e-ISSN 2581-0405
Asian Journal of Applied Research for Community Development and Empowerment
Journal home page: http://ajarcde-safe-network.org ISSN 2581-0405

Bioavailability of Curcumin in Various Nanoformulations: *A Critical Review*

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ARTICLE INFO

Article History:
Received: 01 December 2025
Final Revision: 14 December 2025
Accepted: 16 December 2025
Online Publication: 17 December 2025

KEYWORDS

curcumin, nanoformulations, bioavailability, pharmacokinetics, clinical

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A B S T R A C T

This critical review evaluates strategies to enhance curcumin bioavailability using nanoformulation-based delivery systems, compares pharmacokinetic and in vivo safety data, and identifies key barriers to clinical translation. Articles published between 2015 and 2025 were retrieved from Scopus, ScienceDirect, and PubMed using keywords related to curcumin, nanoformulations, bioavailability, pharmacokinetics, safety, and clinical translation. Eligible peer-reviewed studies were compared based on formulation type, bioavailability enhancement, in vivo tolerability, and translational limitations. Various systems—including polymeric nanoparticles, lipid-based carriers, micelles, nanoemulsions, cyclodextrin complexes, phytosomes, dendrimers, and exosomes—improve curcumin solubility, stability, permeability, and delivery. Overall, nanoformulations increase systemic exposure from moderate to substantial levels, with lipid–polymer systems showing the most consistent gains. Most studies report acceptable safety at therapeutic doses; however, dose dependence, formulation-specific effects, limited long-term human data, scalability issues, and regulatory challenges remain major constraints. While nanoformulations significantly improve curcumin bioavailability and therapeutic potential, standardized manufacturing, comprehensive safety evaluation, and well-designed clinical trials are required for clinical implementation.

Contribution to Sustainable Development Goals (SDGs):
SDG 3: Good Health and Well Being
SDG 9: Industry, Innovation and Infrastructure
SDG 12: Responsible Consumption and Production
SDG 17: Partnerships for the Goals

1. INTRODUCTION

1.1. Research Background

Polyphenolic compounds extracted from the rhizome of *Curcuma longa* have attracted significant scientific attention owing to their broad pharmacological properties, including anti-inflammatory, antioxidant, anticancer, antimicrobial, and neuroprotective effects. Characteristics have established curcumin as a potential therapeutic agent for the prevention and treatment of diverse chronic diseases, including cancer, metabolic disorders, neurodegenerative diseases, and inflammatory conditions [1], [2], [3], [4]. Although curcumin has considerable therapeutic potential and a good safety record, its use in clinical settings remains challenging.

The primary constraint hindering curcumin's clinical application is its significantly low oral bioavailability. Native

curcumin has low water solubility, is rapidly broken down in the intestines, is not readily absorbed through the gastrointestinal epithelium, and is quickly eliminated from the body, resulting in very low plasma concentrations after oral administration [5], [6], [7]. These undesirable pharmacokinetic properties necessitate the administration of elevated doses to achieve therapeutic efficacy, which is impractical and may compromise patient adherence [1, 2].

To address these challenges, significant research has focused on developing nanoformulation-based delivery systems to enhance the solubility, stability, absorption, and overall bioavailability of curcumin. Numerous nanocarriers, such as liposomes, micelles, nanoemulsions, polymeric nanoparticles, dendrimers, and solid lipid nanoparticles, have been developed and assessed in both preclinical and clinical settings [3], [4], [8], [9], [10]. These nanoformulations have demonstrated significant enhancements in curcumin's pharmacokinetic profile, with specific systems achieving up to a nine-fold increase in oral bioavailability compared to native curcumin [1, 2, 11].

Nanoformulations enhance curcumin's bioavailability by increasing its water solubility, protecting it from chemical and enzymatic degradation, increasing intestinal permeability, and facilitating targeted or sustained release [12, 13]. Despite promising preclinical results, the application of nanoformulated curcumin in standard clinical practice remains limited. Regulatory constraints, safety concerns, scalability issues, and insufficient long-term clinical data continue to impede widespread adoption [10], [14], [15].

