



HERBAL DRUG NANOTECHNOLOGY: A REVIEW

Periketi Sowmya Sri¹, Neerudu Supriya¹, Edgi Laxmikanth Goud¹,
Suraj Vinod Gupta¹, Amar Anand¹, Vangala Kiran Kumar^{2*}

¹Bharat Institute of Technology, Mangalpally, Ibrahimpatnam, Hyderabad, Telangana, India.

²Department of Pharmacy, University College of Technology, Osmania University, Hyderabad, Telangana, India.

*Corresponding author E-mail: drkiranpharmacy@gmail.com

ARTICLE INFO

Key words:

Herbal drugs, novel drug delivery systems, nanotechnology, phytotherapeutics.

Access this article online
Website:
<https://www.jgtps.com/>
Quick Response Code:



ABSTRACT

The WHO has recently defined traditional medicine (including herbal drugs) as comprising therapeutic practices that have been in existence, often for hundreds of years, before the development and spread of modern medicine and are still in use today. Herbal remedies have been utilised extensively throughout history, and consumers and medical experts alike have acknowledged the greater therapeutic efficiency of these remedies due to their lower potential for side effects when compared to contemporary medications. For phytotherapeutics to maximise patient adherence and avoid recurrent administration, a methodical approach to element delivery throughout time is required. Developing innovative drug delivery systems (NDDSs) for herbal components might help achieve this. NDDSs lessen the need for further dosages to correct non-compliance by decreasing toxicity and improving bioavailability, which increases therapeutic efficacy. One day, delivery methods for herbal medications in nanosized form may improve efficacy and solve issues with plant-based medications. The purpose of this study is to review nanotechnology-based drug delivery systems and herbal medicines.

INTRODUCTION:

First of all, from ancient times, medical disorders have been treated using herbal items and methods. Thousands of compounds work together in herbal remedies, as opposed to the commonly utilised allopathic approach, to cure the specific condition at hand. Phytotherapeutics need to administer the components in a sustained way using a scientific method to increase patient compliance and avoid repeated dosing. One approach to do this is to develop innovative drug delivery systems (NDDS) for herbal medicines. NDDSs reduce the need for repeated administration to overcome non-compliance and enhance the therapeutic value in a number of ways, including by lowering toxicity and enhancing bioavailability.

Objectifying the herbal extracts into the new expression method has various other advantages, which may be overcome, such as lower immersion and bulk dose. This is the primary problem drawing attention to significant medicinal plants. Nanotechnology is an applied science and technology sector which aim is to produce bias and lozenge shapes as tiny as feasible, between 1 and 100 nm [1,2]. The traditional use of plants, both used directly and extracted, for medicinal purposes has existed since ancient times. Plants are a source of various phytochemicals and have been used for human health because of their low side effects, low cost, and high acceptance by the general public. Conventional medicine delivery mechanisms such as pills, capsules,

syrops, and decoctions cannot compete with the benefits of herbal pharmaceuticals stated above. However, nanotechnology in herbal medicine has demonstrated tremendous effectiveness in natural medication delivery. It has been shown to be useful in a variety of medical sciences sectors, including artificial implants, tissue/organ imaging, biosensors, nanorobotics, and sophisticated drug delivery, such as targeted, controlled, or sustained drug administration, among others [3,4]. The world market for product using nanotechnology is estimated to reach US\$ 1trillion by 2015. In 2006 India and Australian government contributes to start Australia-India Science Research Funding Program. The market value of the worldwide nanomedicine industry was \$63.8 billion and \$72.8 billion in 2010-2011 respectively. The market is estimated to grow up to \$130.9 billion by fiscal year 2016. Evaluation of herbal preparation is a fundamental requirement of industry and other organization dealing with ayurvedic and herbal products. Standardization is an important step for the establishment of a consistent biological activity, a consistent chemical profile, or simply a quality assurance program for production and manufacturing of an herbal drug [5,6]. The concept of nanomedicine is as old as *Ayurveda*, where they use nanoparticles of metals like *Bhasma* in therapeutics. The *Bhasma* (ash) preparation process is known as "*Bhasmikarana*", where the metal ions and herbal drugs are converted into a higher oxidative state called metal ion-nanoparticles. These metal nanoparticles have superior properties like better absorption, improved stability, and compatibility for the human body. Metals like silver (Ag, Rajata), mercury (Hg, Parada), zinc (Zn, Yasada), iron (Fe, Loha/Aayasa), tin (Sn, Vanga), lead (Pb, Naga/Sisaka), copper (Cu, Tamra) and gold (Au, Swarna) are commonly used to prepare the *Dhatu Bhasma*. Herbal medicines using

