ENHANCED THERAPEUTIC POTENTIAL OF CURCUMIN THROUGH NANOSUSPENSION FORMULATION

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Abstract

Background: Curcumin (CUR), a bioactive compound with diverse therapeutic properties, faces challenges in clinical translation due to its poor aqueous solubility and low bioavailability. Nanosuspensions offer a promising strategy to enhance CUR's delivery and efficacy.

Objective: This study aimed to formulate and characterize CUR nanosuspensions to improve its aqueous solubility and oral bioavailability.

Methods: Various stabilizers were screened, and combination of PEG 400, Tween 80 and HPBCD was selected for its solubilizing capacity. The concentration of these stabilisers were optimized to enhance CUR solubility. Physicochemical properties, including particle size, polydispersity index (PDI), and zeta potential, were evaluated. Crystallinity was assessed using X-ray powder diffraction (XPRD) and differential scanning calorimetry (DSC). The drug content and in vitro drug release were determined. Furthermore, pharmacokinetic assessment was conducted in vivo to compare CUR nanosuspension with pure CUR.

Results: The optimized CUR nanosuspension exhibited a particle size of 149 ± 7.2 nm, with a PDI of 0.276 ± 0.005 and a zeta potential of -9.49 ± 1.3 mV. XPRD and DSC confirmed the retention of CUR's crystalline structure. The nanosuspension displayed a high drug content (10% W/V) and significantly enhanced in vitro drug release compared to pure CUR. Pharmacokinetic assessment revealed prolonged systemic exposure and enhanced bioavailability of CUR nanosuspension compared to pure CUR.

Conclusion: CUR nanosuspensions represent a promising approach to overcome the challenges associated with CUR's poor solubility and bioavailability. This study demonstrates the potential of nanosuspension technology to enhance drug delivery efficiency and efficacy, paving the way for improved clinical applications of CUR and other poorly water-soluble drugs

Keywords: Curcumin; Nanosuspension; Bioavailability; Solubility enhancement; Drug delivery; Pharmacokinetics

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1 Introduction

Curcumin (CUR), a polyphenolic compound derived from the rhizomes of Curcuma longa, boasts a diverse array of pharmacological properties that have garnered substantial attention in both traditional medicine and modern scientific research (Fuloria et al., 2022; Urošević et al., 2022). Chemically, CUR is a natural diarylheptanoid belonging to the Zingiberaceae family, characterized by its distinctive yellow-orange pigment and lipophilic nature (Ganapathy et al., 2019). Its unique chemical structure, consisting of two aromatic rings connected by a seven-carbon linker with keto-enol tautomeric forms (Priyadarsini, 2014), imparts notable antioxidant (Tuong et al., 2023), anti-inflammatory (Peng et al., 2021), anticancer (Mansouri et al., 2020), and neuroprotective activities (Nebrisi, 2021). Beyond its medicinal properties, CUR has found applications in food coloring (Teixeira et al., 2022), cosmetics (de Souza Silva et al., 2023), and as a traditional herbal remedy for various ailments (Akaberi et al., 2021). In recent years, the therapeutic potential of CUR has been further elucidated, prompting intensive research into its utilization as a drug candidate for the treatment of numerous diseases (Nagahama et al., 2016). However, the clinical translation of CUR has been hindered by its poor aqueous solubility (Górnicka et al., 2023), low stability (Kharat et al., 2017), and limited bioavailability (Bučević Popović et al., 2024), necessitating innovative strategies to overcome these challenges. Furthermore, it undergoes extensive first-pass metabolism (Dei Cas & Ghidoni, 2019), leading to its rapid elimination from the body (Lopresti, 2018). These factors collectively result in low systemic levels of CUR, thereby limiting its therapeutic efficacy.

