

REVIEW



Harnessing nanoparticles for phytochemical delivery: a comprehensive review of safety and therapeutic potential

Sharon Oladipupo^a, Damilare Emmanuel Rotimi^b, Emmanuel Henry Ezenabor^c, Adebola Busola Ojo^d, Oluwatomisin Aderonke Akinsola^e and Oluwafemi Adeleke Ojo^f

^aChemistry and Industrial Chemistry Programme, Bowen University, Iwo, Nigeria; ^bDepartment of Biochemistry, Landmark University, Omu-Aran, Nigeria; ^cBiochemistry Programme, Bowen University, Iwo, Nigeria; ^dDepartment of Environmental Management and Toxicology, University of Ilesha, Ilesha, Nigeria; ^eMicrobiology Programme, Bowen University, Iwo, Nigeria; ^fResearch Centre for Integrative Physiology and Pharmacology, Institute of Biomedicine, University of Turku, Turku, Finland

ABSTRACT

Nanoparticle encapsulation has emerged as a relevant technology with the potential to revolutionize multiple fields, including medicine, food technology, cosmetics, and environmental monitoring. This review discusses the fundamental aspects of nanoparticle encapsulation, highlighting its benefits, such as enhanced solubility, stability, and bioavailability of phytochemicals. The data for this report were obtained via an extensive review of the peer-reviewed scientific literature. We reviewed various types of nanoparticles used in encapsulation, the efficacy of nanoparticle-encapsulated phytochemicals, and the challenges faced, including formulation complexity and regulatory hurdles. The review also considers current and future applications, providing examples of how advanced technologies such as artificial intelligence and novel manufacturing methods contribute to innovation in this field. As nanoparticle technology progresses, addressing safety and regulatory issues will be critical for its successful integration and commercialization. This review underscores the promising future of nanoparticle technology.

ARTICLE HISTORY

Received 25 March 2025
Accepted 1 October 2025

KEYWORDS

Nanoparticles;
encapsulation; toxicity;
phytochemicals

1. Introduction

Nanoparticles (NPs) are materials with dimensions on the nanoscale, generally under 100 nm. In recent years, these tiny structures have become significant in modern medicine, serving various roles from contrast agents in medical imaging to carriers for gene delivery at the cellular level. Compared with those of bulk materials, their unique properties, attributed to their small size, include enhanced chemical reactivity, improved energy absorption, and greater biological mobility [1]. NPs have the potential to enhance the delivery and efficacy of various compounds, including phytochemicals. These nanoscale carriers can improve the solubility, stability, and bioavailability of encapsulated substances, thereby addressing many limitations that natural compounds face [2].

Phytochemicals, derived from the Greek words “phyto” (meaning plant) and “chemical” (indicating a biologically active compound), are natural compounds found in plants that offer potential therapeutic benefits. These compounds, including antioxidants and anti-inflammatory agents, help plants defend against environmental stress, and when ingested by humans, they can support overall health [3]. Examples include curcumin from turmeric, resveratrol from grapes, and quercetin from various fruits and vegetables, which have been explored for their health benefits (Figure 1) [4].

However, the therapeutic application of phytochemicals is often limited by their low bioavailability, necessitating the

exploration of nanoparticle encapsulation to increase their efficacy [5]. Nanoparticle encapsulation improves the solubility, stability, and absorption of phytochemicals within the body. This process prevents rapid degradation, allows the compounds to reach target tissues more efficiently, and keeps them active for longer durations, reducing the need for large dosages [6].

Despite their benefits, the small size of nanoparticles raises safety concerns because it enables them to interact with tissues in ways that can lead to unexpected effects, potentially resulting in harmful outcomes. Therefore, thoroughly assessing the safety and effectiveness of phytochemicals encapsulated in nanoparticles is crucial [7]. This review examines how nanoparticle technology can enhance the transport and effectiveness of phytochemicals, the various types of nanoparticles used, and potential safety risks.

The primary aim of this review is to consolidate and critically evaluate recent advances in nanoparticle-encapsulated phytochemicals with a focus on translational potential. Given the rapid growth in nanotechnology and its intersection with natural product-based therapeutics, our goal is to highlight formulation strategies, therapeutic applications, and commercial relevance, thereby informing future research and development efforts in this evolving field. It will also address challenges such as maintaining nanoparticle stability, scaling up production, meeting regulatory requirements, and identifying future research areas.

Article highlights

- Phytochemicals possess significant therapeutic potential but are limited by poor bioavailability, instability, and off-target effects, necessitating advanced delivery strategies
- Nanoparticle-based delivery systems such as liposomes, polymeric nanoparticles, solid lipid nanoparticles (SLNs), dendrimers, and metallic nanoparticles have emerged as promising platforms to enhance phytochemical delivery
- The review discusses both passive targeting (via EPR effect) and active targeting (via ligand-receptor interactions) to improve drug accumulation in specific tissues
- Most widely studied examples of phytochemicals like curcumin, quercetin, berberine, artemisinin, and resveratrol are discussed in the context of their nanoformulations and enhanced pharmacokinetics.

2. Review methodology

The relevant literature was sourced by using major scientific catalogs such as Google Scholar, PubMed, Scopus, and ScienceDirect to obtain information. Terms such as ‘nanoparticle encapsulation’ together with ‘phytochemicals,’ ‘nanoparticle encapsulation safety,’ and ‘clinical trials and ‘extraction’ were searched, and over 70 published papers were gathered, with a major focus on work performed between 2007 and 2025. Papers that were not written in English were not used. The relevant literature from the articles’ references was also explored.

3. Phytochemical encapsulation within nanoparticles

Nanoparticle encapsulation involves embedding phytochemicals within nanoscale carriers composed of biocompatible substances such as lipids, polymers, or metals [2]. Nanoparticles, which are typically smaller than 100 nm, offer an increased surface area that enhances drug solubility and absorption. They protect phytochemicals from degradation,

thereby improving their stability and extending their circulation time in the body. Encapsulating phytochemicals in nanoparticles is a cutting-edge technique for drug delivery and preservation. This process involves embedding phytochemicals into nanoscale carriers composed of biocompatible substances such as lipids, polymers, or metals [8]. These nanoparticles, which are usually less than 100 nanometers in diameter, provide multiple benefits for optimizing the effectiveness of phytochemicals.

Nanoparticle encapsulation gives rise to a major advantage in the form of increased nanoparticle surface area. Their small size increases the surface area-to-volume ratio, which increases their solubility and facilitates the absorption of phytochemicals in bodily fluids [9]. This is particularly beneficial for compounds that have poor solubility in their natural form. By encapsulating these phytochemicals in nanoparticles, their bioavailability is significantly improved, ensuring that a larger portion of the active compound reaches its intended target [10].

NPs not only increase their solubility but also protect against degradation. By encapsulating phytochemicals, a barrier is formed to shield them from environmental elements such as light, oxygen, and moisture, which would otherwise cause degradation. This protective layer guarantees the stability and effectiveness of phytochemicals for extended periods, preserving their therapeutic potential and prolonging their shelf life until they reach their target destination [11].

Furthermore, nanoparticles provide the benefit of regulated release. Encapsulation can be tailored to release phytochemicals slowly. This regulated release system assists in maintaining optimal levels of the active compound at the intended location, decreasing the need for frequent dosing and minimizing the risk of side effects [12]. By customizing nanoparticles to react to specific physiological conditions, such as alterations in pH or the presence of particular enzymes, scientists can adjust the release patterns to meet different therapeutic requirements.

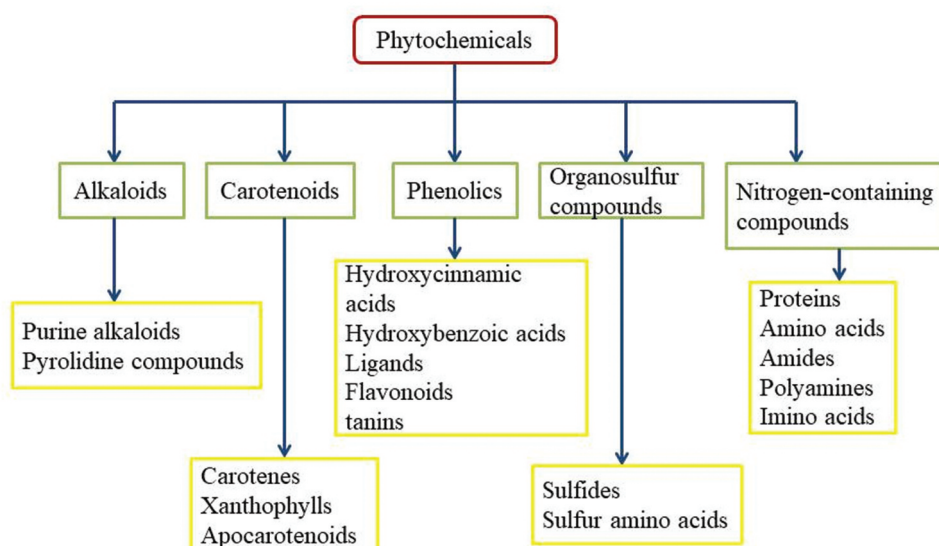


Figure 1. Basic groups and subgroups of phytochemicals.

Nanoparticle encapsulation offers an important advantage by extending the amount of time that phytochemicals circulate throughout the body. Since nanoparticles are very small, they can evade the immune system's quick destruction, remain in the bloodstream for extended periods of time and have a more powerful impact. This prolonged circulation period increases the overall effectiveness of phytochemicals and contributes to their sustained therapeutic influence [13].

The utilization of nanoparticle encapsulation leverages the benefits of tiny carriers to increase the solubility, stability, and effectiveness of phytochemicals [14]. NPs serve as a potent mechanism to enhance drug delivery systems and increase the solubility of bioactive chemicals to improve their function, safeguarding against degradation, regulating release, and prolonging circulation time [15]. This technology has the potential to greatly impact diverse industries, including medicine, pharmaceuticals, food technology, and cosmetics.

3.1. Advantages of nanoparticle encapsulation

Nanoparticles have significant benefits in improving the delivery of phytochemicals by increasing their stability and therapeutic effectiveness. One of the main advantages of utilizing nanoparticles is their ability to increase the stability of delicate phytochemicals. These naturally occurring compounds from plants are often susceptible to deterioration. When subjected to environmental conditions such as heat, light, and oxygen, materials can undergo significant changes [16]. NPs serve as protective carriers, shielding the enclosed phytochemicals from these detrimental elements. In particular, solid lipid nanoparticles (SLNs), which are lipid-based, are highly productive in creating a stable environment [17]. By preventing degradation, these systems ensure that the active compounds retain their potency and efficacy over their lifespan, thus preserving their therapeutic potential [18].

NPs offer crucial benefits by improving the solubility of phytochemicals with low water solubility [19]. Many naturally occurring compounds have limited solubility, which hinders their absorption into the bloodstream and reduces their bioavailability [20]. Encapsulation by nanoparticles can significantly increase the dissolution rate of these compounds, leading to better absorption. An illustrative case is curcumin, which has low water solubility and bioavailability in its free state. Nonetheless, curcumin has improved solubility and increased absorption when enclosed in nanoparticles, thereby enhancing its therapeutic effectiveness [21].

NPs also enable the controlled release of phytochemicals. They can be engineered to deliver their contents over an extended period, providing sustained therapeutic effects. For example, polymeric nanoparticles are designed to release their payload gradually, ensuring the consistent and prolonged delivery of phytochemicals. This controlled release reduces the need for frequent dosing, offering more convenience to patients and enhancing overall treatment outcomes [22].