Consequently, this critical review aims to systematically analyze contemporary nanoformulation strategies for curcumin delivery, evaluate their effects on bioavailability and therapeutic efficacy, investigate the mechanisms underlying absorption enhancement, and identify essential translational challenges and research deficiencies that need to be addressed to promote clinical application.

1.2. Literature Review

Nanoformulation-based delivery systems have emerged as a crucial approach to addressing the inherent physicochemical and pharmacokinetic challenges of curcumin, particularly its limited aqueous solubility, chemical instability, and restricted oral bioavailability. A broad array of nanoformulation platforms has been created, each distinguished by unique structural attributes and functional benefits that collectively seek to improve curcumin delivery and therapeutic efficacy [16], [17], [18].

1.2.1 Liposomes

Liposomes are one of the most well-studied nanoformulation systems for delivering curcumin. Liposomes are made up of phospholipid bilayers that surround an aqueous core. They can trap hydrophobic substances, such as curcumin, in their lipid membranes. This structure keeps curcumin from breaking down chemically and makes it much more stable and soluble in living things [16, [17]. Liposomes can also help cells take them up more readily and stay in the body longer, making them especially useful for treating cancer and inflammatory diseases [18].

1.2.2. Nanoparticles made of Polymers

Polymeric nanoparticles, typically made from biodegradable polymers such as poly(lactic-co-glycolic acid) (PLGA) and chitosan, are highly useful for controlled and sustained drug release. Systems enable precise control over the rate of curcumin release, and they can be modified with targeting ligands to enhance delivery to specific tissues [19]. Nanoparticles are useful for both systemic and localised therapeutic applications because they are biocompatible and their physicochemical properties can be tailored [16], [17].

Lipid nanoparticles (SLNs) are made up of a solid lipid core that is held together by surfactants. This makes them more stable and protects drugs from breaking down. SLNs have shown better oral bioavailability and longer release profiles for curcumin, and they also use fewer organic solvents during production [20], [21]. These characteristics make SLNs especially useful for nutraceutical and food-related uses, as well as for long-term medical use [18].

1.2.3. Micelles

Amphiphilic molecules spontaneously assemble in water to form micellar systems. These systems have hydrophobic cores that can dissolve curcumin. Polymeric micelles have demonstrated significant encapsulation efficiency and improved intestinal absorption, especially when designed to react to environmental factors such as pH [22]. Their relatively small size makes them easier to pass through biological membranes, increasing their bioavailability [16].

1.2.4. Nanoemulsions

A standard method for delivering curcumin is through nanoemulsions, which are typically oil-in-water or water-in-oil dispersions. These formulations have a large interfacial surface area, which significantly increases curcumin solubility and accelerates its absorption [23]. Shown better bioavailability than regular curcumin supplements and are often used in functional foods and medicines[8], [24].

1.2.5. Nanogels

Nanogels are three-dimensional crosslinked polymer networks capable of encapsulating curcumin and releasing it in a sustained and controlled manner. Their high water content and tunable swelling behaviour enable localised, site-specific delivery, making nanogels particularly suitable for topical, ocular, and inflammatory disease applications [16], [17].

1.2.6. Cyclodextrin Complexes

Cyclodextrin complexes increase the solubility of curcumin by forming inclusion complexes, which partially enclose the hydrophobic curcumin molecule in the cyclodextrin cavity. These systems make curcumin more stable in water and less prone to chemical breakdown, without significantly altering its molecular structure [25]. Cyclodextrin-based carriers are especially appealing for food and oral formulations because they are safe [26].

1.2.7. Phytosomes

Phytosomes, which are made by combining curcumin with phospholipids, make membranes more permeable and help the body absorb curcumin better through the gut. Phytosomes are different from regular liposomes because they involve interactions between curcumin and phospholipids at the

 https://doi.org/10.29165/ajarcde.v9i3.861

molecular level. This makes them more bioavailable and stable in the body [16], [17].

