid ratio may reduce formulation costs and minimise lipid-associated toxicity by requiring less lipid to deliver an effective drug dose.

The entrapment efficiency (EE) and drug loading (DL) of the formulations range from 55.41% to 92.38% and from 6.52% to 13.58% respectively.

Measurement of zeta potential

The zeta potential measurements of the formulations varied between −0.3 mV and −12.4 mV, indicating a generally negative surface charge across all samples. These results align with those reported by Chen *et al*., (2014), who investigated brucine-incorporated liposomes prepared with HSPC and DPPC, which exhibited zeta potentials ranging from −5.96 to −3.20 mV [29]. Despite being within the moderate range of electrostatic stabilisations (±30 mV), the formulations demonstrated good physical stability, likely due to uniform particle size and lipid composition.

In vitro drug release

Five formulations were tested, including four liposomal preparations (F1 = F14, F6 = F7, F16 = F17, F4 = F3) and a pure drug suspension. The release profiles demonstrated a biphasic pattern for all formulations, characterised by an initial moderate release followed by a sustained release phase.

Among the formulations, F16 = F17 exhibited the highest cumulative drug release (87.29% at 14 h), attributed to its low HSPC content, which possibly led to higher membrane permeability. In

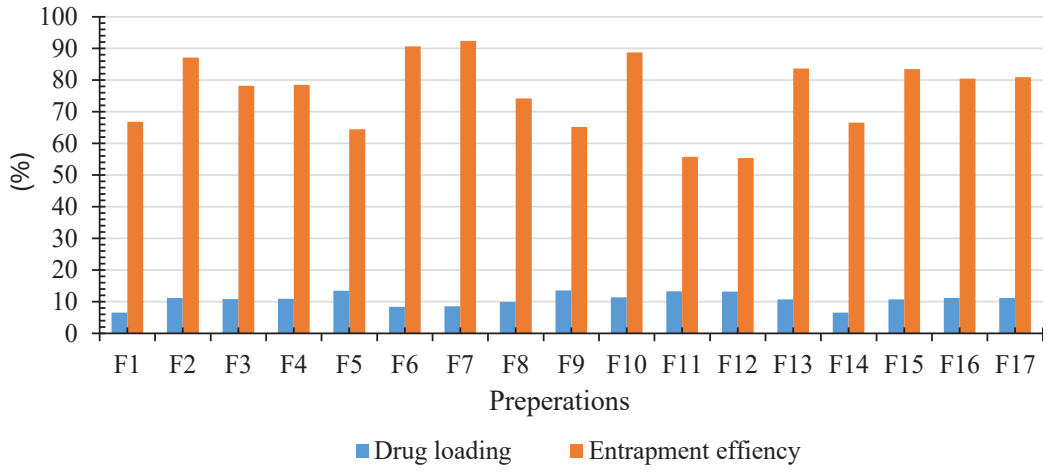

Fig. 2. Comparison of entrapment efficiency (EE) and drug loading (DL) of carvedilol-loaded liposomes for all prepared formulations (F1–F17), illustrating the impact of varying DPPC, HSPC, and cholesterol concentrations on encapsulation performance.

contrast, F6 = F7, with a high cholesterol content (8 mg), showed a more sustained release profile (77.44% at 14 h), confirming the role of cholesterol in stabilising the lipid bilayer and retarding drug diffusion. F1 = F14 demonstrated an intermediate release behaviour (81.3% at 14 h), while F4 = F3 showed relatively rapid release due to lower DPPC content. The pure carvedilol suspension exhibited a non-controlled release pattern, reaching only 64.48% at 14 hours, likely due to its limited aqueous solubility, even in the presence of Tween 80.

These findings suggest that the lipid composition, particularly the ratio of cholesterol and phospholipids, has a considerable influence on the drug release kinetics from liposomal carriers. these observations are supported by the data shown in Fig. 3.

Fourier transform infrared spectroscopy

The FTIR analysis was performed on carvedilol powder to assess the drug's purity and to evaluate its compatibility with the phospholipids and cholesterol. The study revealed distinctive peaks at 3346.5 cm^{-1}, corresponding to the stretching vibrations of N–H and O–H groups, and at 1255.66 cm^{-1}, attributed to C–O and O–H bending vibrations. These findings are in agreement

Table 2. Characterisation results for carvedilol liposomes formulations.