It is possible to tailor nanoparticles for specific delivery, in addition to increasing their solubility and release. Altering the surface of nanoparticles enables them to be guided to specific tissues or cells, ensuring that the phytochemicals reach their desired action site. This precise targeting is very useful

in the treatment of diseases such as cancer, where reducing harm to healthy tissues is imperative. For example, ligands or antibodies that recognize and bind to particular receptors on cancer cells can be used to functionalize nanoparticles. This allows phytochemicals to be directly delivered to the tumor location, increasing therapeutic effectiveness and decreasing adverse effects [23]. The stability, solubility, controlled release, and targeted distribution of phytochemicals are all much improved by nanoparticles, which makes them effective tools for enhancing the medicinal potential of natural compounds [24].

4. Nanoparticle toxicity mechanisms and dose-response relationships

4.1. Nanoparticle toxicity mechanisms

The mechanisms underlying the toxic effects of nanoparticles are complex and depend on various factors such as their size, shape, surface chemistry, and other physicochemical properties. A primary mechanism of nanoparticle-induced toxicity is the generation of reactive oxygen species (ROS), which leads to oxidative stress. This can damage cellular components like proteins, lipids, and DNA, ultimately causing cell dysfunction or death. Nanoparticles can trigger ROS production directly through their surface reactivity or by interacting with cellular components like mitochondria [25]. Other toxicity mechanisms include:

- a. Direct cell membrane interaction: Nanoparticles can physically damage cell membranes or initiate signaling pathways that lead to cellular damage [26].
- b. Dissolution and ion release: Some nanoparticles can dissolve and release toxic ions that can impair enzyme function or interact with DNA [26].
- c. Inflammation: Nanoparticles can activate the immune system, leading to the release of pro-inflammatory cytokines and chronic inflammation, which is a risk factor for various diseases [27].

4.2. Dose-response relationships

The dose-response relationship is a fundamental concept in toxicology that describes how the magnitude of a toxic response is related to the dose of the substance. For nanoparticles, this relationship can be complex and non-linear. Factors that influence the dose-response relationship for nanoparticles include:

- a. Size and Shape: Smaller nanoparticles generally exhibit greater toxicity due to their larger surface area and ability to penetrate biological membranes.
- b. Surface Chemistry: The surface properties of nanoparticles, such as charge and functionalization, can affect their interactions with biological systems.
- c. Aggregation: The tendency of nanoparticles to clump together can influence their toxicity and dose-response relationship.

Establishing clear dose-response relationships for nanoparticles is challenging due to the complexity of their toxicity mechanisms and the variability in their physicochemical properties. Some studies have shown that for certain toxic effects, like lung inflammation, the best dose metric may be surface area or particle number rather than mass.

4.3. Accumulation in organs

Following exposure, nanoparticles can be distributed throughout the body and accumulate in various organs, which can lead to organ-specific toxicity. The primary routes of exposure are inhalation, ingestion, and skin contact [28] in the following organs:

- a. Lungs: The lungs are a major site of nanoparticle accumulation, especially after inhalation. This can lead to inflammation, fibrosis, and other respiratory problems.
- b. Liver and Spleen: After intravenous administration, a significant portion of nanoparticles accumulate in the liver and spleen. This accumulation can cause liver toxicity and affect the immune system [29].
- c. Kidneys: The kidneys are involved in the clearance of some nanoparticles, and accumulation in this organ can lead to renal toxicity [28].
- d. Brain: Some nanoparticles are small enough to cross the blood-brain barrier and accumulate in the brain, raising concerns about neurotoxicity [28].

The biodistribution and accumulation of nanoparticles are influenced by their physicochemical properties. For example, surface modifications can alter the accumulation of nanoparticles in specific organs. Long-term accumulation of non-biodegradable nanoparticles, such as some metal-based nanoparticles, is a significant concern for chronic toxicity [29].

The passive targeting mechanism exploits the enhanced permeability and retention (EPR) effect observed in tumor tissues or inflamed sites, allowing nanoparticles to accumulate due to leaky vasculature and poor lymphatic drainage [30]. In contrast, active targeting involves functionalizing nanoparticles with ligands (e.g., antibodies, peptides, or small molecules) that bind selectively to overexpressed receptors on target cells, thereby enhancing cellular uptake and site-specific drug delivery [31].

5. Nanocarriers for phytochemical delivery

There are several kinds of nanoparticles, each offering distinct advantages in terms of encapsulating and delivering phytochemicals. These different nanoparticle systems not only improve the bioavailability of these compounds but also offer enhanced stability, solubility, and focused distribution, which gives them great versatility for medical use [32].

5.1. Lipid-based nanoparticles

Lipid-based nanoparticles, such as liposomes and solid lipid nanoparticles (SLNs), are widely used. Liposomes are spherical vesicles made of a lipid bilayer. They have the ability to

contain both hydrophilic and hydrophobic substances [33]. This capability makes liposomes effective at enhancing the stability and soluble nature of phytochemicals. They are often used in medication delivery systems to increase the bioavailability of encapsulated compounds and protect them from degradation during storage and transport [34]. Additionally, liposomes help increase the efficiency of the phytochemicals supplied by being able to target particular tissues [35]. Another lipid-based solution is provided by solid lipid nanoparticles (SLNs), which consist of a surfactant-encapsulated solid lipid core [36]. These nanoparticles ensure improved stability and controlled release, safeguarding sensitive phytochemicals from degradation while releasing them steadily over time. In situations where prolonged release is advantageous, SLNs prove to be highly effective, reducing the need for repeated doses and improving patient adherence [37].

Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) are prominent lipid-based systems. They are composed of solid lipids at room temperature, offering advantages such as good biocompatibility, biodegradability, and low toxicity [38]. They can encapsulate both hydrophilic and lipophilic phytochemicals, protecting them from degradation and enhancing their stability. SLN and NLC have shown significant potential in improving the bioavailability of plant sourced bioactive compounds. Preclinical studies have demonstrated their effectiveness in delivering phytochemicals for various therapeutic applications, including antioxidant, anti-inflammatory, and anticancer treatments. Surface modification of these nanoparticles is a key strategy to enhance their stability and enable targeted delivery to specific tissues or cells [38].

5.2. Polymeric nanoparticles

Polymeric nanoparticles (PNPs) are versatile nanocarriers made from biodegradable and biocompatible polymers. They offer excellent control over drug release kinetics, high drug loading capacity, and the ability to be functionalized for targeted delivery [39]. PNPs can protect encapsulated phytochemicals from enzymatic degradation and improve their cellular uptake. PNPs have been widely explored for delivering phytochemicals in various therapeutic areas, including cancer therapy, inflammatory diseases, and neurodegenerative disorders. Recent innovations include the development of 'smart' PNPs that respond to specific physiological stimuli (e.g., pH, temperature, enzyme activity) to achieve precise and on-demand drug release at the target site. This responsiveness enhances therapeutic efficacy and minimizes off-target effects. Despite their promise, challenges such as potential toxicity of certain polymers, scalability of production, and regulatory hurdles need to be addressed for widespread clinical translation. Future research focuses on developing novel biocompatible polymers, optimizing fabrication techniques, and integrating artificial intelligence for rational design and optimization of PNPs [39]. Polymeric nanoparticles are commonly utilized in drug delivery via the use of poly (lactic-co-glycolic acid) (PLGA), a biodegradable polymer. Owing to its biocompatibility, PLGA is commonly employed because of its capacity to

provide sustained release of encapsulated compounds [40]. This polymer significantly improves the bioavailability and therapeutic efficacy of phytochemicals, ensuring that the active compounds remain in the body long enough to provide therapeutic benefits. The adaptability of PLGA nanoparticles allows their use in various formulations [41]. Derived from crustacean shells, chitosan is a natural polymer that provides a biodegradable and biocompatible nanoparticle system. These nanoparticles made from chitosan are especially valuable for increasing the absorption of phytochemicals by the GI tract and their stability and solubility [42]. Consequently, chitosan nanoparticles are well suited for use in oral medication administration systems, providing phytochemicals with defenses against stomach breakdown and improving blood-stream absorption [43].

5.3. Magnetic nanoparticles

Magnetic nanoparticles (MNPs) are being extensively investigated for their applications in targeted drug delivery, particularly in cancer therapy, where they can deliver phytochemicals directly to tumor sites under the influence of an external magnetic field. Beyond drug delivery, MNPs are also used in magnetic resonance imaging (MRI) for diagnostic purposes and in hyperthermia for cancer treatment. Innovations include the development of multifunctional MNPs that combine therapeutic and diagnostic capabilities [44]. Magnetic nanoparticles and metal-based nanoparticles such as gold and silver are utilized in the encapsulation and transport of phytochemicals, providing distinct characteristics that improve their therapeutic potential [45]. Gold nanoparticles are well known for their excellent biocompatibility and unique optical properties, making them highly useful in applications related to imaging and therapy. For precision distribution, they can be targeted to particular cells or tissues by attaching particular ligands or antibodies. Photothermal therapy uses gold nanoparticles, which are heated by light to kill cancer cells [46]. Silver nanoparticles have strong antimicrobial characteristics that make them appropriate for use in applications involving wound healing and infection control. They can be added to creams, gels, or wound dressings to transport phytochemicals with antibacterial effects to the infection site, thereby facilitating quicker healing and inhibiting the growth of harmful microorganisms [47]. Magnetic nanoparticles possess the unique ability to be directed by external magnetic fields, enabling the targeted delivery of phytochemicals to particular organs or tissues. This characteristic is especially helpful for treating cancer, as they can be targeted to tumor sites for both diagnostic and therapeutic purposes. Moreover, magnetic nanoparticles can be filled with phytochemicals and steered to specific areas of the body for localized treatment, minimizing general side effects [48]. MNPs are widely used for phytochemical delivery, particularly in cancer therapy, where they can enhance the efficacy of phytochemicals through synergistic effects or by acting as photothermal/photodynamic agents. Innovations include the development of smart metal based nanocarriers that respond to specific stimuli for controlled drug release, and their integration into diagnostic platforms

for theragnostic applications. Challenges associated with metal-based nanoparticles include potential toxicity, long-term stability in biological systems, and issues related to their synthesis and scalability. Future research is focused on developing biocompatible and biodegradable metal-based nanoparticles, exploring novel synthesis methods (e.g., green synthesis), and optimizing their surface modifications for enhanced targeting and reduced toxicity [49].

Lipid-based, polymeric, and metal-based nanoparticles have specific advantages for encapsulating phytochemicals. They enhance solubility, improve stability, provide controlled release, and target specific tissues, all of which contribute significantly to enhancing the effectiveness of phytochemical-based therapies [15,50]. Magnetic Nanoparticles (MNPs), typically composed of iron oxides, are gaining significant attention due to their unique magnetic properties, which allow for external manipulation and targeted delivery. They offer advantages such as remote control over drug localization, noninvasive targeting, and potential for hyperthermia therapy. MNPs can be functionalized with various biomolecules to enhance their biocompatibility and targeting efficiency [44]. Metal-based nanoparticles (MNPs), including gold nanoparticles (AuNPs), silver nanoparticles (AgNPs), and others, possess unique optical, electronic, and catalytic properties that make them highly attractive for biomedical applications. They offer advantages such as high surface area for drug loading, tunable surface chemistry for functionalization, and inherent therapeutic properties (e.g., anticancer, antimicrobial) [49].