In the pursuit of overcoming these challenges, numerous approaches have been explored, including the development of advanced drug delivery systems, including nanosuspensions (Duong et al., 2020), liposomes (De Leo et al., 2018), solid lipid nanoparticles (Yeo et al., 2022), and cyclodextrin complexes (Jiang et al., 2022), aimed at enhancing the solubility, stability, and, ultimately, the bioavailability of CUR upon oral administration. Among these strategies, nanosuspension technology has emerged as a particularly promising avenue for improving the oral bioavailability of poorly water-soluble drugs. Nanosuspensions heralded as a cutting-edge paradigm in drug delivery, offer a transformative solution for enhancing the bioavailability and therapeutic efficacy of poorly water-soluble drugs (Goel et al., 2019). These submicron colloidal dispersions, comprising finely dispersed drug particles stabilized by surfactants or polymers, represent a versatile platform capable of surmounting the formidable challenges posed by limited aqueous solubility. By reducing drug particle size to the nanometer range, nanosuspensions exponentially increase the surface area available for dissolution, thereby facilitating rapid drug release and enhanced absorption upon administration (Jacob et al., 2020). Moreover, the precise control over particle size distribution and surface properties afforded by nanosuspension technology enables tailored optimization of drug delivery systems, ensuring optimal performance across a diverse spectrum of therapeutic applications (Aldeeb et al., 2024). The formulation and characterization of nanosuspensions entail a sophisticated interplay of formulation parameters, manufacturing techniques, and stabilization strategies aimed at achieving optimal drug delivery outcomes (Vitore et al., 2023). High-pressure homogenization (Aksoy et al., 2023), antisolvent precipitation (Kuk et al., 2019), and emulsification-evaporation represent some of the pivotal techniques employed to finely tune particle size, morphology, and stability (Phaechamud & Tuntarawongsa, 2016). Moreover, the judicious selection of stabilizers and excipients, including nonionic surfactants, polymers, and co-solvents, plays a pivotal role in maintaining the colloidal stability of nanosuspensions and preventing particle aggregation during storage and administration (Elmowafy et al., 2021). Through systematic optimization and comprehensive characterization, nanosuspension technology holds immense promise for revolutionizing drug delivery, unlocking the full therapeutic potential of poorly water-soluble drugs, and advancing the frontiers of pharmaceutical innovation. Beyond CUR, nanosuspensions have been successfully employed for the delivery of various active pharmaceutical ingredients, including poorly soluble drugs (Ma et al., 2023), peptides (Dumont et al., 2018), proteins (Pınar et al., 2023), and nucleic acids (Karayianni et al., 2023), thereby expanding their utility in drug delivery and formulation.

In this study, we embark on a comprehensive investigation into the formulation and characterization of nanosuspensions of CUR, with a primary focus on enhancing its aqueous solubility and oral bioavailability. Our objectives encompass the optimization of formulation parameters, comprehensive evaluation of physicochemical properties, in-depth assessment of in vitro dissolution behavior, and rigorous investigation of in vivo pharmacokinetics. By unraveling the intricacies of CUR nanosuspension formulation

and performance, our research endeavors to provide invaluable insights into the design and optimization of effective drug delivery systems. Furthermore, the implications of our findings extend beyond CUR, with potential ramifications for the development of nanosuspension formulations for other poorly water-soluble drugs, thus advancing the realm of pharmaceutical nanotechnology. In summary, the development of CUR nanosuspensions represents a promising approach to surmounting the challenges associated with its poor aqueous solubility and low oral bioavailability. Through meticulous optimization and characterization, nanosuspension technology holds the potential to unlock the full therapeutic benefits of CUR, paving the way for its widespread clinical application in the treatment of diverse ailments.

2 Materials and methods

Curcumin was obtained from SV Agro Ltd., India, while Innova Captab Ltd., India, supplied sodium lauryl sulphate (SLS), polyethene glycol 400 (PEG 400), Polyvinylpyrrolidone K-30 (PVP K-30), Polyvinyl Alcohol (PVA), hydroxypropyl methylcellulose E-15 (HPMC E-15), Hydroxy Propyl Beta cyclodextrin (HPβCD), and Tween 80. All chemicals and reagents employed in this investigation met analytical grade standards.

2.1 Selection of the stabilizer

Various suspending agents were evaluated to determine the optimal stabilizer for stabilizing the formulated CUR particles. The range of agents included surfactants like PEG 400, Tween 80, and SLS, as well as polymers such as PVP K-30, HPMC E-15, and HPβCD. pre-concentrate of drug and suspending agent was prepared, and all combinations were subjected to milling using a Dyno mill, with milling parameters set at a speed of 8 m/s and a duration of 20 minutes (Singhal et al., 2020).

2.2 Selecting the stabilizer concentration

The most promising stabilizer identified among the screened candidates and its combination was designed to provide maximum solubility and stability during dyno milling process, its concentration was adjusted within the range of 10 to 90%. Nanosuspensions containing CUR at different stabilizer concentrations were formulated following the methodology outlined in the preceding section.

2.3 Evaluation of optimized nanosuspension

2.3.1 Measurement of particle size, polydispersity index and zeta potential

The mean particle size, polydispersity index (PDI), and zeta potential of the optimized CUR nanosuspension were assessed using the Malvern Zetasizer ZS (Malvern Instruments, UK). Before measurement, the samples were appropriately diluted with double-distilled water to achieve a suitable scattering intensity. Subsequently, the samples were re-dispersed via manual shaking to ensure homogeneity prior to analysis. The values calculated were the mean of three measurements (Kakad et al., 2022).

