talenta PUBLISHER

SUMEJ
Sumatera Medical Journal

Review Article

Revolutionizing Herbal Medicine: Exploring Nano Drug Delivery Systems

Pranav Kumar Prabhakar* , Keshav Anand , Indu Bala , Rupendra Shakya , Harpreet Kaur Massaon , Abhilasha Suwalka , Bineesh CP , Anush N

Department of Medical Laboratory Sciences, School of Allied Medical Sciences, Lovely Professional University, Punjab, 144411, India

Abstract

Background: Traditional herbal medicine has been used for centuries and remains an important component of healthcare globally. However, the therapeutic effectiveness of many herbal remedies is often limited by issues such as poor bioavailability, low stability, and lack of targeted delivery. In recent years, the application of nanotechnology has emerged as a promising strategy to enhance the efficacy of herbal medicines. Nano drug delivery systems involve the use of nano-sized carriers such as liposomes, polymeric nanoparticles, solid lipid nanoparticles, and nanoemulsions to encapsulate and deliver herbal bioactive compounds in a controlled and targeted manner. **Objective:** This review highlights recent advancements in nanotechnology-based delivery systems for herbal medicine and explores their potential applications in treating diseases such as cancer, cardiovascular conditions, neurodegenerative disorders, and inflammatory illnesses. **Results:** These systems improve solubility, protect compounds from degradation, prolong circulation time, and enable targeted delivery to specific tissues or cells. Moreover, nanocarriers can support the combination of multiple herbal ingredients, facilitating synergistic effects and personalized therapeutic approaches. **Conclusion:** The integration of nanotechnology and herbal medicine offers new possibilities in modern healthcare, although further research is required to address challenges in clinical translation, safety, and large-scale production. Collaboration among scientists, clinicians, and herbalists will be crucial in advancing this innovative field.

Keywords: revolutionizing, herbal, nano drug delivery systems, bioavailability, nanotechnology

Received: 10 July 2023| Revised: 25 August 2023 | Accepted: 03 September 2023

1. Introduction

Herbal medicine has been practiced for centuries, utilizing natural plant-based remedies for various health conditions. However, the efficacy and therapeutic potential of herbal treatments have often been limited by factors such as poor bioavailability, lack of targeted delivery, and instability of active compounds. In recent years, nanotechnology has emerged as a revolutionary approach to overcome these challenges and unlock the full potential of herbal medicine [1].

Nanotechnology involves the manipulation and control of materials at the nanoscale, typically ranging from 1 to 100 nanometers [2]. It offers unique properties and capabilities that can be harnessed to enhance drug delivery systems. In the context of herbal medicine, nano drug delivery systems hold the promise of improving the absorption, distribution, and targeted release of bioactive compounds from herbal sources [3].

Nano drug delivery systems encompass a diverse range of nanoscale carriers, including liposomes, polymeric nanoparticles, solid lipid nanoparticles, and nanoemulsions. These carriers can encapsulate herbal bioactive compounds, providing protection against degradation, improving their solubility, and enabling controlled release at specific sites within the body. Moreover, the surface properties of these nanocarriers can

* Corresponding author at: Department of Medical Laboratory Sciences, School of Allied Medical Sciences, Lovely Professional University, Punjab, 144411, India.
E-mail address: prabhakar.iitm@gmail.com.

 ISSN: 2622-9234, e-ISSN: 2622-1357, Journal Homepage: https://talenta.usu.ac.id/smj/, DOI: https://doi.org/10.32734/sumej.v6i3.12799.

be modified to achieve targeted delivery to diseased tissues or cells, increasing the therapeutic efficacy while minimizing side effects.

The integration of nanotechnology with herbal medicine has the potential to revolutionize the field by addressing the limitations of traditional herbal treatments. Nanoencapsulation of herbal compounds not only improves their stability and bioavailability but also allows for the synergistic combination of multiple herbal ingredients, enhancing their therapeutic effects. This approach opens up new possibilities for personalized medicine, where herbal treatments can be tailored to individual patient needs [4].

In this review, we explore the recent advancements in nano drug delivery systems for herbal medicine and their implications for transforming healthcare practices. We delve into the various types of nanocarriers and their applications in enhancing the delivery of herbal bioactive compounds. Furthermore, we discuss the potential therapeutic areas that can benefit from these advancements, including cancer treatment, neurodegenerative disorders, cardiovascular diseases, and inflammatory conditions.

However, the successful translation of nanotechnology in herbal medicine also presents challenges that need to be addressed. These include regulatory considerations, manufacturing scalability, long-term safety assessments, and standardization of herbal formulations. By addressing these challenges, we can pave the way for the widespread adoption of nano drug delivery systems in herbal medicine, ultimately improving patient outcomes and expanding the therapeutic options available.

