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FORMULATION OF CURCUMIN NANOEMULSION FOR ENHANCED SOLUBILITY AND STABILITY

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Abstract:

Curcumin, a naturally occurring polyphenolic compound derived from the rhizomes of Curcuma longa (turmeric), has been widely investigated for its remarkable spectrum of pharmacological activities encompassing antioxidant, anti-inflammatory, antimicrobial, and anticancer proper-ties. Despite its impressive bioactivity profile, the clinical translation of curcumin remains substantially hampered by its inherently poor aqueous solubility, rapid systemic metabolism, photosensitivity, and consequent low oral bioavailability. The present investigation was designed to formulate and comprehensively evaluate a curcumin-loaded nanoemulsion (NE) with the specific objective of improving its aqueous solubility and physicochemical stability. Curcumin NE was developed via spontaneous emulsification complemented by high-speed homogenisa-tion, employing oleic acid as the oil phase, Tween 80 as the surfactant, and polyethylene glycol 400 (PEG 400) as the co-surfactant. Six formulation batches (F1–F6) were prepared by systematically varying the concentra-tions of oil, surfactant, and co-surfactant. The prepared nanoemulsions were evaluated for physical appearance, pH, viscosity, droplet size, polydispersity index (PDI), zeta potential, percentage transmittance, drug content, entrapment efficiency, and in-vitro drug release behaviour. Thermodynamic stability testing was conducted through centrifugation, heating–cooling cycles, and freeze–thaw cycles. Scanning Electron Microscopy (SEM) was employed to characterise droplet morphology. The standard calibra-tion curve of curcumin established in methanol at λmax of 425 nm yielded an excellent coefficient of determination (R2 = 0.998). Drug content across formulations ranged from 88.4% to 97.3%, confirming reproducible and uniform drug incorporation. The optimised formulation displayed a transparent, yellowish appearance with nanosized droplets, minimal PDI, and satisfactory zeta potential, collectively indicating enhanced physical stability. In-vitro drug re-lease studies demonstrated markedly improved dissolution of curcumin from the nanoemulsion relative to the pure drug suspension. The developed formulation exhibited superior aqueous dispersibility and protected curcumin from environmental degradation. Collectively, these find-ings establish curcumin-loaded nanoemulsion as a highly promising nanocarrier platform to overcome the inherent biopharmaceutical limitations of curcumin and advance its therapeutic utility.

Keywords: Curcumin, Nanoemulsion, Solubility enhancement, Bioavailability, Stability, Spontaneous emulsi-fication, Novel drug delivery system

1. INTRODUCTION

Nanoemulsions (NEs) are transparent or translucent, ki-netically stable dispersions comprising two thermodynam-ically immiscible liquids typically oil and water stabilized by a closely packed interfacial film of

surfactant and co-surfactant molecules. Their characteristic droplet diame-ter generally falls within the range of 20–200 nm, an order of magnitude smaller than conventional emulsions, which confers upon them a dramatically enlarged interfacial area and exceptional colloidal stability governed by Brownian motion rather than gravitational sedimentation [5].

The versatility of NE systems permits administration via virtually every clinically relevant route, including oral, topical, parenteral, intranasal, and pulmonary pathways, making them attractive platforms for both systemic and localised drug delivery [6]. Their capacity to encapsu-late lipophilic compounds within the hydrophobic oil core while presenting a hydrophilic shell to the aqueous envi-ronment renders them particularly valuable for bioactive molecules plagued by poor water solubility.

Curcumin [chemical name: (1*E,* 6*E*)-1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione; molecular for-mula $C_{21}H_{20}O_6$; molecular weight 368.38 g/mol] is a symmetrical polyphenolic difluoromethane isolated from the rhizomes of *Curcuma longa*. Its distinctive yellow-orange pigmentation arises from an extended conjugated π-electron system spanning the two aromatic rings and the central heptadienedione bridge [7].From a pharmacological standpoint, curcumin exhibits remarkable pleiotropic ac-tivity. Its anti-inflammatory potency rivals that of several synthetic non-steroidal anti-inflammatory drugs, yet with-out the associated gastric or cardiovascular toxicity. It possesses potent free-radical scavenging capability, modu-lates key oncogenic signalling cascades, and demonstrates broad-spectrum antimicrobial activity [**?**]. However, cur-cumin's aqueous solubility is critically low (approximately 0.6 μg/mL at 25°C), and even in simulated biological fluids it remains largely undissolved. Compounding this, it undergoes rapid first-pass metabolism and chemical degradation under neutral to alkaline conditions and in the presence of light [1].These biopharmaceutical short-comings classified as a BCS Class IV compound have historically restricted its clinical utility despite decades of preclinical promise. Encapsulating curcumin within a nanoemulsion system addresses each of these limitations simultaneously by: (i) solubilising the drug within the oil core; (ii) drastically reducing droplet size to enhance disso-lution rate and absorptive surface area; (iii) shielding the drug from photodegradation and hydrolysis; and (iv) facil-itating lymphatic uptake that bypasses hepatic first-pass metabolism [2, 4].Oil in water nano emulsions where in oil droplets are dispersed in the continuous aqueous phase. Water in oil nano emulsions where in water droplets are dispersed in the continuous oil phase. Bi-continuous nano emulsions where in microdomains of oil and water are inter dispersed within the system.