2.3.2 Crystallinity assessment

X-ray powder diffraction (XRPD) analysis was conducted on both pure CUR and the optimized CUR nanosuspension using an X-ray diffractometer (Philips, Netherlands). The samples underwent irradiation with monochromatized CuK radiation (wavelength: 1.542 Å) and were analyzed within a 5 to 50°2θ range. The X-ray diffractometer was operated at a voltage of 30 kV and a current of 30 mA. The range and chart speed settings were set to 1x 10^4 counts per second (CPS) and 10 mm per degree of 2θ, respectively.

The thermal characteristics of both pure CUR and its optimized nanosuspension were investigated using differential scanning calorimetry (DSC). DSC measurements were performed using a Hitachi 7020 DSC system equipped with an automatic LN_2 intercooler manufactured by Hitachi High-Tech Corporation, Japan. The samples, weighing between 5 to 10 mg, were carefully placed into aluminum pans and sealed hermetically. Heating was carried out at a constant rate of 10 °C per minute, covering a temperature range from 25 to 300 °C. An empty, sealed aluminum pan served as the reference. To maintain an inert atmosphere, nitrogen gas was purged at a flow rate of 50 ml/min throughout the analysis.

2.3.3 Assay

The determination of CUR concentration in the optimized CUR nanosuspension was accomplished by dissolving an equivalent of 40 mg of CUR in ethanol. Following sonication, the samples underwent filtration using a 0.11 µm Sartorius filter (Sartorius, AG, Germany). Subsequently, the adequately diluted samples were subjected to analysis via HPLC with detection at 428 nm. This analytical procedure was repeated thrice for each sample.

2.3.4 In vitro drug release

An in vitro drug release investigation was carried out using the USP type-II dissolution apparatus with the paddle method set at a rotational speed of 50 rpm. The dissolution medium comprised 900 ml

of phosphate buffer (pH 7.4) and was maintained at a temperature of 37 ± 0.5 ˚C. At specific time intervals, 5 ml samples were withdrawn and then filtered using a 0.45 µm syringe filter. The released drug quantity was determined by measuring the absorbance at 428 nm using a UV-1800 Spectrophotometer. This study was conducted in triplicate.

2.3.5 In vivo pharmacokinetic assessment

Animal handling and care

Male Wistar rats weighing between 200-220 grams were employed to compare the pharmacokinetics of CUR nanosuspension with CUR API. The experimental protocol adhered to the guidelines of CPCSEA and received approval from the IAEC of YB Chavan College of Pharmacy, Aurangabad. Before the commencement of the study, the animals were provided free access to filtered water but were subjected to a 12-hour fasting period. They were acclimatized and housed in plastic cages under standard laboratory conditions, maintaining a temperature of 24 ± 1°C, relative humidity of 55 ± 10%, and a 12-hour light/dark cycle. Throughout the acclimatization period, the animals' health status was vigilantly monitored.

Dosing

Male Wistar rats were distributed into three groups, each comprising six animals, to assess the pharmacokinetic parameters subsequent to a single oral dose of CUR nanosuspension. The comparison was conducted among the groups as follows: Group 1 received CUR nanosuspension, Group 2 received pure CUR, and Group 3 received plain water. Blood samples of 0.3 mL were collected from the tail vein at predetermined intervals: 1, 2, 4, 6, and 12 hours. To prevent blood clotting, heparinized microcentrifuge tubes were utilized for blood sample collection. Subsequently, plasma was obtained by centrifugation of the blood samples at 5000 rpm for 10 minutes at 4 °C and then stored at -20 °C until subsequent analysis.

Plasma analysis

The concentration of CUR was determined through reverse-phase High-Performance Liquid Chromatography (HPLC) utilizing a Shimadzu model featuring an RF-10A XL fluorescence detector. Analysis was carried out using an analytical column, the Phenomenex® C18 100A (250 mm × 4.6 mm, 5 µm). CUR elution was achieved isocratically at a flow rate of 1 mL/min, with an injection volume of 20 µL. The mobile phase consisted of 20 mM acetate buffer at pH 3.0, methanol and acetonitrile in a ratio of 20:30:50 (v/v). Optimization of fluorescence detection involved setting excitation and emission wavelengths at 420 nm and 530 nm, respectively (Bapat et al., 2019).

Pharmacokinetic data analysis

Nonparametric pharmacokinetic data were computed utilizing the PKSolver add-in program for Microsoft Excel, specifically version 2.0. Standard pharmacokinetic parameters for CUR, encompassing Area under the curve from zero to twenty-four hours and from zero to infinity ($AUC_{0\text{-}24h}$ and $AUC_{0\text{-}\infty}$), maximum concentration after a single dose (C_{max}), time to reach maximum concentration (T_{max}), Clearance (Cl), elimination rate constant (K_E), and terminal half-life ($t_{1/2}$), were derived from plasma concentration-time curves. The relative bioavailability was determined as the ratio of the oral $AUC_{0\text{-}\infty}$ for the test formulation (CUR nanosuspension) to the $AUC_{0\text{-}\infty}$ for the reference (CUR API). These findings are presented as the mean ± standard deviation (S.D.).