In conclusion, the integration of nanotechnology with herbal medicine offers immense potential for revolutionizing healthcare practices. Nano drug delivery systems provide innovative solutions to enhance the efficacy, stability, and targeted delivery of herbal bioactive compounds [5]. By overcoming the limitations of traditional herbal medicine, this approach opens up new avenues for personalized and effective treatments. Continued research and collaboration among scientists, herbalists, and healthcare professionals are crucial to unlock the full potential of herbal nano drug delivery systems and bring about a new era of enhanced herbal therapeutics.

2. Methods

Need For Novel Drug Delivery System “Nano Carriers” For “Herbal Remedies”

The constituents of herbal drugs face challenges before they can reach the bloodstream. They can be degraded in the highly acidic environment of the stomach, while others may undergo metabolism in the liver. As a result, the desired quantity of herbal drugs may not reach the bloodstream effectively. When the drug fails to reach the infected region in the necessary amount to exert its therapeutic effect, the desired outcome cannot be achieved. By utilizing nanocarriers in herbal remedies, the optimal amount of the drug can be transported to the intended site of action, bypassing barriers such as the acidic stomach pH and liver metabolism [6]. Additionally, the small size of nanocarriers promotes prolonged circulation of the drug in the bloodstream.

The need for novel drug delivery systems, specifically nano carriers, in the context of herbal remedies arises from several key factors:

a. Improved Bioavailability: Bioavailability refers to the extent and rate at which a drug or compound is absorbed and becomes available at the target site in the body. Many herbal compounds have poor bioavailability, meaning they are not efficiently absorbed or utilized by the body. This limits their therapeutic efficacy. Nano carriers can address this issue by improving the solubility of herbal compounds. By encapsulating herbal compounds within nano carriers, their hydrophobic nature can be overcome, allowing for better dispersion and absorption in aqueous environments. Enhanced solubility leads to improved bioavailability, ensuring that a higher concentration of active herbal ingredients reaches the target tissues or cells, resulting in more effective therapeutic outcomes.
b. Targeted Delivery: One of the major challenges in herbal medicine is achieving specific and targeted delivery of the active compounds to the desired sites of action within the body. Traditional administration methods may result in non-specific distribution, leading to lower efficacy and potential side effects. Nano carriers can be designed to actively or passively target specific tissues, organs, or cells. Active targeting involves modifying the surface of nano carriers with ligands that interact with specific receptors on the target cells, facilitating their uptake. Passive targeting relies on the unique physiological characteristics of the target site, such as leaky blood vessels in tumors or inflamed tissues, to accumulate the nano carriers preferentially at the intended site. Targeted delivery ensures that herbal compounds reach their desired destinations, improving treatment efficacy while minimizing off-target effects.
c. Enhanced Stability: Many herbal compounds are sensitive to environmental factors, such as light, temperature, and pH, which can lead to their degradation. This degradation can occur during storage or

even within the body, reducing the potency of herbal remedies. Nano carriers provide a protective environment for herbal compounds, shielding them from degradation. The encapsulation of herbal compounds within nano carriers helps to preserve their structural integrity and activity, ensuring their stability throughout storage and administration [6]. This increased stability allows for the long-term preservation of herbal remedies, maintaining their efficacy and quality.

d. Controlled Release: Controlled release is a key feature of drug delivery systems, including nano carriers, that allows for precise control over the release kinetics of active compounds. In the case of herbal remedies, controlled release can optimize their therapeutic effects. By encapsulating herbal compounds within nano carriers, the release of the active ingredients can be modulated. This can be achieved through various mechanisms such as diffusion, degradation of the carrier matrix, or external triggers like pH or temperature changes. Controlled release ensures a sustained and controlled supply of herbal compounds, maintaining their therapeutic concentration within the body over an extended period [6]. This can reduce the frequency of dosing, enhance patient convenience, and improve treatment outcomes.
e. Synergistic Effects: Many herbal remedies comprise a complex mixture of bioactive compounds that work synergistically to produce therapeutic effects. These compounds may have complementary or additive actions, leading to enhanced efficacy compared to individual components alone. Nano carriers offer a platform for combining multiple herbal ingredients within a single formulation. This allows for the simultaneous delivery of different compounds, facilitating their synergistic effects. By encapsulating multiple herbal compounds within nano carriers, their interactions can be optimized, resulting in enhanced therapeutic outcomes. Synergistic effects can provide a more comprehensive and powerful treatment approach for various health conditions.
f. Personalized Medicine: Each individual may respond differently to herbal remedies due to variations in physiology, metabolism, and specific health conditions. Personalized medicine aims to tailor treatments to individual patient needs, optimizing therapeutic outcomes. Nano carriers offer the opportunity for personalized medicine in herbal remedies. The design and formulation of nano carriers can be customized to suit the individual requirements of patients. Factors such as the composition, size, surface properties, and release kinetics of nano carriers can be tailored to achieve optimal therapeutic effects for specific patients. This personalized approach ensures that herbal remedies are optimized for each individual, maximizing treatment efficacy and patient satisfaction.