Different classes of nanoparticles including liposomes, polymeric nanoparticles, and metallic nanoparticles, each offer distinct advantages and limitations in the delivery of phytochemicals. Liposomes, composed of phospholipid bilayers, are highly biocompatible and can encapsulate both hydrophilic and lipophilic phytochemicals, such as curcumin and quercetin. Their ability to mimic biological membranes allows for efficient cellular uptake and reduced toxicity. However, liposomes often suffer from limited physical stability, susceptibility to oxidation, and relatively short shelf life [51]. In contrast, polymeric nanoparticles, made from natural or synthetic polymers like PLGA or chitosan, provide controlled release, improved drug loading, and enhanced protection from enzymatic degradation. These features make them particularly suitable for poorly water-soluble phytochemicals and chronic therapeutic regimens. Yet, they may face biocompatibility or biodegradability issues, depending on the polymer used [52].

Metallic nanoparticles for example gold (AuNPs), silver (AgNPs), and iron oxide nanoparticles are increasingly explored for targeted delivery and diagnostic (theranostic) applications due to their unique optical and magnetic properties. Their high surface area allows for functionalization with ligands or targeting moieties, enhancing site-specific delivery of phytochemicals like resveratrol or epigallocatechin gallate (EGCG). Nonetheless, concerns remain regarding their long-term toxicity, accumulation in organs, and lack of biodegradability, which may limit clinical use [53]. Overall, the choice of nanoparticle system should be guided by the physicochemical properties of the phytochemical, the intended route of administration, and the therapeutic target. For instance, liposomes are favored for topical or intravenous delivery, polymeric NPs

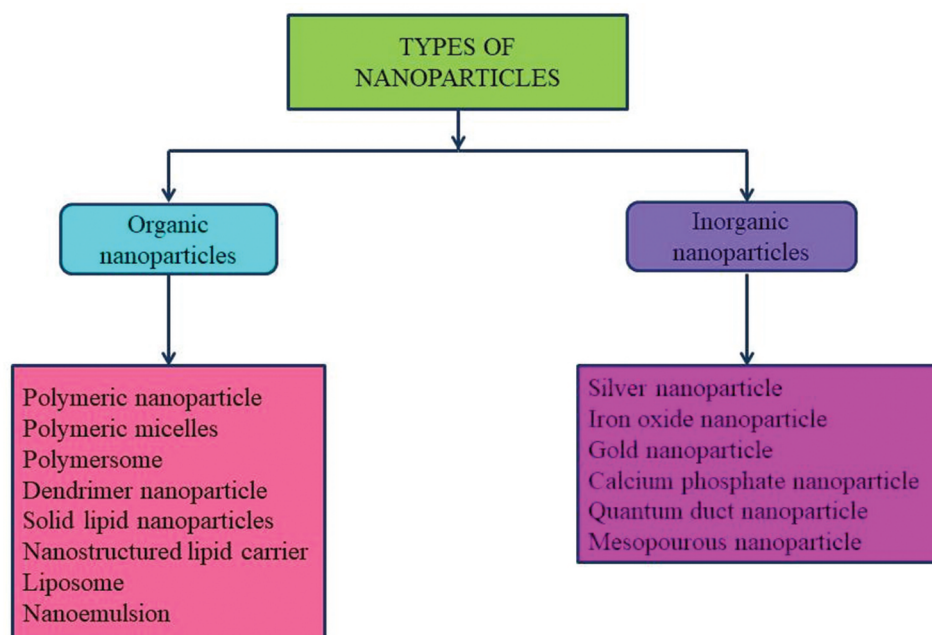


Figure 2. Types of nanoparticles.

for oral and sustained-release formulations, and metallic NPs for imaging-guided therapies and precision oncology. A depiction of the types of nanoparticles is presented in Figure 2.

5.4. Advantages and limitations of different nanoparticle systems

Lipid-based nanoparticles, including liposomes and solid lipid nanoparticles (SLNs), are noted for their biocompatibility and biodegradability, which stems from a composition that is similar to that of cell membranes [54,55]. This similarity facilitates efficient cellular uptake and minimizes toxicity risks, making them suitable for delivering a wide range of therapeutic agents. They can be used for various routes of administration, including dermal, pulmonary, oral, and intravenous. However, there are some limitations to lipid-based systems, such as the potential for instability, low drug-loading capacity, and rapid clearance from the bloodstream by the immune system [17].

Polymeric nanoparticles are a highly versatile platform for drug delivery, offering the ability to tune their properties for specific applications. These nanoparticles can be engineered to control the release of drugs, improve their stability, and target specific tissues or cells [55,56]. The surface of these nanoparticles can be modified with ligands to enhance cellular uptake and minimize nonspecific interactions. Despite these advantages, the use of polymeric nanoparticles is not without its challenges. Concerns about their biodegradability and the potential for long-term toxicity are significant limitations. Additionally, the manufacturing process can be complex and difficult to scale up, which can hinder their clinical translation [57].

Metal-based nanoparticles, such as those made of gold and iron oxide, possess unique optical and magnetic properties that make them useful for both diagnostic and therapeutic

purposes [58]. For instance, gold nanoparticles can be used in photothermal therapy to selectively destroy cancer cells, while iron oxide nanoparticles can serve as contrast agents in magnetic resonance imaging (MRI) [59]. However, a major drawback of metal-based nanoparticles is their potential for toxicity and long-term accumulation in the body. Their non-biodegradable nature raises concerns about their safety and environmental impact, which can limit their clinical applications [60].

6. Efficacy of nanoparticle-encapsulated phytochemicals

Nanoparticle encapsulation offers multiple advantages for enhancing the delivery and therapeutic efficacy of phytochemicals. These benefits include extended release, targeted precision, improved absorption, and increased stability. Collectively, these advantages make nanoparticle-based delivery systems crucial tools in modern drug development, allowing phytochemicals to overcome their inherent limitations and achieve their full therapeutic potential [14]. The revolution of drug delivery systems utilizing nanoparticle encapsulation has significantly enhanced the therapeutic efficacy of phytochemicals. Phytochemicals, which are derived from plants, are bioactive compounds that frequently encounter obstacles such as poor bioavailability, stability issues, and ineffective delivery to their intended locations. NPs present a promising remedy for these constraints, allowing for more efficient and accurate delivery. There are various bioactive phytochemicals encapsulated in nanoparticle formulations which are listed in Table 1.

The advancement of nanoparticle-based delivery systems for phytochemicals is driven by multiple interrelated challenges and therapeutic goals. While improving bioavailability remains a critical focus due to the poor solubility, low

Table 1. Nanoparticle development for phytochemicals.

Study Title	Phytochemical	Nanoparticle Type	Encapsulation Method	Clinical Application	Outcomes/Findings	Reference
Curcumin Nanoparticles as Promising Therapeutic Agents for Drug Targets	Curcumin	Lipid Nanoparticles	Solid lipid nanoparticles	Cancer therapy (targeted drug delivery)	Enhanced bioavailability and therapeutic effect in cancer patients	[61]
Resveratrol-loaded PLGA nanoparticles: enhanced stability, solubility and bioactivity of resveratrol for nonalcoholic fatty liver disease therapy	Resveratrol	Polymeric Nanoparticles	Nanoemulsions	Antioxidant and anti-inflammatory effects	Increased stability and prolonged release	[62]
Green synthesis of gold nanoparticles using quercetin biomolecule from mangrove plant, <i>Ceriops tagal</i> : Assessment of antiproliferative properties, cellular uptake and DFT studies	Quercetin	Gold Nanoparticles	Solvent evaporation method	Anti-inflammatory, cardiovascular health	Improved absorption and bioavailability	[63]
Acid-activatable polymeric curcumin nanoparticles as therapeutic agents for osteoarthritis	Curcumin	Chitosan Nanoparticles	Ionic gelation	Osteoarthritis management	Better joint health, reduced inflammation	[64]
Solidified reverse micellar solution-based chitosan-coated solid lipid nanoparticles as a new approach to enhance oral delivery of artemether in malaria treatment	artemisinin	Solid-lipid nanoparticle	Micelles	Antimalaria and anticancer properties	improve intracellular uptake and selective cytotoxicity in cancer cells	[65]
Bioavailability Enhancement of Paclitaxel via a Novel Oral Drug Delivery System: Paclitaxel-Loaded Glycyrrhizic Acid Micelles	Paclitaxel (PTX)	Polymeric nanoparticle	Micelles	Breast cancer, Refractory human ovarian, Non-small-cell lung carcinoma	promising carrier for the oral delivery of PTX	[66]
Berberine encapsulated phenylboronic acid-conjugated pullulan nanoparticles: Synthesis, characterization and anticancer activity validated in A431 skin cancer cells and 3D spheroids	Berberine	Phenylboronic acid-conjugated pullulan-stearic acid nanoparticles	Self-assembly of amphiphilic pullulan conjugate with berberine	Skin cancer therapy	Effective drug delivery system for skin cancer therapy.	[67]
Enhancing apoptosis-mediated anticancer activity of evodiamine through protein-based nanoparticles in breast cancer cells	Evodiamine	bovine serum albumin (BSA) nanoparticles	Desolvation	Anticancer activity	Improved cytotoxicity, positioning ENPs as a propitious strategy for advancing breast cancer treatment	[68]
Synthesis, characterization, <i>in-silico</i> and <i>in-vitro</i> anticancer studies of Plumbagin encapsulated albumin nanoparticles for breast cancer treatment	Plumbagin	Bovine serum albumin (BSA)-based nanoparticles	Desolvation	Anticancer studies	Improving the therapeutic efficacy of the hydrophobic drug PLB using biocompatible albumin	[69]
Folate conjugated albumin as a targeted nanocarrier for the delivery of fisetin: <i>in silico</i> and <i>in vitro</i> biological studies	Fisetin	Folic acidconjugated bovine serum albumin nanoparticles	Selfassembled	Cancer therapy	FFNPs as a promising targeted drug delivery nanocarrier for effective FST delivery in cancer therapy.	[69]

permeability, and rapid metabolism of many plant-derived compounds, other critical drivers have emerged. One major impetus is the need for targeted delivery to enhance tissue specificity and reduce off-target effects, especially for compounds like curcumin, quercetin, and resveratrol, which exhibit broad but nonselective bioactivity. Nanoparticles can be functionalized with targeting ligands (e.g., folate, peptides, antibodies) to exploit receptor-mediated uptake pathways in diseased cells such as tumors or inflamed tissues [15]. Additionally, nanoparticles enable protection of labile phytochemicals from degradation due to pH, enzymes, and oxidative stress, thereby preserving their bioactivity until reaching the target site [70,71]. Controlled or sustained release profiles are also crucial, particularly for chronic diseases, allowing for reduced dosing frequency and improved patient compliance. Furthermore, the ability to co-deliver multiple therapeutic agents (e.g., phytochemicals with chemotherapeutics or synergistic natural compounds) in a single nanoparticle

enhances efficacy and may overcome drug resistance [72]. The development of stimuli-responsive nanocarriers, which release their payload in response to pH, redox potential, or enzymatic activity, further exemplifies the precision sought in modern phytochemical delivery strategies. Collectively, these drivers represent a transformative shift in phytochemical research from basic supplementation to targeted, controlled, and clinically relevant nanomedicine platforms. NPs help increase the effectiveness of phytochemicals by gradually releasing the encapsulated compounds in a controlled manner. This ensures that the phytochemicals are delivered slowly over time instead of all at once, maintaining optimal therapeutic levels and reducing potential side effects. Additionally, nanoparticles may react specifically to certain physiological cues at the intended location, ensuring precise release when needed, thus improving therapeutic efficacy and minimizing the risk of overdose or toxicity. The advantages are listed below;

6.1. Cancer therapy

In cancer therapy, encapsulation of phytochemicals such as curcumin, quercetin, and resveratrol in polymeric or lipid-based nanoparticles has shown improved cellular uptake, sustained release, and enhanced cytotoxicity against various cancer cell lines, while minimizing systemic toxicity. For instance, curcumin-loaded PLGA nanoparticles have demonstrated superior anti-proliferative effects in breast and colorectal cancer models compared to free curcumin [73,74]. Treatment precision can be significantly improved by using nanoparticles that are specifically designed for targeted distribution and controlled release. Researchers can precisely bind to receptors on particular cells or tissues by adding targeting ligands on the surface of nanoparticles [75]. By precisely delivering phytochemicals to the desired locations, this focused technique maximizes their therapeutic benefits and reduces any unintended effects on healthy tissues. A notable example involves the use of Herceptin-functionalized nanoparticles for breast cancer treatment. Herceptin, an antibody that targets the HER2 receptor, was conjugated to nanoparticles that encapsulate curcumin, an anticancer phytochemical. This modification significantly improved the accumulation of nanoparticles in HER2-positive cancer cells, resulting in increased apoptosis and reduced tumor growth in preclinical models [76].

