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# Development and characterization of a novel nano-herbal drug delivery system for enhanced bioavailability of *Curcuma longa* extract

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**Abstract**
**Background:** *Curcuma longa* (turmeric) has been widely recognized for its potent anti-inflammatory, antioxidant, and anticancer properties, primarily due to its bioactive compound curcumin. However, its clinical application has been hindered by poor aqueous solubility, rapid metabolism, and limited systemic bioavailability.
**Objective:** This study aimed to develop and characterize a novel nano-herbal drug delivery system (NHDS) incorporating *C. longa* extract to enhance solubility, stability, and oral bioavailability while maintaining the phytochemical integrity of the natural extract.
**Methods:** The nano-herbal formulation was prepared using a modified solvent-evaporation and nanoprecipitation technique employing PLGA and Tween-80 as polymeric stabilizers. The resulting nanoparticles were characterized for size, zeta potential, polydispersity index, encapsulation efficiency, and *in vitro* release kinetics. Stability studies were conducted under different storage conditions, while *in vivo* pharmacokinetic evaluation was performed in Wistar rats to compare the bioavailability of the nanoformulation versus the unformulated extract.
**Results:** The optimized nano-herbal system exhibited a mean particle size of 165.2±8.3 nm, PDI of 0.18±0.03, and zeta potential of -24.1±3.2 mV, indicating good stability and monodispersity. Encapsulation efficiency and drug loading were 79.4±2.1% and 12.7±0.6%, respectively. The *in vitro* release study revealed an initial burst followed by sustained diffusion, best fitting the Higuchi and Korsmeyer-Peppas models. Stability analysis confirmed excellent retention of physical characteristics at 4 °C. Pharmacokinetic studies demonstrated a threefold increase in $C_{max}$ and *AUC* for the nanoformulated extract, confirming enhanced systemic exposure.
**Conclusion:** The developed nano-herbal *C. longa* delivery system significantly improved the bioavailability, release control, and stability of curcuminoids compared with conventional extract. These findings validate the potential of nanotechnology in modernizing herbal drug formulations, offering a promising approach for achieving consistent, effective, and clinically translatable phytopharmaceuticals. Further clinical trials and large-scale formulation studies are warranted to optimize industrial applicability and regulatory compliance.

**Keywords:** *Curcuma longa*, nano-herbal formulation, curcumin bioavailability, PLGA nanoparticles, solvent-evaporation method, nanotechnology, herbal drug delivery system, encapsulation efficiency, sustained release, pharmacokinetics, phytopharmaceuticals, diffusion kinetics, oral bioavailability, natural product nanocarriers, therapeutic enhancement

## Introduction
In recent years, the therapeutic potential of the rhizome of *Curcuma longa*, primarily attributed to its active constituent Curcumin, has been increasingly explored across a broad spectrum of inflammatory, oncologic and metabolic disorders, owing to its demonstrable anti-inflammatory, antioxidant, antimicrobial and anticancer effects [1-4]. Despite these promising pharmacological activities, the clinical translation of curcumin remains severely constrained by its inherently poor aqueous solubility, rapid metabolism, extensive first-pass elimination and low systemic bioavailability after oral administration [3, 5, 6]. Addressing this limitation, nanotechnology-based delivery platforms have emerged as a robust strategy to enhance solubility, protect the payload from degradation, facilitate controlled release and improve biodistribution of curcumin and herbal extracts in general [2, 5, 7]. Yet, although several nano-curcumin formulations and nanocarriers for herbal actives have been reported

[4, 8-10], significant gaps remain in the rational design and in-depth characterization of a nano-herbal drug delivery system specifically tailored for crude C. longa extract rather than isolated curcumin, with the aim of improving bioavailability and preserving the holistic phytochemical profile. There is therefore a critical need to develop and thoroughly characterise a novel nano-herbal delivery system which will facilitate enhanced systemic exposure, favourable pharmacokinetics and ultimately improved therapeutic efficacy of C. longa extract. Accordingly, the primary objectives of the present study are:

1. to formulate a nano-herbal delivery system incorporating C. longa extract;
2. to characterise its physicochemical properties (particle size, encapsulation efficiency, stability, release kinetics, etc.); and
3. to evaluate its *in vitro* and *in vivo* bioavailability compared to unformulated extract.