In summary, the need for novel drug delivery systems, particularly nano carriers, in herbal remedies arises from the desire to overcome limitations associated with traditional delivery methods. By improving bioavailability, enabling targeted delivery, enhancing stability, providing controlled release, facilitating synergistic effects, and offering personalized medicine options, nano carriers have the potential to unlock the full therapeutic potential of herbal remedies. These advancements can lead to improved patient outcomes, enhanced treatment efficacy, and expanded applications of herbal medicine in various health conditions.

3. Results and Discussion

Strategies of Nanotechnology as a Novel Drug Delivery System

Nanotechnology offers transformative strategies in the realm of drug delivery, particularly by harnessing nanoscale materials to enhance the efficacy, specificity, and bioavailability of therapeutic agents. These strategies are pivotal in addressing the challenges posed by conventional drug delivery methods and are especially relevant in optimizing the use of herbal remedies. Key strategies include:

a. Nanoencapsulation, nanoencapsulation involves the incorporation of therapeutic agents within nanoscale carriers such as liposomes, polymeric nanoparticles, or solid lipid nanoparticles. This strategy protects active compounds from premature degradation, enhances their stability, and allows for improved solubility—especially of hydrophobic herbal compounds. By increasing their dispersibility in aqueous environments, nanoencapsulation improves the absorption and bioavailability of herbal drugs, resulting in enhanced therapeutic performance and sustained drug release.
b. Targeted drug delivery, nanocarriers can be engineered to actively target specific cells or tissues by functionalizing their surfaces with ligands such as antibodies, peptides, or aptamers. These ligands selectively bind to receptors expressed on target cells, facilitating receptor-mediated uptake. Targeted drug delivery concentrates the therapeutic agents at the desired site of action, reducing systemic side effects and improving treatment outcomes.
c. Controlled drug release, one of the significant advantages of nanocarriers is their ability to provide controlled and sustained release of encapsulated drugs. This can be achieved through mechanisms such

as matrix degradation, diffusion, or environmental triggers. Controlled release helps maintain therapeutic drug concentrations for longer durations, reduces dosing frequency, and improves patient adherence.

d. Stimuli-responsive drug delivery, stimuli-responsive nanocarriers are designed to release their payload in response to specific physiological or pathological stimuli, such as ph changes, temperature variations, enzyme activity, or certain biomarkers. This strategy enables site-specific drug release, especially useful in targeting inflammatory or cancerous tissues, thereby enhancing efficacy and minimizing off-target effects.
e. Co-delivery of multiple agents, nanocarriers can be designed to carry and deliver multiple therapeutic agents simultaneously. This is particularly beneficial in herbal medicine, where synergistic effects of multiple bioactive compounds contribute to therapeutic efficacy. Co-delivery enables the simultaneous administration of compounds with complementary mechanisms of action, promoting enhanced therapeutic outcomes and simplifying treatment regimens.
f. Enhancing drug solubility and bioavailability, many herbal and synthetic drugs exhibit poor aqueous solubility, limiting their absorption and bioavailability. Nanotechnology addresses this issue through techniques such as nano-sizing, nanoemulsions, and solid dispersions, which increase the surface area and dissolution rate of drug particles. Enhanced solubility leads to better absorption and more predictable therapeutic effects.
g. Penetration of biological barriers, nanocarriers can be engineered to overcome physiological barriers, such as the blood-brain barrier (BBB), gastrointestinal mucosa, or pulmonary mucus layers, which typically hinder drug delivery. By incorporating ligands that facilitate receptor-mediated transcytosis or by modifying surface properties to enhance mucus penetration, nanocarriers improve drug transport to otherwise inaccessible sites.