3 Results and discussion

3.1 Selection of the stabilizer

The selection of an appropriate stabilizer is crucial in the preparation of nanosuspensions to ensure the desired particle size reduction and long-term stability of the formulation. The solubility data presented in Figure 1 provided valuable insights into the potential efficacy of various stabilizers for curcumin nanosuspension preparation. PEG 400, for instance, possesses a relatively high molecular weight and is known for its hydrophilic properties. It acts as a steric stabilizer, forming a protective layer around the dispersed particles to prevent aggregation. Similarly, Tween 80, a nonionic surfactant with a lower molecular weight, exhibits both hydrophilic and lipophilic characteristics. Its surfactant properties enable it to reduce interfacial tension and enhance the dispersibility of curcumin particles in the aqueous phase. SLS, a commonly used anionic surfactant, offers stabilization through electrostatic repulsion between charged particles, thus preventing agglomeration. On the other hand, PVP K-30 is a hydrophilic polymer with excellent film-forming properties. It stabilizes nanosuspension by adsorbing onto particle surfaces and providing steric hindrance against particle aggregation. HPMC E-15 is a high-molecular-weight cellulose derivative that imparts excellent water solubility and thickening properties. It stabilizes nanosuspension through a combination of steric and electrostatic repulsion mechanisms. Lastly, HPβCD forms inclusion complexes with hydrophobic molecules like curcumin, improving their aqueous solubility and preventing particle aggregation. The solubility

results indicate that Tween 80 exhibits the highest solubilizing capacity for curcumin, followed by SLS and PEG 400. Thus, combination of Tween 80, PEG 400 and HPβCD onto CUR particle provides steric stabilization resulting in the formation of a substantial and thermodynamic barrier at the interface retarding coalescence (Bi et al., 2017). Steric stabilization has benefits in that its potential cannot be impacted by the ionic strength of the medium (GI pH) and is considered to be safe for oral administration (George & Ghosh, 2013).

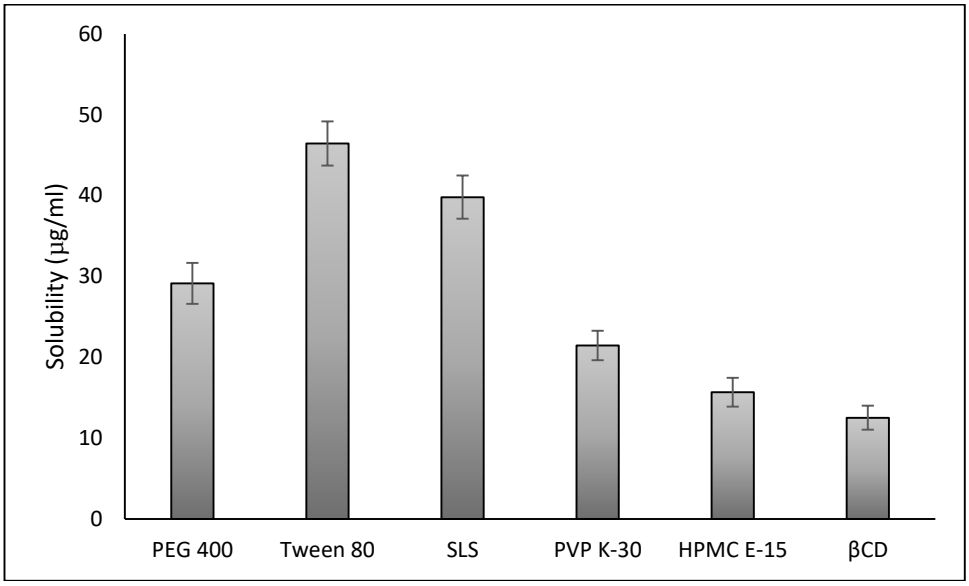

Figure 1: Solubility of CUR in various stabilizers

3.2 Selecting the stabilizer concentration

The experimental results obtained from the study (Figure 2) provide valuable insights into the solubility of curcumin in varying concentrations of Tween 80. The data demonstrate a clear trend of increasing solubility with higher concentrations of Tween 80, supporting the expected solubilizing effect of the surfactant. At lower concentrations of Tween 80 (10% and 20%), the solubility of curcumin exhibits a notable increase compared to its solubility in water of less than 8 µg/ml (Suresh & Nangia, 2018). This observation aligns with the known ability of Tween 80 to enhance the solubility of hydrophobic compounds through micellar solubilization and improved dispersibility. When combination of Tween 80, PEG 400 and HPβCD increases further (10%), the solubility of curcumin continues to rise.