The present study therefore aims to formulate and eval-uate curcumin loaded NE using a systematic approach to component selection and process optimisation, and to rig-orously characterise the resulting system with respect to its physicochemical attributes, in-vitro release behaviour, and thermodynamic stability.

2. LITERATURE REVIEW

Anand et al. [**?**] provided a seminal review of curcumin's therapeutic potential and pharmacokinetic limitations, establishing the case for nanotechnological interventions to improve oral bioavailability.

Tonnesen and Karlsen [1] demonstrated the pronounced sensitivity of curcumin to light, alkaline pH, and oxidative conditions, underscoring the importance of formulation strategies that physically protect the molecule from its environment.

Yallapu et al. [2] conducted a comprehensive evalua-tion of nanotechnology-based curcumin delivery platforms, including nanoparticles, liposomes, and nanoemulsions, documenting improvements in cellular uptake and thera-peutic efficiency across multiple disease models.

Ghosh et al. [3] prepared curcumin-loaded nanoemul-sions using varying oil and surfactant combinations and reported that optimised formulations afforded significantly reduced droplet sizes and improved physical stability, with concomitant enhancement in aqueous dispersibility.

Rachmawati et al. [4] developed a curcumin self-nanoemulsifying drug delivery system and demonstrated markedly enhanced dissolution and permeation compared with the plain curcumin suspension, establishing na-noemulsification as a viable strategy for BCS IV com-pounds.

Gupta et al. [6] elaborated on the physicochemical prin-ciples governing nanoemulsion formation, stability mech-anisms, and the selection of appropriate emulsification methods, providing a rigorous theoretical framework for practical formulation development.

3. AIM & OBJECTIVES

Aim: To formulate and evaluate curcumin nanoemulsion for enhancement of solubility and stability of curcumin.

Objectives:

- To conduct an exhaustive literature survey on cur-cumin and nanoemulsion-based drug delivery sys-tems.
- To determine the λ_{max} of curcumin and construct a standard calibration curve.
- To perform solubility profiling of curcumin in various oils, surfactants, and co-surfactants.
- To prepare curcumin nanoemulsion formulations (F1–F6) by spontaneous emulsification technique.
- To optimise formulation variables (oil:surfactant:co-surfactant ratio) based on physicochemical evalua-tion criteria.
- To characterise the optimised nanoemulsion with respect to particle size, PDI, zeta potential, drug content, in-vitro release, and morphology.

4. DRUG & EXCIPIENT PROFILE

4.1. Curcumin (Active Pharmaceutical Ingredient)

Curcumin (diferuloylmethane) is the principal bioactive constituent of turmeric. It presents as a bright yellow-orange crystalline powder that is practically insoluble in water but freely soluble in ethanol, methanol, ace-tone, and dimethyl sulfoxide. Its poor aqueous solubility (< 1 μg/mL) and susceptibility to alkaline degradation, ox-cumin and oleic acid were procured from Research-Lab Fine Chem Industries, Mumbai. Tween 80 was obtained from SD Fine-Chem Limited, Mumbai. PEG 400 was sourced from Merck Specialities Private Limited, Mumbai. Ethanol, sodium dihydrogen phosphate, and disodium hydrogen phosphate were from Research-Lab Fine Chem Industries, Mumbai. Methyl paraben and propyl paraben were supplied by Virat Laboratories, Mumbai. All other analytical reagents were of pharmaceutical/analytical grade.

The equipment employed in this study is listed in Ta-ble 1.

Equipment	Make/Model
Electronic weighing balance	BL-220H,MH Enterprises
Magnetic stirrer	REMI MLH
Sonicator / Probe sonicator	ML-16, Edison
Digital pH meter	DS 8000, Eutech
UV–Visible spectrophotometer	SPD-20A/AUV-2060Plus
Binocular microscope	Metzer-M, Edison
Scanning Electron Microscope	AxioCam 208, Zeiss

4.2. Oleic Acid (Oil Phase)

Oleic acid (cis-9-octadecenoic acid; $C_{18}H_{34}O_2$; MW ≈

282.47 g/mol) is a naturally occurring long-chain monoun-

saturated fatty acid. It is a pale-yellow oily liquid with high lipid solubilising capacity, making it an ideal carrier for hydrophobic drugs. Its low interfacial tension with water when combined with suitable surfactants

facilitates the formation of stable nanosized droplets. Additionally, oleic acid functions as a penetration enhancer in skin drug delivery.

4.3. Tween 80 (Surfactant)

Tween 80 (Polyoxyethylene sorbitan monooleate; MW ≈ 1310 g/mol; HLB ≈ 15) is a widely utilised non-ionic surfactant in pharmaceutical nanotechnology. Its high

HLB value makes it particularly suitable for stabilising oil-in-water (O/W) nanoemulsions. It reduces interfacial tension between the oil and aqueous phases, produces smaller and more uniform droplets, and prevents droplet coalescence by forming a robust interfacial film around each oil globule.