Moreover, peptides such as RGD (arginine-glycine-aspartate) have been employed to functionalize nanoparticles to target integrin receptors, which are overexpressed in angiogenic blood vessels associated with tumors. This strategy has substantially improved the delivery of encapsulated phytochemicals, such as resveratrol, to tumor sites, leading to improved antiangiogenic and anticancer effects [77]. Anticancer phytochemicals can be delivered directly to tumor areas via nanoparticles that are designed with antibodies or peptides that identify particular markers on cancer cells. This precision not only enhances treatment outcomes but also reduces overall treatment toxicity, safeguarding healthy cells from unnecessary damage [78].

Another crucial benefit of nanoparticle encapsulation is the enhancement of bioavailability. Many phytochemicals have poor solubility, which limits their ability to be absorbed into the bloodstream. By making these substances more soluble and promoting greater absorption, especially in the gastrointestinal system, nanoparticles can assist in overcoming this problem [79]. Additionally, the encapsulation process shields phytochemicals from degradation, which might occur because of the harsh conditions in the body. This protection allows a greater amount of the active compound to reach the bloodstream and ultimately the target site, hence increasing the treatment efficacy [80].

NPs increase the stability of phytochemicals, which are usually susceptible to deterioration caused by light, heat, and oxygen in the environment. By encapsulating phytochemicals, nanoparticles form a protective barrier that guards against these harmful conditions. This greatly extends the shelf-life of phytochemicals, ensuring that they remain stable and effective for their intended duration [10]. Additionally, nanoparticle treatment has demonstrated significant promise. One study produced a hydrogel nanocomposite to transport quercetin, a phytochemical with

anticancer effects, using chitosan, halloysite, and graphitic-carbon nitride. The excellent encapsulation efficiency and loading capacity of the nanocomposite resulted in increased apoptotic activity in MCF-7 breast cancer cells [81]. Long-lasting therapeutic effects are facilitated by the sustained release of quercetin from the nanoparticles, which decreases the frequency of dosage while increasing the overall efficacy of treatment. The application of nanoparticle encapsulation is not limited to pharmaceuticals; it extends to food and healthcare products as well. For example, the stability and bioavailability of bioactive substances in functional foods have been enhanced by the introduction of nanoparticles. The potent antioxidant epigallocatechin gallate (EGCG) from green tea has been encapsulated in potato starch nanoparticles. When food is processed at high temperatures, nanoencapsulation improves the stability of EGCG, maintaining its nutritional value [82]. This application shows how nanoparticles can ensure that bioactive compounds in foods remain potent, even under harsh processing conditions.

6.2. Wound healing

In wound healing, the encapsulation of phytochemicals with anti-inflammatory and antioxidant properties has been proven to accelerate the healing process and improve tissue regeneration. A notable example is nanoencapsulated curcumin, which has been integrated into wound dressings to accelerate healing and decrease inflammation. When delivered via nanoparticles, the natural therapeutic properties of curcumin are better preserved and more effectively utilized at the wound site [83]. Studies by [84], have demonstrated that nanoparticles significantly enhance the direct application of healing ingredients to the site, improving therapeutic results and hastening healing. In wound healing, nanoparticles carrying flavonoids, tannins, or alkaloids can accelerate tissue regeneration through enhanced antioxidant and anti-inflammatory activity [85]. Chitosan-based NPs loaded with *Centella asiatica* extract have been shown to promote collagen deposition and re-epithelialization in diabetic wounds [86].

6.3. Other pharmacological activities

As antioxidants, phytochemical-loaded NPs help scavenge free radicals more efficiently by ensuring controlled release and deeper tissue penetration, which is particularly beneficial in neurodegenerative diseases and oxidative stress-related conditions. Moreover, in antimicrobial applications, silver or zinc oxide nanoparticles functionalized with plant-derived compounds such as eugenol or catechins exhibit synergistic antimicrobial activity against resistant bacterial strains [87]. Additional emerging uses include anti-inflammatory, anti-diabetic, neuroprotective, and cardioprotective applications, making phytochemical-based nanodelivery systems a versatile tool in precision therapeutics.

NPs have also been employed in the delivery of anthocyanins, a group of phytochemicals known for their antioxidant and anticancer properties. For example, carboxymethyl chitosan (CMC) nanoparticles were utilized to encapsulate C3G, a particular type of anthocyanin. When these nanoparticles were tested in lung cancer cell lines, they showed minimal

cytotoxicity and greatly increased the antioxidant capacity of the anthocyanins. This approach shows great potential for targeted delivery to lung cancer tissues, providing a more effective and less toxic treatment option [88]. The enhanced bioavailability and therapeutic efficacy of anthocyanins through nanoencapsulation open new possibilities for treating lung cancer and other diseases where antioxidants play a vital role. The encapsulation of nanoparticles has become a potent technique for augmenting the medicinal properties of phytochemicals in diverse domains, ranging from the development of food and medical products to wound healing and cancer treatment. By improving their stability, bioavailability, and targeted delivery, nanoparticles are unlocking new potential for these natural compounds in modern medicine and beyond.

In addition, curcumin-loaded liposomes and solid lipid nanoparticles have been evaluated in clinical trials for cancer and inflammatory diseases, showing improved bioavailability and therapeutic efficacy compared to unformulated curcumin [89]. Quercetin-loaded PLGA nanoparticles have demonstrated promising results in preclinical studies targeting cardiovascular and metabolic disorders and are being optimized for human application due to their controlled release and reduced cytotoxicity [90]. Additionally, resveratrol-loaded nanocarriers, such as polymeric micelles and nanostructured lipid carriers (NLCs), are in advanced preclinical and early-phase clinical trials for neurodegenerative and cardiovascular conditions [91]. Furthermore, berberine nanoformulations, including chitosan and albumin-based nanoparticles, are being explored for their enhanced glucose-lowering and lipid-regulating effects in type 2 diabetes management.

Excipients are critical to the success of nanocarrier systems, serving not only as structural or stabilizing agents but also as key enhancers of pharmacokinetic and therapeutic profiles. For example, biodegradable polymers such as poly (lactic-co-glycolic acid) (PLGA) and polycaprolactone (PCL) are commonly used for their biocompatibility and controlled release properties, helping to extend the circulation time of encapsulated phytochemicals like curcumin and quercetin [92]. Lipids such as phosphatidylcholine, cholesterol, and glyceryl monostearate play structural roles in forming liposomes and solid lipid nanoparticles, improving encapsulation efficiency and protecting labile compounds from degradation.

In addition, surfactants like Tween 80, poloxamers, and lecithin are employed to reduce interfacial tension and stabilize nanoparticles during formulation and storage. They can also enhance permeability across biological membranes. Some excipients, such as chitosan and alginate, provide mucoadhesive properties or enable pH-sensitive release, ideal for targeting specific regions of the gastrointestinal tract or tumor microenvironments [56]. Moreover, targeting ligands like folic acid or transferrin are sometimes conjugated to the nanoparticle surface to improve site-specific delivery. By elaborating on these functional roles, the revised manuscript now offers a clearer understanding of how excipients are strategically selected to optimize stability, bioavailability, targeting, and therapeutic action of phytochemicals in nanoparticle-based systems.

7. Relevant patents related to nanoparticle-encapsulated phytochemicals

There are key patents related to nanoparticle-encapsulated phytochemicals, which underscores the field's translational and commercial potential. Several patents in recent years have focused on improving the stability, bioavailability, and therapeutic targeting of phytochemicals using nanocarrier systems. For example, US Patent No. 10,493,056 B2 discloses curcumin-loaded nanostructured lipid carriers designed for enhanced absorption and sustained release in cancer therapy applications. Similarly, a resveratrol-loaded nanoparticle formulation using biocompatible polymers aimed at treating inflammatory and neurodegenerative disorders. Another example, covers a berberine-encapsulated chitosan nanoparticle system for improved antidiabetic efficacy through oral delivery. These patents highlight not only technical innovation but also growing global interest in commercializing nanophytomedicine platforms for chronic diseases such as cancer, diabetes, and neuroinflammation [15,91].

8. Current and future applications of nanoparticle encapsulation

Nanoparticle encapsulation has revolutionized various fields, providing innovative solutions to challenges in food technology, healthcare, cosmetics, and environmental monitoring. Increasing the functionality, stability, and bioavailability of drugs encapsulated with nanoparticles has created new opportunities for enhancing product performance and medicinal results [93].

In food technology, significant strides have been made in the development of nanoparticles by improving the stability and functional properties of food ingredients. A key example is the encapsulation of epigallocatechin gallate (EGCG), a strong antioxidant presents in green tea, within potato starch nanoparticles. This process enhances the thermal stability of EGCG, making it suitable for use in functional food products such as cookies, bread, and cakes without losing its beneficial properties during high-temperature processing [94]. Additionally, nanoparticle technology can improve the nutritional profile of food by protecting sensitive nutrients such as vitamins and minerals from degradation during processing, storage, and consumption. This ensures that consumers receive the full benefits of these bioactive compounds, resulting in more nutritious food products [95]. Furthermore, by serving as a barrier against oxygen, moisture, and other elements that cause spoil, nanoparticles have the potential to increase the shelf-life of food products. By adding nanoparticles to food packaging or directly into a product, producers can extend the shelf life of the product, reduce waste, and increase food safety [96].

In healthcare, nanoparticle encapsulation has a significant impact, especially in the area of cancer treatment. Researchers have developed liposomal micelles containing bilberry anthocyanins, which have high bioavailability and stability in the gastrointestinal tract. The greater cytotoxic effects of these encapsulated anthocyanins on cancer cells present a promising avenue for cancer treatment in the future [97].

NPs increase the effectiveness of treatments while reducing negative effects by improving the targeted delivery of therapeutic substances to malignant areas. Additionally, by lowering the frequency of dosage, continuous and controlled drug release made possible by nanoparticles can improve patient compliance. This approach is not limited to cancer therapy but extends to other areas of medicine, where precise and efficient drug delivery is critical for effective treatment outcomes [98].