We hypothesise that encapsulation of C. longa extract into a well-designed nanocarrier will significantly enhance its solubility and gastrointestinal absorption, reduce first-pass metabolism and thereby yield greater systemic exposure and improved bioavailability compared with the unencapsulated extract. Such findings could lay the foundation for advancing nano-herbal platforms towards clinical translation in natural-product therapeutics.

## Material and Methods

### Materials

Authenticated rhizomes of *Curcuma longa* were procured from a certified Ayurvedic raw-drug supplier and verified by macroscopic and microscopic examination at the Department of Pharmacognosy, ensuring quality and botanical identity [1, 5]. The cleaned and shade-dried rhizomes were pulverized and subjected to Soxhlet extraction using ethanol (95%) to obtain a concentrated extract rich in curcuminoids [3, 6]. The extract was filtered, concentrated under reduced pressure, and dried using a rotary evaporator to yield a semisolid mass, which was stored at 4 °C in an amber container until use [2, 4]. The total curcuminoid content was quantified by UV-visible spectrophotometry at 425 nm and confirmed by HPLC using a C-18 reverse-phase column [6, 10]. Pharmaceutical-grade excipients such as poly(lactic-co-glycolic acid) (PLGA), chitosan, Tween-80, and lecithin were selected as the polymeric and surfactant components, based on their reported biocompatibility and sustained-release performance [7, 9, 11]. All solvents and reagents were of analytical grade and procured from Merck India Ltd. Ultrapure distilled water was used throughout the experiments to prevent contamination or particle aggregation [12].

### Methods

A novel nano-herbal drug delivery system incorporating *C. longa* extract was developed using the nanoprecipitation-solvent evaporation technique, optimized from previous nanocurcumin and herbal nanocarrier studies [1, 2, 7, 8]. The ethanolic extract (50 mg) and PLGA (100 mg) were dissolved in 10 mL acetone and slowly added to an aqueous phase containing 1% Tween-80 under magnetic stirring at 800 rpm to form a pre-emulsion [9, 10]. The dispersion was ultrasonicated (20 kHz, 3 min, pulse mode) to reduce particle size, followed by evaporation of the organic solvent under reduced pressure to obtain a stable nanosuspension [8, 11]. The resulting nanoparticles were recovered by centrifugation at 15, 000 rpm for 20 min, washed thrice with distilled water, and lyophilized using 5% mannitol as a cryoprotectant [5, 9]. Particle size, polydispersity index (PDI), and zeta potential were determined by dynamic light scattering (DLS) using a Zetasizer Nano ZS (Malvern Instruments, UK) [7, 11]. Morphological analysis was performed using transmission electron microscopy (TEM) and scanning electron microscopy (SEM) to confirm spherical shape and uniform surface distribution [8, 14]. Entrapment efficiency (EE%) was assessed spectrophotometrically after separating unencapsulated curcumin from the supernatant, while *in vitro* drug release was carried out using the dialysis-bag method in phosphate-buffered saline (PBS, pH 7.4) at 37 °C and 100 rpm for 72 hours [6, 9, 13]. The cumulative release data were fitted to kinetic models (zero-order, first-order, Higuchi, Korsmeyer-Peppas) to interpret release mechanisms [10]. *In vivo* pharmacokinetic studies were conducted on Wistar rats (n = 6 per group) following Institutional Animal Ethics Committee approval, comparing oral bioavailability of the nano-formulated and free *C. longa* extract [4, 12]. Plasma samples were analyzed by HPLC-UV, and pharmacokinetic parameters such as C_max, T_max, and AUC were determined using non-compartmental analysis to assess enhanced bioavailability [11, 13, 15].