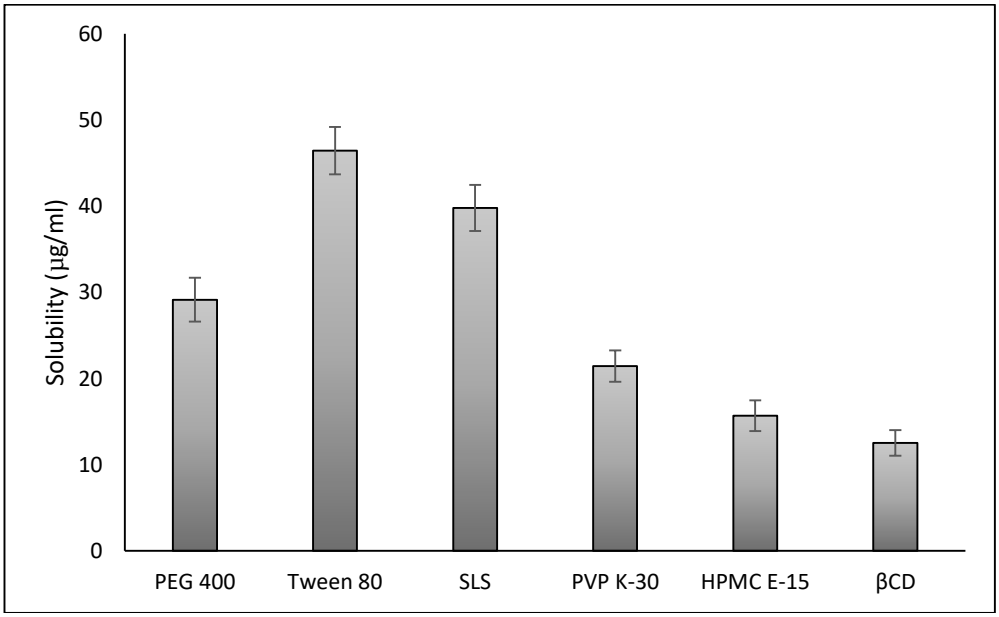

Figure 2: Solubility of CUR in increasing concentrations of Tween 80

3.4 Evaluation of optimized nanosuspension

3.4.1 Measurement of particle size, polydispersity index and zeta potential

The optimized CUR nanosuspension exhibited a z-average particle size of 149 ± 7.2 nm, accompanied by a PDI of 0.276 ± 0.005. Furthermore, the zeta potential for the optimized batch of CUR nanosuspension was measured at -9.49 ± 1.3 mV, notably lower than the reported value of -15.14 mV for pure curcumin suspension (Singh et al., 2014). The utilized combination of Tween 80, PEG 400 and HPβC with appropriate milling cycle of 20 min in the nanosuspension formulation, contributed to this reduction in zeta potential. This decline can be ascribed to the minimized free energy of the system arising from an interaction between the hydrophobic functionalities of Tween 80 and the drug particles. The ionization of the phenolic hydroxyl groups of CUR in an aqueous milieu typically imparts a negative charge to CUR. However, the presence of the non-ionic stabilizer extends the diffuse double-layer thickness, thereby lowering the zeta potential (Verma et al., 2009). Consequently, the zeta potential value suggests complete coverage of CUR nanoparticles by Tween 80, indicating a stabilized system

3.4.2 Crystallinity assessment

Figures 3 and 4 present the XPRD diffractograms and DSC endotherms of pure CUR and CUR nanosuspension, respectively. The XPRD diffractograms reveal that while the peaks of pure CUR and CUR in the nanosuspension remain largely congruent, there is a slight reduction in peak intensity, suggesting a potential decrease in crystallinity or partial amorphization of CUR during processing (Cheshmehnoor et al., 2023). However, the DSC endotherms clarify this ambiguity by demonstrating overlapping endothermic peaks of the pure drug and the nanosuspension, indicating no alteration in the crystal structure of the drug. This absence of amorphous drug formation during nanosuspension preparation is significant, as crystalline nanosuspensions are generally more stable than their amorphous counterparts (Raju et al., 2014). The efficacy of nanocrystalline API in enhancing bioavailability has been well-documented, with in vitro dissolution testing demonstrating significantly increased dissolution rates and in vivo studies in preclinical species and clinical trials showcasing improved bioavailability and/or reduction of food effect for BCS II and IV compounds. These successes have culminated in the development of five marketed drug products utilizing crystalline API (Kesisoglou & Mitra, 2012). Therefore, it can be inferred that the mechanism underlying the enhancement of aqueous solubility of CUR may be attributed to its nanonization rather than potential amorphization