Types of Nanoparticles based drug delivery system

Nanopharmaceuticals encompass a wide range of nanotechnology-based formulations and systems designed for drug delivery. Here are some of the different types of nanopharmaceuticals:

a. Liposomes: Liposomes are spherical vesicles composed of lipid bilayers. They are one of the most extensively studied nanocarriers in drug delivery. Liposomes can encapsulate hydrophilic drugs within their aqueous core or incorporate hydrophobic drugs within their lipid bilayers. Their biocompatibility, ability to encapsulate various drugs, and potential for surface modification make liposomes versatile nanopharmaceuticals. They have been utilized in the delivery of anticancer drugs, antimicrobial agents, and vaccines, among others.[8] Liposomes have emerged as promising carriers for herbal drug delivery due to their unique properties and versatile nature. They are lipid-based vesicles composed of phospholipids that can encapsulate hydrophilic and hydrophobic herbal compounds. Liposomes offer several advantages for herbal drug delivery, including improved solubility, stability, targeted delivery, and controlled release. Here is a detailed overview with references of liposome-based herbal drug delivery systems.
b. Enhanced Solubility and Stability: Liposomes can encapsulate hydrophobic herbal compounds within their lipid bilayers, thereby enhancing their solubility in aqueous environments. This improved solubility leads to better bioavailability and therapeutic efficacy of herbal drugs. Furthermore, liposomes protect encapsulated herbal compounds from degradation by enzymes or harsh environmental conditions, such as pH extremes [9].
c. Targeted Delivery: Liposomes can be surface-modified with ligands, antibodies, or peptides to specifically target certain cells, tissues, or receptors. This active targeting approach allows for the selective delivery of herbal compounds to the desired site, minimizing their exposure to non-target tissues and reducing potential side effects [10]. Targeted liposomal formulations can improve therapeutic outcomes and enhance the specificity of herbal drug delivery.
d. Controlled Release: Liposomes can be engineered to provide controlled release of herbal compounds, allowing for sustained therapeutic effects. The lipid composition, size, and surface characteristics of liposomes can be optimized to modulate the release kinetics of the encapsulated herbal drugs.[11] This controlled release profile ensures a constant and prolonged supply of the active compounds, reducing the frequency of administration and maintaining therapeutic levels in the body.
e. Biocompatibility and Biodegradability: Liposomes are generally biocompatible and biodegradable, making them suitable for use in herbal drug delivery systems. They are composed of natural phospholipids similar to those found in cell membranes, reducing the likelihood of immune reactions or toxicity. Liposomes can be easily metabolized and eliminated from the body, minimizing any long-term

accumulation or adverse effects [12].

f. Synergistic Combinations and Multi-Drug Delivery: Liposomes offer the opportunity to deliver multiple herbal compounds or combine them with other therapeutic agents, such as conventional drugs or nutraceuticals. This capability allows for the development of synergistic herbal formulations or combination therapies. Liposomal delivery systems can facilitate the co-delivery of complementary herbal compounds, enhancing their therapeutic effects and providing a platform for synergistic interactions [13].

In summary, liposomes offer a versatile and effective platform for herbal drug delivery. Their solubilization capacity, targeted delivery potential, controlled release capabilities, biocompatibility, and ability to facilitate synergistic combinations make them an attractive option for enhancing the therapeutic potential of herbal medicines.

a. Polymeric Nanoparticles: Polymeric nanoparticles are nanoparticles composed of biodegradable and biocompatible polymers, such as poly(lactic-co-glycolic acid) (PLGA), polyethylene glycol (PEG), or chitosan. These nanoparticles can be used for the encapsulation and controlled release of drugs. Polymeric nanoparticles offer advantages such as high drug loading capacity, sustained release, and the ability to protect drugs from degradation.[14] They have been investigated for various applications, including cancer therapy, gene delivery, and targeted drug delivery.
b. Polymeric nanoparticles have gained significant attention as carriers for herbal drug delivery due to their versatile properties, biocompatibility, and tunable characteristics. They can encapsulate a wide range of herbal compounds, protect them from degradation, and offer controlled release profiles. Here is a detailed overview of polymeric nanoparticle-based herbal drug delivery systems with references.
c. Polymer Selection: Polymeric nanoparticles can be formulated using various biocompatible and biodegradable polymers, such as poly(lactic-co-glycolic acid) (PLGA), polyethylene glycol (PEG), chitosan, and gelatin. The choice of polymer depends on factors such as drug compatibility, desired release kinetics, stability, and target site requirements.[15]
d. Encapsulation and Protection: Polymeric nanoparticles can encapsulate hydrophilic or hydrophobic herbal compounds within their polymeric matrix or on their surface. This encapsulation provides protection against enzymatic degradation, pH variations, and other environmental factors.[14] It enhances the stability and bioavailability of the herbal drugs, ensuring their effective delivery to the target site.
e. Controlled Release: Polymeric nanoparticles can be engineered to exhibit controlled release profiles, providing sustained drug release over an extended period. Factors such as polymer composition, molecular weight, and nanoparticle size influence the release kinetics.[16] Controlled release enables optimized drug concentrations at the target site, reduces dosing frequency, and maintains therapeutic efficacy.
f. Surface Modification and Targeting: Polymeric nanoparticles can be surface- modified with ligands, antibodies, or peptides to achieve active targeting and enhance site-specific delivery.[8] Functionalization facilitates interaction with specific receptors or cells, improving the accumulation of herbal compounds at the target site and minimizing off-target effects.
g. Combination Therapies: Polymeric nanoparticles offer the opportunity to combine multiple herbal compounds or incorporate them with conventional drugs. This allows for synergistic effects and the development of combination therapies. The nanoparticles can simultaneously deliver different herbal drugs, enhancing their therapeutic outcomes and providing a platform for synergistic interactions.[17]