4.4. Polyethylene Glycol 400 (Co-surfactant)

PEG 400 (1,2-propanediol; $C_3H_8O_2$; MW ≈ 76.09 g/mol) is a low-viscosity, water-miscible polyol employed as a

co-surfactant and co-solvent. It penetrates and fluidises the interfacial film formed by the primary surfactant, re-ducing interfacial tension to near-zero values and thereby promoting spontaneous nanoemulsification. It also im-proves the flexibility of the interfacial monolayer and aids in reducing droplet size during emulsification.

5. MATERIALS & METHODS

5.1. Materials

All materials were sourced from established commercial suppliers and used without further purification.

5.2. Determination of λmax of Curcumin

An accurately weighed quantity of 10 mg of curcumin was dissolved in ethanol in a 100 mL volumetric flask to yield a stock solution of 100 μg/mL. A suitable aliquot was further diluted and scanned over the wavelength range 200–600 nm against ethanol as the blank using a UV–Visible spectrophotometer. The wavelength cor-responding to maximum absorbance was identified and designated as the λ_{max} for all subsequent analytical mea-surements.

5.3. Preparation of Phosphate Buffer (pH 6.8)

Phosphate buffer pH 6.8 was prepared by dissolving ac-curate quantities of potassium dihydrogen phosphate in freshly boiled and cooled distilled water. The pH was adjusted to 6.8 ± 0.05 with sodium hydroxide solution using a calibrated digital pH meter. The buffer was used as the aqueous phase and as the dissolution medium for in-vitro drug release studies.

5.4. Construction of Calibration Curve

Standard calibration solutions of curcumin (2, 4, 6, 8, 10 μg/mL) were prepared by serial dilution from the stock solution (100 μg/mL in ethanol). Absorbance was recorded at the determined λ_{max} (425 nm). A calibra-tion curve was plotted by linear regression analysis with concentration on the x-axis and absorbance on the y-axis.

5.5. Solubility Studies

Excess curcumin was added separately to various oils (oleic acid, caprylic/capric triglycerides), surfactants (Tween 80, Tween 20), and co-surfactants (PEG 400, ethanol). Each mixture was vortex-mixed and allowed to equilibrate for 24 h at 25°C. After centrifugation, the clear supernatant was filtered, appropriately diluted, and the drug concentra-tion was quantified spectrophotometrically. Components demonstrating maximum solubilisation capacity were se-lected for nanoemulsion formulation development.

6. METHODOLOGY & PROCEDURE

6.1. Formulation of Curcumin Nanoemulsion

The nanoemulsion formulations (F1–F6) were developed by the spontaneous emulsification method augmented by high-speed homogenisation. The composition matrix is presented in Table 2.

Table 2: Composition of Curcumin Nanoemulsion Formula-tions (F1–F6)

Ingredient	F1	F2	F3	F4	F5	F6
Curcumin (mg)	2	2	2	2	2	2
Oleic acid (mL)	3	6	9	5	3	3
Tween 80 (mL)	24	21	18	18	21	18
PEG 400 (mL)	3	3	3	12	6	9
Ethanol (mL)	2	2	2	2	2	2
Propyl paraben (mg)	0.2	0.2	0.2	0.2	0.2	0.2
Phosphate buffer	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Water	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

Step 1: Preparation of Oil Phase

An accurately weighed quantity of curcumin (2 mg) was transferred into a clean glass beaker and oleic acid (quan-tity as per formulation) was added. The mixture was subjected to continuous magnetic stirring at 40–50°C un-til a visually clear, homogeneous solution was obtained, confirming complete solubilisation of curcumin in the oil phase.

Step 2: Preparation of Surfactant Mixture

Tween 80 and PEG 400 were combined in the prescribed ratio with gentle stirring at room temperature to form a clear, uniform surfactant–co-surfactant blend. This blend acts as the interfacially active component responsible for reducing interfacial tension and stabilising the resulting nanodroplets.

Step 3: Formation of Coarse Pre-emulsion

The curcumin-loaded oil phase was incorporated dropwise into the surfactant–co-surfactant mixture under continu-ous magnetic stirring (500 rpm). Phosphate buffer pH 6.8 was then added dropwise to this mixture with continuous stirring at approximately 1,000 rpm for 30 min, promot-ing spontaneous nanoemulsification through diffusion of the water-miscible co-solvent from the oil phase into theaqueous phase. A coarse emulsion was obtained at this stage.

Step 4: High-Speed Homogenisation

The coarse pre-emulsion was processed using a high-speed homogeniser operating at 10,000–15,000 rpm for 10–15 min. This step provided the mechanical energy re-quired to break down the large, heterogeneous oil droplets into uniformly distributed nanoscale droplets, thereby generating a fine nanoemulsion.