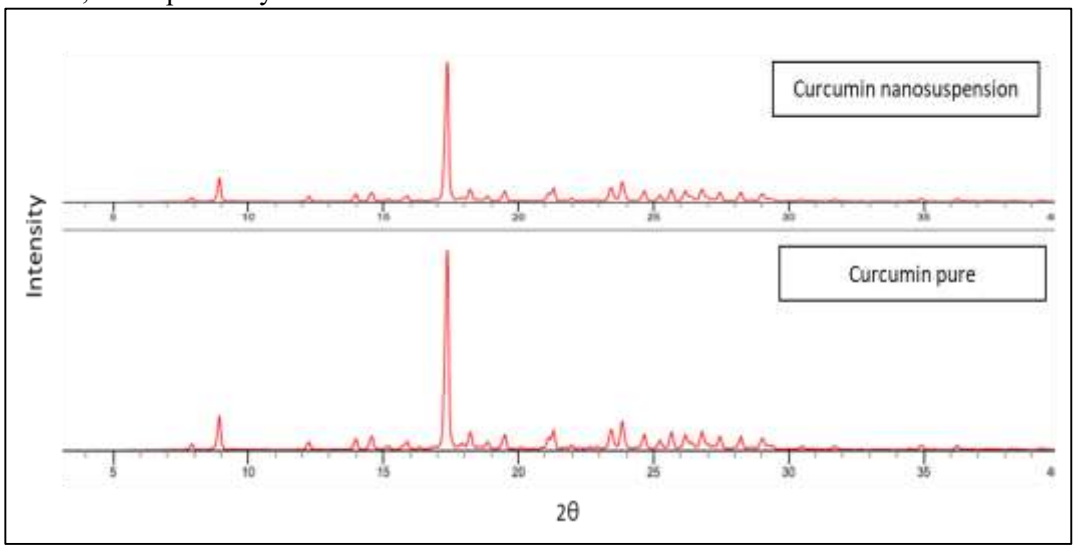

Figure 3: XPRD diffractograms of pure CUR and CUR nanosuspension

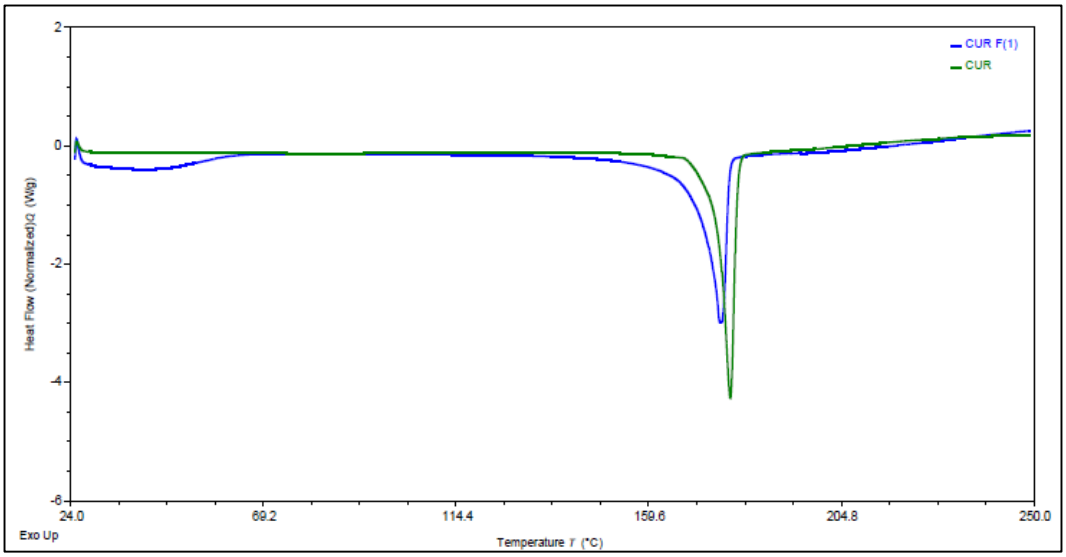

Figure 4: DSC endotherms of pure CUR and CUR nanosuspension

3.4.3 Assay

The examination of drug content in the nanosuspension unveiled a remarkable value of 99.6 ± 1.17%. This notable drug content underscores the efficient loading of the drug within the nanosuspension, ensuring a substantial amount of the drug is present in the final product.