1.2.8. Dendrimers

Dendrimers are polymers that have numerous branches and are all the same size. They can hold a lot of drugs and have exact structural control. For functionalization with targeting moieties, enabling drug delivery to specific sites and enhancing their effectiveness [18]. Still worries about long-term safety and how hard it is to make.

1.2.9. Gold.Metallic Nanoparticles

Metallic nanoparticles, including gold and magnetic nanoparticles, provide multifunctional capabilities such as imaging, targeting, and enhanced stability. These inorganic systems facilitate theranostic applications but require careful evaluation of toxicity and long-term accumulation [27].

1.2.10. Niosomes

Niosomes are vesicular nanoformulations composed of non-ionic surfactants that form bilayer structures like liposomes. This makes them effective at encapsulating hydrophobic compounds, such as curcumin. The Main benefit is that they are more stable in terms of their physical and chemical properties than phospholipid-based vesicles. This makes them less likely to break down when exposed to oxygen, and as a result, the formulation becomes stronger [26], [28]. Enhance delivery efficiency by preventing premature breakdown of curcumin and facilitating its passage across biological membranes. Niosomes can also be used as multifunctional delivery platforms, allowing them to be loaded with metallic nanoparticles to achieve both antimicrobial and antibiofilm effects that work synergistically, making them even more effective for treating diseases [27].

1.2.11. Exososmes/Biological Carriers

Exosomes and other biological carriers are unique nanoformulations derived from vesicles secreted by cells. They are unique because they are derived from nature, are highly biocompatible, and can cross biological barriers on their own. These characteristics enable exosomes to serve as effective, biologically compatible carriers for curcumin, thereby promoting improved cellular uptake and intracellular delivery via endogenous vesicular transport pathways [18]. Consequently, exosome-based systems are increasingly recognised as promising next-generation delivery platforms for curcumin, particularly for applications that require efficient tissue penetration and reduced immunogenicity.

Table 1 summarises the main strategies for nanoformulation developed to deliver curcumin. It shows their structural characteristics, key functional features, and some examples of references.

1.3. Research Objective

This study aimed to critically evaluate the bioavailability of curcumin across various nanoformulation strategies, focusing on delivery mechanisms, enhancement efficiency, and translational challenges for clinical and therapeutic applications.

Table 1. Major Nanoformulation Types for Curcumin Delivery

Type of Nanoformulation	Description and Important Features	References
Liposomes	Spherical vesicles made of phospholipid bilayers that keep curcumin from breaking down and make it easier to dissolve	[16], [17], [18]
Polymeric Nanoparticles	Biodegradable polymer-based systems (e.g., PLGA, chitosan) facilitate controlled release and targeted delivery.	[16], [17], [18], [19]
Nanoparticles of Solid Lipids (SLN)	Solid lipid core structures enhance stability, prolonged release, and oral bioavailability.	[16], [17], [18], [20], [21]
Micelles	Self-assembled amphiphilic molecules that dissolve curcumin and make it easier to absorb	[16], [17], [18], [22]
Nanoemulsions	Droplets of oil in water or water in oil make things easier to dissolve and help them absorb more quickly.	[8], [16], [17], [18], [23], [24]
Nanogels	Crosslinked polymer networks allow for sustained release and targeted delivery.	[16], [17], [18]
Cyclodextrin Complexes	Cyclic oligosaccharides form inclusion complexes, making them more soluble in water.	[16], [17], [18], [25], [26]
Phytosomes	Curcumin-phospholipid complexes enhance absorption and bioavailability.	[16], [17], [18]
Dendrimers	Highly branched polymers; high drug-loading capacity and potential for targeting	[16], [17], [18]
Gold/Metallic Nanoparticles	Inorganic nanocarriers (e.g., gold, magnetic) enable imaging, targeting, and improved stability	[16], [17], [18]
Niosomes	Non-ionic surfactant vesicles; similar to liposomes, improve stability and delivery	[26], [27], [28]
Exosomes/Biological Carriers	Cell-derived vesicles; natural, biocompatible, and can cross biological barriers	[18]

2. MATERIALS AND METHODS

This study employed a critical review methodology to systematically assess and integrate contemporary evidence regarding the bioavailability, pharmacokinetics, safety, and translational obstacles of curcumin nanoformulations. The review aimed to critically evaluate not only the reported outcomes but also the robustness, consistency, and limitations of current studies, to identify knowledge gaps and inform future research directions.

