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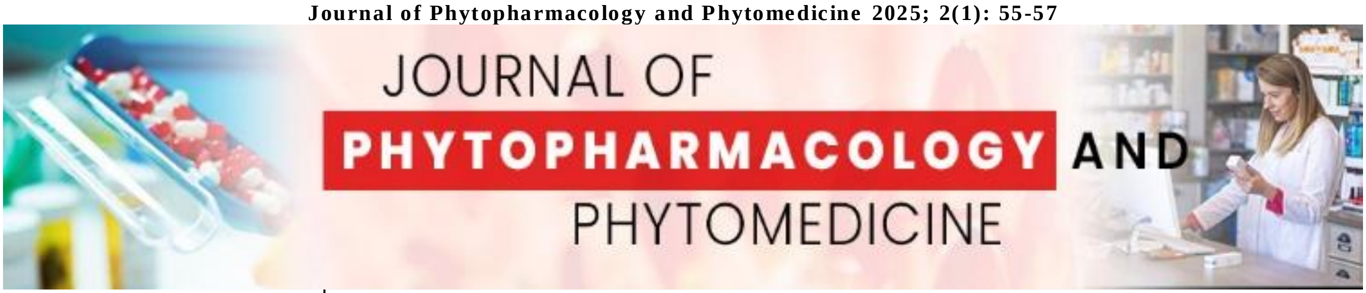

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Nanotechnology-enabled delivery systems in phytomedicine enhancing the bioavailability of polyphenols, alkaloids, and Terpenoids

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Abstract
Phytomedicine, the use of plant-based compounds for therapeutic purposes, has attracted significant attention due to its potential health benefits. Among the myriad of bioactive plant-derived compounds, polyphenols, alkaloids, and terpenoids stand out for their diverse pharmacological properties. Despite their promising therapeutic potential, these compounds often suffer from poor bioavailability when administered in their natural form. This limitation is primarily due to their low solubility, instability, and rapid metabolism. Nanotechnology has emerged as a transformative strategy to overcome these barriers and enhance the bioavailability of phytochemicals. This paper explores the role of nanotechnology-based delivery systems in improving the pharmacokinetics of polyphenols, alkaloids, and terpenoids with a focus on the various nanocarriers and their mechanisms of action. Furthermore, the paper discusses the challenges associated with nanotechnology-enabled delivery systems and their future prospects in the realm of phytomedicine.

Keywords: Terpenoids, polyphenols, alkaloids, phytomedicine, phytochemicals, nanotechnology, poor bioavailability, phytomedicine enhancing, bioavailability, delivery systems

Introduction

Phytochemicals are plant-derived compounds that offer numerous health benefits, and many of them have been used in traditional medicine for centuries. Among the various classes of phytochemicals, polyphenols, alkaloids, and terpenoids are especially noted for their antioxidant, anti-inflammatory, antimicrobial, and anticancer properties. However, despite their therapeutic potential, the clinical application of these compounds is hindered by poor bioavailability. This is mainly due to their low solubility in water, susceptibility to rapid degradation, and poor absorption in the gastrointestinal tract (Patra *et al*., 2018) [5]. For example, curcumin, a polyphenol found in turmeric, is widely studied for its anti-inflammatory properties, but its clinical use is limited due to its poor solubility and rapid metabolism (Parvin, 2025) [4].

Nanotechnology offers promising solutions to overcome these limitations. By utilizing nanocarriers, it is possible to enhance the solubility, stability, and bioavailability of bioactive compounds. Nanocarriers such as liposomes, nanoparticles, and micelles can encapsulate these compounds, protect them from degradation, and ensure their sustained release, thus enhancing their therapeutic efficacy (Bonifácio, 2013) [1]. This paper explores the role of nanotechnology-based drug delivery systems (DDS) in enhancing the bioavailability of polyphenols, alkaloids, and terpenoids, focusing on the mechanisms through which nanocarriers improve the pharmacokinetic profiles of these bioactive compounds.

Main Objectives

The main objectives of this paper are:

- To explore the role of nanotechnology in enhancing the bioavailability of polyphenols, alkaloids, and terpenoids.
- To review the different nanocarrier systems used for delivering these phytochemicals and examine their mechanisms of action.
- To discuss the challenges and future prospects of nanotechnology-based DDS in phytomedicine.

