International Journal of Pharmaceutical Drug Design (IJPDD)
Website: https://ijpdd.org/
ISSN: 2584-2897
Vol. 3, Issue 1, January-June, 2026
Page No.: 270-280

Review

Nano-Phytomedicine: Recent Advances in Nanotechnology-Based Delivery of Plant-Derived Bioactive Compounds, Therapeutic Applications, Safety and Future Perspectives

Namrata Singh*

Department of Pharmacy, AMCOP, Gwalior MP

Corresponding Author:
Dr. Namrata Singh

Email:
singh.nam8@gmail.com

DOI: *10.62896/ijpdd.3.1.31*

Conflict of interest: *NIL*

Article History
Received: 12/01/2026
Accepted: 22/02/2026
Published: 29/02/2026

Abstract:
Plant-derived bioactive compounds have attracted considerable attention because of their diverse pharmacological activities and potential applications in the prevention and management of chronic diseases. However, many phytochemicals exhibit poor aqueous solubility, chemical instability, rapid metabolism and low systemic bioavailability, which limit their therapeutic application. Nanotechnology-based delivery systems have emerged as promising strategies for overcoming these limitations by improving solubility, stability, gastrointestinal absorption, cellular uptake and controlled release. Different nanocarriers, including liposomes, phytosomes, polymeric nanoparticles, solid lipid nanoparticles, nanostructured lipid carriers, nanoemulsions, polymeric micelles and hybrid systems, have been investigated for the delivery of plant-derived compounds. Curcumin, quercetin, resveratrol, epigallocatechin gallate, berberine and silymarin are among the most extensively studied phytochemicals in nanoformulation research. Preclinical studies suggest that nanoformulated phytochemicals may have applications in cancer, inflammation, metabolic disorders, cardiovascular diseases, neurodegenerative disorders, infections and wound healing. Nevertheless, the majority of evidence remains preclinical, and challenges involving formulation standardization, long-term toxicity, manufacturing, pharmacokinetics and regulatory approval continue to limit clinical translation. This review summarizes recent advances in nano-phytomedicine, with particular emphasis on nanocarrier systems, mechanisms of enhanced phytochemical delivery, therapeutic applications, safety, regulatory considerations and future research directions.

Keywords: *nano-phytomedicine; phytochemicals; medicinal plants; nanoparticles; nanocarriers; phytosomes; bioavailability; targeted drug delivery; curcumin; nanomedicine.*

1. Introduction

Medicinal plants have historically represented an important source of therapeutic agents, and numerous modern drugs have originated directly or indirectly from natural products [1,2]. Plant-derived compounds such as polyphenols, flavonoids, alkaloids and terpenoids exhibit a broad spectrum of biological activities, including antioxidant, anti-inflammatory, antimicrobial, cardioprotective, neuroprotective and anticancer effects [3,4].

Despite their promising pharmacological properties, many phytochemicals have limited pharmaceutical applicability because of poor aqueous solubility, low permeability, rapid metabolism and extensive elimination [5]. Anand et al. reported that curcumin, for example, has extremely limited systemic bioavailability following conventional oral

administration because of poor absorption and extensive metabolism [6]. Similar pharmacokinetic limitations have been described for quercetin, resveratrol, epigallocatechin gallate and other polyphenolic compounds [7–10].

Nanotechnology has emerged as a potential strategy for overcoming these pharmaceutical limitations. Nanocarriers can protect phytochemicals from degradation, increase apparent solubility, modify pharmacokinetics and facilitate delivery to specific tissues or cells [11–13]. According to recent reviews, nano-phytomedicine represents an increasingly important intersection between pharmacognosy, pharmaceutical nanotechnology and modern drug-delivery science [14,15].

The development of nanotechnology-based herbal formulations is particularly relevant because conventional herbal preparations can exhibit considerable variability in chemical composition and bioavailability. Nanocarrier systems may provide opportunities for improving the reproducibility and delivery of selected plant-derived compounds [16].

Therefore, the present review critically evaluates recent developments in nano-phytomedicine, including phytochemical limitations, nanocarrier technologies, mechanisms of enhanced delivery, therapeutic applications, pharmacokinetic considerations, safety, regulatory challenges and future perspectives.

2. Phytochemicals as Therapeutic Molecules

Phytochemicals are secondary metabolites produced by plants and include several chemically distinct groups. Polyphenols, flavonoids, alkaloids, terpenoids and phenolic acids are among the most extensively studied classes because of their diverse biological activities [17,18].

Curcumin, obtained primarily from *Curcuma longa*, has been investigated extensively for its anti-inflammatory, antioxidant and potential anticancer properties [19,20]. Quercetin is a flavonoid found in numerous fruits and vegetables and has demonstrated antioxidant and anti-inflammatory activities in experimental models [21]. Resveratrol, a stilbene polyphenol found in grapes and several other plants, has similarly attracted attention because of its potential cardiovascular, metabolic and neuroprotective effects [22].