This study searched major scientific databases, including Scopus, Elsevier (ScienceDirect), and PubMed, for all articles published between 2015 and 2025. The search strategy utilized combinations of keywords, including curcumin, nanoformulation, bioavailability, pharmacokinetics, toxicity, safety, and clinical translation. Only English-language articles that had been peer-reviewed were taken into account.

Relevant studies were selected based on title, abstract, and full-text review. Data analysis was qualitative, comparing nanoformulation types, reported bioavailability enhancements, safety outcomes, and translational limitations. Emphasis was placed on identifying trends, inconsistencies, and methodological limitations rather than analysis, consistent with a critical review framework.

3. RESULT AND DISCUSSION

3.1. Comparative Pharmacokinetic Evidence of Curcumin Bioavailability Enhancement

Table 2 presents a clear picture of how various nanoformulation strategies enhance curcumin bioavailability compared to free curcumin. In general, the data show that nanoformulations can increase systemic exposure by about 3 to over 100 times. The degree of improvement depends heavily on the formulation type and the study model. Table 1 provides a comprehensive list of nanoformulation platforms developed for delivering curcumin. Table 2, on the other hand, only shows formulations for which quantitative pharmacokinetic data on bioavailability enhancement are available. Consequently, numerous nanoformulation systems are excluded from Table 2 due to the lack of analogous in vivo or clinical bioavailability assessments.

Table 2 shows that solid lipid nanoparticles (SLN) consistently improve bioavailability by 12-70 times in animal models and by even more in human studies. This is because they help the intestines absorb nutrients better and release them over time [20], [29], [30]. Polymeric nanoparticle systems, such as PLGA and chitosan-based formulations, exhibit analogous trends, generally resulting in 9- to 11.5-fold enhancements in rats, due to mechanisms that prevent degradation and regulate release [1], [33], [34]. These results demonstrate that polymeric and lipid-based carriers are effective for enhancing curcumin's pharmacokinetics.

Systems based on proteins and surfactants also show significant improvements, though not as large. In animal models, zein nanoparticles increase by about 7.5-9 times, while saponin-coated nanoparticles and sophorolipid micelles increase by about 2.7-8.9 times. This is because they dissolve and absorb more effectively, not because they remain in the body longer [31], [32]. Self-nanoemulsifying drug delivery systems (SNEDDS) demonstrate substantial enhancements in bioavailability in both in vitro and in vivo studies. However, specific fold values are not consistently documented, which restricts direct quantitative comparison [35].

Table 2. Summarizing fold increase in curcumin bioavailability for various nanoformulations

Nanoformulation Type	Fold Increase vs. Free Curcumin	Study Model	References
Solid Lipid Nanoparticles (SLN)	12–70×	In vivo dan Humans	[20], [29], [30]
Zein Nanoparticles	7.5–9×	In vivo	[31], [32]
Saponin-coated Nanoparticles	8.9×	In vivo	[32]
Chitosan Nanoparticles	11.5×	In vivo	[33]
PLGA Nanoparticles	9×	In vivo	[1], [34]
Self-nanoemulsifying Drug Delivery Systems (SNEDDS)	Significant (exact value not stated)	In vitro, In vivo	[35]
Commercial Nanoformulations (CurcuWIN®)	9–136×	Humans	[30]
Clinical Nanoformulations (various)	9–185×	Humans	[36]
Sophorolipid Micelles	2.7–3.6×	In vivo	[32]

Table 2 also illustrates the significant effects observed in clinical settings, which is important. Commercially and clinically assessed nanoformulations, including CurcuWIN®, have been shown to increase efficacy by 9-136 times in humans, while systematic clinical reviews report enhancements of up to 185 times [30]. Nonetheless, as indicated in the table, cross-study comparisons remain challenging due to differences in dosing regimens, analytical methods, and study designs. This is an important limitation to keep in mind when evaluating these pharmacokinetic gains.