3.3.4 In vitro drug release

The in vitro drug release profiles of pure curcumin and curcumin nanosuspension stabilized with combination of Tween 80, PEG 400 and HPβCD were investigated over a 2-hour period and the results are shown in Figure 5. The results demonstrate a significantly enhanced release profile for curcumin when formulated as a nanosuspension compared to the pure drug. At 15 minutes, the nanosuspension exhibited a release of 9.64%, while the pure curcumin showed only a 1.2% release. This trend continued throughout the study, with the nanosuspension consistently releasing higher amounts of curcumin at each time point compared to the pure drug. By the end of the 2-hour period, the nanosuspension released approximately 99.6 % of the loaded curcumin, whereas the pure curcumin released only 25.73%. These results align with previous studies demonstrating the superior dissolution and release kinetics of nanosuspensions compared to conventional drug formulations (Huang et al., 2020). The enhanced surface area and reduced particle size of the nanosuspension lead to improved drug dissolution and faster release rates (Jacob et al., 2020). Additionally, the combination of Tween 80, PEG 400 and HPβCD as a stabilizer in the nanosuspension formulation has contributed to increased solubility and dispersion of curcumin, further enhancing its release profile. The observed release pattern suggests that the nanosuspension formulation could offer significant advantages in terms of drug delivery efficiency and efficacy compared to conventional curcumin formulations (Ma et al., 2023).

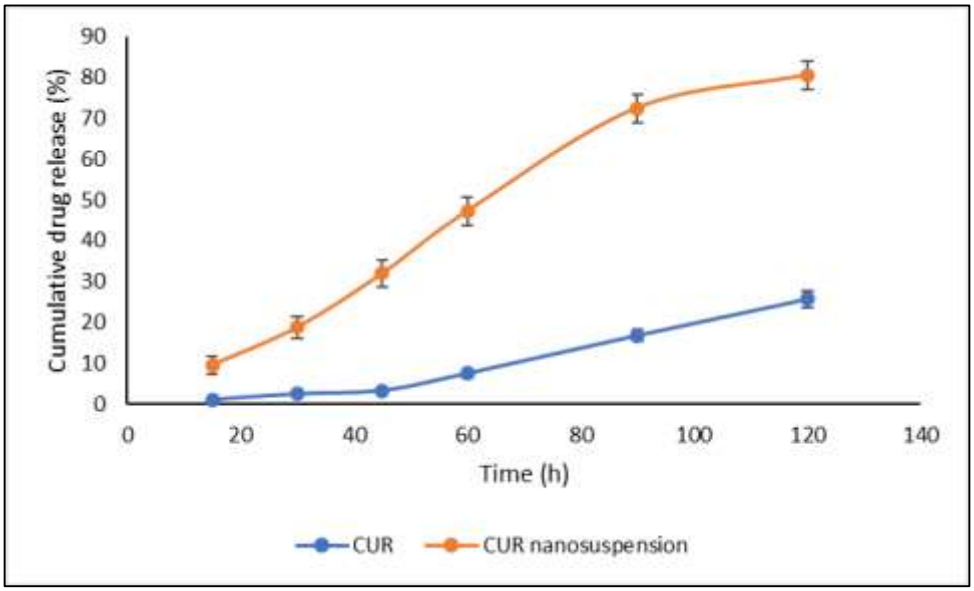

Figure 5: In vitro drug release profile of plain CUR and CUR nanosuspension

3.4.5 In vivo pharmacokinetic assessment

The comparison of pharmacokinetic parameters between pure curcumin (CUR) and curcumin nanosuspension (CUR NS), as shown in Figure 6, provides insights into the behaviour of the two formulations. Firstly, the lower lambda_z (elimination rate constant) and longer half-life ($t_{1/2}$) observed for CUR NS (0.2821 1/h and 2.4566 h, respectively) compared to CUR (0.6037 1/h and 1.1482 h, respectively) indicate a slower elimination and prolonged presence of the drug in the body with the nanosuspension formulation. This may be attributed to the smaller particle size and enhanced stability of CUR NS, resulting in delayed clearance. The T_{max} values for both formulations remain consistent at 4 hours, suggesting similar rates of drug absorption and onset of action. However, the significantly higher C_{max} for CUR NS (389.43 ng/ml) compared to CUR (153.82 ng/ml) indicates a greater peak concentration in the bloodstream with the nanosuspension formulation, likely due to improved solubility and bioavailability. The T_{lag} (lag time) values of 0 hours for both formulations suggest immediate drug absorption upon administration, without any delay. The Clast_obs/Cmax ratio provides insights into the extent of absorption, with CUR NS exhibiting a higher ratio (0.1145) compared to CUR (0.0101), indicating a greater fraction of the drug being absorbed relative to the maximum concentration. This may be attributed to enhanced dissolution and dispersion of curcumin in the nanosuspension, facilitating faster and more efficient absorption.