nanotechnology-based delivery systems have great potential and unique properties, such as being able to convert less soluble, poorly absorbed, unstable substances into promising drugs. Therefore, nanotechnology-based delivery systems represent a promising prospect for enhancing herbal activity and overcoming the dilemmas associated with herbal medicine [7-9].

Nanotechnology-based drug delivery system for phytochemical compounds:

According to the literature, 70% of the active ingredients obtained from plants are hydrophobic. New technology has been used as a strategy to increase the bioavailability/bioactivity of phytochemical compounds. In order to develop new nanotechnology-based therapies, the ability to design suitable formulations for drug delivery is of the utmost importance. Phytochemical delivery is essential for effective disease prevention and treatment. These delivery systems include lipid-based delivery systems and polymer-based delivery systems, which have the potential to increase the bioactivity of phytochemical compounds. New drug delivery systems based on nanotechnology have been developed for effective herbal drug delivery. Lipid-based carrier systems consisting of vesicular systems (liposomes, phytosomes, transfersomes, ethosomes, and niosomes), lipid particulates (SLN and NLC), and nanoemulsions have garnered particular interest for phytochemical delivery aimed at increasing bioactivity and bioavailability, as well as the stability of phytochemical compounds. Vesicular drug delivery systems can be defined as highly ordered assemblies consisting of one or more concentric bilayers formed as a result of self-assembly in the presence of water. SLN and NLC are two types of nanoparticle systems consisting of lipid cores formed from solid lipids or mixtures with liquid lipids. Nanoemulsions are used to increase the bioavailability of hydrophobic drugs and drugs with a high

first-pass metabolism. The components of the nanoemulsion system include oils, lipids, surfactants, water-soluble cosolvents, and water. Lipid-based nano systems represent the largest and most investigated nanocarrier category. Typically, these carriers exhibit a lower toxicity profile and a more reasonable cost compared to polymer carriers. Among all approaches, the delivery of liposomes and phytosomes is considered to be very effective. With high biocompatibility and biodegradability, liposomes offer the ability to improve the solubility, efficacy, and bioavailability of drugs. Liposomes can be used to encapsulate hydrophilic and lipophilic drugs [10-12].

Nanoformulations of herbal medicines:

Pharmaceutical firms find it difficult to develop a full herbal medication since a variety of elements affect the plant herb's biological efficacy and repeatability of its therapeutic potential. Certain illnesses, including asthma, pain, fever, etc., require medications to have a quick start of action; conversely, chronic therapies like diabetes, cancer, and hypertension, among others, may also require longer acting times. However, because of their physiochemical characteristics, herbal treatments are severely limited in both phases. These elements have undoubtedly lessened their hegemony in contemporary medicine. To provide herbal medications with successful outputs, significant research investments have been undertaken in recent years. However, to obtain the desired efficacy of herbal drugs, nanotechnology strategy is incorporated to manipulate the effectiveness of active phytoconstituents in the system. Nanotechnology has proved to increase the chance of implementation of herbal-based drugs by improving the potential of drug action, promoting the sustained release of active constituents, reducing the required dosage and improving the biological activity. Nanomaterials such as polymeric

