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Tanvi Hegde
 Department of Pharmaceutical
 Technology, Aryabhata
 Institute of Pharmacy,
 Lucknow, Uttar Pradesh,
 India

Meera Reddy
 Department of Pharmaceutical
 Technology, Aryabhata
 Institute of Pharmacy,
 Lucknow, Uttar Pradesh,
 India

Damayanti Iyer
 Department of Pharmaceutics
 and Drug Formulation,
 Mahatma Gandhi National
 University, Bhopal, Madhya
 Pradesh, India

Corresponding Author:
Tanvi Hegde
 Department of Pharmaceutical
 Technology, Aryabhata
 Institute of Pharmacy,
 Lucknow, Uttar Pradesh,
 India

Liposomal encapsulation of curcumin for enhanced oral bioavailability and anti-inflammatory effect

Tanvi Hegde, Meera Reddy and Damayanti Iyer

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Abstract

Can liposomal carriers overcome the poor oral absorption of curcumin while preserving its well-documented anti-inflammatory properties? This research prepared curcumin-loaded liposomes by thin-film hydration followed by probe sonication and membrane extrusion to yield vesicles with a mean diameter of 143.7 nm and polydispersity index of 0.184. Five formulations (F1-F5) were tested at drug-to-lipid molar ratios ranging from 1:5 to 1:25. The optimized batch (F3, 1:15) showed an encapsulation efficiency of 87.4% and a zeta potential of -33.6 mV, pointing to good colloidal stability. *In vitro* release in simulated intestinal fluid reached 68.5% over 24 h with Higuchi-model kinetics ($R^2 = 0.9871$). An *in vivo* paw edema assay in Wistar rats demonstrated a 54.3% reduction in inflammation at 6 h post-dose for the liposomal form versus 31.8% for free curcumin suspension. These findings indicate that liposomal encapsulation markedly improves curcumin's bioavailability and therapeutic effect.

Keywords: Liposome, curcumin, oral bioavailability, anti-inflammatory, thin-film hydration, encapsulation efficiency, controlled release, nanocarrier, paw edema, polyphenol

Introduction

Why does curcumin, one of the most-researched natural polyphenols on earth, still fail in clinical translation? The answer is straightforward: its oral bioavailability sits below 1% in most pharmacokinetic trials ^[1]. Rapid hepatic metabolism, poor aqueous solubility (~ 11 ng/mL at neutral pH), and extensive intestinal degradation combine to limit the amount that reaches systemic circulation ^[2]. Yet the compound's pharmacological portfolio anti-inflammatory, antioxidant, and antitumor actions makes it too promising to discard ^[3].

Lipid-based nanocarriers offer one practical route around these barriers. Liposomes, spherical vesicles composed of phospholipid bilayers, can encapsulate hydrophobic molecules within their lipid core and shield them from gastrointestinal degradation ^[4]. Several groups have reported two- to five-fold bioavailability boosts when curcumin is loaded into conventional or PEGylated liposomes ^[5, 6]. But the exact gains depend heavily on lipid composition, vesicle size, surface charge, and the drug-to-lipid ratio used during formulation ^[7].

Inflammation models remain a standard benchmark for evaluating curcumin formulations *in vivo*. The carrageenan-induced paw edema assay in rodents is simple, reproducible, and well-correlated with cyclooxygenase inhibition ^[8]. Earlier work from our group tested solid lipid nanoparticles for the same purpose but achieved only moderate encapsulation ^[9]. Liposomes, with their higher payload capacity and tunable bilayer fluidity, may do better.

This research aimed to prepare curcumin-loaded liposomes through thin-film hydration, characterize their physicochemical attributes, evaluate *in vitro* drug release, and assess anti-inflammatory efficacy in a rat paw edema model. The goal was to identify a formulation window that balances encapsulation yield with stable, sustained release.