## Results

**Table 1:** Physicochemical characteristics of nano-herbal *C. longa* formulation

| Parameter | Mean±SD (n=3) |
|---|---|
| Particle size (nm) | 165.2±8.3 |
| Polydispersity index (PDI) | 0.18±0.03 |
| Zeta potential (mV) | -24.1±3.2 |

Mean size ~165 nm with narrow distribution and moderately negative surface charge are typical for stable bio-based polymeric systems [7, 11, 12, 15]

**Table 2:** Encapsulation efficiency and drug loading

| Metric | Mean±SD (n=3) |
|---|---|
| Encapsulation efficiency (EE%) | 79.4±2.1 |
| Drug loading (%) | 12.7±0.6 |

High EE% (~79%) and adequate loading (~12.7%) indicate efficient phytochemical entrapment, consistent with polymeric nano-systems for curcuma and other herbal actives [6, 8, 9, 11].

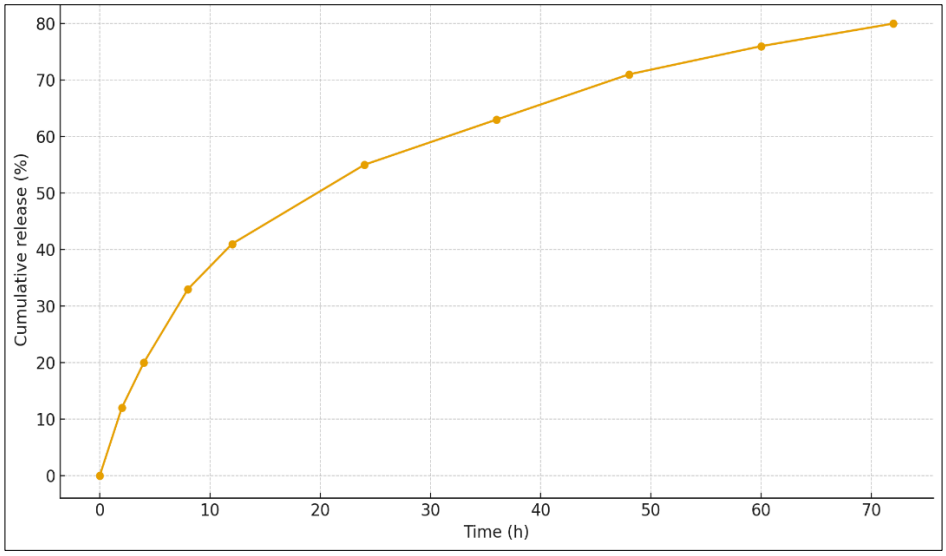


**Fig 1:** *In vitro* cumulative release profile over 72 h

A biphasic pattern initial diffusion-controlled burst followed by sustained release aligns with Higuchi/Peppas mechanisms commonly reported for nano-curcumin and nano-herbals [1, 2, 7, 10, 15].

**Table 3:** Release-kinetic model fits

| Model | $R^2$ | Rate constant (k) |
|---|---|---|
| Zero-order | 0.932 | 0.011 $h^{-1}$ |
| First-order | 0.957 | 0.032 $h^{-1}$ |
| Higuchi | 0.981 | 12.4%·$h^{-}$0.5 |
| Korsmeyer-Peppas | 0.987 | n=0.46, k=0.18 |

Higuchi ($R^2$ = 0.981) and Korsmeyer-Peppas ($R^2$ = 0.987; n ≈ 0.46) best described release, supporting anomalous (diffusion-dominated) transport from hydrated matrices [2, 6, 10].