Formulation	Particle size (nm)	Polydispersity	Entrapment effiency%	Drug loading%	Zeta potential
F1	119	0.029	66.86	6.554	-1.2
F2	84.3	0.034	87.085	11.164	-6.1
F3	84	0.056	78.25	10.868	-1.6
F4	87.7	0.062	78.525	10.909	-2.9
F5	66.2	0.087	64.51	13.439	-3.367
F6	144	0.016	90.645	8.393	-6.1
F7	147	0.014	92.38	8.553	-5.505
F8	84	0.028	74.255	9.9	-0.9992
F9	68	0.066	65.2	13.583	-4.169
F10	85.2	0.032	88.805	11.385	-5.505
F11	63.7	0.043	55.715	13.264	-0.3037
F12	61.1	0.065	55.415	13.192	-0.4017
F13	91.6	0.051	83.705	10.731	-3.9
F14	120	0.031	66.545	6.523	-1.8
F15	90.8	0.031	83.525	10.708	-3.367
F16	78.7	0.041	80.5	11.18	-9.4
F17	77.9	0.034	80.91	11.237	-12.4

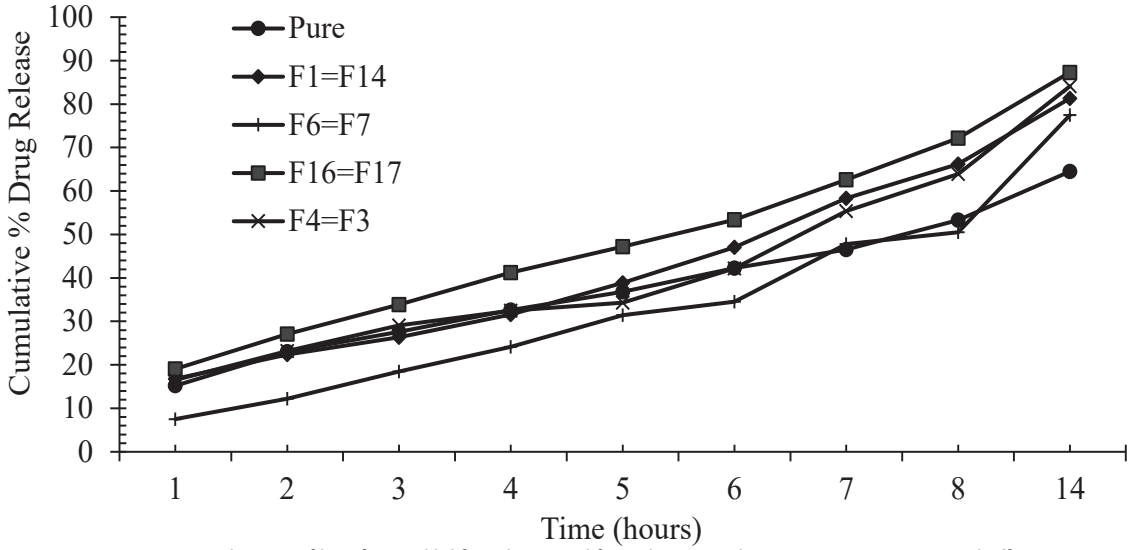

Fig. 3. In vitro release profiles of carvedilol from liposomal formulations and pure suspension in pH 6.8 buffer.

with Rehab *et al*., (2021), who reported that pure carvedilol exhibits peaks at 3344.66 cm^{-1} and 1255.39 cm^{-1}, respectively [30]. The peak at 2924.09 cm^{-1} corresponds to C–H stretching vibrations, while the peak at 1602.85 cm^{-1} results from bending vibrations of the N–H group. These