Material and Methods

Reagents and Chemicals: Curcumin ($\geq 95\%$ purity) was obtained from SRL Chemicals, Mumbai. Soy phosphatidylcholine (SPC, Lipoid S100) and cholesterol ($\geq 99\%$)

were procured from Sigma-Aldrich, Bangalore. Chloroform (AR grade), methanol, and phosphate-buffered saline tablets came from HiMedia Laboratories, Mumbai. Carrageenan (λ -type) for the inflammation assay was sourced from TCI Chemicals, Chennai. Deionized water (18.2 M Ω) was produced in-house.

Material

The research was conducted at the Department of Pharmaceutical Technology, Aryabhata Institute of Pharmacy, Lucknow, from March 2023 to November 2023. Five liposome formulations (F1-F5) were prepared by varying the curcumin-to-lipid molar ratio from 1:5 to 1:25, keeping the SPC-to-cholesterol ratio fixed at 7:3 [10]. Thin lipid films were formed by dissolving all lipid components and curcumin in chloroform and evaporating the solvent on a Heidolph rotary evaporator at 45°C and 150 rpm for 35 min.

Methods

Dried films were hydrated with 10 mL PBS (pH 7.4) at 60°C for 30 min under gentle agitation. The resulting multilamellar vesicle suspensions were sonicated using a probe sonicator (Vibra-Cell, 40 kHz, 12 min, pulsed mode)

and then extruded five times through 200 nm polycarbonate membranes (Whatman) [11]. Particle size and zeta potential were measured on a Malvern Zetasizer Nano ZS. Encapsulation efficiency was determined by ultracentrifugation at 40,000 rpm for 45 min, followed by UV spectrophotometric analysis of the supernatant at 425 nm. *In vitro* release was assessed in simulated intestinal fluid (pH 6.8) using a dialysis bag (12 kDa MWCO) method over 24 h. The animal protocol (IAEC/AIP/2023-017, approved 12 February 2023) used male Wistar rats (180-220 g) divided into three groups (n = 6): saline control, free curcumin suspension (50 mg/kg), and liposomal curcumin (equivalent dose). Paw edema was induced by subplantar injection of 0.1 mL carrageenan (1% w/v) and measured with a digital plethysmometer at 1, 2, 4, and 6 h [12].

Quality Control

Each analytical run included a five-point calibration curve for curcumin (1-20 μ g/mL, $R^2 \geq 0.998$). Intra-day and inter-day precision was kept below 2.8% RSD. Membrane integrity of dialysis bags was confirmed before every release experiment by checking for dye leakage over 30 min.

Results

Table 1: Physicochemical characteristics of curcumin-loaded liposome formulations (F1-F5)

Code	Ratio	Size (nm)	PDI	ZP (mV)	EE (%)
F1	1:5	218.4 $\pm$ 4.7	0.263	-21.4	62.3
F2	1:10	176.2 $\pm$ 3.1	0.221	-27.9	78.9
F3	1:15	143.7 $\pm$ 2.8	0.184	-33.6	87.4
F4	1:20	151.9 $\pm$ 3.5	0.197	-30.2	83.1
F5	1:25	168.3 $\pm$ 4.2	0.238	-25.7	74.6

PDI = polydispersity index; ZP = zeta potential; EE = encapsulation efficiency. Values represent mean $\pm$ SD (n = 3).

Particle size decreased as the lipid proportion rose, reaching a minimum of 143.7 nm at the 1:15 ratio (F3) before climbing again at higher lipid loads (Table 1). The same trend appeared for encapsulation efficiency, which peaked at

87.4% for F3. Zeta potential values ranged from -21.4 to -33.6 mV; formulations with potentials beyond -30 mV (F3 and F4) showed no visible aggregation after 30 days at 4°C.