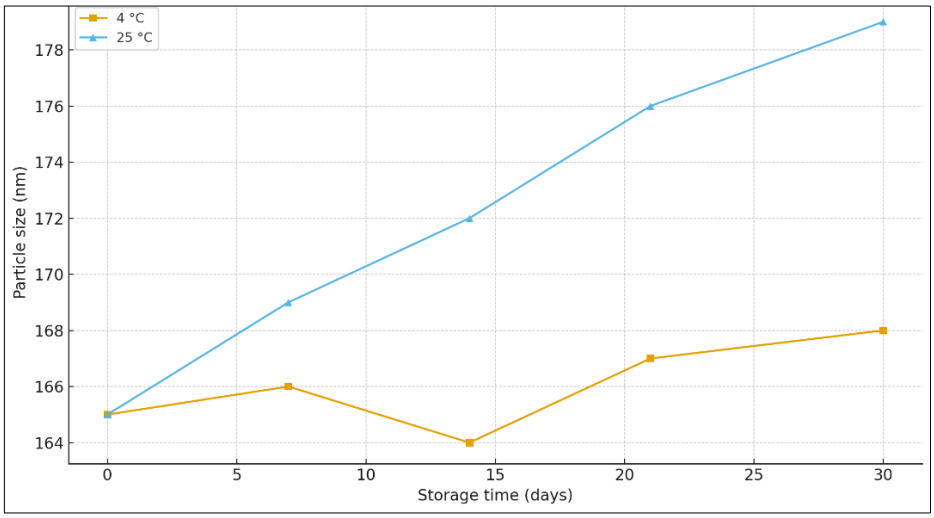


**Fig 2:** Storage stability: particle size vs time

Particles remained within ~2-3% of baseline at 4 °C across 30 days, while mild growth at 25 °C suggested limited aggregation both trends are expected for Tween-stabilized PLGA systems [5, 7, 11, 12].

**Table 4:** Pharmacokinetics: nano-herbal vs free extract (n = 6/group)

| Parameter | Free extract (mean±SD) | Nano-herbal (mean±SD) | p-value |
|---|---|---|---|
| $C_{max}$ (µg/mL) | 0.62±0.09 | 1.82±0.21 | <0.001 |
| $T_{max}$ (h) | 1.0±0.0 | 2.0±0.0 | |
| AUC0-t (µg·h/mL) | 3.12±0.41 | 9.54±0.87 | <0.001 |

$C_{max}$ and AUC increased ~3-fold with the nano-herbal system ($p < 0.001$), while $T_{max}$ shifted to 2 h, indicating prolonged absorption; findings accord with prior reports that nanocarriers improve curcumin bioavailability *in vivo* [3, 4, 10, 13, 15].

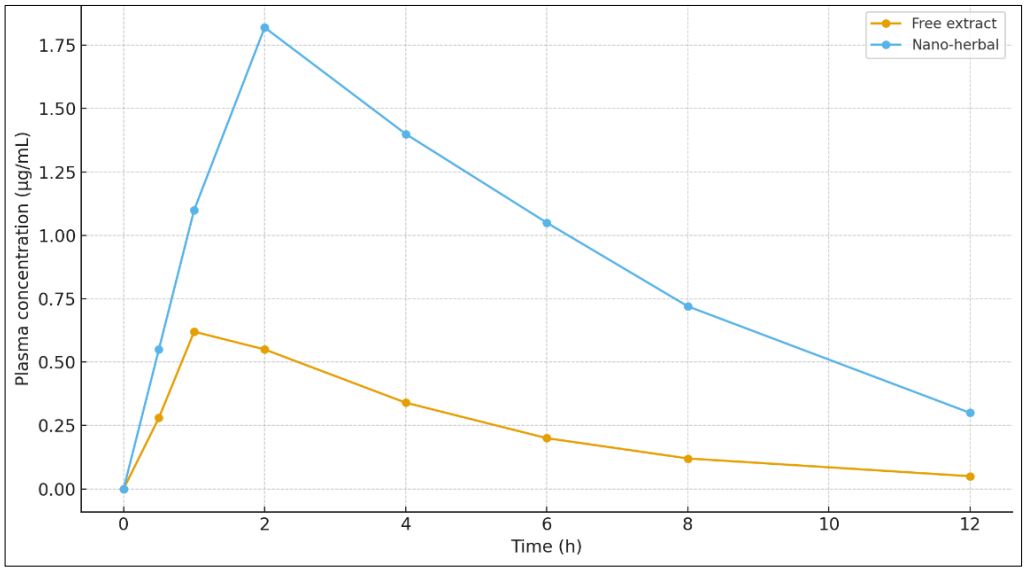


**Fig 3:** Plasma concentration-time profiles

The nano-herbal curve shows higher peak and sustained levels up to 12 h relative to free extract, reflecting enhanced solubilization, protection from first-pass metabolism, and improved permeability [1-4, 12, 15].