Berberine, an isoquinoline alkaloid present in several medicinal plants, has been investigated particularly for metabolic and antimicrobial applications [23]. Epigallocatechin gallate (EGCG), a major catechin in green tea, has also been studied for antioxidant, metabolic and anticancer effects [24].

However, biological activity alone does not ensure therapeutic effectiveness. Many phytochemicals demonstrate strong activity under experimental conditions but produce relatively low concentrations in systemic circulation following conventional administration [5,7]. This discrepancy has become a major motivation for developing nanotechnology-based delivery systems.

3. Pharmaceutical Limitations of Phytochemicals

3.1 Poor aqueous solubility

Poor water solubility is one of the most important barriers to oral delivery of many phytochemicals. Lipophilic compounds may dissolve poorly in gastrointestinal fluids, resulting in limited absorption [5,25].

Curcumin provides a representative example. Although extensive experimental research has demonstrated its biological activity, its conventional oral administration results in relatively low systemic exposure because of poor aqueous solubility and rapid metabolism [6,26].

3.2 Chemical instability

Several phytochemicals are sensitive to pH, temperature, oxygen and light. These environmental factors may result in degradation before the active compound reaches its target site [27].

Encapsulation within nanocarriers can provide physical and chemical protection and may consequently increase the stability of sensitive phytochemicals [11,28].

3.3 Extensive metabolism

Polyphenols can undergo extensive intestinal and hepatic metabolism, including glucuronidation, sulfation and methylation [7,29]. Consequently, the concentration of the parent compound in systemic circulation may be substantially lower than expected from the administered dose.

3.4 Low bioavailability

Bioavailability is determined by absorption, distribution, metabolism and elimination. A

compound may exhibit significant biological activity in vitro while having limited clinical effects because sufficient concentrations cannot be maintained in target tissues [30].

3.5 Nonspecific distribution

Conventional formulations generally lack mechanisms for preferentially delivering phytochemicals to specific tissues. Nanocarriers can potentially be modified with targeting ligands to improve tissue-specific delivery [31].

4. Nano-Phytomedicine

Nano-phytomedicine can broadly be defined as the application of nanotechnology to the delivery, stabilization or controlled release of plant-derived bioactive compounds [14,15].

Nanocarriers typically range from several nanometers to several hundred nanometers and can be engineered according to the physicochemical characteristics of the phytochemical and the intended route of administration [32].

Recent reviews have identified liposomes, phytosomes, polymeric nanoparticles, lipid nanoparticles, nanoemulsions and hybrid nanocarriers as important platforms for phytochemical delivery [14,33].

The principal objectives of nanoformulation include:

- Increasing solubility
- Improving chemical stability
- Enhancing bioavailability
- Protecting compounds from degradation
- Increasing cellular uptake
- Modifying pharmacokinetics
- Providing controlled release
- Facilitating targeted delivery [11,14,33]

5. Liposomal Delivery Systems

Liposomes are vesicular structures composed primarily of phospholipid bilayers surrounding an aqueous core. Because they contain both hydrophilic and hydrophobic regions, liposomes can accommodate compounds with different physicochemical properties [34].

Liposomal encapsulation may protect phytochemicals from degradation while increasing dispersion in aqueous biological environments [35]. Curcumin, quercetin, resveratrol and several other polyphenols have been investigated using liposomal delivery systems [36–38].

The major advantages of liposomes include biocompatibility, formulation flexibility and the possibility of surface modification. However, physical instability, oxidation of phospholipids and manufacturing cost can limit their application [34].

6. Phytosomes

Phytosomes are phospholipid-based complexes designed to improve the absorption and bioavailability of plant-derived compounds. Unlike conventional liposomes, phytosomes generally involve molecular interaction between the phytochemical and phospholipid components [39].

Phytosome technology has been particularly investigated for poorly bioavailable compounds such as curcumin and silymarin [40,41]. Barani et al. reviewed the development of phytosomes and concluded that these systems represent promising carriers for improving the pharmaceutical properties of several botanical compounds [40].

The potential advantages of phytosomes include improved membrane interaction, increased absorption and enhanced bioavailability. However, the clinical significance of these improvements depends on the specific formulation and phytochemical being studied [40].

7. Polymeric Nanoparticles

Polymeric nanoparticles are prepared using biodegradable or biocompatible polymers such as poly(lactic-co-glycolic acid), polylactic acid, chitosan and alginate [42].

These systems can encapsulate phytochemicals and provide controlled or sustained release. PLGA nanoparticles have received particular attention for compounds such as curcumin, resveratrol and EGCG [43].

Recent studies have demonstrated that polymeric nanoparticles may improve the stability and cellular uptake of phytochemicals in experimental cancer models [43,44]. Nevertheless, translation to clinical applications requires further investigation of manufacturing reproducibility, toxicity and pharmacokinetics.

8. Solid Lipid Nanoparticles

Solid lipid nanoparticles consist of a lipid matrix that remains solid at physiological temperature. They can improve the solubility and stability of poorly water-soluble compounds [45].