nanoparticles, solid lipid nanoparticles (SLN), lipid crystal (LC) systems, liposomes, and nanoemulsions have been attempted as carrier vehicles to protect the herbal drugs from an external source of degradation and increase their bioavailability. Research in polymeric nanoparticles has predominantly grown in the present decade due to their inherent ability to target the site and response to the external stimuli factors. In designing a polymeric nanoparticle for herbal drug formulation, biotoxicity and stability of the polymer should be taken into considerations. Hence, the mechanism of delivery of such herbal compounds is very effectively practiced by biodegradable and biocompatible polymers such as PLA (polylactic acid), PLGA (poly (lactic-co-glycolic acid)), chitosan, etc. Some polymers like chitosan offer an excellent range of benefits for transdermal delivery application by enhancing the features like sustained, targeted drug release, high biocompatibility and biodegradability properties. The present opinion of this review paper summarizes; Though many polymeric nanoparticles have been extensively studied for herbal formulations, nanogels deserve a special consideration due to their favourable physiochemical properties for controlled drug delivery and affinity to aqueous solutions, superior colloidal stability, high cellular internalization property, and tendency to remain inert in the bloodstream is the major requirement in this modern pharmaceutical era [3,13,14]. Herbal remedies were selected for delivery through a nano delivery system because of the following properties:

- ✓ Effective chloroform, petrol, acetone, and methanolic extracts are available which may not be suitable for delivery as such.
- ✓ These are the bulk drugs so dose reduction is intended.

- ✓ Currently marketed formulations lack target specificity for various chronic diseases.
- ✓ Some other side effects are associated with currently marketed formulations.
- ✓ Patient non-compliance due to large doses and less effectiveness with the available formulations.

Advantages of herbal nanomedicine:

Herbal nanomedicine offers several advantages over traditional forms of herbal therapy and conventional pharmaceuticals. By combining the therapeutic benefits of herbal compounds with the advanced delivery mechanisms of nanotechnology, these formulations can significantly improve health outcomes. Here are some of the key advantages:

Enhanced bioavailability: Improved solubility: Nanoparticles can increase the solubility of poorly water-soluble herbal compounds, enhancing their absorption and bioavailability. Efficient absorption: Nanocarriers facilitate better absorption of herbal drugs through biological barriers, such as the gastrointestinal tract, skin, and blood-brain barrier.

Targeted drug delivery:

- Specific targeting: Nanoparticles can be engineered to target specific cells or tissues, delivering herbal compounds directly to the site of action and reducing systemic side effects.
- Reduced dosage: Targeted delivery allows for lower doses of the active ingredient to achieve therapeutic effects, minimizing potential toxicity.

Stability and shelf-life:

- Improved stability: Encapsulation of herbal compounds in nanoparticles protects them from environmental

factors such as light, heat, and oxygen, enhancing their stability and shelf-life.

- Protection from degradation: Nanoparticles can protect sensitive herbal compounds from degradation in the gastrointestinal tract or during storage.

Reduced side effects:

- Minimized systemic exposure: Targeted and controlled release reduces the exposure of non-target tissues to the herbal drug, minimizing adverse effects and improving safety.
- Better tolerability: Improved delivery mechanisms often result in better tolerability of herbal compounds, making treatments more comfortable for patients.

Enhanced efficacy:

- Increased therapeutic effectiveness: By enhancing bioavailability and targeting specific sites, nanoparticles can significantly increase the therapeutic efficacy of herbal compounds.
- Synergistic effects: Combining multiple herbal compounds in a single nanoparticle formulation can create synergistic effects, enhancing overall treatment efficacy.

Versatility in administration routes:

- Multiple routes of administration: Herbal nanoparticles can be administered through various routes, including oral, topical, transdermal, intravenous, and inhalation, providing flexibility in treatment options.
- Improved patient compliance: Convenient administration routes, such as oral and topical, can improve

patient compliance and acceptance of herbal treatments.

Potential for novel therapies:

- New therapeutic applications: Nanotechnology enables the use of herbal compounds in new therapeutic areas, such as neurodegenerative diseases, cancer, and chronic inflammatory conditions.
- Innovative treatment modalities: Herbal nanomedicine opens up possibilities for innovative treatment modalities, such as theranostics (combined therapy and diagnostics) and personalized medicine.

Eco-friendly and sustainable approaches:

- Green synthesis: Using eco-friendly methods for nanoparticle synthesis aligns with the principles of sustainability and reduces the environmental impact of pharmaceutical production.
- Biocompatibility and biodegradability: Natural and biodegradable materials used in nanoparticles enhance biocompatibility and reduce long-term environmental and health risks.