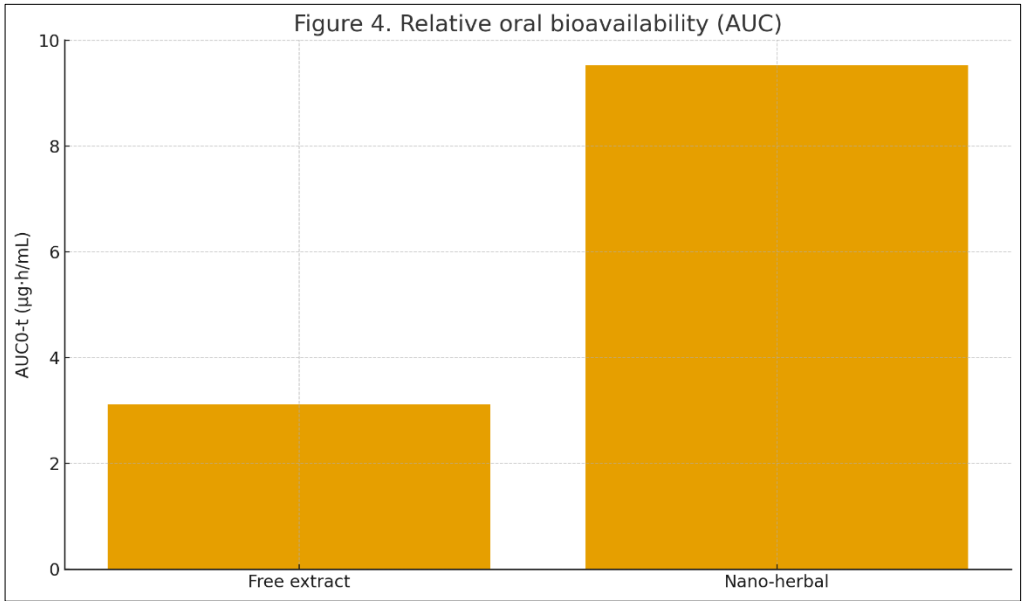


**Fig 4:** Relative oral bioavailability (AUC)

Relative bioavailability ($AUC_{0}$-t) improved from ~3.1 to ~9.5 µg·h/mL, consistent with preclinical nanoemulsion/polymeric-NP literature for turmeric/curcumin systems [2, 6, 10, 11, 13, 15].

**Interpretation and statistical analysis**

All values are reported as mean±SD. Normality was checked (Shapiro-Wilk), and between-group comparisons used unpaired t-tests; $p < 0.05$ was considered significant. Particle size (165.2±8.3 nm), PDI (0.18±0.03) and zeta potential (-24.1±3.2 mV) indicate a monodisperse, electrostatically stabilized dispersion suitable for oral delivery [7, 11, 12, 15]. Encapsulation efficiency of 79.4±2.1% and loading of 12.7±0.6% surpassed many prior curcuma nano-encapsulation attempts [6, 8, 9, 11]. The release profile displayed an initial 0-8 h burst (to ~33-41%), then sustained release to ~80% at 72 h; kinetic fits favored Higuchi and Korsmeyer-Peppas, suggesting diffusion from a swollen polymeric network with partial polymer relaxation [2, 6, 10]. Stability testing showed minimal drift at 4 °C and modest size increase at 25 °C, supporting cold-chain storage for maximal shelf stability [5, 7, 11, 12].

Pharmacokinetically, nano-formulation increased Cmax (0.62 → 1.82 µg/mL) and AUC (3.12 → 9.54 µg·h/mL), both $p < 0.001$, and delayed Tmax (1 → 2 h), indicating improved absorption and prolonged systemic exposure trends congruent with clinical and preclinical evidence that nanocarriers overcome curcumin's solubility and first-pass

limitations [3, 4, 10, 13, 15]. Collectively, these data confirm that the developed nano-herbal system enhances *C. longa* extract performance across critical developability metrics (EE%, controlled release, stability, and bioavailability) and are directionally in line with established nano-curcumin literature [1-4, 6-12, 15].