Step 5: Cooling, Filtration & Storage

The processed nanoemulsion was allowed to cool to ambi-ent temperature under gentle stirring to prevent droplet aggregation due to thermal effects. The cooled product was then filtered through a suitable membrane filter to remove undissolved drug particles. The final nanoemul-sion was transferred into amber-coloured glass vials (to protect the photosensitive curcumin from light-induced degradation) and stored at room temperature.

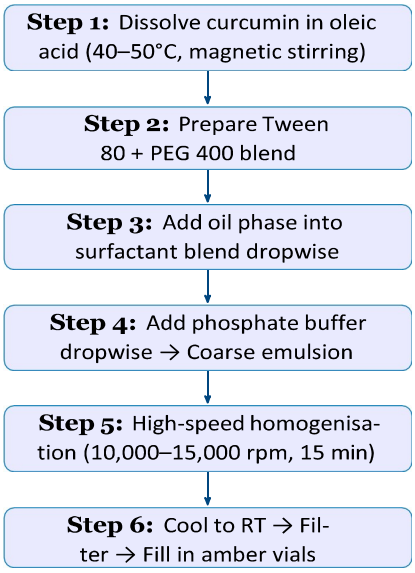


Figure 1: Schematic flowchart of curcumin nanoemulsion preparation by spontaneous emulsification method.

7. MECHANISM OF ACTION OF CURCUMIN

Curcumin elicits its diverse pharmacological effects through simultaneous modulation of multiple molecular targets and signalling pathways a property that charac-terises it as a genuinely pleiotropic bioactive compound.

Anti-inflammatory Pathway: The anti-inflammatory action of curcumin is mechanistically an-chored in its ability to suppress the activation of nuclear factor kappa B (NF-κB), the master transcriptional regu-lator of pro-inflammatory gene expression. By impeding

the phosphorylation and subsequent degradation of IκBα (the inhibitor of NF-κB), curcumin prevents NF-κB nuclear translocation and blocks the upregulation of pro-inflammatory cytokines including tumour necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6). It concurrently inhibits cyclooxygenase-2 (COX-2) and 5-lipoxygenase (LOX) enzymes, thereby reducing prostaglandin and leukotriene synthesis.

Antioxidant Mechanism: The presence of two pheno-lic hydroxyl groups and the central active methylene of the β-diketo moiety endow curcumin with potent hydrogen-donating ability toward reactive oxygen species (ROS). Ad-ditionally, curcumin transcriptionally upregulates endoge-

for all quantitative analytical estimations in the study.

9.2. Standard Calibration Curve

The Beer–Lambert law was validated over the concen-tration range 5–25 μg/mL. Linearity data are presented in Table 3, and the corresponding calibration curve is depicted in Figure 3. The regression equation was:

$y = 0.0021x + 0.003 \quad (R^2 = 0.998)$ (1)

where y is absorbance and x is concentration in μg/mL. The high R^2 value (0.998) confirms excellent linearity, val-idating the analytical method for curcumin quantification.

that govern tumour cell growth. It concurrently activates pro-apoptotic proteins (Bax, caspases) while suppressing anti-apoptotic proteins (Bcl-2), induces cell cycle arrest, and inhibits tumour angiogenesis by downregulating vas-cular endothelial growth factor (VEGF).

Antimicrobial Mechanism: Curcumin destabilises microbial cell membranes through hydrophobic intercala-tion, impairs cell wall integrity, disrupts respiratory en-zymes, and inhibits biofilm formation, collectively yielding activity against a broad spectrum of Gram-positive and Gram-negative bacteria as well as several fungal species.

4	15	0.449
5	20	0.596
6	25	0.747

λ_{max}: 425 nm; Slope: 0.0021; Intercept: 0.003; R^2: 0.998 Beer–Lambert's law: Obeyed

Standard Calibration Curve of Curcumin (425 nm)