The cosmetics industry is also benefiting from advancements in nanoparticle technology, particularly in enhancing the stability and efficacy of skin-care products. Lipid-based nanoparticles facilitate improved absorption and more obvious cosmetic effects by delivering active substances deep into the skin [99]. These nanoparticles also stabilize sensitive ingredients, preventing them from breaking down and maintaining their potency over time. In addition to improving the performance of skin-care products, lipid nanoparticles offer skin benefits such as increased hydration and protection. By forming a barrier on the skin, they help retain moisture and shield the skin from environmental damage, making them valuable in developing advanced skin-care formulations that offer long-lasting effects [100].

NPs also play a crucial role in environmental monitoring and control. The ability of these sensors to detect pollutants and pathogens at low concentrations makes them ideal for use in advanced sensors that provide early warnings of contamination in water or air [101]. These nanoparticle-based sensors are highly sensitive and selective, offering a powerful tool for safeguarding public health. Moreover, nanoparticles have the potential to contribute to water and air purification efforts by capturing harmful materials such as viruses, organic contaminants, and heavy metals. NPs are an effective way to eliminate pollutants from water, but in air purification systems, they help improve air quality by trapping airborne toxins [102].

In summary, nanoparticle encapsulation technology is pushing the boundaries of innovation across multiple industries. The quality and efficacy of products in the food, health-care, cosmetics, and environmental sectors are improved by the use of nanoparticles through the enhancement of the stability, bioavailability, and delivery of key chemicals. It is anticipated that as nanoparticle technology research advances, its applications will grow even more, presenting fascinating new chances for creativity and problem solving in the years to come [44].

9. Challenges and solutions in nanoparticle encapsulation

Nanoparticle encapsulation has emerged as a revolutionary technique with vast potential across various industries, especially in drug delivery, food technology, cosmetics, and environmental monitoring [103]. However, several challenges remain, particularly concerning controlled release, material and production costs, stability, shelf-life, and safety. Overcoming these hurdles is critical for realizing the full potential of nanoparticles in therapeutic applications [104]. Achieving controlled release is a prominent challenge in

nanoparticle encapsulation, particularly in drug delivery. The ideal scenario involves nanoparticles releasing their therapeutic payload only at a target site or upon exposure to specific stimuli such as pH, temperature, or enzymes. Premature release during transit can severely compromise the therapeutic effect, especially for sensitive compounds such as phytochemicals or anticancer drugs, which may degrade before reaching the intended site [105]. A key example of overcoming this challenge is the development of liposomal nanoparticles for anticancer therapy. Liposomes, with their lipid bilayers mimicking cell membranes, are engineered to encapsulate both hydrophobic and hydrophilic drugs. These nanoparticles can be designed to release their cargo only at specific locations, such as tumor sites, where an acidic pH or specific enzymes trigger the breakdown of the nanoparticle [106]. The liposomal formulation of doxorubicin, known as Doxil, is an example. It releases the chemical drug in response to the acidic environment in cancer cells, minimizing its toxicity to healthy tissues and enhancing the drug's efficacy [107]. In addition to liposomal nanoparticles, polymeric nanoparticles, such as poly (lactic-co-glycolic acid) (PLGA), have shown promise for controlled drug release.

PLGA nanoparticles have been successfully used to encapsulate anti-inflammatory drugs, releasing them in a sustained manner over extended periods, which helps prevent premature degradation during delivery [108]. The production of nanoparticles is often costly due to the high-value materials needed, including gold, silver, and specialized polymers, in addition to the complex machinery needed for their synthesis. This poses a significant barrier to the widespread use of nanoparticles, especially in consumer products such as food and cosmetics. To mitigate these costs, researchers have turned to more sustainable and cost-effective materials. Natural polymers such as chitosan, alginate, and starch are being used to create nanoparticles that are not only more affordable but also biocompatible. For example, the successful encapsulation of curcumin in starch-based nanoparticles provides a less expensive and more eco-friendly alternative to synthetic polymers.

Green chemistry techniques, such as the use of plant extracts to reduce metal salts, also enable the cost-effective synthesis of metal nanoparticles, making them viable for food and cosmetic applications [109]. Further solutions to cost issues lie in scaling up nanoparticle production via automated, efficient manufacturing techniques. For example, microfluidic platforms have been developed to produce nanoparticles that are more controlled and reproducible at larger scales, reducing costs and improving the consistency of nanoparticle formulations [110].

Once nanoparticles are produced, maintaining their stability is crucial to ensure their long-term effectiveness [111]. Environmental factors such as temperature, pH, and light exposure can degrade nanoparticles, altering their structure and diminishing their performance [112]. This issue is particularly critical in pharmaceuticals, where the stability of drug formulations is essential for maintaining therapeutic efficacy and safety [113]. To address this, researchers have developed stabilizing agents and protective coatings that increase the stability of nanoparticles. For example, polyethylene glycol

(PEG) is often added to nanoparticles to prevent aggregation and prolong the circulation time in the body. The PEGylation of nanoparticles, a process of attaching PEG molecules to their surfaces, is a common strategy to improve both their stability and biocompatibility. A notable example is Abraxane, a nanoparticle formulation of paclitaxel, which is encapsulated in albumin nanoparticles coated with PEG to increase its stability and improve drug delivery efficiency [114]. Additionally, thermoresponsive nanoparticles, whose structure changes in response to temperature fluctuations, have been developed to maintain stability during storage and transport, further increasing their shelf-life [115].

One of the most significant challenges facing nanoparticle-based products is ensuring their safety. Owing to their small size, nanoparticles have unique properties that allow them to interact with biological systems in ways that larger particles cannot. While these properties make nanoparticles highly effective for targeted drug delivery and enhancing bioavailability, they also raise concerns about potential toxicity and long-term health effects. Addressing these safety concerns requires extensive toxicological research to assess the potential risks associated with nanoparticle exposure. In vivo studies are essential for understanding how nanoparticles interact with cells, tissues, and organs and whether they may accumulate in the body and cause adverse effects. Furthermore, bio-distribution and pharmacokinetics studies are critical for determining how nanoparticles are absorbed, distributed, metabolized, and excreted by the body [116]. To mitigate these risks, interest in the design of biocompatible and biodegradable nanoparticles that degrade safely in the body is increasing [117]. For example, polymeric nanoparticles can breakdown into nontoxic byproducts, making them safer alternatives to metal-based nanoparticles. To address safety concerns, regulatory agencies such as the Food and Drug Administration (FDA) and the European Food Safety Authority (EFSA) are developing guidelines for the use of nanoparticles in food, medicine, and cosmetics. For example, the FDA requires comprehensive toxicological assessments of nanoparticle drug delivery systems before they can be approved for clinical use. These guidelines are crucial for ensuring the safety of nanoparticle-based products before they reach consumers [118].

10. Future prospects and innovations

The development of nanoparticle technology is on track to make significant progress, especially in the customization of nanoparticle formulations to meet specific requirements across different sectors. Tailored nanoparticle formulations are expected to be a key focus in research and development, as the ability to customize nanoparticles to optimize their size, surface characteristics, and release profiles can greatly increase their efficacy in specialized uses [119]. In the field of personalized medicine, it is possible to create nanoparticles to deliver medication in a way that best suits each patient's individual needs, such as by targeting specific disease indicators or adjusting release rates on the basis of metabolic functions [105]. Similarly, customized nanoparticle

formulations could benefit functional foods by improving the absorption of nutrients, ensuring that consumers receive maximum nutritional advantages. Furthermore, the cosmetics industry might witness the emergence of more advanced cosmetic products that utilize nanoparticles customized for different skin types, environmental conditions, or targeted treatments, leading to more accurate and efficient skincare solutions [120].

When combined with cutting-edge technologies such as advanced manufacturing and artificial intelligence (AI), nanoparticle technology is promising. By using algorithms to predict and improve the characteristics of nanoparticle formulations meant for certain applications, artificial intelligence (AI) has the potential to revolutionize the design of nanoparticles. This data-centered approach has the potential to simplify the process of creating nanoparticles that fulfill strict performance standards, thereby accelerating innovation and minimizing trial-and-error in formulation procedures [121]. Furthermore, advanced manufacturing methods, including 3D printing and nanofabrication, could increase the efficiency of nanoparticle production, decrease expenses and make nanoparticle-based products more widely available. By employing the capabilities of AI and state-of-the-art manufacturing, nanoparticle technology can continue to develop, resulting in more intelligent and effective solutions across various industries [122].

However, the ongoing expansion of this technology will require ongoing advancements in regulation and safety to guarantee the safety of nanoparticles for human use and the environment. With the increasing integration of nanoparticles into various consumer goods, such as food, cosmetics, and pharmaceuticals, the establishment of strong regulatory frameworks is imperative [123]. These frameworks not only address nanoparticle toxicity but also consider their long-term health effects and environmental impact. Adhering to safety standards will be crucial for the successful introduction of nanoparticle-based innovations. Regulatory authorities must anticipate technological advancements by developing thorough safety protocols and conducting rigorous testing to minimize potential hazards [124]. The ongoing development of nanoparticle technology will drive its full potential through advancements in customization, integration with emerging technologies, and regulatory frameworks, ultimately fostering groundbreaking innovations in healthcare, food, cosmetics, and environmental fields.

11. Conclusion

In summary, rapid advancements in nanoparticle technology could have a large impact on a number of areas, such as environmental monitoring, food technology, cosmetics, healthcare, and cosmetics. As researchers continue to investigate and enhance the capabilities of nanoparticles, the customization of formulations will be key in improving their effectiveness in meeting specific requirements. Adapting nanoparticles to optimize their size, surface characteristics, and release patterns offers the promise of substantial advancements in personalized medicine, functional foods, and advanced cosmetic products.

The combination of nanoparticle technology with emerging technologies such as artificial intelligence and advanced manufacturing methods holds great potential for further progress. AI-driven design and optimization can expedite innovation, whereas advanced manufacturing techniques can increase production efficiency and cost-effectiveness. Together, these advancements could result in more intelligent, more efficient solutions and broaden the scope of nanoparticle technology applications.

The advancement of technology requires careful consideration of the associated regulatory and safety challenges. It is crucial to establish strong regulatory frameworks and safety standards to guarantee the environment and people's safety when items containing nanoparticles are used. Thorough safety evaluations and strict adherence to guidelines are vital for supporting the successful adoption and commercialization of these innovations.

In summary, the future of nanoparticle technology looks promising, offering the potential to transform industries and enhance people's lives. Continuous research, strategic integration with emerging technologies, and dedication to safety and regulatory excellence are essential for unleashing the full potential of nanoparticles and driving substantial progress in various fields.

Acknowledgments

Dr. Oluwafemi Ojo has been co-funded by the European Union's Horizon Europe Framework Programme for Research and Innovation 2021–2027 under the Marie Skłodowska-Curie action grant agreement No. 101126611.

Author contributions

OAO.: Conceptualization, Supervision, Writing- Original draft, Writing-review and editing; **S.O., D.E.R., E.H.E.**: Visualization, Writing- Original draft, Formal analysis, Data curation; **A.B.O., O.A.A.**: Writing- review and editing; **A.B.O.**: Validation, Project administration, Resources.

Disclosure statement

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

Reviewer disclosures

Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

Funding

This paper was not funded.