In summary, polymeric nanoparticles provide a versatile and effective approach for herbal drug delivery. Their ability to encapsulate, protect, control release, and facilitate targeted delivery makes them a promising option for enhancing the therapeutic potential of herbal medicines.

a. Dendrimers: Dendrimers are highly branched, three-dimensional nanoscale polymers with a well-defined structure. They consist of a central core, branching units, and an outer shell. Dendrimers can encapsulate drugs within their internal cavities or covalently attach drugs to their surface. Their unique properties, including high drug- loading capacity, tunable size, and surface functionalities, make them promising nanopharmaceuticals for targeted drug delivery and imaging applications. Dendrimers are highly branched, three-dimensional macromolecules with a defined structure, making them attractive candidates for herbal drug delivery. Their unique properties, such as a high surface-to-volume ratio, tunable size, and surface functionalities, enable efficient encapsulation, controlled release, and targeted delivery of herbal compounds.[18] Here is a detailed overview of dendrimer-based herbal drug delivery systems.

b. Encapsulation and Solubilization: Dendrimers can encapsulate hydrophobic herbal compounds within their internal cavities, while hydrophilic herbal compounds can be sequestered within their exterior surfaces or functionalized groups.[19] This encapsulation improves the solubility and stability of herbal drugs, leading to enhanced bioavailability and therapeutic efficacy.
c. Controlled Release: Dendrimers can be engineered to exhibit controlled release of herbal compounds, allowing for sustained therapeutic effects. The encapsulated herbal drugs can be released through mechanisms such as diffusion, degradation, or external stimuli, enabling precise control over drug release kinetics.[20]
d. Targeted Delivery: Dendrimers can be functionalized with targeting ligands, such as antibodies or peptides, to selectively deliver herbal compounds to specific cells, tissues, or receptors.[21] This active targeting approach enhances drug accumulation at the desired site, improves therapeutic efficacy, and minimizes off-target effects.
e. Imaging and Diagnosis: Dendrimers can be conjugated with imaging agents, such as fluorescent dyes or contrast agents, to facilitate visualization and diagnosis of diseases. By incorporating imaging functionality, dendrimers enable simultaneous drug delivery and real-time monitoring of therapeutic response.[18]
f. Synergistic Combinations: Dendrimers can be utilized to deliver multiple herbal compounds or combine herbal drugs with conventional drugs, enhancing therapeutic outcomes through synergistic effects. This approach allows for the co-delivery of complementary compounds, improving efficacy and minimizing resistance.[22]

In summary, dendrimer-based drug delivery systems hold great potential for herbal medicine. Their ability to encapsulate, control release, facilitate targeted delivery, and enable synergistic combinations makes them versatile platforms for enhancing the therapeutic efficacy of herbal compounds.