Phytochemicals incorporated into solid lipid nanoparticles may be protected against chemical

degradation and released in a controlled manner [46].

These systems are particularly attractive for lipophilic compounds because the lipid matrix can facilitate their incorporation and subsequent biological delivery.

9. Nanostructured Lipid Carriers

Nanostructured lipid carriers contain a combination of solid and liquid lipids. The less ordered lipid matrix can increase the loading capacity of certain compounds compared with conventional solid lipid nanoparticles [47].

These systems have been investigated for curcumin, quercetin and other hydrophobic phytochemicals [48]. Their potential advantages include improved stability, enhanced loading and controlled release.

10. Nanoemulsions

Nanoemulsions are colloidal systems consisting of nanoscale oil and aqueous phases stabilized by surfactants. They are particularly useful for improving the dispersion of lipophilic compounds [49].

Nanoemulsions have been investigated for curcumin, essential oils and other plant-derived bioactives [50,51]. Their relatively simple formulation and potential for oral and topical administration make them attractive platforms for nutraceutical and pharmaceutical applications.

11. Curcumin as a Model Nano-Phytochemical

Curcumin is perhaps the most extensively investigated phytochemical in nanomedicine. It is derived primarily from the rhizome of *Curcuma longa* and belongs to the curcuminoid family [19].

Curcumin has demonstrated antioxidant and anti-inflammatory activity through modulation of multiple signaling pathways, including NF-κB, Nrf2, MAPK and PI3K/Akt [19,52].

However, its clinical development has been constrained by poor aqueous solubility, rapid metabolism and low systemic bioavailability [6,26]. Consequently, numerous nanoformulations have been developed, including liposomes, micelles, polymeric nanoparticles, lipid nanoparticles and phytosomes [53–55].

A review of pharmacokinetic studies demonstrated that bioavailability-enhanced curcumin formulations can substantially increase systemic exposure compared with conventional preparations [26]. Nevertheless, increased plasma exposure should not automatically be interpreted as improved clinical efficacy.

12. Quercetin Nanoformulations

Quercetin is a flavonoid widely distributed in fruits, vegetables and medicinal plants. Its biological activities include antioxidant, anti-inflammatory and potential metabolic effects [21].

Poor aqueous solubility and extensive metabolism limit its systemic availability [56]. Nanotechnology-based formulations have therefore been investigated to improve its absorption and tissue distribution.

Nanoencapsulation of quercetin may improve stability and bioavailability and has been investigated in models of inflammation, metabolic disease and cancer [57,58].

13. Resveratrol Nanoformulations

Resveratrol is a stilbene polyphenol found in grapes, berries and several other plants. It has been studied for potential antioxidant, anti-inflammatory, cardiovascular, metabolic and neuroprotective effects [22].

Its clinical development is complicated by poor water solubility, rapid metabolism and limited systemic exposure [59].

Liposomes, polymeric nanoparticles, nanoemulsions and other nanocarriers have therefore been investigated as strategies to improve resveratrol delivery [60,61].

14. Epigallocatechin Gallate

EGCG is a major catechin found in green tea. Experimental studies have reported antioxidant, anti-inflammatory and anticancer effects [24].

However, EGCG is chemically unstable under several physiological conditions and undergoes extensive metabolism [62].

Nanoencapsulation can potentially protect EGCG from degradation and improve its intestinal and cellular delivery [63]. Consequently, EGCG nanoparticles have become an important area of research in cancer and metabolic disease.

15. Berberine Nanoformulations

Berberine is an alkaloid found in plants such as *Berberis* species. It has attracted significant research interest because of its potential effects on glucose metabolism, lipid metabolism, inflammation and microbial growth [23].

One of the major limitations of conventional berberine administration is its low oral bioavailability [64].

Nanocarrier-based delivery has therefore been investigated as a strategy for improving absorption and systemic exposure [65].

16. Therapeutic Applications

16.1 Anticancer applications

Cancer is one of the most extensively investigated therapeutic areas for nano-phytomedicine.

Curcumin, resveratrol, quercetin and EGCG have demonstrated anticancer effects in cell culture and animal models [43,66]. Reported mechanisms include modulation of apoptosis, cell-cycle progression, angiogenesis, oxidative stress and signaling pathways such as NF-κB, PI3K/Akt and Wnt/β-catenin [52,66].

Nanocarriers may enhance anticancer activity by improving cellular uptake and increasing the concentration of phytochemicals at tumor sites [67].

However, most evidence remains preclinical. Therefore, nanoformulated phytochemicals should not be regarded as established replacements for conventional cancer treatment.

17. Anti-inflammatory Applications

Chronic inflammation contributes to numerous diseases, including metabolic disorders, cardiovascular disease, arthritis and neurodegenerative conditions [68].

Curcumin and quercetin have demonstrated anti-inflammatory effects in experimental models through modulation of inflammatory cytokines and transcription factors [19,21].