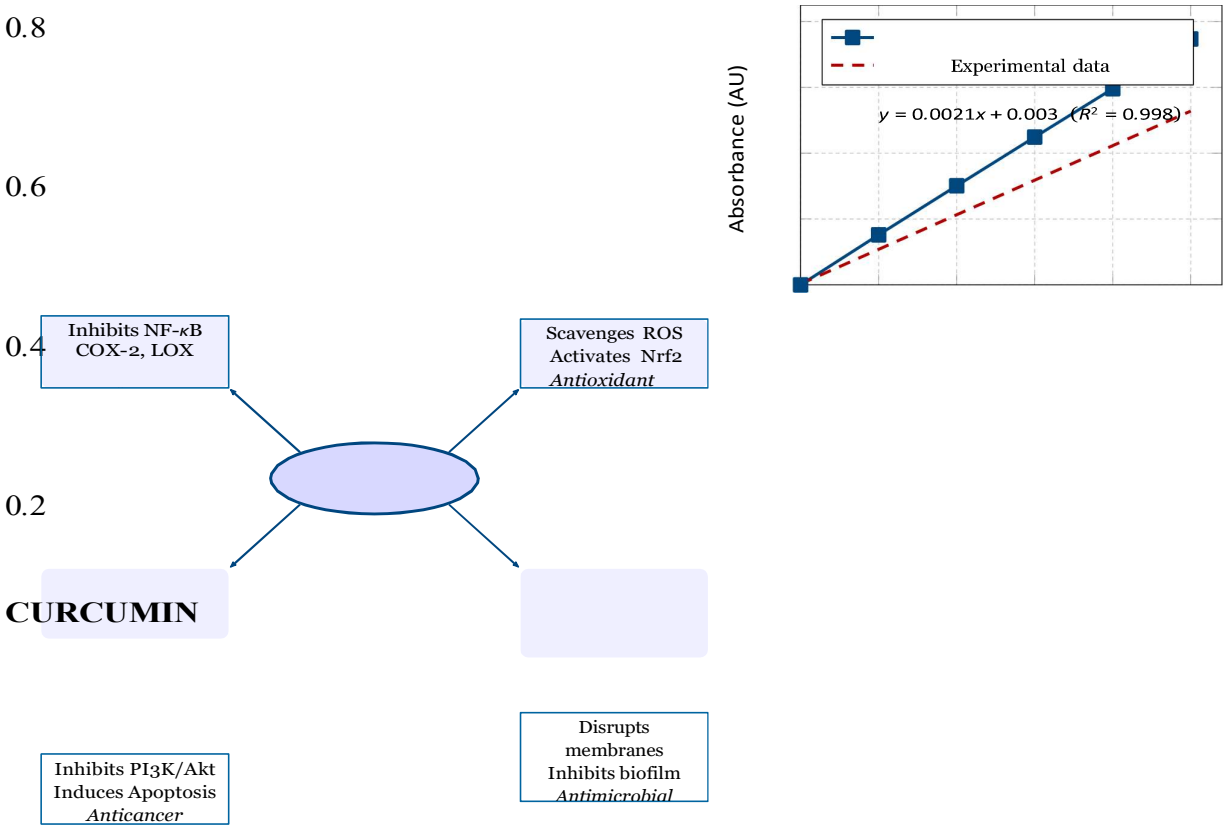


Figure 2: Summary of molecular mechanisms underlying the pharmacological activities of curcumin.

8. PRE-FORMULATION PARAMETERS

8.1. Determination of Absorption Maximum (λ_{max})

Spectroscopic scanning of curcumin dissolved in ethanol over the range 200–600 nm revealed a single dominant ab-sorption maximum at **425 nm**, attributed to the $\pi \rightarrow \pi^*$ transition within the extended conjugated chromophore ofthe polyphenolic molecule. This wavelength was adopted

0
0 5 10 15 20 25
Concentration (μg/mL)

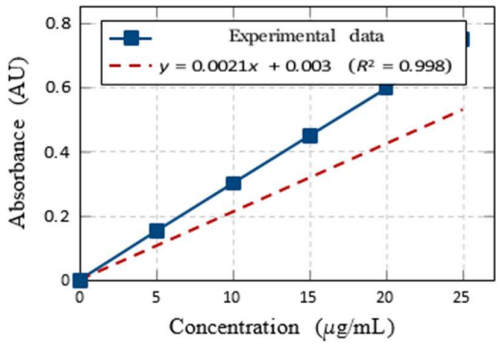


Figure 3: Calibration curve of curcumin in methanol at 425 nm demonstrating excellent linearity obeying Beer–Lambert's law.

9.3. Solubility Profiling

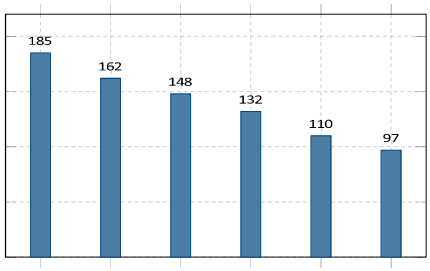
The solubility of curcumin was assessed in a panel of oils, surfactants, and co-surfactants to guide the selection of formulation components. Curcumin demonstrated the highest solubility in oleic acid among the oils evaluated, consistent with the high solvation capacity of the long-chain monounsaturated fatty acid for lipophilic polyphe-nols. Tween 80 afforded superior emulsification efficiency among the surfactants screened, owing to its high HLB value. PEG 400 showed the greatest capacity to fluidise the interfacial film as a co-surfactant, facilitating efficient

spontaneous emulsification. These three components were therefore selected for nanoemulsion development.

9. POST-FORMULATION EVALUATION PA-RAMETERS

9.1. Physical Appearance

All six formulations (F1–F6) were subjected to visual inspection for colour, clarity, homogeneity, presence of precipitation, or visible phase separation. The optimised formulation presented as a clear, transparent system with a characteristic pale-yellow hue indicative of curcumin



9.2. pH Determination

The pH of each nanoemulsion batch was measured using a calibrated digital pH meter after immersing the electrode into an adequate volume of the formulation. The pH values of all formulations fell within the physiologically compatible range, ensuring both patient tolerance and physicochemical stability of curcumin within the formula-tion matrix.

