

Nano-Emulsion Formulation of Curcumin for Enhanced Bioavailability

Parag Deshmukh¹, Akash Jain²

Department of Pharmaceutics

Bombay College of Pharmacy, Mumbai, Maharashtra, India

Abstract—Curcumin, the principal bioactive polyphenol of turmeric (*Curcuma longa*), exhibits potent anti-inflammatory, antioxidant, and anticancer properties, yet its clinical utility remains severely limited by poor aqueous solubility, rapid metabolism, and consequently low oral bioavailability. This study reports the formulation and characterization of an oil-in-water nano-emulsion delivery system to enhance the solubility and bioavailability of curcumin. Nano-emulsions were prepared by the aqueous phase titration method using varying oil, surfactant, and co-surfactant ratios, and optimized using a pseudo-ternary phase diagram approach. The optimized formulation was characterized for droplet size, polydispersity index, zeta potential, drug entrapment efficiency, in-vitro drug release, and stability under accelerated storage conditions. The optimized nano-emulsion exhibited a mean droplet size of 78.4 nm, a polydispersity index below 0.25, and entrapment efficiency exceeding 92%, with sustained in-vitro release over 24 hours following Higuchi release kinetics. Comparative in-vitro dissolution studies indicated an approximately 6-fold increase in apparent aqueous solubility of curcumin relative to the unformulated drug. Accelerated stability studies over three months showed no significant change in droplet size or drug content, indicating adequate formulation stability. These findings support nano-emulsion technology as an effective strategy for overcoming the solubility and bioavailability limitations of curcumin, with potential application in oral nutraceutical and pharmaceutical formulations.

Index Terms—Curcumin, Nano-Emulsion, Bioavailability Enhancement, Pseudo-Ternary Phase Diagram, Drug Delivery, Solubility Enhancement, Zeta Potential, In-Vitro Release.

I. INTRODUCTION

Curcumin, a hydrophobic polyphenolic compound derived from the rhizome of *Curcuma longa*, has attracted extensive research interest for its wide-ranging pharmacological activities including anti-inflammatory, antioxidant, antimicrobial, and anticancer effects. Despite this pharmacological promise, clinical translation of curcumin has been severely constrained by its extremely poor aqueous solubility, chemical instability at physiological pH, rapid first-pass metabolism, and consequently negligible oral bioavailability.

Numerous strategies have been explored to overcome these limitations, including liposomal encapsulation, solid lipid nanoparticles, phospholipid complexes, and nano-emulsion systems. Among these, nano-emulsions are particularly attractive owing to their thermodynamic formulation simplicity, ability to solubilize lipophilic drugs within a nanoscale oil-in-water dispersion, and potential to enhance both solubility and lymphatic absorption of the encapsulated drug.

This study aims to formulate and characterize an optimized curcumin-loaded nano-emulsion using a

C. Construction of Pseudo-Ternary Phase Diagrams

Phase diagrams were constructed for surfactant-to-co-surfactant (Smix) ratios of 1:1, 2:1, and 3:1, using the aqueous titration method, to identify the nano-emulsion existence region for each Smix ratio.

D. Preparation of Curcumin Nano-Emulsion

Curcumin was dissolved in the oil phase, combined with the Smix blend, and titrated with distilled water under continuous magnetic stirring to obtain the final nano-emulsion, which was further optimized based on droplet size and clarity.

E. Characterization Techniques

The optimized formulation was characterized for droplet size and polydispersity index by dynamic light scattering, zeta potential by electrophoretic light scattering, entrapment efficiency by ultracentrifugation, and morphology by transmission electron microscopy.

IV. FORMULATION OPTIMIZATION

Based on solubility screening, curcumin exhibited maximum solubility in Capryol 90 among tested oils, and in Tween 80 and Transcutol P among tested

pseudo-ternary phase diagram approach, and to evaluate its physicochemical properties, in-vitro release behavior, and short-term stability as a foundation for enhanced oral bioavailability.

II. LITERATURE REVIEW

A. Bioavailability Challenges of Curcumin

Prior pharmacokinetic studies have consistently reported that orally administered curcumin undergoes extensive glucuronidation and sulfation in the intestine and liver, along with poor intestinal absorption due to its high log P value, resulting in very low measurable plasma concentrations even at high oral doses.

B. Nano-Emulsion Delivery Systems

Nano-emulsion systems, typically comprising an oil phase, surfactant, co-surfactant, and aqueous phase, have been widely reported to enhance the apparent solubility and membrane permeability of poorly water-soluble drugs, with reported droplet sizes generally in the range of 20-200 nm imparting improved physical stability compared to conventional emulsions.

C. Formulation Optimization Approaches

Pseudo-ternary phase diagrams constructed using varying surfactant-to-co-surfactant (Smix) ratios are a widely used approach to identify the nano-emulsion region and optimize formulation composition, providing a systematic basis for selecting stable, low-viscosity formulations suitable for oral delivery.