- To provide insights into the potential applications of nanotechnology in improving the therapeutic efficacy of phytochemicals, focusing on specific bioactive compounds like curcumin, resveratrol, and quercetin.

Literature Review

The use of nanotechnology in enhancing the bioavailability of phytochemicals has garnered significant interest in recent years. Researchers have explored various types of nanocarriers, including polymeric nanoparticles, lipid-based nanoparticles, and micelles, for the delivery of bioactive phytochemicals.

Polymeric nanoparticles, made from materials such as poly(lactic-co-glycolic acid) (PLGA) and chitosan, have been extensively studied for their ability to encapsulate hydrophobic and hydrophilic compounds (Lv, 2024) [2]. These nanoparticles not only improve the solubility of phytochemicals but also provide controlled release, which can enhance their therapeutic effects. In addition to PLGA, chitosan-based nanoparticles have been investigated for their mucoadhesive properties, which improve the absorption of phytochemicals in the gastrointestinal tract (Bonifácio, 2013) [1].

Lipid-based nanoparticles, such as liposomes and solid lipid nanoparticles (SLNs), have been used to encapsulate lipophilic phytochemicals like terpenoids. These systems improve the solubility and stability of phytochemicals, thus enhancing their bioavailability. For example, liposomes have been successfully used to deliver curcumin, a polyphenol, which is poorly soluble in water (Patra *et al*., 2018) [5]. Additionally, SLNs, which provide a stable matrix for the encapsulation of phytochemicals, have been shown to enhance the bioavailability of compounds like resveratrol.

Micelles, which are self-assembled structures formed from amphiphilic surfactants, offer a versatile platform for the delivery of hydrophobic compounds such as polyphenols and alkaloids. Their ability to solubilize these compounds in their core improves their bioavailability (Ghosh, 2025) [6]. Furthermore, nanostructured lipid carriers (NLCs), which combine the advantages of SLNs and liquid lipid systems, have been explored for delivering various phytochemicals. NLCs offer superior stability and controlled release, making them an attractive option for enhancing the bioavailability of bioactive compounds (Patra *et al*., 2018) [5].

Recent studies have demonstrated that the use of nanotechnology in phytomedicine can significantly improve the pharmacokinetics of polyphenols, alkaloids, and terpenoids. For instance, nanoparticles loaded with curcumin have been shown to increase its bioavailability by several folds, enabling its therapeutic use in conditions like cancer and inflammatory diseases (Parvin, 2025) [4]. Similarly, nanocarriers have been used to enhance the bioavailability of alkaloids such as morphine and quinine, which are effective but often suffer from poor absorption (Awlqadr, 2025) [3]. Additionally, terpenoids such as limonene and menthol have shown enhanced solubility and bioavailability when encapsulated in lipid-based nanocarriers (Bonifácio, 2013) [1].

Despite the promising advancements, several challenges remain in the development of nanotechnology-based DDS for phytochemicals. These include the scalability of production, the potential toxicity of nanomaterials, and regulatory hurdles. Future research must address these issues to fully realize the potential of nanocarriers in improving the bioavailability and therapeutic efficacy of phytochemicals.

Nanotechnology-based drug delivery systems

The application of nanotechnology to phytomedicine has led to the development of various nanocarriers capable of encapsulating and delivering bioactive compounds in a controlled and efficient manner. These carriers range from nanoparticles made of lipids, polymers, and proteins to micelles and nanoemulsions. The small size of these carriers, typically in the range of 1-100 nm, allows them to navigate biological barriers such as cell membranes, enhancing the delivery of poorly bioavailable compounds.

Polymeric nanoparticles, often made from biocompatible and biodegradable materials like poly(lactic-co-glycolic acid), (PLGA) and chitosan, have been widely used for delivering phytochemicals. These nanoparticles can encapsulate both hydrophilic and hydrophobic compounds, improving their solubility and protecting them from degradation. The release of the encapsulated phytochemicals can be controlled by adjusting the polymer composition, particle size, and surface properties, allowing for a sustained release of the active compound over time. This controlled release can significantly improve the therapeutic efficacy of phytochemicals by maintaining their concentration at the target site for a prolonged period.