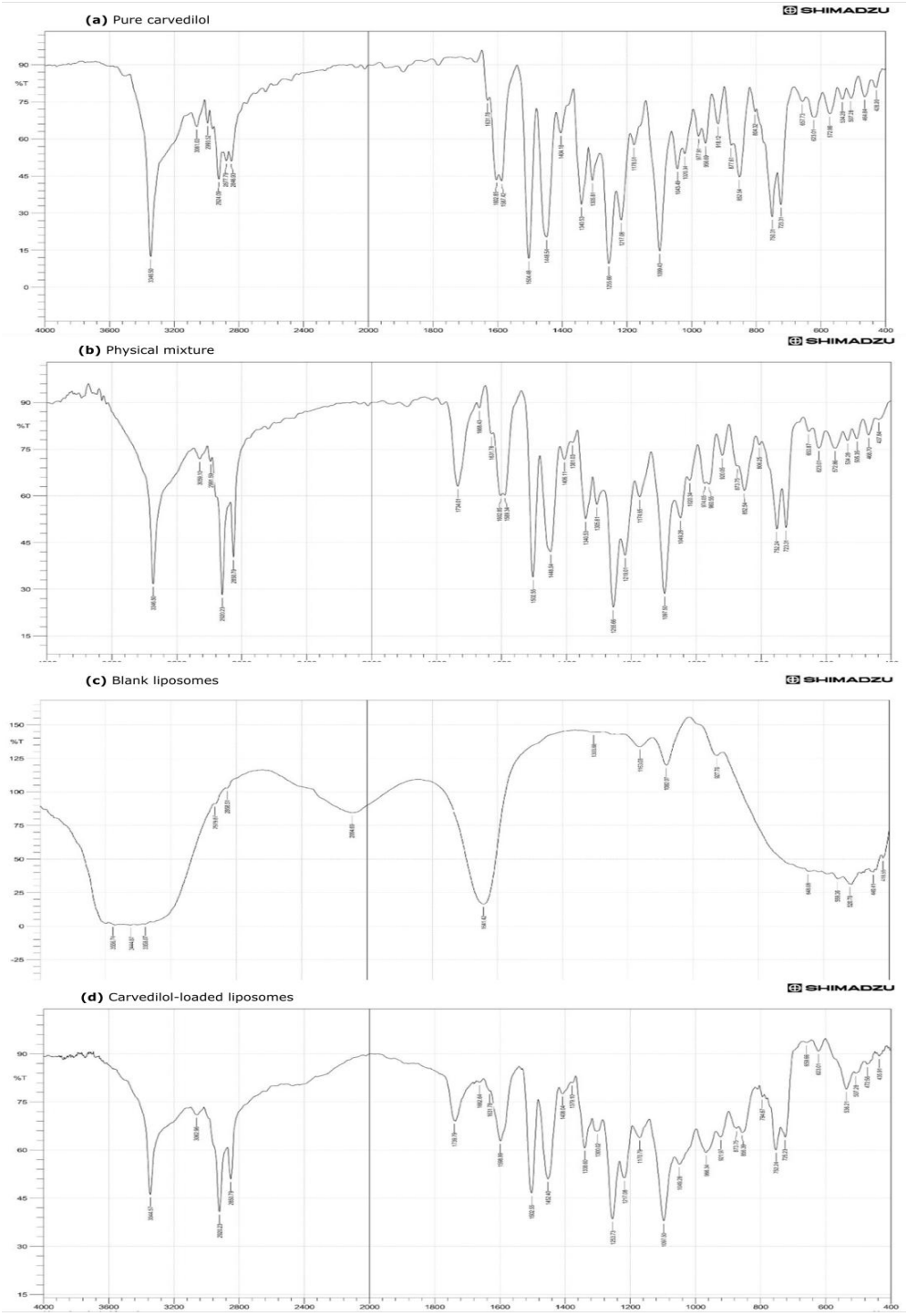

Fig. 4. The FTIR spectra of (a) pure carvedilol, (b) physical mixture of carvedilol with lipids and cholesterol, (c) blank liposomes, and (d) carvedilol-loaded liposomal formulation.

results are in agreement with Alves *et al*., (2016), who reported that carvedilol exhibits peaks at 2924 cm^{-1} and 1598 cm^{-1}, respectively [20]. These characteristic peaks observed in the FTIR spectrum confirm the purity of the carvedilol powder, as shown in Fig. 3.