3.2. Comparative Superiority of Liposomal and Polymeric Nanoparticles in Curcumin Nanoformulation

Liposomes and polymeric nanoparticles are clearly the two most advanced and widely used platforms, accounting for the majority of systems that have advanced closer to clinical use. These are lipid-based. Polymer-based nanocarriers comprise the majority of nanomedicine products approved or evaluated by the FDA and EMA, underscoring their importance for translation [10], [37], [38].

Liposomes, as lipid-based nanocarriers, are characterized by phospholipid bilayer structures that closely resemble the structure of biological membranes. This makes them highly biocompatible and relatively non-toxic. Liposomes have a good safety record, are easy to modify, and are widely accepted by regulators, especially for cancer and infectious disease treatments [39], [40]. However, their clinical performance is limited by moderate to low physicochemical stability, susceptibility to oxidation and vesicle fusion, and the potential for burst release, which can render the formulation less stable during storage and circulation [41, 42]. As

https://doi.org/10.29165/ajarcde.v9i3.861

a result, liposomal curcumin formulations usually only improve bioavailability by about 5–6 times compared to free curcumin [10].

Table 3. Key Comparative Aspects of Liposomes and Polymeric Nanoparticles for Curcumin Delivery

Aspect	Liposomes	Polymeric Nanoparticles	References
Biocompatibility	Very high	High (polymer-dependent)	[10], [37], [41]
Stability	Low to moderate	High	[39], [41], [43]
Surface Modification	Easy (limited)	Highly flexible	[39], [41], [43]
Curcumin Bioavailability	5–6× (vs. free curcumin)	9–11× (vs. free curcumin)	[10], [42], [44]
Safety Profile	Generally safe, minimal toxicity	Potential toxicity of synthetic polymers	[37], [41]
Regulatory Status	Widely approved by FDA/EMA	Partially approved, under development	[38], [39]

Polymeric nanoparticles, such as those made of PLGA and chitosan, are matrix-based carriers that are more stable in terms of sterics and offer more flexible surface engineering options. Table 3 shows that polymeric nanoparticles are less likely to break down in the environment, can be controlled more precisely in their release rate, and remain in the body longer, especially when modified on the surface with PEGylation or ligand attachment [41], [43]. Polymeric systems exhibit a significantly greater enhancement in bioavailability (approximately 9–11-fold) than liposomes, indicating superior pharmacokinetic efficacy for curcumin delivery [10, 42, 44]. Still, the potential toxicity of polymers and the use of organic solvents during synthesis remain important considerations.

The table's evidence indicates that polymeric nanoparticles are more effective at enhancing curcumin bioavailability and improving formulation stability. On the other hand, liposomes remain preferable because they are safer, more biocompatible, and better established under regulatory standards. Choosing the best platform, then, depends on balancing the formulation's stability with the biological safety needs of the intended clinical use.

3.3. Comparative In Vivo Toxicity and Safety Profiles of Curcumin Nanoformulations

Table 4 summarises in vivo toxicity and safety data, providing a clear picture of how well curcumin nanoformulations interact with various carrier systems. The evidence suggests that most nanoformulated curcumin systems, including polymeric nanoparticles, liposomes, micelles, and nanoemulsions, are safe at therapeutic doses. They do not have any significant adverse effects on blood parameters, liver function, or major organs in animal models [19], [45], [46], [47].

Table 4 shows that polymeric nanoparticles (like PLGA, PVP, and PHA-based systems) are usually safe and do not cause irritation at pharmacologically relevant doses. However, toxicity may develop in a dose-dependent manner at higher concentrations [48], [49], [50], [51]. Liposomal formulations also exhibit high biocompatibility, with few reports of toxicity, even in cancer models, indicating that they are safe for systemic use [45, 52, 53]. Micellar systems are generally well tolerated; however, weak teratogenic or developmental effects have been observed at elevated doses in embryo-based models, underscoring the need for dose optimisation [54], [55].