Integration with traditional medicine:

- Cultural acceptance: Herbal nanomedicine can be more culturally acceptable in regions where traditional herbal medicine is widely practiced, facilitating integration into local healthcare systems.
- Complementary approaches: Combining traditional herbal knowledge with modern nanotechnology can create comprehensive and culturally sensitive therapeutic approaches.

Overall, the advantages of herbal nanomedicine lie in its ability to enhance the therapeutic potential of natural compounds through improved delivery, stability, efficacy, and safety, while also providing innovative and sustainable healthcare solutions.

Applications of herbal nanotechnology: Herbal nanotechnology holds significant promise for enhancing the therapeutic potential of herbal compounds. By leveraging nanotechnology, these natural substances can be delivered more efficiently, effectively, and safely. Here are some notable applications:

Cancer therapy: Targeted drug delivery: Nanoparticles can deliver herbal anticancer compounds directly to tumor cells, enhancing therapeutic efficacy while minimizing side effects. For instance, curcumin, derived from turmeric, can be encapsulated in nanoparticles for targeted delivery to cancer cells. Combination therapies: Combining herbal compounds with conventional chemotherapy drugs in nanocarriers to achieve synergistic effects and reduce drug resistance.

Anti-inflammatory treatments:

- Enhanced bioavailability: Nanoparticles can improve the bioavailability and stability of herbal anti-inflammatory agents like resveratrol, curcumin, and quercetin, leading to more effective treatment of chronic inflammatory diseases such as rheumatoid arthritis.

Anti-microbial and anti-viral agents:

- Enhanced efficacy: Herbal compounds with antimicrobial properties, such as tea tree oil and eucalyptus oil, can be encapsulated in nanoparticles to enhance their

penetration and efficacy against bacterial and viral infections.

- **Wound healing:** Nanoparticle formulations can be used in topical applications to improve the wound healing properties of herbal extracts by providing sustained release and better skin penetration.

Neuroprotection and neurological disorders: Brain delivery: Nanoparticles can cross the blood-brain barrier more effectively, delivering neuroprotective herbal compounds such as ginkgo biloba extract or bacoside-A to treat neurodegenerative diseases like Alzheimer's and Parkinson's.

Cardiovascular health: Anti-oxidant delivery: Herbal antioxidants like green tea polyphenols and flavonoids can be delivered using nanoparticles to reduce oxidative stress and improve cardiovascular health. Cholesterol management: Nanoparticle formulations of herbal compounds like berberine can aid in better management of cholesterol levels and overall cardiovascular health.

Cosmetics and skin care: Anti-aging: Nanoparticles can enhance the delivery of herbal anti-aging agents like aloe vera and grape seed extract, improving skin hydration, reducing wrinkles, and protecting against UV damage. Skin conditions: Herbal nanoparticles can be used to treat skin conditions such as acne, psoriasis, and eczema by delivering active compounds more effectively to the affected areas.

Gastrointestinal health: Anti-ulcer and anti-inflammatory effects: Nanoparticles can improve the stability and bioavailability of herbal compounds like licorice and ginger, providing more effective treatment for gastrointestinal disorders.

- **Probiotics and prebiotics delivery:** Encapsulation of probiotics and

prebiotics in nanoparticles can protect them from stomach acid and enhance their delivery to the gut, promoting better digestive health.

Respiratory disorders: Enhanced delivery: Herbal compounds with anti-asthmatic and anti-inflammatory properties, such as those from eucalyptus and thyme, can be formulated in nanoparticles for improved delivery via inhalation therapies.

Bone and joint health: Osteoporosis and arthritis: Nanoparticles can enhance the delivery of herbal compounds like phytoestrogens and anti-inflammatory agents, improving the management of osteoporosis and arthritis.

Anti-obesity treatments: Fat metabolism: Herbal compounds that influence fat metabolism, such as garcinia cambogia and green tea extract, can be delivered using nanoparticles to enhance their efficacy in weight management.

Dental applications: Oral hygiene: Herbal nanoparticles can be incorporated into dental care products to provide sustained release of anti-microbial and anti-inflammatory agents, improving oral hygiene and preventing dental diseases. By addressing the challenges associated with the bioavailability, stability, and targeted delivery of herbal compounds, herbal nanotechnology has the potential to significantly advance the efficacy of natural therapies across a wide range of medical and health applications.