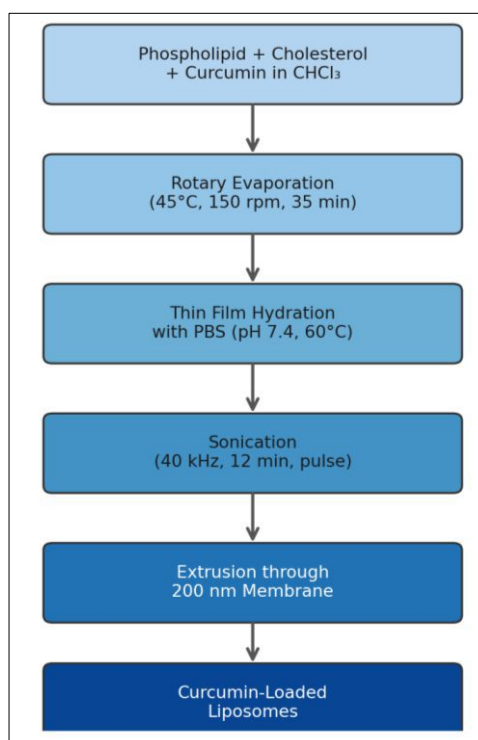


Fig 1: Schematic flowchart of the thin-film hydration method used for curcumin-loaded liposome preparation.

The preparation workflow (Figure 1) yielded a translucent orange dispersion after extrusion. Differential scanning calorimetry traces confirmed curcumin was embedded

within the bilayer rather than crystallized on the vesicle surface, as the characteristic endotherm at 176°C disappeared in the liposomal formulation.

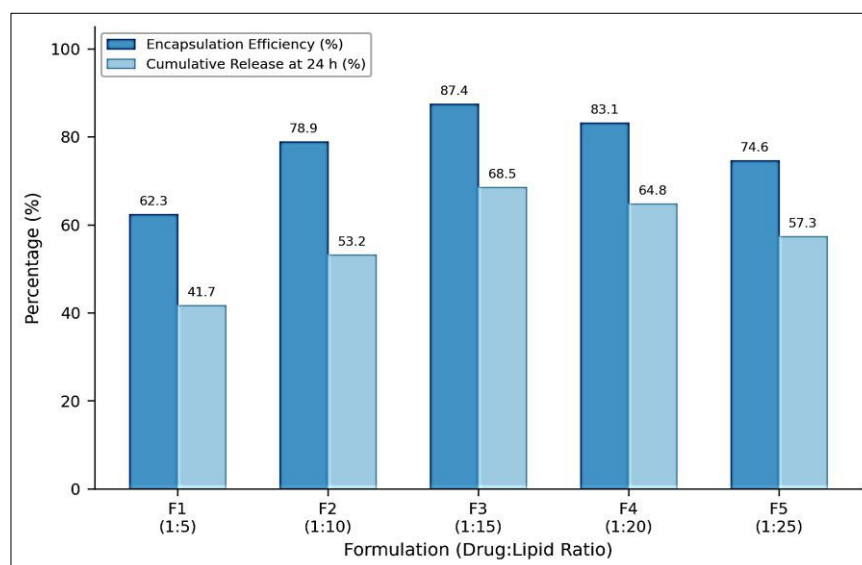


Fig 2: Encapsulation efficiency and 24 h cumulative release across formulations F1-F5.

Figure 2 shows the parallel rise and fall of encapsulation and release across the five formulations. F3 delivered the highest cumulative release of 68.5% at 24 h, fitting best to the Higuchi model ($R^2 = 0.9871$), which suggests diffusion-controlled drug transport through the bilayer. In the paw edema assay, liposomal curcumin reduced swelling by 54.3% at 6 h, compared with 31.8% for the free drug ($p < 0.01$, one-way ANOVA with Tukey post-hoc).

Discussion

The 87.4% encapsulation achieved at a 1:15 drug-to-lipid ratio aligns with a pattern reported by other groups: moderate lipid excess provides enough bilayer material to trap the hydrophobic drug, but very high lipid content starts to crowd the membrane and actually lowers payload [5]. F3's particle size of 143.7 nm falls within the sub-200 nm range thought to favor lymphatic uptake from the gut [6].