The FTIR compatibility test was conducted to confirm that carvedilol is compatible with the other liposomal ingredients and to identify any potential chemical interactions. This was achieved by comparing the FTIR spectrum of pure carvedilol to the spectra of the physical mixture and the carvedilol-loaded liposome formulation. The spectra revealed no significant shifts or disappearance of characteristic peaks, indicating that the functional groups remained essentially unchanged. These results suggest the absence of any chemical interaction between carvedilol and the excipients, thereby confirming their compatibility, as shown in Fig. 4.

CONCLUSION

In this study, carvedilol-loaded liposomal nanoparticles were successfully developed using the thin-film hydration method and then subjected to particle size reduction *via* extrusion. The findings demonstrate that careful selection and optimisation of phospholipid and cholesterol concentrations, optimised by Design Expert® software, can produce liposomes with desirable particle size, high encapsulation efficiency, and good stability properties that are essential for enhancing the solubility and potential bioavailability of poorly water-soluble drugs like carvedilol. This approach highlights the potential of liposomal nanocarriers as a practical strategy for improving drug delivery and therapeutic outcomes.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

REFERENCES

1. Hupe M. StatPearls. Journal of Electronic Resources in Medical Libraries. 2024;21(3):147-152.
2. Kar S, Singh SK. Cationic nanoliposomes of carvedilol for intranasal application: In vitro, in vivo and in silico studies. J Drug Deliv Sci Technol. 2023;80:104178.
3. Ghassemi S, Haeri A, Shahhosseini S, Dadashzadeh S. Labrasol-Enriched Nanoliposomal Formulation: Novel Approach to Improve Oral Absorption of Water-Insoluble Drug, Carvedilol. AAPS PharmSciTech. 2018;19(7):2961-2970.
4. Liu D, Pan H, He F, Wang X, Li J, Yang X, et al. Effect of particle size on oral absorption of carvedilol nanosuspensions: in vitro and in vivo evaluation. International Journal of Nanomedicine. 2015:6425.
5. Maherani B, Arab-Tehrany E, R. Mozafari M, Gaiani C, Linder M. Liposomes: A Review of Manufacturing Techniques and Targeting Strategies. Current Nanoscience. 2011;7(3):436-452.
6. Umbarkar M, Thakare S, Surushe T, Giri A, Chopade V. Formulation and Evaluation of Liposome by Thin Film Hydration Method. Journal of Drug Delivery and Therapeutics. 2021;11(1):72-76.
7. Godbole MD, Mathur VB. Selection of Phospholipid and Method of Formulation for Optimum Entrapment and Release of Lamivudine from Liposome. Journal of Drug Delivery and Therapeutics. 2018;8(5-s):175-183.
8. Lee M-K. Liposomes for Enhanced Bioavailability of Water-Insoluble Drugs: In Vivo Evidence and Recent Approaches. Pharmaceutics. 2020;12(3):264.
9. Pattni BS, Chupin VV, Torchilin VP. New Developments in Liposomal Drug Delivery. Chem Rev. 2015;115(19):10938-10966.
10. Joshi H, Shelat P, Dave D. Development and Characterization of Liposomal formulation for ophthalmic delivery of Prednisolone Acetate. International Journal of Pharmaceutical Sciences and Drug Research. 2020:175-180.
11. Nsairat H, Khater D, Sayed U, Odeh F, Al Bawab A, Alshaer W. Liposomes: structure, composition, types, and clinical applications. Heliyon. 2022;8(5):e09394.
12. Danaei M, Dehghankhold M, Ataei S, Hasanzadeh Davarani F, Javanmard R, Dokhani A, et al. Impact of Particle Size and Polydispersity Index on the Clinical Applications of Lipidic Nanocarrier Systems. Pharmaceutics. 2018;10(2):57.
13. Janga KY, Jukanti R, Velpula A, Sunkavalli S, Bandari S, Kandadi P, et al. Bioavailability enhancement of zaleplon via proliposomes: Role of surface charge. Eur J Pharm Biopharm. 2012;80(2):347-357.
14. Shawka Al-Asadi LJA, Al-Edresi S. REDUCTION OF TIME AND COST IN PREPARATION OF NANOFIBERS FROM PVA, PEO AND HPMC USING DESIGN-EXPERT® SOFTWARE. International Journal of Applied Pharmaceutics. 2024:257-266.
15. Nesalin JAJ, B N C. Formulation and Optimization of Rabeprazole Sodium-Loaded Liposomes using Design Expert Software. Asian Journal of Research in Pharmaceutical Sciences. 2025:237-244.
16. A.S. Al Janabi M, Edresi SSNAL. Preparation and validation of nanofibers loaded with silver sulfadiazine from zein/poly (ε -caprolactone)/poly (ethylene oxide) for topical dosage forms to improve release behaviour. Journal of Research in Pharmacy. 2024;28(6)(28(6)):2114-2125.
17. Abdelwahab NS. Spectrophotometric methods for simultaneous determination of Carvedilol and Hydrochlorothiazide in combined dosage form. Arabian Journal of Chemistry. 2016;9:S355-S360.
18. R. Atiyah S, Al-Edresi S. PREPARATION AND JUSTIFICATION OF NANOFIBRES-LOADED MAFENIDE USING ELECTROSPINNING TECHNIQUE TO CONTROL RELEASE. International Journal of Applied Pharmaceutics. 2024:224-230.
19. Al-Edresi S, Albo Hamrah K, Al-Shaibani A. Figure 5 from: Al-Edresi S, Albo Hamrah K, Al-Shaibani A (2024) Formulation and validation of Candesartan cilexetil-loaded nanosuspension to enhance solubility. Pharmacia 71: 1-13.