III. MATERIALS AND METHODS

A. Materials

Curcumin (analytical grade, purity greater than 95%) was procured from a certified supplier. Capryol 90 was selected as the oil phase, Tween 80 as the surfactant, and Transcutol P as the co-surfactant, based on preliminary solubility screening of curcumin in a panel of candidate oils, surfactants, and co-surfactants.

B. Solubility Studies

Equilibrium solubility of curcumin in various oils, surfactants, and co-surfactants was determined by adding excess drug to each vehicle, shaking for 72 hours at 25°C, centrifuging, and quantifying drug content in the supernatant by UV-visible spectrophotometry at 425 nm.

surfactants and co-surfactants respectively, guiding the selection of these components for nano-emulsion formulation. Nine formulations (F1-F9) were prepared by varying the oil concentration (5-15% w/w) and Smix ratio (1:1, 2:1, 3:1), and screened for droplet size, polydispersity index, and physical stability under centrifugation and freeze-thaw cycling.

Formulation F5, containing 10% w/w oil phase and a 2:1 Smix ratio, was selected as the optimized formulation based on its minimum droplet size, narrow size distribution, and satisfactory thermodynamic stability. The composition of the optimized formulation is presented in Table I.

V. IN-VITRO EVALUATION

A. Droplet Size, PDI, and Zeta Potential

Droplet size, polydispersity index, and zeta potential of the optimized formulation were measured in triplicate using dynamic light scattering and electrophoretic light scattering techniques.

B. Entrapment Efficiency

Entrapment efficiency was determined by separating untrapped curcumin through ultracentrifugation and quantifying free drug content by UV-visible spectrophotometry, with entrapment efficiency calculated as the percentage of total drug incorporated within the nano-emulsion droplets.

C. In-Vitro Drug Release

In-vitro release of curcumin from the optimized nano-emulsion was studied using the dialysis bag method in phosphate buffer (pH 6.8) containing 0.5% w/v sodium lauryl sulfate to maintain sink conditions, with samples withdrawn at predetermined intervals over 24 hours and analyzed spectrophotometrically.

D. Stability Studies

Accelerated stability studies were conducted at 25°C/60% RH and 40°C/75% RH for three months as per standard stability testing guidelines, with periodic evaluation of droplet size, zeta potential, and drug content.

TABLE I — Composition of Optimized Curcumin Nano-Emulsion (Formulation F5)

Component	Role	Quantity (% w/w)
Curcumin	Active drug	1.0
Capryol 90	Oil phase	10.0

Component	Role	Quantity (% w/w)
Tween 80	Surfactant	26.7
Transcutol P	Co-surfactant	13.3
Distilled water	Aqueous phase	q.s. to 100

VI. RESULTS AND DISCUSSION

A. Solubility and Phase Behavior

Curcumin solubility was highest in Capryol 90 (18.6 mg/mL) among the oils screened, and the 2:1 Smix ratio produced the largest nano-emulsion existence region in the pseudo-ternary phase diagram, indicating superior self-emulsification efficiency compared to the 1:1 and 3:1 ratios.

B. Droplet Size, PDI, and Zeta Potential

The optimized formulation (F5) exhibited a mean droplet size of 78.4 nm with a polydispersity index of 0.21, indicating a narrow and uniform size distribution. Zeta potential was measured at -24.6 mV, suggesting adequate electrostatic stabilization against droplet coalescence.

C. Entrapment Efficiency and Drug Release

Entrapment efficiency of the optimized formulation was 92.3%, and in-vitro release studies showed 88.6% cumulative curcumin release over 24 hours, following predominantly Higuchi release kinetics, consistent with diffusion-controlled release from the nano-emulsion droplets.

D. Comparative Solubility Enhancement

Comparative dissolution studies indicated an approximately 6-fold increase in apparent aqueous solubility of curcumin when formulated as a nano-emulsion, relative to plain unformulated curcumin powder, attributable to the reduced droplet size and solubilization within the oil-surfactant matrix.

VII. STABILITY EVALUATION

Over three months of accelerated storage, the optimized formulation showed no statistically significant change in droplet size, polydispersity index, or drug content at 25°C/60% RH, while minor increases in droplet size and slight drug content reduction were observed at 40°C/75% RH, indicating that the formulation is suitable for storage under standard, non-extreme conditions. A summary of stability data is presented in Table II.

VIII. CHALLENGES AND LIMITATIONS

Challenges in curcumin nano-emulsion development include the relatively high surfactant concentration required for adequate solubilization, potential for gastrointestinal irritation from surfactant load at scale-up, and the need for further in-vivo pharmacokinetic validation beyond the in-vitro release data presented in this study. Long-term physical and chemical stability of curcumin, which is prone to degradation at alkaline pH and under light exposure, also requires further packaging-level mitigation.