References

Papers of special note have been highlighted as either of interest (*) or of considerable interest () to readers.**

- Murthy SK. Nanoparticles in modern medicine: state of the art and future challenges. *Int J Nanomed*. 2007;2(2):129–141.
- Sahoo SK, Labhasetwar V. Nanoparticle-based drug delivery systems. *J Nanosci Nanotechnol*. 2003;3(4):301–316.
- Huang Y, Di X, Burton-Freeman BM, et al. Chemical changes of bioactive phytochemicals during thermal processing. *Ref Mod Food Sci*. 2016. doi: 10.1016/B978-0-08-100596-5.03055-9
- Zou Y, Qian Y, Rong X, et al. Encapsulation of quercetin in biopolymer-coated zein nanoparticles: formation, stability, antioxidant capacity, and bioaccessibility. *Food Hydrocolloids*. 2021;120:106980. doi: 10.1016/j.foodhyd.2021.106980
- Lopez FR, Patel JA, Gupta M. Challenges in the delivery of poorly soluble drugs: formulation strategies and tools. *Ther Deliv*. 2016;7(1):33–48.
- Doroudian M, Zanganeh S, Abbasgholinejad E, et al. Nanomedicine in lung cancer immunotherapy. *Front Bioeng Biotechnol*. 2023;11:1144653. doi: 10.3389/fbioe.2023.1144653
- Domb AJ, Sharifzadeh G, Nahum V, et al. Safety evaluation of nanotechnology products. *Pharm*. 2021;13(10):1615. doi: 10.3390/pharmaceutics13101615
- Natalia Ž, Świeca M, Pawłowska A, et al. Microencapsulation of blueberry (*Vaccinium myrtillus* L.) extracts via ionotropic gelation: in vitro assessment of bioavailability of phenolic compounds and their activity against colon cancer cells. *Appl Sci*. 2024;4(17):7842.
- Mozafari MR, Mazaheri E, Dormiani K. Simple equations pertaining to the particle number and surface area of metallic, polymeric, lipidic, and vesicular nanocarriers. *Sci Pharm*. 2021;89(2):15. doi: 10.3390/scipharm89020015
- Wang S, Su R, Nie S, et al. Application of nanotechnology in improving bioavailability and bioactivity of diet-derived phytochemicals. *J Nutr Biochem*. 2014;25(4):363–376. doi: 10.1016/j.jnutbio.2013.10.002
- Jha AK, Sit N. Encapsulation of bioactive compounds extracted from haritaki pulp (*Terminalia chebula* Retzius): characterization of physical, thermal, and morphological properties. *Sustain Food Technol*. 2024;2(2):362–372. doi: 10.1039/D3FB00131H
- Alu'datt M, Alrosan M, Gammoh S, et al. Encapsulation-based technologies for bioactive compounds and their application in the food industry: a roadmap for food-derived functional and health-promoting ingredients. *Food Biosci*. 2022;101:101971.
- Liu Y, Zhang T, Liang J, et al. Nanoparticle encapsulation: enhancing the bioavailability and therapeutic efficacy of phytochemicals. *J Nanobiotechnol*. 2022;20(1):188.
- Goktas Z, Zu Y, Abbasi M, et al. Recent advances in nanoencapsulation of phytochemicals to combat obesity and its comorbidities. *J Agric Food Chem*. 2020;68(31):8119–8131. doi: 10.1021/acs.jafc.0c00131
- Ahmad R, Srivastava S, Ghosh S, et al. Phytochemical delivery through nanocarriers: a review. *Colloids And Surfaces B, Biointerfaces*. 2021;197:111389. doi: 10.1016/j.colsurfb.2020.111389
- Zhou F, Peterson T, Fan Z, et al. The commonly used stabilizers for phytochemical-based nanoparticles: stabilization effects, mechanisms, and applications. *Nutri Full*. 2023;15(18):3881. doi: 10.3390/nu15183881
- Mehta M, Bui TA, Yang X, et al. Lipid-based nanoparticles for drug/gene delivery: an overview of the production techniques and difficulties encountered in their industrial development. *ACS Mater Au*. 2023;3(6):569–733.
- Subroto E, Andoyo R, Indarto R. Solid lipid nanoparticles: review of the current research on encapsulation and delivery systems for active and antioxidant compounds. *Antiox*. 2023;12(3):633. doi: 10.3390/antiox12030633
- Shakeri A, Sahebkar A. Nanotechnology: a successful approach to improve oral bioavailability of phytochemicals. *Curr Drug Disc Technol*. 2016;10(1):4–6.
- Alshamrani M, Khan MK, Khan BA, et al. Technologies for solubility, dissolution and permeation enhancement of natural compounds. *Pharmaceutics*. 2022;5(6):653.
- Gera M, Sharma N, Ghosh M, et al. Nanoformulations of curcumin: an emerging paradigm for improved remedial application. *Oncotarget*. 2017;8(39):66680–66698. doi: 10.18632/oncotarget.19164
- Gagliardi A, Giuliano E, Venkateswararao E, et al. Biodegradable polymeric nanoparticles for drug delivery to solid tumors. *Front Pharmacol*. 2021;12:601626. doi: 10.3389/fphar.2021.601626

23. Yao Y, Zhou Y, Liu L, et al. Nanoparticle-based drug delivery in cancer therapy and its role in overcoming drug resistance. *Front Mol Biosci.* 2020;7:193. doi: [10.3389/fmolb.2020.00193](https://doi.org/10.3389/fmolb.2020.00193)
24. Vuppu S, Mishra T, Mishra S, et al. Phytochemical-loaded nanoparticles in COVID-19 management. *NRFHH.* 2024;4(1):51–72. doi: [10.53365/nrfhh/176325](https://doi.org/10.53365/nrfhh/176325)
25. Xuan L, Ju Z, Skonieczna M, et al. Nanoparticles-induced potential toxicity on human health: applications, toxicity mechanisms, and evaluation models. *MedComm.* 2023;4(4):e327. doi: [10.1002/mco.327](https://doi.org/10.1002/mco.327)
- **This article is of considerable interest because it provides insight into the applications toxicity mechanisms and evaluation models involved in nanoparticles induction in human health.**
26. Buchman JT, Hudson-Smith NV, Landy KM, et al. Understanding nanoparticle toxicity mechanisms to inform redesign strategies to reduce environmental impact. *Acc Chem Res.* 2019;52(6):1632–1642. doi: [10.1021/acs.accounts.9b00053](https://doi.org/10.1021/acs.accounts.9b00053)
27. Nakamura A. The impact of nanoparticles on cellular oxidative stress and its mechanisms. *J Nanomed Biotherapeutic Discov.* 2024;14:275.
28. Missaoui WN, Arnold RD, Cummings BS. Toxicological status of nanoparticles: what we know and what we don't know. *Chem Biol Interact.* 2018;295:1–12.
29. Kumar M, Kulkarni P, Liu S, et al. Nanoparticle biodistribution coefficients: a quantitative approach for understanding the tissue distribution of nanoparticles. *Adv Drug Deliv Rev.* 2023;194:114708. doi: [10.1016/j.addr.2023.114708](https://doi.org/10.1016/j.addr.2023.114708)
30. Maeda H, Wu J, Sawa T, et al. Tumor vascular permeability and the EPR effect in macromolecular therapeutics: a review. *J Control Release.* 2000;65(1–2):271–284. doi: [10.1016/S0168-3659\(99\)00248-5](https://doi.org/10.1016/S0168-3659(99)00248-5)
31. Danhier F, Feron O, Préat V. To exploit the tumor microenvironment: passive and active tumor targeting of nanocarriers for anti-cancer drug delivery. *J Control Release.* 2010;148(2):135–146. doi: [10.1016/j.jconrel.2010.08.027](https://doi.org/10.1016/j.jconrel.2010.08.027)
32. Solanki R, Jodha B, Prabina KE, et al. Recent advances in phytochemical based nano-drug delivery systems to combat breast cancer: a review. *J Drug Deliv Sci Technol.* 2022;77:103832. doi: [10.1016/j.jddst.2022.103832](https://doi.org/10.1016/j.jddst.2022.103832)
33. Pande S. Liposomes for drug delivery: review of vesicular composition, factors affecting drug release and drug loading in liposomes. *Artif Cells, Nanomed Biotechnol.* 2023;51(1):428–440. doi: [10.1080/21691401.2023.2247036](https://doi.org/10.1080/21691401.2023.2247036)
34. Singh M, Devi S, Rana VS, et al. Delivery of phytochemicals by liposome cargos: recent progress, challenges, and opportunities. *J Microencapsul.* 2019;36(3):1–55.
35. Chavda VP, Vihol D, Mehta B, et al. Phytochemical-loaded liposomes for anticancer therapy: an updated review. *Nanomed.* 2022;17(8):547–568. doi: [10.2217/nnm-2021-0463](https://doi.org/10.2217/nnm-2021-0463)
36. Mishra V, Bansal KK, Verma A, et al. Solid lipid nanoparticles: emerging colloidal nano drug delivery systems. *Pharmaceutics.* 2018;10(4):191. doi: [10.3390/pharmaceutics10040191](https://doi.org/10.3390/pharmaceutics10040191)
37. Munir M, Zaman M, Waqar MA, et al. Solid lipid nanoparticles: a versatile approach for controlled release and targeted drug delivery. *J Liposome Res.* 2023;34(2):335–348. doi: [10.1080/08982104.2023.2268711](https://doi.org/10.1080/08982104.2023.2268711)
38. Fathi F, Machado TOX, de AC, et al. Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) for the delivery of bioactives sourced from plants: part II - applications and preclinical advancements. *Exp Opin Drug Deliv.* 2024;21(10):1491–1499.
- **This article is of interest because it provides extensive explanations of the delivery of bioactive sourced from plants through solid lipid nanoparticles and nanostructured lipid carriers, their applications as well as preclinical developments.**
39. Eltaib L. Polymeric nanoparticles in targeted drug delivery: unveiling the impact of polymer characterization and fabrication. *Polymers.* 2025;17(7):833. doi: [10.3390/polym17070833](https://doi.org/10.3390/polym17070833)
- **This article is important because it discusses the impact of polymeric nanoparticles, characterization and fabrication impact in targeted drug delivery.**
40. Nie H, Lee LY, Tong H, et al. Plga/chitosan composites from a combination of spray drying and supercritical fluid foaming techniques: new carriers for DNA delivery. *J Control Release.* 2008;129(3):207–214. doi: [10.1016/j.jconrel.2008.04.018](https://doi.org/10.1016/j.jconrel.2008.04.018)
41. Das A, Adhikari S, Deka D, et al. An updated review on the role of nanoformulated phytochemicals in colorectal cancer. *Medicina (B Aires).* 2023;59(4):685. doi: [10.3390/medicina59040685](https://doi.org/10.3390/medicina59040685)
42. Herdiana Y, Husni P, Nurhasanah S, et al. Chitosan-based nano systems for natural antioxidants in breast cancer therapy. *Polymers.* 2023;15(13):2953. doi: [10.3390/polym15132953](https://doi.org/10.3390/polym15132953)
43. Liang J, Yan H, Puligundla P, et al. Applications of chitosan nanoparticles to enhance absorption and bioavailability of tea polyphenols: a review. *Food Hydrocolloids.* 2017;69:286–292. doi: [10.1016/j.foodhyd.2017.01.041](https://doi.org/10.1016/j.foodhyd.2017.01.041)
44. Singh AK, Pal P, Pandey B, et al. Development of “smart foods” for health by nanoencapsulation: novel technologies and challenges. *Food Chem X.* 2023;20:100910. doi: [10.1016/j.fochx.2023.100910](https://doi.org/10.1016/j.fochx.2023.100910)
45. Bhilkar PR, Bodhne AS, Yerpude ST, et al. Phyto-derived metal nanoparticles: prominent tool for biomedical applications. *OpenNano.* 2023;14:100192. doi: [10.1016/j.onano.2023.100192](https://doi.org/10.1016/j.onano.2023.100192)
46. Vines JB, Yoon JH, Ryu NE, et al. Gold nanoparticles for photothermal cancer therapy. *Front Chem.* 2019;7:1–16. doi: [10.3389/fchem.2019.00167](https://doi.org/10.3389/fchem.2019.00167)
47. Almatroudi A. Silver nanoparticles: synthesis, characterization and biomedical applications. *Open Life Sci.* 2020;15(1):819–839. doi: [10.1515/biol-2020-0094](https://doi.org/10.1515/biol-2020-0094)
48. Dürr S, Janko C, Lye S, et al. Magnetic nanoparticles for cancer therapy. *Nanotechnol Rev.* 2013;2(4):395–409. doi: [10.1515/ntrev-2013-0011](https://doi.org/10.1515/ntrev-2013-0011)
49. Chandrakala V, Aruna V, Angajala G. Review on metal nanoparticles as nanocarriers: current challenges and perspectives in drug delivery systems. *Emergent Mater.* 2022;4(5):1593–1615. doi: [10.1007/s42247-021-00335-x](https://doi.org/10.1007/s42247-021-00335-x)
50. Ferreira K, Valle A, Paes C, et al. Nanostructured lipid carriers for the formulation of topical anti-inflammatory nanomedicines based on natural substances. *Pharmaceutics.* 2021;13(9):1454. doi: [10.3390/pharmaceutics13091454](https://doi.org/10.3390/pharmaceutics13091454)
51. Bozzuto G, Molinari A. Liposomes as nanomedical devices. *Int J Nanomed.* 2015;10:975–999. doi: [10.2147/IJN.S68861](https://doi.org/10.2147/IJN.S68861)
52. Makadia HK, Siegel SJ. Poly lactic-co-glycolic acid (PLGA) as biodegradable controlled drug delivery carrier. *Polymers.* 2011;3(3):1377–1397. doi: [10.3390/polym3031377](https://doi.org/10.3390/polym3031377)
53. Hussain A, Singh S, Sharma D, et al. Elastic liposomes as novel carriers: recent advances in drug delivery. *Int J Nanomed.* 2017;12:5087–5108. doi: [10.2147/IJN.S138267](https://doi.org/10.2147/IJN.S138267)
54. Waheed I, Ali A, Tabassum H, et al. Lipid-based nanoparticles as drug delivery carriers for cancer therapy. *Front Oncol.* 2024;14:1296091. doi: [10.3389/fonc.2024.1296091](https://doi.org/10.3389/fonc.2024.1296091)
- **This article discussed lipid-based nanoparticles as a drug delivery approach in cancer treatment.**
55. Geszke-Moritz M, Moritz M. Biodegradable polymeric nanoparticle-based drug delivery systems: comprehensive overview, perspectives and challenges. *Polymers.* 2024;16(17):2536. doi: [10.3390/polym16172536](https://doi.org/10.3390/polym16172536)
- **This article is of importance because it provides indepth analysis of biodegradable polymeric nanoparticles based drug delivery, its success and challenges.**
56. Begines B, Ortiz T, Pérez-Aranda M, et al. Polymeric nanoparticles for drug delivery: recent developments and future prospects. *Nanomaterials.* 2020;10(7):1403. doi: [10.3390/nano10071403](https://doi.org/10.3390/nano10071403)
57. Beach MA, Nayanathara U, Gao Y, et al. Polymeric nanoparticles for drug delivery. *Chem Rev.* 2024;124(9):5505–5516. doi: [10.1021/acs.chemrev.3c00705](https://doi.org/10.1021/acs.chemrev.3c00705)
58. Karami MH, Abdouss M, Maleki B. The state-of-the-art metal nanoparticles in drug delivery systems: a comprehensive review. *Nanomed J.* 2024;11(3):222–249.
59. Zhang N, Xiong G, Liu Z. Toxicity of metal-based nanoparticles: challenges in the nano era. *Front Bioeng Biotechnol.* 2022;10:1001572. doi: [10.3389/fbioe.2022.1001572](https://doi.org/10.3389/fbioe.2022.1001572)
60. Bi J, Mo C, Li S, et al. Immunotoxicity of metal and metal oxide nanoparticles: from toxic mechanisms to metabolism and