Novel strategies: Herbal medication delivery systems with nanoscale capabilities may improve biological activity and solve issues with plant-based remedies. Still, there are a lot of obstacles in the way of putting clinically sound treatments into practice in this area.

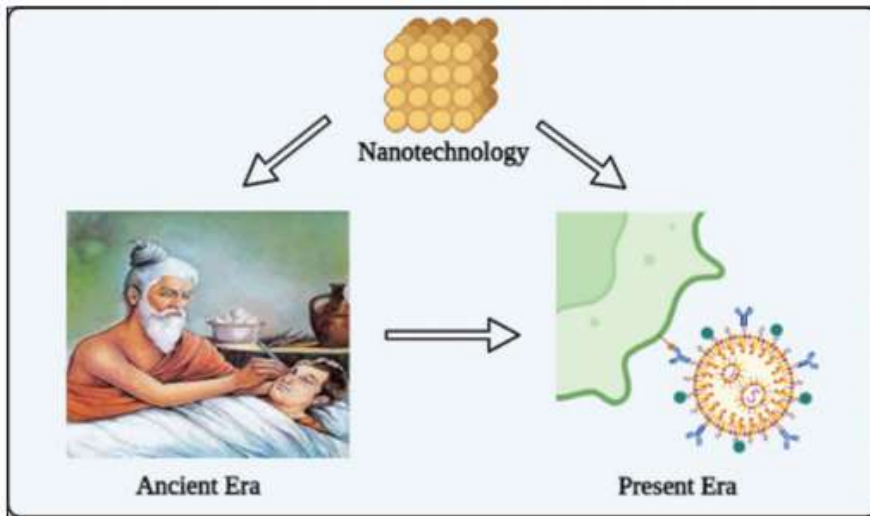


Figure 1: Nanotechnology from ancient to present era

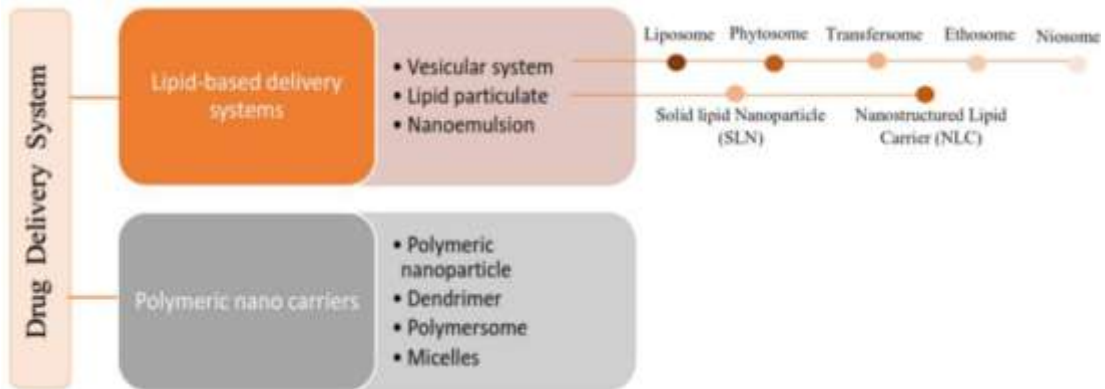


Figure 2: Nanotechnology-based delivery system for phytochemicals

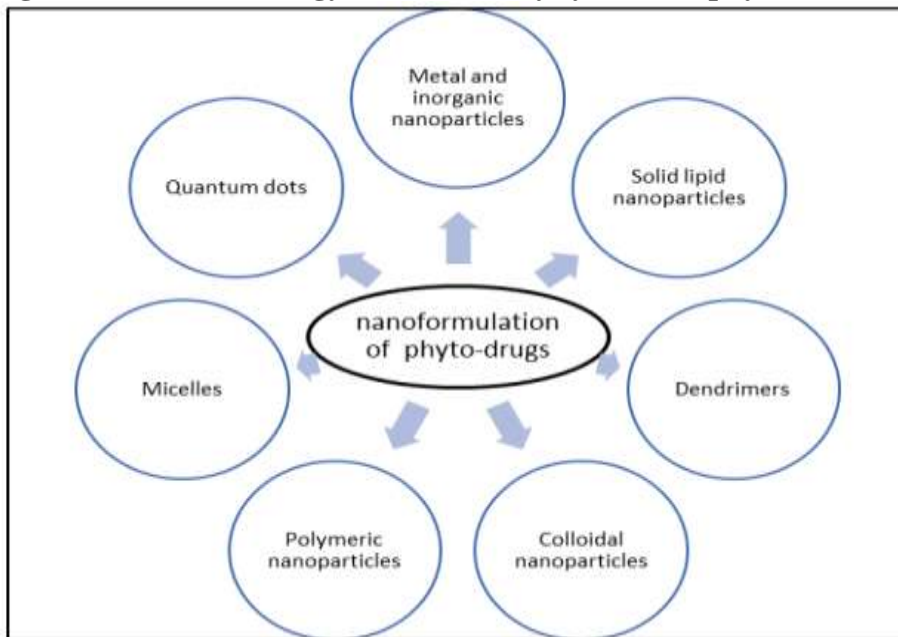


Figure 3: Different types of herbal nanoformulations

One of the main obstacles to converting these technologies into medicines is the testing of innovative approaches to regulate the interactions of nanomaterials with biological systems. The possibility of obtaining multifunctional systems to satisfy multiple biological and therapeutic requirements, as well as the viability of scaling up processes to quickly bring novel therapeutic techniques to market, are new challenges in the development of nanotechnology-based drug delivery systems. Testing the effectiveness of nanoparticle targeting and meeting global requirements for their toxicological and biocompatibility are a few more novel problems [2,15].

Current trends and future directions

- ✓ *Advanced Nanocarriers*: Researchers are currently exploring more advanced nanocarriers, such as dendrimers, quantum dots, and gold nanoparticles, for their potential in herbal drug delivery.
- ✓ *Personalized Medicine*: The integration of herbal drug nanotechnology with personalized medicine is a promising area, where nanotechnology could help tailor herbal treatments to individual patients based on their genetic and metabolic profiles.
- ✓ *Sustainability and Green Nanotechnology*: The development of eco-friendly and sustainable nanotechnology processes for herbal drug formulation is gaining attention, aligning with the broader movement towards green chemistry and sustainability in the pharmaceutical industry.

CONCLUSION

The application of nanotechnology-based delivery systems for phytochemical constituents plays an important role in public