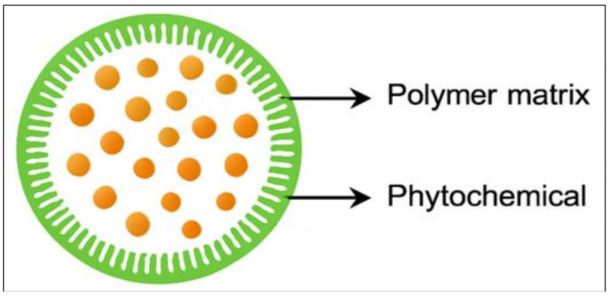

Fig 1: Polymeric nanoparticles for phytochemical delivery

Lipid-based nanocarriers, such as liposomes and solid lipid nanoparticles (SLNs), are another promising platform for phytochemical delivery. Liposomes, which are composed of phospholipid bilayers, can encapsulate both hydrophilic and lipophilic compounds, providing an effective means of improving the solubility and stability of bioactive phytochemicals. SLNs, on the other hand, offer advantages over liposomes in terms of stability and drug loading capacity. These lipid-based systems have been particularly useful in enhancing the bioavailability of lipophilic compounds such as terpenoids, which are poorly soluble in water.

Another nanocarrier that has gained attention in recent years is the micelle. Micelles are self-assembled structures made of amphiphilic surfactants, which can solubilize hydrophobic compounds in their core. These nanocarriers are particularly effective for delivering hydrophobic phytochemicals, such as polyphenols and alkaloids, improving their solubility in aqueous environments and enhancing their absorption.

Nanostructured Lipid Carriers (NLCs), which combine the advantages of SLNs and liquid lipid systems, have also been explored for the delivery of phytochemicals. These carriers provide a stable environment for encapsulating bioactive compounds, ensuring their protection from degradation and facilitating controlled release. NLCs have shown promise in enhancing the bioavailability of a wide range of phytochemicals, including polyphenols, alkaloids, and terpenoids.

Enhancement of Bioavailability

Nanotechnology-based DDS enhance the bioavailability of phytochemicals through several key mechanisms. The first mechanism is improved solubility. Many phytochemicals, especially polyphenols, alkaloids, and terpenoids, have poor water solubility, which limits their absorption in the gastrointestinal tract. Nanocarriers increase the surface area of these compounds, facilitating their dissolution in aqueous media and enhancing absorption.

The second mechanism is the protection of phytochemicals from degradation. Phytochemicals are often sensitive to environmental factors such as light, heat, and oxygen, which can lead to their degradation before they reach their target site. Encapsulation within nanocarriers protects these compounds from such degradation, ensuring their stability and enhancing their therapeutic efficacy. This protection is particularly important for sensitive compounds like polyphenols and terpenoids, which are prone to oxidation and enzymatic degradation.

The third mechanism involves controlled release. Nanocarriers can be engineered to release their payload in a controlled manner, ensuring that the active compounds are delivered over an extended period. This sustained release not only improves the pharmacokinetic profile of the compounds but also reduces the frequency of administration, improving patient compliance.

Finally, nanocarriers can facilitate targeted delivery. Surface modification of nanoparticles with ligands that specifically recognize receptors on target cells or tissues allows for the selective delivery of phytochemicals. This targeted delivery reduces systemic side effects and ensures that the therapeutic compounds are concentrated at the desired site of action, further enhancing their bioavailability and efficacy.

Conclusion

Nanotechnology has the potential to revolutionize phytomedicine by enhancing the bioavailability of polyphenols, alkaloids, and terpenoids, thereby improving their therapeutic efficacy. Through the development of various nanocarriers, these bioactive compounds can be delivered more efficiently, overcoming the limitations of poor solubility, rapid metabolism, and low systemic absorption. While significant progress has been made in this field, challenges related to scalability, safety, and regulatory approval must be addressed before nanotechnology-based DDS can be widely adopted in clinical settings. Continued research and development in this area hold the promise of providing more effective and targeted treatments for a variety of diseases, ultimately benefiting public health.

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