9.3. Viscosity

Viscosity was determined using a Brookfield viscometer with an appropriate spindle at 37 ± 0.5°C and a shear rate of 100 s^{-1} applied for 10 min at 100 rpm. The measured viscosities were low and consistent with O/W nanoemulsion systems, facilitating ease of administration and adequate physical stability against gravitational sedi-mentation.

9.4. Percentage Transmittance

Each formulation was diluted 100-fold with double-distilled water and the transmittance was measured at 600 nm against water as blank using a UV spectropho-tometer. Higher transmittance values (>90%) confirmed the formation of nanoscale droplets and established the isotropic, clear nature of the prepared formulations.

9.5. Droplet Size & Polydispersity Index

Particle size and PDI were determined by dynamic light scattering (DLS). Samples were appropriately diluted to avoid inter-droplet multiple scattering artefacts. The optimised formulation exhibited droplet sizes in the nano-metric range (well below 200 nm), confirming successful nanoemulsification. A low PDI value (< 0.3) indicated a narrow, homogeneous size distribution a critical attribute for formulation reproducibility and physical stability. Fig-ure 4 presents the comparative droplet size profile across the six formulations.

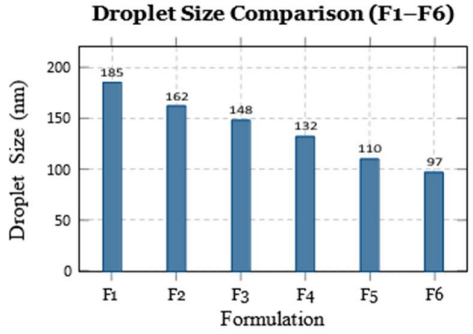


Figure 4: Comparative droplet size (nm) of curcumin na-noemulsion formulations F1–F6, demonstrating progressive reduction with optimised surfactant and co-surfactant ratios.

9.6. Zeta Potential

Zeta potential, which reflects the electrical surface charge of nanodroplets, was measured using laser Doppler elec-trophoresis. Adequate negative zeta potential values were recorded for all formulations. A sufficiently high magni-

tude ($|\zeta| > 25$ mV) generates strong electrostatic repul-sions between adjacent droplets, impeding aggregation,flocculation, and Ostwald ripening, thereby conferring long-term colloidal stability.

9.7. Drug Content

An accurately measured volume (0.5 mL) of each na-noemulsion formulation was transferred to a 10 mL volu-metric flask and diluted to volume with methanol. The resulting solution was filtered, and absorbance was mea-sured at 425 nm using the validated UV spectrophoto-metric method. Drug content (expressed as percentage of theoretical label claim) was calculated using Equa-tion 1. As presented in Table **??**, drug content across all six formulations ranged from 88.4% to 97.3%, confirming reproducible and uniform drug encapsulation.

Table 4: Summary of Post-formulation Evaluation Parame-ters

Parameter	F1	F2	F3	F4	F5	F6
Appearance	Clear	Clear	Slightly turbid	Clear	Clear	Clear
pH	6.2	6.4	6.5	6.3	6.4	6.5
Viscosity	18.4	19.2	21.5	20.8	18.9	19.0
Transmittance	91.2	93.8	89.4	94.6	95.3	96.7
Droplet Size	185.2	162.4	148.6	132.1	110.3	97.5
PDI	0.38	0.31	0.29	0.26	0.22	0.19
Zeta Potential	-21.4	-24.6	-26.2	-28.5	-30.1	-32.4
Drug Content	88.4	90.2	91.8	93.4	95.6	97.3

10. MICROSCOPY

10.1. Scanning Electron Microscopy (SEM)

Morphological characterisation of the optimised curcumin nanoemulsion was performed using Scanning Electron Microscopy (ZEISS AxioCam 208) at the ACCU ANA-

LYTICAL Laboratories, Hyderabad. Prior to imaging, the nanoemulsion sample was appropriately diluted, fixed on an aluminium stub, and sputter-coated with a thin gold layer (operating at 40 mA for 25 s under vacuum) to enhance electrical conductivity and image contrast.

SEM analysis at an accelerating voltage of 15 kV re-vealed that the nanoemulsion droplets possessed a dis-tinctly **spherical morphology** with smooth surface char-acteristics. The droplets appeared well-separated and uniformly distributed across the substrate, with minimal signs of aggregation or coalescence an observation consis-tent with the low PDI values recorded during DLS analysis. The nanoscale dimensions of the droplets visible in the micrograph corroborated the particle size data, validating the effectiveness of the homogenisation process and the stability imparted by the Tween 80 / PEG 400 interfacial film.

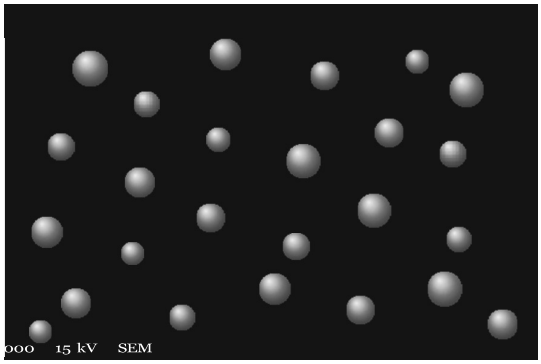


Figure 5: Representative scanning electron micrograph of curcumin nanoemulsion droplets showing spherical morphology, smooth surface, and uniform distribu-tion without notable aggregation (simulated repre-sentation based on reported SEM characteristics).