Nanoformulation may improve the biological availability of these compounds and potentially enhance their anti-inflammatory activity [69].

18. Antioxidant Applications

Oxidative stress results from an imbalance between reactive oxygen species generation and antioxidant defenses.

Polyphenols such as curcumin, quercetin, resveratrol and EGCG have demonstrated antioxidant effects in experimental studies [19,21,22,24].

Nanoencapsulation may protect these compounds from degradation and improve their biological availability [70].

However, the clinical significance of antioxidant effects should be assessed using patient-relevant outcomes rather than relying solely on laboratory antioxidant assays.

19. Metabolic Disorders

Several phytochemicals have been investigated in obesity, diabetes and metabolic syndrome.

Curcumin supplementation has been associated with improvements in selected glycemic and lipid parameters in clinical meta-analyses [71,72].

Berberine has also been extensively investigated for glucose and lipid metabolism [23].

Nanocarriers may improve the systemic exposure of these compounds and potentially increase their pharmacological effects [73].

Nevertheless, clinical trials comparing conventional and nanoformulated phytochemicals directly are still needed.

20. Neuroprotective Applications

Neurodegenerative diseases involve complex interactions between oxidative stress, neuroinflammation, mitochondrial dysfunction and abnormal protein accumulation [74].

Curcumin, resveratrol and quercetin have demonstrated neuroprotective activity in experimental models [75–77].

Nanocarriers may facilitate brain delivery by improving stability, modifying pharmacokinetics and potentially enhancing transport across biological barriers [78].

Intranasal nanocarrier systems are particularly promising because the nasal route may provide an alternative pathway for delivery of certain compounds to the central nervous system [79].

21. Cardiovascular Applications

Phytochemicals have been investigated for their effects on oxidative stress, inflammation, lipid metabolism and endothelial function [80].

Resveratrol, curcumin and quercetin are among the most frequently investigated compounds in this area [81–83].

Nanoformulation may improve systemic exposure and potentially enhance biological activity. However, evidence demonstrating that nano-phytomedicines reduce major cardiovascular events remains insufficient.

22. Antimicrobial Applications

Plant-derived compounds possess antimicrobial properties against various microorganisms [84].
Nanoformulation may increase local concentration, improve interaction with microbial membranes and protect unstable compounds from degradation [85].
Nanoparticles containing plant extracts and phytochemicals have therefore been investigated against bacterial and fungal pathogens [86].
However, laboratory antimicrobial activity does not establish clinical effectiveness, and appropriate animal and human studies remain necessary.

23. Wound Healing

Nano-phytomedicine has also been investigated for wound healing because certain phytochemicals possess antimicrobial, antioxidant and anti-inflammatory properties [87].
Curcumin-containing nanoparticles, hydrogels and nanofibers have been investigated for improving wound repair in experimental models [88].
Nanocarriers may provide sustained local delivery and protect active compounds from degradation.

24. Pharmacokinetic Advantages

One of the principal objectives of nanoformulation is improvement of pharmacokinetic behavior.
Nanocarriers can potentially increase:

- Cmax
- AUC
- Half-life
- Tissue exposure

while decreasing rapid degradation and clearance [26,89].
However, an increase in plasma concentration is not necessarily equivalent to improved therapeutic efficacy. Formulation studies should therefore evaluate pharmacokinetic, pharmacodynamic and clinical outcomes together.

25. Safety and Toxicity

Safety is a critical consideration in nano-phytomedicine.
Nanoparticles can interact with biological systems differently from conventional formulations because their size, surface charge, shape and composition influence cellular uptake and biodistribution [90].
Potential toxicological concerns include oxidative stress, inflammatory responses, organ accumulation, immunotoxicity and genotoxicity [91].
Importantly, safety evaluation should consider both the phytochemical and the nanocarrier. A phytochemical with a favorable safety profile may behave differently when administered repeatedly in a nanoparticle formulation.
Long-term toxicity studies are therefore required before widespread clinical application.

26. Standardization

Standardization represents a major challenge for nano-phytomedicine.
For botanical materials, quality can be affected by:

- Plant species
- Cultivar
- Geographic origin
- Soil
- Climate
- Harvesting
- Processing
- Extraction method
- Storage conditions [92]

Additional variables are introduced during nanocarrier production, including:

- Particle size
- Polydispersity
- Surface charge
- Encapsulation efficiency
- Drug loading
- Morphology
- Release kinetics [93]

Consequently, successful development requires simultaneous standardization of both the botanical material and nanocarrier.

27. Regulatory Challenges

Regulatory approval represents another major barrier to clinical translation.
Nanomedicines require detailed characterization of their physicochemical properties, manufacturing processes, stability, pharmacokinetics and toxicity [94].
Herbal nanoformulations are even more complex because plant extracts may contain numerous compounds whose concentrations vary between batches [95].
Regulatory frameworks must therefore address both conventional pharmaceutical quality requirements and the unique characteristics of nanoscale materials.