https://doi.org/10.3897/pharmacia.71.e114943. Pensoft Publishers; 2024. http://dx.doi.org/10.3897/pharmacia.71.e114943.figure5
20. Alves JMV, Prado LD, Rocha HVA. Evaluation and correlation of the physicochemical properties of carvedilol. Pharmaceutical Development and Technology. 2015;21(7):856-866.
21. Ayuhastuti A, Syah I, Megantara S, Chaerunisaa A. Nanotechnology-Enhanced Cosmetic Application of Kojic Acid Dipalmitate, a Kojic Acid Derivate with Improved Properties. Cosmetics. 2024;11(1):21.
22. Atiyah SR, Al-Edresi S. Preparation And Characterization of Polyvinyl Alcohol Nanofiber Loaded With Mafenide For Sustain Release. Journal Port Science Research. 2024;7(1):43-50.
23. Al-Hamadani MH, Al-Edresi S. Formulation and Characterization of Hydrogel of Proniosomes Loaded Diclofenac Sodium. INTERNATIONAL JOURNAL OF DRUG DELIVERY TECHNOLOGY. 2022;12(01):132-136.
24. López-Pinto JM, González-Rodríguez ML, Rabasco AM. Effect of cholesterol and ethanol on dermal delivery from DPPC liposomes. Int J Pharm. 2005;298(1):1-12.
25. Kuntsche J, Freisleben I, Steiniger F, Fahr A. Temoporfin-loaded liposomes: Physicochemical characterization. Eur J Pharm Sci. 2010;40(4):305-315.
26. El-Nesr OH, Yahiya SA, El-Gazayerly ON. Effect of formulation design and freeze-drying on properties of fluconazole multilamellar liposomes. Saudi Pharmaceutical Journal. 2010;18(4):217-224.
27. Najlah M, Jain M, Wan K-W, Ahmed W, Albed Alhnan M, Phoenix DA, et al. Ethanol-based proliposome delivery systems of paclitaxel for in vitro application against brain cancer cells. J Liposome Res. 2016;28(1):74-85.
28. Kadhim MJ, Al-Edresi S. Preparation and Characterization of Electrospun Ketoconazole Loaded Nanofibers as Dermal Patch. Journal of Contemporary Medical Sciences. 2024;10(4).
29. Chen J, He C-Q, Lin A-H, Xu F, Wang F, Zhao B, et al. Brucine-loaded liposomes composed of HSPC and DPPC at different ratios: in vitro and in vivo evaluation. Drug Development and Industrial Pharmacy. 2013;40(2):244-251.
30. Abdelmonem R, Elhabal SF, Abdelmalak NS, El-Nabarawi MA, Teaima MH. Formulation and Characterization of Acetazolamide/Carvedilol Niosomal Gel for Glaucoma Treatment: In Vitro, and In Vivo Study. Pharmaceutics. 2021;13(2):221.