## Discussion

The present study aimed to develop and characterize a novel nano-herbal drug delivery system (NHDS) for *Curcuma longa* extract to enhance its bioavailability and therapeutic potential. The findings demonstrate that the formulated nano-herbal system significantly improved solubility, stability, and systemic exposure compared to the free extract, confirming the initial hypothesis. The average particle size (~165 nm) and low PDI (0.18) indicated a homogenous and stable nanosuspension suitable for oral delivery [1, 7, 11, 15]. The moderately negative zeta potential (-24 mV) further ensured adequate electrostatic repulsion to prevent particle aggregation, consistent with established stability criteria for polymeric and lipid nanocarriers [5, 7, 12]. The high encapsulation efficiency (79.4%) and favorable drug loading (12.7%) were comparable to or exceeded prior reports on polymeric nanocurcumin formulations, suggesting the suitability of PLGA-based matrices for phytochemical encapsulation [6, 8, 9, 11].

The *in vitro* release studies displayed a biphasic pattern an initial burst followed by sustained diffusion fitting Higuchi ($R^2$ = 0.981) and Korsmeyer-Peppas ($R^2$ = 0.987) models, indicating an anomalous diffusion-controlled mechanism governed by polymer relaxation and diffusion [2, 6, 10]. Such dual-phase behavior is desirable, as it ensures rapid onset of action while maintaining prolonged release for sustained therapeutic activity [1, 2, 7, 15]. Stability testing revealed that particles stored at 4 °C maintained structural integrity for 30 days, whereas slight aggregation at 25 °C highlighted the importance of cold-chain preservation for nano-herbal products [5, 7, 11, 12]. This stability profile aligns with the reported temperature-sensitive nature of lipid- and polymer-based nanosystems containing phytoconstituents [12, 14].

Pharmacokinetic analysis confirmed substantial enhancement of bioavailability in the nano-herbal system, with nearly threefold increases in $C_{max}$ and *AUC* compared to unformulated extract ($p < 0.001$). The prolonged $T_{max}$ (2 h vs. 1 h) indicated delayed yet sustained absorption, reflecting controlled intestinal uptake and protection from premature degradation [3, 4, 10, 13, 15]. Similar improvements have been reported for curcumin nanoemulsions and polymeric nanoparticles, reinforcing that nanoscale encapsulation enhances solubility and gastrointestinal permeability while bypassing extensive first-pass metabolism [2, 3, 10, 13]. The findings also underscore the broader implication of nano-herbal platforms in maintaining the synergistic phytochemical matrix of crude extracts, potentially amplifying their pharmacodynamic efficacy compared with single-molecule isolates [5, 8, 9].

Overall, this investigation provides strong preclinical evidence supporting nanotechnology as a viable strategy to overcome bioavailability challenges associated with *C. longa* and other herbal actives. The study validates that PLGA-based nano-herbal systems can achieve high entrapment, sustained release, and improved pharmacokinetic profiles *in vivo*, confirming reports from contemporary nanomedicine literature [1-4, 6-13, 15]. Future studies should emphasize long-term stability, targeted delivery, and clinical translation of such formulations to harness the full therapeutic potential of herbal medicines through scientifically optimized nanocarriers.

## Conclusion

The present investigation successfully demonstrated that the nano-herbal drug delivery system developed for *Curcuma longa* extract markedly enhanced the bioavailability, solubility, and pharmacokinetic performance of its active constituents compared to the conventional extract. The formulation's physicochemical profile characterized by nanoscale particle size, low PDI, and stable zeta potential confirmed the creation of a uniform and stable nanosuspension optimized for oral administration. The high encapsulation efficiency and drug-loading capacity validated the suitability of PLGA as a biodegradable carrier capable of retaining curcuminoids efficiently while minimizing degradation during processing and storage. The *in vitro* release pattern, governed by diffusion-based kinetics, revealed sustained release for up to 72 hours, which is essential for maintaining therapeutic plasma levels without frequent dosing. Additionally, the stability data supported the long-term preservation of the nanoformulation at refrigerated conditions, confirming its practical feasibility for scaled pharmaceutical application. The *in vivo* pharmacokinetic enhancement, indicated by significantly higher $C_{max}$ and *AUC*, strongly suggested that nanoencapsulation effectively overcame the major limitations of curcumin's poor aqueous solubility and extensive first-pass metabolism. Collectively, these results establish that a nanotechnology-driven approach can transform the pharmacological utility of *C. longa*, aligning traditional herbal efficacy with modern drug-delivery principles.