TABLE II — Physicochemical Characterization and Stability Data of Optimized Formulation

Parameter	Initial	3 Months (25°C/60% RH)	3 Months (40°C/75% RH)
Droplet size (nm)	78.4	79.1	86.7
Polydispersity index	0.21	0.22	0.27
Zeta potential (mV)	-24.6	-24.1	-22.3
Drug content (%)	99.2	98.6	95.4
Entrapment efficiency (%)	92.3	91.8	89.5

IX. FUTURE SCOPE

Future work should include in-vivo pharmacokinetic and bioavailability studies in animal models to confirm the in-vitro solubility and release improvements translate into enhanced systemic

X. CONCLUSION

An optimized oil-in-water nano-emulsion of curcumin was successfully developed using Capryol 90, Tween 80, and Transcutol P, guided by pseudo-ternary phase diagram optimization. The formulation exhibited

exposure, along with evaluation of gastrointestinal tolerability at scaled surfactant concentrations. Incorporation of the optimized nano-emulsion into solid dosage forms such as self-nanoemulsifying pellets or capsules, and exploration of mucoadhesive or targeted-release modifications, represent promising directions for translating this formulation toward clinical and nutraceutical products.

favorable droplet size, narrow size distribution, high entrapment efficiency, sustained in-vitro release, and short-term storage stability, along with an approximately 6-fold increase in apparent aqueous solubility relative to unformulated curcumin. These results support nano-emulsion technology as a viable and practical strategy for enhancing the oral bioavailability of curcumin, warranting further in-vivo validation toward pharmaceutical and nutraceutical application.

XI. REFERENCES

- [1] Anand, P., Kunnumakkara, A.B., Newman, R.A., and Aggarwal, B.B. (2007). Bioavailability of curcumin: Problems and promises. *Molecular Pharmaceutics*, 4(6), 807-818.
- [2] Aggarwal, B.B., Sundaram, C., Malani, N., and Ichikawa, H. (2007). Curcumin: The Indian solid gold. *Advances in Experimental Medicine and Biology*, 595, 1-75.
- [3] Gupta, S.C., Patchva, S., and Aggarwal, B.B. (2013). Therapeutic roles of curcumin: Lessons learned from clinical trials. *AAPS Journal*, 15(1), 195-218.
- [4] Wang, Y.J., Pan, M.H., Cheng, A.L., et al. (1997). Stability of curcumin in buffer solutions and characterization of its degradation products. *Journal of Pharmaceutical and Biomedical Analysis*, 15(12), 1867-1876.
- [5] Prajapati, B.G., et al. (2019). Formulation and evaluation of curcumin nanoemulsion for enhanced oral bioavailability. *Journal of Drug Delivery Science and Technology*, 51, 529-538.
- [6] Lawrence, M.J., and Rees, G.D. (2000). Microemulsion-based media as novel drug delivery systems. *Advanced Drug Delivery Reviews*, 45(1), 89-121.
- [7] Date, A.A., Desai, N., Dixit, R., and Nagarsenker, M. (2010). Self-nanoemulsifying drug delivery systems: Formulation insights, applications and advances. *Nanomedicine*, 5(10), 1595-1616.
- [8] Ahmed, K., Li, Y., McClements, D.J., and Xiao, H. (2012). Nanoemulsion- and emulsion-based delivery systems for curcumin: Encapsulation and release properties. *Food Chemistry*, 132(2), 799-807.
- [9] Wang, X., Jiang, Y., Wang, Y.W., Huang, M.T., Ho, C.T., and Huang, Q. (2008). Enhancing anti-inflammation activity of curcumin through O/W nanoemulsions. *Food Chemistry*, 108(2), 419-424.
- [10] Flanagan, J., and Singh, H. (2006). Microemulsions: A potential delivery system for bioactives in food. *Critical Reviews in Food Science and Nutrition*, 46(3), 221-237.
- [11] Sethacheewakul, S., Mahattanadul, S., Phadoongsombut, N., Pichayakorn, W., and Wiwattanapatapee, R. (2010). Development and evaluation of self-microemulsifying liquid and pellet formulations of curcumin, and absorption studies in rats. *European Journal of Pharmaceutics and Biopharmaceutics*, 76(3), 475-485.
- [12] Yu, H., and Huang, Q. (2012). Improving the oral bioavailability of curcumin using novel organogel-based nanoemulsions. *Journal of Agricultural and Food Chemistry*, 60(21), 5373-5379.
- [13] Rachmawati, H., Al Shaal, L., Muller, R.H., and Keck, C.M. (2013). Development of curcumin nanocrystal: Physical aspects. *Journal of Pharmaceutical Sciences*, 102(1), 204-214.
- [14] Tonnesen, H.H., Masson, M., and Loftsson, T. (2002). Studies of curcumin and curcuminoids. XXVII. Cyclodextrin complexation: Solubility, chemical and photochemical stability. *International Journal of Pharmaceutics*, 244(1-2), 127-135.
- [15] Anand, P., Nair, H.B., Sung, B., et al. (2010). Design of curcumin-loaded PLGA nanoparticles formulation with enhanced cellular uptake, and increased bioactivity in vitro and superior bioavailability in vivo. *Biochemical Pharmacology*, 79(3), 330-338.
- [16] Indian Pharmacopoeia Commission. (2018). *Indian Pharmacopoeia*, Ghaziabad, India.
- [17] ICH Harmonised Guideline. (2003). *Stability testing of new drug substances and products Q1A(R2)*. International Council for Harmonisation.