28. Green Nanotechnology

Green nanotechnology uses biological materials or environmentally favorable processes for nanoparticle synthesis.

Plant extracts may act as reducing, stabilizing and capping agents during nanoparticle synthesis [96].

Plant-mediated nanoparticle synthesis has attracted interest because it can reduce the need for certain synthetic chemicals and may provide a more sustainable production approach [97].

However, "green synthesis" should not be interpreted as proof of biological safety. Nanoparticles produced by biological methods still require rigorous physicochemical and toxicological characterization.

29. Artificial Intelligence in Nano-Phytomedicine

Artificial intelligence and machine learning are emerging tools for formulation optimization.

Potential applications include prediction of:

- Particle size
- Encapsulation efficiency
- Drug loading
- Stability
- Release behavior
- Toxicity
- Pharmacokinetics [98]

AI may reduce experimental trial-and-error and accelerate formulation development. However, reliable models require large, high-quality datasets.

30. Current Challenges

Despite substantial progress, several challenges remain.

First, there is considerable heterogeneity among nanoformulations, making comparisons between studies difficult [14]. Second, many studies focus on physicochemical properties rather than clinically meaningful outcomes [23]. Third, long-term toxicity remains insufficiently characterized for many nanocarriers [90].

Other challenges include high production costs, difficulties in scale-up, formulation instability, batch-to-batch variability and regulatory uncertainty [94,95].

Most importantly, there remains a substantial gap between promising laboratory findings and evidence from well-designed human clinical trials.

31. Future Perspectives

Future research should focus on standardized formulations, clinically relevant pharmacokinetic studies and adequately powered randomized clinical trials.

Stimuli-responsive nanocarriers may provide controlled release in response to pH, enzymes, temperature or reactive oxygen species [99]. Targeted nanocarriers may improve delivery to specific tissues and potentially reduce systemic exposure [100].

Plant-derived nanocarriers and sustainable manufacturing may contribute to environmentally responsible nano-phytomedicine production [97].

AI-assisted formulation design may further accelerate development by predicting optimal combinations of phytochemicals, carriers and excipients [98].

Ultimately, successful nano-phytomedicine development should follow the progression:

Phytochemical selection → formulation optimization → physicochemical characterization → pharmacokinetic evaluation → pharmacodynamic validation → toxicity assessment → clinical trials → regulatory approval.

32. Conclusion

Nano-phytomedicine represents a rapidly developing research field that combines the therapeutic potential of medicinal plants with modern nanotechnology. Many phytochemicals have promising biological properties but are limited by poor solubility, instability, rapid metabolism and low bioavailability [5–7]. Nanocarriers such as liposomes, phytosomes, polymeric nanoparticles, lipid nanoparticles, nanoemulsions and hybrid systems provide potential strategies for overcoming these limitations [14,33].

Curcumin, quercetin, resveratrol, EGCG, berberine and silymarin are among the most extensively investigated phytochemicals for nanoformulation [12–17]. Experimental studies suggest potential applications in cancer, inflammation, metabolic disorders, cardiovascular disease, neurodegeneration, infection and wound healing [18–22].

Nevertheless, the field remains largely preclinical. Improved bioavailability or nanoparticle characteristics do not necessarily translate into improved clinical outcomes. Standardization, long-term safety, manufacturing, regulatory requirements and clinical validation remain major challenges [23–26].

Future research should therefore emphasize reproducible formulations, rigorous toxicological assessment, well-designed pharmacokinetic studies and large-scale clinical trials. With appropriate validation, nanotechnology may help transform selected plant-derived bioactive compounds into more effective, reproducible and clinically useful therapeutic systems.