- outcomes. *Biomater Sci.* **2023**;11(12):4151–4183. doi: [10.1039/D3BM00271C](https://doi.org/10.1039/D3BM00271C)
61. Chopra H, Dey PS, Das D, et al. Curcumin nanoparticles as promising therapeutic agents for drug targets. *Mol.* **2021**;26(16):4998. doi: [10.3390/molecules26164998](https://doi.org/10.3390/molecules26164998)
 62. Wan S, Zhang L, Quan Y, et al. Resveratrol-loaded PLGA nanoparticles: enhanced stability, solubility, and bioactivity of resveratrol for nonalcoholic fatty liver disease therapy. *R Soc Open Sci.* **2018**;5(181457):181457. doi: [10.1098/rsos.181457](https://doi.org/10.1098/rsos.181457)
 63. Parthiban A, Sachithanandam V, Sarangapany S, et al. Green synthesis of gold nanoparticles using quercetin biomolecule from mangrove plant, *Ceriops tagal*: assessment of antiproliferative properties, cellular uptake, and DFT studies. *J Mol Struct.* **2022**;1272:134167.
 64. Kang C, Jung E, Hyeon H, et al. Acid-activatable polymeric curcumin nanoparticles as therapeutic agents for osteoarthritis. *Nanomed Nanotechnol Biol Med.* **2020**;23:102104. doi: [10.1016/j.nano.2019.102104](https://doi.org/10.1016/j.nano.2019.102104)
 65. Kenechukwu FC, Ugwu KC, Offorbuikwe CS, et al. Solidified reverse micellar solution-based chitosan-coated solid lipid nanoparticles as a new approach to enhance oral delivery of artemether in malaria treatment. *BMC Chem.* **2025**;19(1):64. doi: [10.1186/s13065-025-01422-4](https://doi.org/10.1186/s13065-025-01422-4)
 66. Yang F-H, Zhang Q, Liang Q-Y, et al. Bioavailability enhancement of paclitaxel via a novel oral drug delivery system: paclitaxel-loaded glycyrrhizic acid micelles. *Molecules.* **2015**;20(3):4337–4356. doi: [10.3390/molecules20034337](https://doi.org/10.3390/molecules20034337)
 67. Solanki R, Parmar B, Jadav M, et al. Berberine encapsulated phenylboronic acid-conjugated pullulan nanoparticles: synthesis, characterization and anticancer activity validated in A431 skin cancer cells and 3D spheroids. *Int J Biol Macromol.* **2024**;273(Pt 1):132737. doi: [10.1016/j.ijbiomac.2024.132737](https://doi.org/10.1016/j.ijbiomac.2024.132737)
 - **This article is of interest because it reported the anticancer activity of berberine encapsulated nanoparticles in skin cancer cells.**
 68. Solanki R, Rajput PK, Jodha B, et al. Enhancing apoptosis-mediated anticancer activity of evodiamine through protein-based nanoparticles in breast cancer cells. *Sci Rep.* **2024**;14(1):2595. doi: [10.1038/s41598-024-51970-3](https://doi.org/10.1038/s41598-024-51970-3)
 - **This article discussed the enhancing apoptosis-mediated anticancer activity of evodiamine in breast cancer cells.**
 69. Solanki R, Srivastav AK, Patel S, et al. Folate conjugated albumin as a targeted nanocarrier for the delivery of fisetin: *in silico* and *in vitro* biological studies. *RSC Adv.* **2024**;14(11):7338–7349. doi: [10.1039/D3RA08434E](https://doi.org/10.1039/D3RA08434E)
 70. Yallapu MM, Jaggi M, Chauhan SC. Curcumin nanoformulations: a future nanomedicine for cancer. *Drug Discov Today.* **2012**;17(1–2):71–80. doi: [10.1016/j.drudis.2011.09.009](https://doi.org/10.1016/j.drudis.2011.09.009)
 71. Ganesan P, Ko HM, Kim IS, et al. Recent trends in the development of nanophytobioactive compounds and delivery systems for their possible role in reducing oxidative stress in Parkinson's disease models. *IJN.* **2015**;10:6757–6772. doi: [10.2147/IJN.S93918](https://doi.org/10.2147/IJN.S93918)
 72. Rizvi SAA, Saleh AM. Applications of nanoparticle systems in drug delivery technology. *Saudi Pharma J.* **2018**;26(1):64–70. doi: [10.1016/j.jsps.2017.10.012](https://doi.org/10.1016/j.jsps.2017.10.012)
 73. Bhawana RK, Buttar HS, Jain VK, et al. Curcumin nanoparticles: preparation, characterization, and antimicrobial study. *J Agric Food Chem.* **2011**;59(5):2056–2061.
 74. Yavarpour-Bali H, Ghasemi-Kasman M, Pirzadeh M. Curcumin-loaded nanoparticles: a novel therapeutic strategy in treatment of central nervous system disorders. *IJN.* **2019**; 14:4449–4460. doi: [10.2147/IJN.S208332](https://doi.org/10.2147/IJN.S208332)
 - **This article is of interest because it reported the novel therapeutic strategy in the management of neurodegenerative disorders using curcumin-loaded nanoparticles.**
 75. Yetisgin AA, Cetinel S, Zuvin M, et al. Therapeutic nanoparticles and their targeted delivery applications. *Mol.* **2020**;25(9):2193. doi: [10.3390/molecules25092193](https://doi.org/10.3390/molecules25092193)
 76. Rahmani F, Imani Fooladi AA, Ajoudanifar H, et al. *In silico* and experimental methods for designing a potent anticancer arazyme-herceptin fusion protein in HER2-positive breast cancer. *J Mol Model.* **2023**;29(5):1–25. doi: [10.1007/s00894-023-05562-z](https://doi.org/10.1007/s00894-023-05562-z)
 77. Javid H, Oryani MA, Rezagholinejad N, et al. Rgd peptide in cancer targeting: benefits, challenges, solutions, and possible integrin–rgd interactions. *Cancer Med.* **2024**;13(2):e6800. doi: [10.1002/cam4.6800](https://doi.org/10.1002/cam4.6800)
 78. Wu P, Onodera Y, Ichikawa Y, et al. Targeting integrins with RGD-conjugated gold nanoparticles in radiotherapy decreases the invasive activity of breast cancer cells. *Int J Nanomed.* **2017**;12:5069–5085. doi: [10.2147/IJN.S137833](https://doi.org/10.2147/IJN.S137833)
 79. Herdiana Y. Functional food in relation to gastroesophageal reflux disease (GERD). *Nutrients.* **2023**;15(16):3583. doi: [10.3390/nu15163583](https://doi.org/10.3390/nu15163583)
 80. Šeregelj V, Četković G, Čanadanović-Brunet J, et al. Encapsulation and degradation kinetics of bioactive compounds from sweet potato peel during storage. *Food Technol Biotechnol.* **2020**;58(3):314–324. doi: [10.17113/ftb.58.03.20.6557](https://doi.org/10.17113/ftb.58.03.20.6557)
 81. Sabzini M, Pourmadadi M, Yazdian F, et al. Development of chitosan/halloysite/graphitic-carbon nitride nanovehicle for targeted delivery of quercetin to enhance its limitation in cancer therapy: an *in vitro* cytotoxicity against MCF-7 cells. *Int J Biol Macromol.* **2022**;226:159–171.
 82. Chidambara Murthy KN, Monika P, Jayaprakasha GK, et al. Nanoencapsulation: an advanced nanotechnological approach to enhance the biological efficacy of curcumin. *Adv Plant Phenolics: From Chem Hum Health.* **2018**;1286:383–405.
 83. Kumari A, Raina N, Wahi A, et al. Wound-healing effects of curcumin and its nanoformulations: a comprehensive review. *Pharmaceutics.* **2022**;14(11):2288. doi: [10.3390/pharmaceutics14112288](https://doi.org/10.3390/pharmaceutics14112288)
 84. Namuga C, Ocan M, Kinengyere AA, et al. Efficacy of nano encapsulated herbal extracts in the treatment of induced wounds in animal models: a systematic review protocol. *Systematic Rev.* **2023**;12(1):215. doi: [10.1186/s13643-023-02370-7](https://doi.org/10.1186/s13643-023-02370-7)
 85. Rajinikanth BS, Rajkumar DSR, Vijayaragavan V. Chitosan-based biomaterial in wound healing: a review. *Cureus.* **2024**;16(2):e55193.
 86. Witkowska K, Paczkowska-Walendowska M, Plech T, et al. Chitosan-based hydrogels for controlled delivery of asiaticoside-rich *Centella asiatica* extracts with wound healing potential. *Int J Mol Sci.* **2023**;24(24):17229. doi: [10.3390/ijms242417229](https://doi.org/10.3390/ijms242417229)
 87. Siafaka PI, Miliotou AN, Okur ME, et al. Nanoformulations loaded with phytochemicals for combating wound infections and promoting wound healing: current applications and innovations. *Appl Sci.* **2025**;15(10):5413. doi: [10.3390/app15105413](https://doi.org/10.3390/app15105413)
 88. Papavassiliou KA, Sofianidi AA, Papavassiliou AG. Anthocyanins in non-small cell lung cancer (NSCLC) treatment and prevention. *Nutrients.* **2024**;16(10):1458. doi: [10.3390/nu16101458](https://doi.org/10.3390/nu16101458)
 89. Gupta SC, Patchva S, Aggarwal BB. Therapeutic roles of curcumin: lessons learned from clinical trials. *Aaps J.* **2013**;5(1):195–218. doi: [10.1208/s12248-012-9432-8](https://doi.org/10.1208/s12248-012-9432-8)
 90. Aggarwal D, Chaudhary M, Mandotra SK, et al. Anti-inflammatory potential of quercetin: from chemistry and mechanistic insight to nanoformulations. *Curr Res Pharmacol Drug Discov.* **2025**;8:100217. doi: [10.1016/j.crphar.2025.100217](https://doi.org/10.1016/j.crphar.2025.100217)
 91. Patel KR, Scott E, Brown VA, et al. Clinical trials of resveratrol. *Ann N Y Acad Sci.* **2011**;1215(1):161–169. doi: [10.1111/j.1749-6632.2010.05853.x](https://doi.org/10.1111/j.1749-6632.2010.05853.x)
 92. Sanna V, Pala N, Sechi M. Targeted therapy using nanotechnology: focus on cancer. *Int J Nanomed.* **2014**;9:467–483.
 93. Chowdhury S, Kar K, Mazumder R. Exploration of different strategies of nanoencapsulation of bioactive compounds and their ensuing approaches. *Future J Pharma Sci.* **2024**;10(1):72. doi: [10.1186/s43094-024-00644-y](https://doi.org/10.1186/s43094-024-00644-y)
 94. Baruah KN, Nagaoka S, Banno A, et al. Nanoencapsulation of epigallocatechin gallate using starch nanoparticles: characterization and insights on *in vitro* micellar cholesterol solubility. *J Food Sci.* **2024**;89(9):5701–5711. doi: [10.1111/1750-3841.17260](https://doi.org/10.1111/1750-3841.17260)
 95. Jagtiani E. Advancements in nanotechnology for food science and industry. *Food Front.* **2022**;3(1):56–82. doi: [10.1002/fft2.104](https://doi.org/10.1002/fft2.104)