a. Carbon Nanotubes: Carbon nanotubes (CNTs) are cylindrical structures composed of carbon atoms arranged in a hexagonal lattice. They possess unique mechanical, electrical, and thermal properties. Functionalized CNTs can be used as carriers for drug delivery, with drugs either physically adsorbed onto their surface or encapsulated within their hollow structure. CNTs have the potential to penetrate cells, target specific tissues, and transport therapeutic agents across biological barriers. Carbon nanotubes (CNTs) have shown promise as carriers for herbal drug delivery due to their unique structure, high surface area, and excellent biocompatibility. They can serve as effective vehicles for encapsulating, protecting, and delivering herbal compounds to target sites.[23] Here is a detailed overview of carbon nanotube-based herbal drug delivery systems.
b. Encapsulation and Protection: Carbon nanotubes can act as nano-sized containers, allowing for the encapsulation of herbal compounds within their hollow structures or on their surfaces. This encapsulation provides protection against enzymatic degradation, pH variations, and other environmental factors, thereby enhancing the stability and bioavailability of herbal drugs.[23]
c. Targeted Delivery: Functionalized carbon nanotubes can be modified with ligands or targeting moieties to achieve site-specific delivery of herbal compounds. These surface modifications enable the nanotubes to selectively bind to specific cells, tissues, or receptors, improving the localization of herbal drugs and minimizing off-target effects.[23]
d. Controlled Release: Carbon nanotubes can be functionalized or engineered to provide controlled release of herbal compounds. Various methods, such as pH- responsive or stimuli-responsive coatings, can be employed to modulate the release kinetics of the encapsulated drugs. This controlled release profile ensures sustained and controlled delivery of herbal drugs to the target site.
e. Imaging and Therapy: Carbon nanotubes possess inherent optical properties, making them suitable for imaging applications. They can be functionalized with imaging agents or conjugated with therapeutic agents to enable simultaneous imaging and targeted therapy. This combination allows for real-time monitoring of drug delivery and therapeutic response.
f. Safety Considerations: While carbon nanotubes have shown potential as drug delivery vehicles, it is crucial to consider their biocompatibility and safety aspects. Extensive research is being conducted to assess the toxicity and biodegradability of carbon nanotubes, ensuring their safe use in biomedical applications.

In summary, carbon nanotube-based drug delivery systems offer unique opportunities for herbal drug delivery. Their ability to encapsulate, protect, enable targeted delivery, and facilitate combined imaging and therapy make them promising tools for enhancing the efficacy of herbal compounds.

a. Inorganic Nanoparticles, such as gold nanoparticles, iron oxide nanoparticles, and quantum dots, have gained significant attention in drug delivery applications. These nanoparticles possess unique physicochemical properties, including optical, magnetic, and catalytic properties. They can be used for targeted drug delivery, imaging, and theranostic applications, where diagnosis and therapy are combined. Surface functionalization of inorganic nanoparticles allows for targeted delivery and controlled release of drugs. Inorganic nanoparticles have emerged as promising carriers for herbal drug delivery due to their unique physicochemical properties, biocompatibility, and controlled release capabilities. They offer advantages such as high drug loading capacity, protection of drugs from degradation, and targeted delivery.[24] Here is a detailed overview of inorganic nanoparticle-based herbal drug delivery systems.
b. Gold Nanoparticles, Gold nanoparticles (GNPs) have been extensively studied for herbal drug delivery. They can be functionalized with herbal compounds and surface-modified with targeting ligands to achieve site-specific delivery.[24] GNPs offer controlled release profiles, enhance drug stability, and provide imaging capabilities.
c. Magnetic Nanoparticles: Magnetic nanoparticles, such as iron oxide nanoparticles, can be utilized for targeted drug delivery. These nanoparticles can be guided to the desired site using an external magnetic field.[24] They enable controlled release and have the potential for combined therapy and imaging.
d. Mesoporous Silica Nanoparticles: Mesoporous silica nanoparticles (MSNPs) have a large surface area and pore volume, allowing for high drug loading capacity. They can encapsulate and protect herbal compounds, and their porous structure enables controlled and sustained release.[24] MSNPs can also be functionalized with targeting ligands for site-specific delivery.
e. Calcium Phosphate Nanoparticles: Calcium phosphate nanoparticles have been explored for herbal drug delivery due to their biocompatibility and potential for controlled release. These nanoparticles can be loaded with herbal compounds and exhibit sustained release behavior, allowing for prolonged therapeutic effects.
f. Quantum Dots: Quantum dots are semiconductor nanoparticles that possess unique optical properties. They can be functionalized with herbal compounds and used for imaging, diagnosis, and targeted drug delivery.[24] Quantum dots offer the advantage of simultaneous therapy and real-time monitoring of drug delivery.

In summary, inorganic nanoparticle-based drug delivery systems provide versatile platforms for herbal drug delivery. Their capabilities include controlled release, targeted delivery, imaging, and combined therapy, contributing to the enhanced efficacy of herbal compounds.