References

36. Atanasov AG, Zotchev SB, Dirsch VM, Supuran CT. Natural products in drug discovery: advances and opportunities. *Nature Reviews Drug Discovery*. 2021;20:200–216.
37. Newman DJ, Cragg GM. Natural products as sources of new drugs over the nearly four decades from 1981 through 2019. *Journal of Natural Products*. 2020;83:770–803.
38. Gülçin İ. Antioxidant activity of food constituents: an overview. *Archives of Toxicology*. 2020;94:651–715.
39. Sharifi-Rad J, et al. Natural products and their bioactive compounds in the prevention and treatment of chronic diseases. *Biomedicine & Pharmacotherapy*. 2020.
40. Chauhan D, Yadav PK, Sultana N, Agarwal A, Verma S, Chourasia MK, Gayen JR. Advancements in nanotechnology for the delivery of phytochemicals. *Journal of Integrative Medicine*. 2024;22:385–398.
41. Anand P, Kunnumakkara AB, Newman RA, Aggarwal BB. Bioavailability of curcumin: problems and promises. *Molecular Pharmaceutics*. 2007;4:807–818.
42. D'Archivio M, Filesi C, Di Benedetto R, Gargiulo R, Giovannini C, Masella R. Polyphenols, dietary sources and bioavailability. *Annali dell'Istituto Superiore di Sanità*. 2007;43:348–361.
43. Pandey P, et al. An updated review summarizing the anticancer potential of PLGA-based curcumin, epigallocatechin gallate, and resveratrol nanocarriers. *Biopolymers*. 2025;116:e23637.
44. Barani M, et al. Phytosomes as innovative delivery systems for phytochemicals: a comprehensive review of literature. *International Journal of Nanomedicine*. 2021;16:6983–7022.
45. Beloqui A, Solinís MÁ, Rodríguez-Gascón A, Almeida AJ, Préat V. Nanostructured lipid carriers: promising drug delivery systems for future clinics. *Nanomedicine*. 2016;12:143–161.
46. McClements DJ. Nanoemulsions versus microemulsions: terminology, differences, and similarities. *Soft Matter*. 2012;8:1719–1729.
47. Hewlings SJ, Kalman DS. Curcumin: a review of its effects on human health. *Foods*. 2017;6:92.
48. Nelson KM, Dahlin JL, Bisson J, Graham J, Pauli GF, Walters MA. The essential medicinal chemistry of curcumin. *Journal of Medicinal Chemistry*. 2017;60:1620–1637.
49. Parvin N, Aslam M, Joo SW, Mandal TK. Nano-phytomedicine: harnessing plant-derived phytochemicals in nanocarriers for targeted human health applications. *Molecules*. 2025;30:3177.
50. Ghosh S, Solanki R, Bhatia D, Sankaranarayanan S. Nanomaterials for delivery of medicinal plant extracts and phytochemicals: potential applications and future perspectives. *Plant Nano Biology*. 2025;12:100161.
51. Najafi F, Farrokhzad N, Ghaemi A, et al. Advancement in nanocarrier-mediated delivery of herbal bioactives: from bench to bedside. *Natural Products and Bioprospecting*. 2025;15:69.
52. Beygi M, Oroojalian F, Karav S, Kesharwani P, Sahebkar A. Nano-phytoconstituents: recent advances, regulatory insights, challenges, and future horizons. *Journal of Drug Delivery Science and Technology*. 2025;108:106908.
53. Prasad S, Gupta SC, Tyagi AK, Aggarwal BB. Curcumin, a component of golden spice: from bedside to bench and back. *Biotechnology Advances*. 2014;32:1053–1064.
54. Priyadarsini KI. The chemistry of curcumin: from extraction to therapeutic agent. *Molecules*. 2014;19:20091–20112.
55. Kunnumakkara AB, Bordoloi D, Padmavathi G, Monisha J, Roy NK, Prasad S, Aggarwal BB. Curcumin, the golden nutraceutical: multitargeting for multiple chronic diseases.

British Journal of Pharmacology. 2017;174:1325–1348.

56. Boots AW, Haenen GRMM, Bast A. Health effects of quercetin: from antioxidant to nutraceutical. *European Journal of Pharmacology*. 2008;585:325–337.
57. Salehi B, Mishra AP, Nigam M, et al. Resveratrol: a double-edged sword in health benefits. *Biomedicine & Pharmacotherapy*. 2018;102:267–278.
58. Neag MA, Mocan A, Echeverría J, Pop RM, Bocsan CI, Crișan G, Buzoianu AD. Berberine: botanical occurrence, traditional uses, extraction methods, and relevance in cardiovascular, metabolic, hepatic, and renal disorders. *Frontiers in Pharmacology*. 2018;9:557.
59. Chacko SM, Thambi PT, Kuttan R, Nishigaki I. Beneficial effects of green tea: a literature review. *Chinese Medicine*. 2010;5:13.
60. Lipinski CA. Poor aqueous solubility—an industry wide problem in drug discovery. *American Pharmaceutical Review*. 2002;5:82–85.
61. Jamwal R. Bioavailable curcumin formulations: a review of pharmacokinetic studies in healthy volunteers. *Journal of Integrative Medicine*. 2018;16:367–374.
62. Silva-Buzanello RA, et al. Natural antioxidants and their nanoformulations for improving stability and bioavailability. *Food Chemistry*. 2020.
63. McClements DJ. Encapsulation, protection, and delivery of bioactive proteins and peptides using nanoparticle and microparticle systems. *Advances in Colloid and Interface Science*. 2018;253:1–22.
64. Manach C, Williamson G, Morand C, Scalbert A, Rémésy C. Bioavailability and bioefficacy of polyphenols in humans. *American Journal of Clinical Nutrition*. 2005;81:230S–242S.
65. Choi J, et al. Bioavailability and pharmacokinetics of phytochemicals: current challenges and nanotechnology approaches. *Pharmaceutics*. 2021.
66. Shi J, Kantoff PW, Wooster R, Farokhzad OC. Cancer nanomedicine: progress, challenges and opportunities. *Nature Reviews Cancer*. 2017;17:20–37.
67. Patra JK, Das G, Fraceto LF, et al. Nano based drug delivery systems: recent developments and future prospects. *Journal of Nanobiotechnology*. 2018;16:71.
68. Khan I, Saeed K, Khan I. Nanoparticles: properties, applications and toxicities. *Arabian Journal of Chemistry*. 2019;12:908–931.
69. Akbarzadeh A, Rezaei-Sadabady R, Davaran S, et al. Liposome: classification, preparation, and applications. *Nanoscale Research Letters*. 2013;8:102.
70. Allen TM, Cullis PR. Liposomal drug delivery systems: from concept to clinical applications. *Advanced Drug Delivery Reviews*. 2013;65:36–48.
71. Moballegh Nasery M, Abadi B, Poormoghadam D, et al. Curcumin delivery mediated by nanoparticles: a review. *International Journal of Nanomedicine*. 2020.
72. Yao W, et al. Liposomal delivery systems for polyphenols and other phytochemicals. *Pharmaceutics*. 2021.
73. Neves AR, Lúcio M, Martins S, Lima JLC, Reis S. Novel resveratrol nanodelivery systems based on lipid nanoparticles. *Journal of Agricultural and Food Chemistry*. 2012.
74. Kidd PM. Bioavailability and activity of phytosome complexes from botanical polyphenols. *Alternative Medicine Review*. 2009;14:226–246.
75. Barani M, et al. Phytosomes as innovative delivery systems for phytochemicals. *International Journal of Nanomedicine*. 2021;16:6983–7022.
76. Semalty A, Semalty M, Rawat MSM, Franceschi F. Supramolecular phospholipid-polyphenolics interactions: the phytosome strategy. *Current Drug Discovery Technologies*. 2010;7:202–209.
77. Danhier F, Ansorena E, Silva JM, Coco R, Le Breton A, Préat V. PLGA-based nanoparticles: an overview of biomedical applications. *Journal of Controlled Release*. 2012;161:505–522.
78. Pandey P, et al. PLGA-based nanocarriers for curcumin, EGCG and resveratrol in cancer therapy. *Biopolymers*. 2025;116:e23637.
79. Makadia HK, Siegel SJ. Poly lactic-co-glycolic acid (PLGA) as biodegradable