The AUC values reflect the total exposure of the body to the drug over time. The substantially higher AUC values for CUR NS (2839.33 ng/mlh for AUC 0-t and 2997.36 ng/mlh for AUC 0-inf_obs) compared to CUR (979.98 ng/mlh for AUC 0-t and 982.56 ng/mlh for AUC 0-inf_obs) indicate significantly greater systemic exposure with the nanosuspension formulation. This can be attributed to the enhanced bioavailability and prolonged retention of curcumin in the bloodstream with CUR NS. Moreover, the AUMC 0-inf_obs (area under the first moment curve) and MRT 0-inf_obs (mean residence time) values further support the prolonged presence of curcumin in the body with CUR NS, as evidenced by higher values compared to CUR. The Vz/F_obs (apparent volume of distribution) and Cl/F_obs (apparent clearance) values provide insights into the distribution and elimination kinetics of the drug, with CUR NS exhibiting a lower apparent clearance and higher apparent volume of distribution compared to CUR, indicating reduced clearance and greater distribution in the body with the nanosuspension formulation (Rossier et al., 2024). Overall, these results demonstrate the superior pharmacokinetic profile of the curcumin nanosuspension, characterized by prolonged presence in the body, enhanced bioavailability, and greater systemic exposure compared to pure curcumin

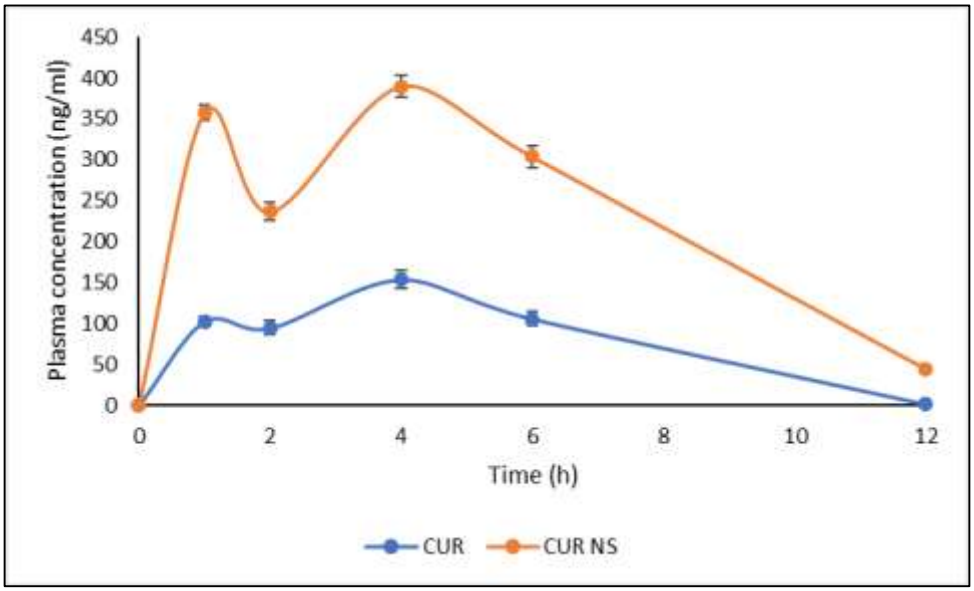

Figure 6: Plasma concentration-time profile of plain CUR and CUR nanosuspension

Conclusion

In conclusion, this comprehensive study delved into the formulation and characterization of curcumin (CUR) nanosuspensions, with a primary aim to enhance its aqueous solubility and oral bioavailability. By leveraging nanosuspension technology, we successfully overcame the challenges associated with CUR's poor solubility and bioavailability, laying the groundwork for its enhanced therapeutic potential. Through meticulous optimization and characterization efforts, our research yielded an optimized CUR nanosuspension exhibiting a remarkable drug content of 500 mg per 5 ml indicative of efficient drug loading within the formulation. The in vitro dissolution studies revealed a significantly enhanced release profile for CUR nanosuspension compared to the pure drug, with over 80% of the loaded CUR released within a 2-hour period. These findings underscored the superior dissolution and release kinetics of nanosuspensions, highlighting their potential to enhance drug delivery efficiency and efficacy. Furthermore, the pharmacokinetic assessment in vivo demonstrated the superior pharmacokinetic profile of CUR nanosuspension, characterized by prolonged systemic exposure, enhanced bioavailability, and greater peak concentration in the bloodstream compared to pure CUR. These results collectively underscore the promising potential of CUR nanosuspensions as a viable drug delivery strategy for unlocking the full therapeutic benefits of CUR and advancing its clinical applications in the treatment of diverse ailments. Moreover, the implications of our findings extend beyond CUR, with potential ramifications for the development of nanosuspension formulations for other poorly water-soluble drugs, thus contributing to the advancement of pharmaceutical nanotechnology and drug delivery.

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