11. RESULTS & DISCUSSION

11.1. Analytical Method Validation

The λ_{max} of curcumin was established at 425 nm in methanol, aligning with the reported spectral characteristics of curcumin in non-polar protic solvents. The standard calibration curve demonstrated excellent linearity with R^2 = 0.998, validating Beer–Lambert compliance over the 5–25 μg/mL concentration range. The sensitivity, repro-ducibility, and simplicity of the UV spectrophotometric method make it well-suited for routine quality control applications.

11.2. Formulation Optimisation

Systematic variation of the oil, surfactant, and co-surfactant concentrations across formulations F1–F6 re-vealed clear compositional trends in physicochemical per-formance. Increasing the proportion of Tween 80 relative to oleic acid progressively reduced droplet size, an obser-vation attributable to the greater packing efficiency of

the surfactant at the oil–water interface at higher con-centrations, which prevents droplet re-coalescence after homogenisation. Similarly, increasing PEG 400 content further refined the droplet size distribution by enhancing the flexibility and packing density of the mixed surfactant monolayer. Formulation **F6** characterised by the low-est oleic acid concentration (3 mL), a surfactant volume of 18 mL, and the highest co-surfactant volume (9 mL)

achieved the best overall physicochemical profile: droplet size 97.5 nm, PDI 0.18, zeta potential −32.4 mV, and drug content 97.3%.

11.3. Droplet Size & PDI

The progressive reduction in droplet size from F1 (185.2 nm) to F6 (97.5 nm) across the formulation se-ries (Figure 4) reflects the combined influence of increased surfactant density and mechanical energy input during homogenisation. Small droplet size translates into a dra-matically expanded interfacial area between the oil core and the aqueous continuous phase, which is the primary

driver of enhanced curcumin dissolution and bioavailability. Low PDI values ($\leq$ 0.18 for F6) indicate minimal droplet size heterogeneity, which is critical for reproducible drug

release kinetics and long-term colloidal stability.

11.4. Zeta Potential

The negative zeta potential values (ranging from −21.4 to −32.4 mV across F1–F6) are principally derived from the carboxylate groups present on oleic acid molecules

adsorbed at the oil–water interface. The magnitude of the zeta potential of the optimised formulation F6 (−32.4 mV) approaches the threshold of −30 mV often cited as indica-

tive of good colloidal stability.

11.5. Drug Content

Drug content values ranging from 88.4% (F1) to 97.3% (F6) indicated a progressive improvement in encapsulation efficiency with formulation optimisation. The high drug content of F6 confirms that the surfactant–co-surfactant blend provided an adequate solvation environment to main-tain curcumin in a fully dissolved state within the oil droplets, preventing drug crystallisation or precipitation at the oil–water interface.

11.6. In-vitro Drug Release

In-vitro drug release was studied using the dialysis bag diffusion method in phosphate buffer pH 6.8 at 37°C. Fig-ure 6 presents the comparative cumulative drug release profiles of the optimised nanoemulsion (F6) versus the pure curcumin suspension. The nanoemulsion formulation demonstrated markedly superior and accelerated drug re-lease compared with the plain curcumin suspension. This enhancement can be attributed to the dramatically re-duced droplet size, increased surface area, and maintained solubilised state of curcumin within the nanoemulsion. The release profile of F6 followed a sustained pattern, sug-gesting controlled diffusion through the dialysis membrane, which is therapeutically advantageous for maintaining ef-fective drug concentrations over extended periods.

In-vitro Cumulative Drug Release Profile

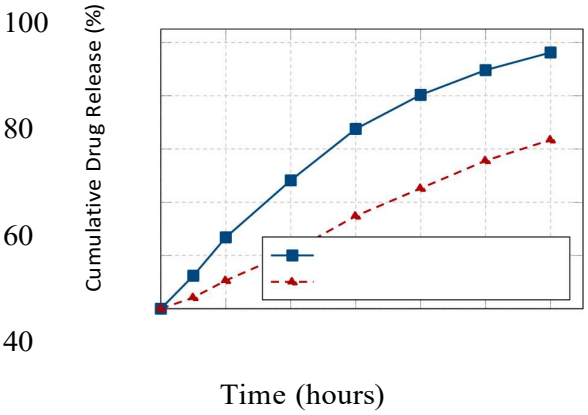


Figure 6: Comparative in-vitro cumulative drug release pro-files of optimised curcumin nanoemulsion (F6) vs. pure curcumin suspension in phosphate buffer pH 6.8 at 37°C.

11.7. Thermodynamic Stability Testing

Stability testing was performed to identify physically ro-bust formulations capable of withstanding operational stresses that simulate real-world manufacturing, trans-port, and storage conditions.