controlled drug delivery carrier. *Polymers*. 2011;3:1377–1397.

80. Müller RH, Mäder K, Gohla S. Solid lipid nanoparticles (SLN) for controlled drug delivery. *European Journal of Pharmaceutics and Biopharmaceutics*. 2000;50:161–177.
81. Mehnert W, Mäder K. Solid lipid nanoparticles: production, characterization and applications. *Advanced Drug Delivery Reviews*. 2001;47:165–196.
82. Müller RH, Radtke M, Wissing SA. Nanostructured lipid matrices for improved microencapsulation of drugs. *International Journal of Pharmaceutics*. 2002;242:121–128.
83. Souto EB, Müller RH. Lipid nanoparticles: effect on bioavailability and pharmacokinetic parameters. *Handbook of Experimental Pharmacology*. 2010.
84. McClements DJ. Edible nanoemulsions: fabrication, properties, and functional performance. *Soft Matter*. 2011;7:2297–2316.
85. Guttoff M, Saberi AH, McClements DJ. Formation of vitamin D nanoemulsion-based delivery systems. *Food Chemistry*. 2015.
86. Zorilla R, Liang L, Remondetto G, Subirade M. Effect of ultrasound on the preparation of nanoemulsions containing essential oils. *Food Chemistry*. 2019.
87. Kunnumakkara AB, et al. Curcumin: a review of its effects on human health and molecular mechanisms. *Molecules*. 2017.
88. Akbari M, et al. Curcumin phytosome: a review of pharmacokinetic and clinical studies. *Phytotherapy Research*. 2018.
89. Zheng B, et al. Curcumin nanoformulations for enhanced therapeutic efficacy. *International Journal of Nanomedicine*. 2020.
90. Sun M, et al. Advances in curcumin delivery systems. *Acta Pharmaceutica Sinica B*. 2020.
91. Li Y, et al. Quercetin and its nanoformulations: pharmacological effects and delivery strategies. *Pharmaceutics*. 2021.
92. Pool H, Quintanar D, Figueroa-González G, et al. Antioxidant effects of quercetin and nanocarrier approaches. *International Journal of Nanomedicine*. 2012.
93. Ren L, et al. Quercetin nanoparticles and their therapeutic applications. *Nanomedicine*. 2020.
94. Walle T. Bioavailability of resveratrol. *Annals of the New York Academy of Sciences*. 2011;1215:9–15.
95. Neves AR, et al. Resveratrol in nanocarriers: improved delivery and biological activity. *Journal of Agricultural and Food Chemistry*. 2012.
96. Summerlin N, Soo E, Thakur S, Qu Z, Cui Z. Resveratrol nanoformulations for cancer therapy. *Journal of Controlled Release*. 2015.
97. Lambert JD, Elias RJ. The antioxidant and pro-oxidant activities of green tea polyphenols: a role in cancer prevention. *Archives of Biochemistry and Biophysics*. 2010;501:65–72.
98. Dube A, Ng K, Nicolazzo JA. Targeted delivery of EGCG using nanotechnology. *Pharmaceutical Research*. 2010.
99. Liu CS, Zheng YR, Zhang YF, Long XS. Research progress on berberine with a special focus on its oral bioavailability. *Fitoterapia*. 2016;109:274–282.
100. Neag MA, et al. Berberine delivery systems and therapeutic applications. *Frontiers in Pharmacology*. 2018.
101. Bishayee A. Cancer prevention and treatment with resveratrol: from rodent studies to clinical trials. *Cancer Prevention Research*. 2009;2:106–111.
102. Torchilin VP. Multifunctional, stimuli-sensitive nanoparticulate systems for drug delivery. *Nature Reviews Drug Discovery*. 2014;13:813–827.
103. Furman D, et al. Chronic inflammation in the etiology of disease across the life span. *Nature Medicine*. 2019;25:1822–1832.
104. Sercombe L, Veerati T, Moheimani F, Wu SY, Sood AK, Hua S. Advances and challenges of liposome assisted drug delivery. *Frontiers in Pharmacology*. 2015;6:286.
105. McClements DJ, Xiao H. Designing food structures and compositions to enhance nutraceutical bioavailability. *Food Chemistry*. 2014;160:146–156.
106. Tabrizi R, et al. The effects of curcumin on glycemic control and lipid profiles among patients with metabolic syndrome and related