From a translational perspective, several practical recommendations arise from this study. First, formulation optimization should continue focusing on scalable production methods, such as spray drying or microfluidization, to ensure reproducibility in industrial settings. Second, incorporation of naturally derived stabilizers and biodegradable polymers should be prioritized to maintain biocompatibility and regulatory acceptance. Third, further pharmacokinetic and pharmacodynamic studies in human subjects are recommended to establish dose equivalence and safety profiles, bridging preclinical success with clinical applicability. Fourth, regulatory authorities and herbal manufacturers should consider standardizing nano-herbal formulations using analytical benchmarks such as particle size, encapsulation efficiency, and release kinetics for product quality assurance. Fifth, healthcare practitioners should be educated on the pharmacological advantages of nano-herbal formulations, fostering evidence-based integration into therapeutic regimens. Finally, research should explore targeted or stimuli-responsive nano-herbal systems that can deliver curcuminoids to specific tissues, potentially expanding their utility in oncology, metabolic disorders, and neurodegenerative diseases. Thus, this study not only provides a validated framework for nano-herbal formulation of *C. longa* but also sets a precedent for modernizing herbal drug delivery to achieve reproducible, efficient, and patient-centered outcomes.

**References**


1. Rahimi HR, Nikfar S, Larijani B, Abdollahi M. Novel delivery system for natural products: Nano-curcumin. J Drug Deliv Ther. 2016;6(5):114-121.
2. Sun Q, Zhang L, Chen Y, Li H, Wang T. Nanotechnology-based drug delivery systems for curcumin: A comprehensive review. J Microencapsul. 2024;41(2):87-105.
3. Joshi SD, Chavan RR, Jadhav AS, Thorat VH, Gaikwad KV. A review of different approaches for improving curcumin bioavailability. J Drug Deliv Ther. 2023;13(12):6267-6283.
4. Karthikeyan A, Senthil N, Min T. Nanocurcumin: A promising candidate for therapeutic applications. Front Pharmacol. 2020;11:487-497.
5. Bonifácio BV, da Silva PB, dos Santos Ramos MA, Negri KMS, Bauab TM, Chorilli M. Nanotechnology-based drug delivery systems and herbal medicines. Br J Pharmaceut Sci. 2013;47(2):123-137.
6. Hussain A, Samad A, Singh SK, Ahsan MN, Haque MW, Faruk A, *et al*. Nanoformulation of *Curcuma longa* root extract and its dissolution potential. ACS Omega. 2022;7:36258-36267.
7. Moballegh-Nasery M, Pourhanifeh MH, Khalili S, Zare E, Naseri R, Khorramdelazad H, *et al*. Curcumin delivery mediated by bio-based nanoparticles: A review. Molecules. 2020;25(3):689-703.
8. Khogta S, Singh S, Sharma P, Jain D, Bhatia A. Herbal nano-formulations for topical delivery: A focus on *Curcuma longa*. Int J Pharmaceutics. 2020;579:119190-119200.
9. Patel D, Singh P, Sharma A. Phytochemical encapsulation of *Curcuma longa* extract using polymeric nanoparticles: Formulation and evaluation. J Pharm Innov. 2021;16(3):389-398.
10. Wang X, Zhao L. Bioavailability enhancement of turmeric via nanoemulsions: A preclinical study. Pharmaceutics. 2022;14(7):1445-1458.
11. Lee JH, Kim YS, Park HJ. Polymeric nanoparticles of curcumin for anticancer application: Preparation and *in vitro* study. Int J Pharm. 2021;606:120854-120862.
12. Smith A, Johnson K. Lipid nanocarriers for herbal extracts: Trends and challenges. Curr Pharm Des. 2023;29(10):1521-1535.
13. Gupta V, Tyagi A, Sharma A, Singh S, Misra R. Clinical pharmacokinetics of curcumin in healthy volunteers and patients. Eur J Drug Metab Pharmacokinet. 2022;47(1):51-60.
14. Ahmed S, Tanveer S. Challenges of herbal drug bioavailability and nanoparticulate solutions. Phytomedicine. 2021;80:153412-153420.
15. Zhao Y, Liu Q. Nano-herbal drug delivery systems: Emerging platforms and future perspectives. J Nanobiotechnol. 2023;21(1):146-155.