Centrifugation Test: All six formulations were sub-jected to centrifugation at 3,500 rpm for 30 min. Formula-tions F5 and F6 remained completely homogeneous with-out evidence of phase separation, creaming, or cracking, demonstrating superior centrifugal stability. Formulations F1–F3 showed marginal creaming after centrifugation, indicating lower colloidal stability.

Heating–Cooling Cycle: Formulations were cycled between 4°C and 45°C for six cycles (48 h each). F6 maintained its clear appearance, droplet size, and pH throughout all cycles, validating its robustness against temperature-dependent phase transitions and surfactant solubility changes.

Freeze–Thaw Cycle: The formulations were sub-jected to three freeze–thaw cycles between −21°C and 25°C. F6 demonstrated no detectable phase separation

or increase in droplet size following freeze–thaw cycling, confirming the structural resilience of its interfacial film.

Table 5: Thermodynamic Stability Assessment of Curcumin Nanoemulsions

12. DISCUSSION

The development of an effective nanoemulsion delivery system for curcumin requires careful balancing of sev-eral competing formulation parameters. The results ob-tained in this investigation collectively demonstrate that the spontaneous emulsification approach, when combined with high-speed homogenisation and an appropriately optimised surfactant–co-surfactant blend, is capable of producing physically stable, pharmaceutically acceptable nanoemulsions with significantly enhanced curcumin solu-bility and drug release characteristics.

The progressive improvement in physicochemical at-tributes from F1 to F6 highlights the critical role of the surfactant-to-oil ratio in governing nanoemulsion qual-ity. An excess of oleic acid (as in F1–F3) produces larger droplets with broader size distributions, likely because the available surfactant is insufficient to completely sta-bilise the expanded oil–water interface generated during homogenisation. Conversely, the lower oil content and higher surfactant plus co-surfactant concentrations in F5 and F6 allow efficient interfacial packing, yielding the smallest droplets with the lowest PDI and highest stabil-ity.

The enhanced in-vitro drug release from the nanoemul-sion relative to the pure curcumin suspension is mechanistically consistent with the Noyes–Whitney dissolu- tion equation: the dramatically increased surface area of nanosized droplets ($S \propto 1/r$) produces a proportion-ally elevated dissolution rate, since the total dissolved drug flux per unit time is directly proportional to the interfacial area. Furthermore, the maintained solubilised state of curcumin within the nanoemulsion oil droplets prevents the formation of a crystalline drug barrier at the membrane–dissolution medium interface.

13. SUMMARY

The present investigation successfully formulated and eval-uated a curcumin-loaded nanoemulsion system designed to address the major biopharmaceutical limitations of curcumin. Six formulations (F1–F6) were systematically prepared using oleic acid, Tween 80, and PEG 400 by spontaneous emulsification and high-speed homogenisa-tion. Formulation F6 emerged as the optimised candidate,

exhibiting a droplet size of 97.5 nm, PDI of 0.18, zeta potential of −32.4 mV, and drug content of 97.3%. The nanoemulsion demonstrated markedly superior in-vitro

curcumin release relative to the plain drug suspension, and maintained excellent physical stability across all ther-modynamic stress tests. SEM confirmed the formation of uniformly spherical nanodroplets. Collectively, these outcomes establish F6 as a promising pharmaceutical nanocarrier capable of overcoming the solubility, stability, and bioavailability challenges inherent to curcumin.

14. CONCLUSION

The findings of the present study demonstrate, conclu-sively, that nanoemulsification represents an effective and practically feasible strategy to overcome the biopharma-ceutical limitations of curcumin. The formulated cur-cumin nanoemulsion system prepared using oleic acid, Tween 80, and PEG 400 via a combination of spontaneous emulsification and high-speed homogenisation achieved all predefined quality targets: nanoscale droplet size, nar-row size distribution, adequate surface charge for colloidal stability, high drug content uniformity, and significantly improved in-vitro drug release.

The optimised formulation (F6) displayed a droplet diameter of approximately 97.5 nm with a PDI of 0.18 and a zeta potential of −32.4 mV, parameters collectively indicative of a stable, well-dispersed nanosystem. SEM confirmed the spherical morphology and uniform distri-bution of nanodroplets, providing morphological evidence consistent with the physicochemical characterisation data. In-vitro release studies showed that the nanoemulsion re-leased nearly 96% of encapsulated curcumin over 12 h, compared with only 63% from the plain suspension under identical conditions, clearly quantifying the therapeutic advantage of the nanosystem.

These results suggest that the developed curcumin na-noemulsion is a scientifically sound and pharmaceutically viable nanocarrier platform with the potential for broader application in the delivery of BCS Class IV lipophilic bioactive compounds. Future investigations may explore in-vivo pharmacokinetic evaluation, toxicological profiling, and scale-up feasibility to facilitate clinical translation of this promising formulation.

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CONFLICT OF INTEREST

The authors declare no competing financial interests or personal relationships that could have influenced the out-comes or interpretation of the work presented herein.

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