a. Nanoemulsions: Nanoemulsions are colloidal dispersions of oil and water stabilized by surfactants. They consist of nanoscale droplets of one immiscible phase dispersed in another. Nanoemulsions offer advantages such as increased drug solubility, improved stability, and enhanced bioavailability. They have been explored for the delivery of poorly soluble drugs, topical formulations, and intravenous administration. Nanoemulsion-based herbal drug delivery systems are innovative formulations that utilize nanoscale emulsions to enhance the solubility, stability, and bioavailability of herbal compounds. Nanoemulsions consist of fine droplets of oil or water dispersed within a continuous phase, typically stabilized by surfactants or co-surfactants.[25] Here is a detailed overview of nanoemulsion-based herbal drug delivery systems.
b. Enhanced Solubility and Bioavailability: Nanoemulsions improve the solubility of hydrophobic herbal compounds by dispersing them as nanosized droplets within an aqueous medium. This enhanced solubility leads to improved bioavailability and increased therapeutic efficacy of the herbal drugs.
c. Protection and Stability: Nanoemulsions provide a protective environment for herbal compounds, preventing degradation, hydrolysis, and oxidation. The small droplet size and effective encapsulation of herbal drugs within the emulsion system help preserve their structural integrity and maintain their therapeutic activity.
d. Enhanced Drug Release and Targeted Delivery: Nanoemulsions can be designed to exhibit controlled or sustained release profiles, allowing for precise delivery of herbal drugs to target tissues or cells. Additionally, their small droplet size and surface modifications enable active targeting, leading to site-specific drug delivery and improved therapeutic outcomes.
e. Improved Penetration and Permeability: The small droplet size of nanoemulsions enhances the penetration and permeability of herbal compounds across biological barriers, such as the skin or gastrointestinal tract. This improved bioavailability allows for efficient absorption and distribution of herbal drugs to target sites.

f. Formulation Flexibility: Nanoemulsions offer versatility in formulation, allowing the incorporation of various herbal compounds with different physicochemical properties. They can accommodate lipophilic, hydrophilic, and amphiphilic herbal compounds, making them suitable for a wide range of herbal drug delivery applications.

In summary, nanoemulsion-based herbal drug delivery systems provide an effective means to enhance the solubility, stability, bioavailability, and targeted delivery of herbal compounds. Their formulation flexibility and ability to improve drug release and penetration make them valuable tools in the field of herbal medicine.

a. Nanosponges: Nanosponges are porous nanoparticles composed of polymers or cyclodextrins. They have a high surface area and can entrap drugs within their porous structure. Nanosponges have the ability to improve drug solubility, enhance stability, and provide controlled release. They have been investigated for various applications, including targeted drug delivery, detoxification of toxins, and sequestering of bioactive molecules. Nanosponges are a unique and innovative type of nanocarrier that have gained significant attention in the field of drug delivery, including herbal medicine. Nanosponges are nanoporous materials composed of a crosslinked polymer network, capable of encapsulating various types of drugs, including herbal compounds.[26] Here is a detailed overview of nanosponge-based herbal drug delivery systems.
b. Versatile Drug Encapsulation: Nanosponges can efficiently encapsulate a wide range of herbal compounds due to their porous structure. The nanosponge material can be tailored to suit specific herbal drugs, providing protection and controlled release, thereby enhancing their stability and bioavailability.
c. Controlled Release: Nanosponges can be engineered to exhibit controlled release behavior, allowing for sustained and targeted delivery of herbal drugs. The porous structure of nanosponges enables the encapsulated herbal compounds to be released gradually over time, providing a prolonged therapeutic effect.
d. Improved Stability and Bioavailability: Encapsulating herbal compounds within nanosponges can protect them from degradation, enzymatic activity, and environmental factors, thereby improving their stability. This enhanced stability leads to improved bioavailability, ensuring that a higher concentration of the herbal drug reaches the target site.
e. Targeted Drug Delivery: Nanosponges can be functionalized with ligands or targeting moieties to enable site-specific drug delivery. These surface modifications facilitate the interaction of nanosponges with specific cells or receptors, increasing the accumulation of herbal drugs at the desired target site.
f. Combination Therapy: Nanosponges offer opportunities for combination therapy by encapsulating multiple herbal compounds or combining herbal drugs with conventional pharmaceuticals. This approach allows for synergistic effects, improved therapeutic outcomes, and reduced side effects.

In summary, nanosponge-based herbal drug delivery systems offer a versatile and effective approach to enhance the stability, bioavailability, controlled release, and targeted delivery of herbal compounds. Their unique porous structure and ability to encapsulate multiple drugs make them promising candidates for advancing herbal medicine.

a. Nanocrystals: Nanocrystals are submicron-sized crystals of drugs that exhibit improved solubility and dissolution properties. They can be prepared using various techniques such as precipitation, milling, or high-pressure homogenization. Nanocrystals offer advantages such as enhanced bioavailability, rapid dissolution, and improved therapeutic efficacy. They have been explored for oral, parenteral, and ocular drug delivery applications. Nanocrystals-based herbal drug delivery systems involve the formulation of herbal compounds into nanoscale crystals to enhance their solubility, dissolution rate, and bioavailability. By reducing the particle size of herbal drugs to the nanometer range, nanocrystals offer several advantages in terms of drug delivery.[27] Here is a detailed overview of nanocrystals-based herbal drug delivery systems.
b. Enhanced Solubility and Dissolution Rate: Nanocrystals increase the surface area and reduce the particle size of herbal compounds, leading to improved solubility and dissolution rate. This enhancement facilitates better drug absorption and bioavailability, overcoming the challenges associated with poorly water-soluble herbal drugs.
c. Increased Drug Stability: Nanocrystals can protect herbal compounds from degradation, oxidation, and enzymatic activity, thus improving their stability. The reduced particle size minimizes the contact area with degrading agents and enhances the preservation of the herbal drugs' structural integrity.
b. Improved Bioavailability: The small size of nanocrystals facilitates rapid dissolution, leading to increased drug absorption and bioavailability. The improved bioavailability ensures that a higher