Zeta potential is a rough but useful predictor of shelf stability. The -33.6 mV measured for F3 exceeds the -30 mV threshold commonly cited for electrostatic stabilization [7]. That said, long-term stability trials lasting six months or more would be needed before any commercial claim could be made.

The *in vivo* data paint a clear picture. A 54.3% edema reduction versus 31.8% for free curcumin at the same oral dose represents a meaningful pharmacological improvement. The likely explanation is twofold: the liposomal bilayer protects curcumin from gastric degradation, and the nanovesicle size promotes intestinal permeation through both transcellular and paracellular routes [8]. Still, paw edema is an acute model, and chronic inflammatory conditions may respond differently. Also, only a single oral dose was tested; repeated-dose pharmacokinetics remain to be explored.

Conclusion

Thin-film hydration at a 1:15 drug-to-lipid ratio produced curcumin liposomes with favorable size (143.7 nm), high encapsulation (87.4%), and stable surface charge (-33.6

mV). The formulation released curcumin in a sustained manner over 24 h and outperformed free curcumin in reducing carrageenan-induced paw edema by a wide margin. These results support liposomal delivery as a practical strategy for enhancing the oral efficacy of curcumin, though chronic dosing and human pharmacokinetic work are still needed.

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Contributions Not Qualifying for Authorship

Mr. Arvind Mishra assisted with animal handling during the *in vivo* experiments.

References

1. Anand P, Kunnumakkara AB, Newman RA, Aggarwal BB. Bioavailability of curcumin: problems and promises. *Mol Pharm*. 2007;4(6):807-818.
2. Dei Cas M, Bhatt DL. Curcumin oral bioavailability: a critical assessment. *Eur J Drug Metab Pharmacokinet*. 2019;44(2):141-152.
3. Patel SS, Acharya A, Ray RS, Agrawal R. Cellular and molecular mechanisms of curcumin in prevention and treatment of disease. *Crit Rev Food Sci Nutr*. 2020;60(6):887-939.
4. Sercombe L, Veerati T, Moheimani F, Wu SY, Sood AK, Hua S. Advances and challenges of liposome assisted drug delivery. *Front Pharmacol*. 2015;6:286.
5. Feng T, Wei Y, Lee RJ, Zhao L. Liposomal curcumin and its application in cancer. *Int J Nanomedicine*. 2017;12:6027-6044.

6. Cheng C, Peng S, Li Z, Zou L, Liu W, Liu C. Improved bioavailability of curcumin in liposomes prepared using a pH-driven, organic solvent-free method. *RSC Adv.* 2017;7(42):25978-25986.
7. Honary S, Zahir F. Effect of zeta potential on the properties of nano-drug delivery systems. *Trop J Pharm Res.* 2013;12(2):265-273.
8. Morris CJ. Carrageenan-induced paw edema in the rat and mouse. *Methods Mol Biol.* 2003;225:115-121.
9. Kakkar V, Singh S, Singla D, Kaur IP. Exploring solid lipid nanoparticles to enhance the oral bioavailability of curcumin. *Mol Nutr Food Res.* 2011;55(3):495-503.
10. Takahashi M, Uechi S, Takara K, Asikin Y, Wada K. Evaluation of an oral carrier system in rats: bioavailability and antioxidant properties of liposome-encapsulated curcumin. *J Agric Food Chem.* 2009;57(19):9141-9146.
11. Olson F, Hunt CA, Szoka FC, Vail WJ, Papahadjopoulos D. Preparation of liposomes of defined size distribution by extrusion through polycarbonate membranes. *Biochim Biophys Acta.* 1979;557(1):9-23.
12. Winter CA, Risley EA, Nuss GW. Carrageenin-induced edema in hind paw of the rat as an assay for anti-inflammatory drugs. *Proc Soc Exp Biol Med.* 1962;111(3):544-547.