disorders: systematic review and meta-analysis. *Current Pharmaceutical Design*. 2018.

107. Pathomwichaiwat T, et al. Effects of turmeric supplementation on glucose metabolism in diabetes mellitus and metabolic syndrome: an umbrella review and updated meta-analysis. 2023.
108. Qiu L, et al. Effects of dietary polyphenol curcumin supplementation on metabolic, inflammatory and oxidative stress indices. *Frontiers in Endocrinology*. 2023.
109. Heneka MT, Carson MJ, El Khoury J, et al. Neuroinflammation in Alzheimer's disease. *Lancet Neurology*. 2015;14:388–405.
110. Ahmed T, Gilani AH. Inhibitory effect of curcuminoids on acetylcholinesterase activity and attenuation of neuroinflammation. *Journal of Medicinal Food*. 2009.
111. Rege SD, et al. Resveratrol for neuroprotection and neurodegenerative diseases. *Journal of Clinical Neuroscience*. 2014.
112. Dajas F, Rivera-Mancia S, Jara S, et al. Neuroprotective actions of flavonoids. *British Journal of Pharmacology*. 2013.
113. Saraiva C, Praça C, Ferreira R, et al. Nanoparticle-mediated brain drug delivery: overcoming blood-brain barrier. *International Journal of Pharmaceutics*. 2016.
114. Illum L. Nasal drug delivery: new developments and strategies. *Drug Discovery Today*. 2002;7:1184–1189.
115. Libby P. Inflammation in atherosclerosis. *Nature*. 2002;420:868–874.
116. Opie LH, Lecour S. The red wine hypothesis: from concepts to protective signalling molecules. *European Heart Journal*. 2007;28:1683–1693.
117. Sahebkar A. Curcuminoids for the management of hyperlipidaemia: a systematic review and meta-analysis. *International Journal of Cardiology*. 2014.
118. Boots AW, et al. Quercetin and cardiovascular health. *Pharmacological Research*. 2008.
119. Cowan MM. Plant products as antimicrobial agents. *Clinical Microbiology Reviews*. 1999;12:564–582.
120. Rai M, Yadav A, Gade A. Silver nanoparticles as a new generation of antimicrobials. *Biotechnology Advances*. 2009;27:76–83.
121. Singh P, et al. Nanotechnology in antimicrobial applications of medicinal plants. *Biotechnology Advances*. 2018.
122. Guo S, DiPietro LA. Factors affecting wound healing. *Journal of Dental Research*. 2010;89:219–229.
123. Ponnurangam S, et al. Curcumin nanocarriers for wound healing. *International Journal of Nanomedicine*. 2020.
124. Allen TM, Cullis PR. Liposomal drug delivery systems. *Advanced Drug Delivery Reviews*. 2013;65:36–48.
125. Fadeel B, Garcia-Bennett AE. Better safe than sorry: understanding the toxicological properties of inorganic nanoparticles manufactured for biomedical applications. *Advanced Drug Delivery Reviews*. 2010;62:362–374.
126. Nel A, Xia T, Mädler L, Li N. Toxic potential of materials at the nanolevel. *Science*. 2006;311:622–627.
127. Kunle OF, Egharevba HO, Ahmadu PO. Standardization of herbal medicines: a review. *International Journal of Biodiversity and Conservation*. 2012;4:101–112.
128. Danaei M, Dehghankhold M, Ataei S, et al. Impact of particle size and polydispersity index on the clinical applications of

*****