healthcare worldwide. The use of herbal medicines is growing worldwide, but their disadvantages of low solubility, bioavailability, and pharmacological activity, as well as being physically and chemically unstable and easily degraded, limit their clinical application as medicines. Therefore, the development of herbal medicines with nanotechnology-based delivery systems might be an alternative strategy for increasing their pharmacological activity. However, the development of these nanotechnology-based delivery systems still needs to be reviewed further, especially regarding safety and toxicity profiles, so that their safety and effectiveness for curing various types of diseases can be ensured. The integration of nanotechnology with herbal medicines presents a promising approach to overcome challenges associated with the bioavailability and efficacy of medicinal plant products. This study emphasizes the potential of nanosystems in delivering active constituents at targeted concentrations throughout the treatment period, particularly in the context of cancer therapy. By developing novel nanocarrier systems, this synergistic approach aims to enhance treatment efficacy while minimizing side effects, providing valuable insights for a more sustainable and potent cancer treatment strategy. The historical roots of herbal medicines, combined with advancements in nanotechnology, showcase the evolution of traditional practices into innovative and scientifically justified formulations, paving the way for future developments in drug delivery system. The advantages of herbal nanoparticle delivery systems, such as high drug concentration at disease sites and reduced side effects, make them a compelling option for improving treatment. The comprehensive exploration of various nanocarrier types and a detailed list of herbal drugs used in cancer therapy further contribute to the understanding of this innovative approach. Overall, the study

provides insights into a potentially potent and more sustainable treatment strategy through the combination of nanotechnology and herbal drugs.

Conflicts of interest: - None -

Ethical approval: Not required.

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