96. de Sousa MS, Schlogl AE, Estanislau FR, et al. Nanotechnology in packaging for food industry: past, present, and future. *Coatings*. 2023;13(8):1411. doi: [10.3390/coatings13081411](https://doi.org/10.3390/coatings13081411)
97. Manzari-Tavakoli A, Babajani A, Tavakoli MM, et al. Integrating natural compounds and nanoparticle-based drug delivery systems: a novel strategy for enhanced efficacy and selectivity in cancer therapy. *Cancer Med*. 2024;13(5):e7010. doi: [10.1002/cam4.7010](https://doi.org/10.1002/cam4.7010)
98. Hristova-Panusheva K, Xenodochidis C, Georgieva M, et al. Nanoparticle-mediated drug delivery systems for precision targeting in oncology. *Pharma*. 2024;17(6):677. doi: [10.3390/ph17060677](https://doi.org/10.3390/ph17060677)
99. Tamrakar DG, Thakur SS. Nanotechnology's application in cosmetics: dermatology and skin care items. *Migr Lett*. 2023;20(S13):1–18.
100. Assali M, Zaid AN. Features, applications, and sustainability of lipid nanoparticles in cosmeceuticals. *Saudi Pharm J*. 2022;30(1):53–65. doi: [10.1016/j.jsps.2021.12.018](https://doi.org/10.1016/j.jsps.2021.12.018)
101. Wassie MA, Goswami N, Zhang X. Nanoparticles for environmental monitoring: advanced sensor applications and their role in pollution control. *Environ Sci Technol*. 2023;57(5):1234–1245.
102. Choi WS, Lee HJ. Nanostructured materials for water purification: adsorption of heavy metal ions and organic dyes. *Polymers*. 2022;14(11):2183. doi: [10.3390/polym14112183](https://doi.org/10.3390/polym14112183)
103. Patra JK, Das G, Fraceto LF, et al. Nanobased drug delivery systems: recent developments and future prospects. *J Nanobiotechnol*. 2018;16(1):71. doi: [10.1186/s12951-018-0392-8](https://doi.org/10.1186/s12951-018-0392-8)
104. Sánchez A, Mejía SP, Orozco J. Recent advances in polymeric nanoparticle-encapsulated drugs against intracellular infections. *Mol*. 2020;25(16):3760. doi: [10.3390/molecules25163760](https://doi.org/10.3390/molecules25163760)
105. Mitchell MJ, Billingsley MM, Haley RM, et al. Engineering precision nanoparticles for drug delivery. *Nat Rev Drug Discov*. 2021;20(2):101–124. doi: [10.1038/s41573-020-0090-8](https://doi.org/10.1038/s41573-020-0090-8)
106. Kumari A, Singla R, Guliani A, et al. Nanoencapsulation for drug delivery. *Excli J*. 2014;13:265–286. doi: [10.1007/s13204-013-0216-y](https://doi.org/10.1007/s13204-013-0216-y)
107. Barenholz Y. Doxil®—the first FDA-approved nanodrug: lessons learned. *J Controlled Release*. 2012;160(2):117–134. doi: [10.1016/j.jconrel.2012.03.020](https://doi.org/10.1016/j.jconrel.2012.03.020)
108. Abdelkader DH, Abosalha AK, Khat tab MA, et al. A novel sustained anti-inflammatory effect of atorvastatin-calcium PLGA nanoparticles. *Vitro Optim In Vivo Evaluation Pharm*. 2021;13(10):1658. doi: [10.3390/pharmaceutics13101658](https://doi.org/10.3390/pharmaceutics13101658)
109. Zhang Y, Poon K, Masonsong GSP, et al. Sustainable nanomaterials for biomedical applications. *Pharma*. 2023;15(3):922. doi: [10.3390/pharmaceutics15030922](https://doi.org/10.3390/pharmaceutics15030922)
110. Gimondi S, Ferreira H, Reis RL, et al. Microfluidic devices: a tool for nanoparticle synthesis and performance evaluation. *ACS Nano*. 2023;17(15):14205–14228. doi: [10.1021/acsnano.3c01117](https://doi.org/10.1021/acsnano.3c01117)
111. Phan HT, Haes AJ. What does nanoparticle stability mean? *J Phys Chem C*. 2019;123(27):16495–16507. doi: [10.1021/acs.jpcc.9b00913](https://doi.org/10.1021/acs.jpcc.9b00913)
112. Xu L, Liang HW, Yang Y, et al. Stability and reactivity: positive and negative aspects for nanoparticle processing. *Chem Rev*. 2018;118(7):3209–3250. doi: [10.1021/acs.chemrev.7b00208](https://doi.org/10.1021/acs.chemrev.7b00208)
113. Kumah EA, Djou Fopa R, Harati S, et al. Human and environmental impacts of nanoparticles: a scoping review of the current literature. *BMC Public Health*. 2023;23(1):1059. doi: [10.1186/s12889-023-15958-4](https://doi.org/10.1186/s12889-023-15958-4)
114. Zhao M, Lei C, Yang Y, et al. Abraxane, the nanoparticle formulation of paclitaxel, can induce drug resistance by upregulation of P-gp. *PLOS ONE*. 2015;10(7):e0131429. doi: [10.1371/journal.pone.0131429](https://doi.org/10.1371/journal.pone.0131429)
115. Sánchez-Moreno P, De Vicente J, Nardecchia S, et al. Thermosensitive nanomaterials: recent advance in synthesis and biomedical applications. *Nanomaterials*. 2018;8(11):935. doi: [10.3390/nano8110935](https://doi.org/10.3390/nano8110935)
116. Wolfram J, Zhu M, Yang Y, et al. Safety of nanoparticles in - medicine. *CDT*. 2015;16(14):1671–1681. doi: [10.2174/1389450115666140804124808](https://doi.org/10.2174/1389450115666140804124808)
117. Sundar DS, Antoniraj MG, Kumar CS, et al. Recent trends of biocompatible and biodegradable nanoparticles in drug delivery: a review. *Curr Med Chem*. 2016;23(32):3730–3751. doi: [10.2174/0929867323666160607103854](https://doi.org/10.2174/0929867323666160607103854)
118. Scientific Committee EFSA, More S, Bampidis V, et al. Guidance on risk assessment of nanomaterials to be applied in the food and feed chain: human and animal health. *Efsa J*. 2021;19(8):e06768.
119. Peer D, Karp JM, Hong S, et al. Nanocarriers as an emerging platform for cancer therapy. *Nat Nanotechnol*. 2007;2(12):751–760. doi: [10.1038/nnano.2007.387](https://doi.org/10.1038/nnano.2007.387)
120. Baroli B. Penetration of nanoparticles and nanomaterials in the skin: fiction or reality? *J Pharm Sci*. 2010;99(1):21–50. doi: [10.1002/jps.21817](https://doi.org/10.1002/jps.21817)
121. Wu J, Wick P, Nowack B. Data-driven prediction of nanoparticle biodistribution from physicochemical descriptors. *ACS Nano*. 2025;19(29):26425–26437. doi: [10.1021/acsnano.5c03040](https://doi.org/10.1021/acsnano.5c03040)
122. Ngo TD, Kashani A, Imbalzano G, et al. Additive manufacturing (3D printing): a review of materials, methods, applications and challenges. *Composites*. 2018;143:172–196. doi: [10.1016/j.compositesb.2018.02.012](https://doi.org/10.1016/j.compositesb.2018.02.012)
123. Fadeel B, Feliu N, Vogt C, et al. Bridge over troubled waters: understanding the synthetic and biological identities of engineered nanomaterials to enhance regulatory decision making. *Nano Today*. 2018;8(6):571–573.
124. Donaldson K, Poland CA. Nanotoxicity: challenging the myth of nanospecific toxicity. *Curr Opin Biotechnol*. 2013;24(4):724–734.