Notably, nanoformulation techniques often reduce the toxicity of free curcumin by decreasing reactive oxygen species production and enhancing overall biocompatibility, as evidenced by studies in zebrafish and rodents [19], [54]. As shown in Table X, nanoemulsions do not cause organ toxicity in vivo, further enhancing their safety profile [56]. Nonetheless, the data collectively highlight that toxicity is formulation- and dose-dependent, underscoring the need for long-term, chronic exposure studies before clinical application [48], [51], [57].

Table 4. Comparative In Vivo Toxicity and Safety Profiles of Curcumin Nanoformulations

Formulation Type	Safety at Therapeutic Dose	Toxicity at High Dose	Key Notes	References
Polymeric Nanoparticles (PLGA, PVP, PHA)	Safe	Possible	Dose-dependent toxicity; generally non-irritant	[48], [49], [50], [51]
Liposomes	Safe	Rare	Good biocompatibility and systemic tolerability	[45], [52], [53]
Micelles	Safe	Possible	Weak teratogenic effects observed at high doses	[54], [55]
Nanoemulsions	Safe	Not reported	No significant organ toxicity in vivo	[56]

3.4. Challenges and Limitations in the Clinical Translation of Curcumin Nanoformulations

Despite substantial progress in formulation design, the clinical translation of curcumin nanoformulations remains constrained by several unresolved challenges spanning pharmacokinetics, safety, manufacturing, and regulatory domains. Although nanoformulation strategies improve curcumin solubility and stability, low oral bioavailability and rapid metabolism persist, frequently resulting in variable and sub-therapeutic systemic exposure across different delivery platforms [10], [16], [18], [58]. In addition, the inconsistent pharmacokinetic behaviour and biodistribution profiles of nanoformulations make it harder to determine the correct dose and predict how well they will perform in the clinic [10], [18].

Concerns about safety and toxicity are a significant roadblock to translation. Although the majority of curcumin nanoformulations exhibit satisfactory tolerability in preclinical models, extensive long-term human safety data remain largely unavailable. Possible risks include the accumulation of drugs in

tissues that are not the intended target, immune responses, and a lack of understanding about the effects of long-term exposure, especially in systems that lack tissue specificity [1], [58], [59]. These uncertainties still make it hard for regulators to be sure.

From a development perspective, producing things at scale and consistently remains technically challenging. At an industrial scale, achieving consistent particle size, encapsulation efficiency, and long-term stability is challenging and expensive. This has a direct impact on quality control and batch-to-batch consistency [10], [18], [60]. Finally, regulatory and clinical limitations further delay translation, as nanomedicines are subject to evolving regulatory standards and only a limited number of well-powered clinical trials have been conducted to date [60], [61](Amekyeh et al., 2022; Boroughani et al., 2024). These challenges underscore the need for standardised production methodologies, comprehensive long-term safety assessments, and robust clinical validation to facilitate the transition of curcumin nanoformulations into clinical practice.

4. CONCLUSION

Curcumin nanoformulations include a wide range of systems, such as liposomes, polymeric nanoparticles, solid lipid nanoparticles, micelles, nanoemulsions, nanogels, cyclodextrin complexes, phytosomes, dendrimers, metallic nanoparticles, niosomes, and exosomes. Each of these systems has its own benefits for making curcumin easier to deliver, more stable, and more effective as a medicine. Nonetheless, despite significant advancements in bioavailability and preclinical efficacy, clinical translation remains hindered by erratic pharmacokinetics, insufficient long-term safety data, manufacturing difficulties, and regulatory complexities. Future advancements will rely on meticulously designed comparative studies, standardized formulation strategies, and robustly powered clinical trials to ascertain the therapeutic efficacy and safety of nanoformulated curcumin in humans.

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