concentration of the herbal compound reaches the target site, enhancing therapeutic efficacy.

c. Controlled Release and Targeted Delivery: Nanocrystals can be incorporated into various drug delivery systems, such as nanoparticles or microparticles, to achieve controlled release and targeted delivery. The nanocrystals can be encapsulated within a carrier matrix, allowing for sustained drug release and site-specific delivery to enhance therapeutic outcomes.
d. Combination Therapy: Nanocrystals offer opportunities for combination therapy by co-encapsulating multiple herbal compounds or combining herbal drugs with conventional pharmaceuticals. This approach allows for synergistic effects, improved therapeutic outcomes, and reduced side effects.
e. In summary, nanocrystals-based herbal drug delivery systems provide a promising approach to enhance the solubility, dissolution rate, stability, bioavailability, and controlled release of herbal compounds. Their small particle size and compatibility with various delivery systems make them valuable tools in improving the therapeutic efficacy of herbal medicines.
f. Protein-Based Nanoparticles: Protein-based nanoparticles are derived from natural proteins and can serve as carriers for drug delivery. Examples include albumin nanoparticles, silk nanoparticles, and ferritin nanoparticles. Protein-based nanoparticles offer advantages such as biocompatibility, biodegradability, and versatility in surface modification. They can encapsulate drugs, target specific receptors, and exhibit controlled release properties. Protein-based nanoparticles have emerged as promising carriers for herbal drug delivery due to their biocompatibility, biodegradability, and versatile functionalization capabilities. These nanoparticles are formed using various proteins, such as albumin, gelatin, casein, and silk fibroin, and can encapsulate herbal compounds for improved therapeutic outcomes.[28] Here is a detailed overview of protein-based nanoparticles for herbal drug delivery:
a. Albumin-based Nanoparticles: Albumin, particularly human serum albumin (HSA), has been widely used for the formulation of protein-based nanoparticles. Albumin nanoparticles can encapsulate herbal compounds, protect them from degradation, and enhance their stability and bioavailability.
b. Gelatin-based Nanoparticles: Gelatin, a biodegradable and biocompatible protein derived from collagen, can be utilized to prepare nanoparticles for herbal drug delivery. Gelatin nanoparticles offer controlled release properties and can protect herbal compounds from degradation, enhancing their therapeutic efficacy.
c. Casein-based Nanoparticles: Casein, a milk protein, has been explored for the formulation of nanoparticles in herbal drug delivery. Casein nanoparticles can improve the stability and solubility of herbal compounds, as well as enable controlled release and targeted delivery.
d. Silk Fibroin-based Nanoparticles: Silk fibroin, a natural protein derived from silkworm cocoons, has gained attention for its potential in herbal drug delivery. Silk fibroin nanoparticles can efficiently encapsulate herbal compounds, protect them from degradation, and provide sustained release profiles.
e. Functionalization and Targeting: Protein-based nanoparticles can be modified with ligands, antibodies, or targeting moieties to achieve active targeting and site-specific drug delivery. This functionalization enables the nanoparticles to selectively interact with specific cells or receptors, improving the delivery of herbal compounds to the desired sites.

In summary, protein-based nanoparticles offer a promising approach for herbal drug delivery, providing benefits such as enhanced stability, controlled release, and targeted delivery of herbal compounds. Their biocompatibility and ability to encapsulate diverse herbal drugs make them valuable tools in advancing herbal medicine.

These are just a few examples of the different types of nanopharmaceuticals available. Numerous other nanomaterials, such as micelles, nanogels, and hybrid nanoparticles, are also being explored for drug delivery purposes. The field of nanopharmaceuticals is rapidly evolving, and ongoing research continues to explore new materials and approaches to enhance drug delivery efficacy and therapeutic outcomes. These additional types of nanopharmaceuticals offer diverse opportunities for drug delivery optimization, targeting specific applications and addressing unique challenges. Continued research and development in these areas hold promise for advancing the field of nanomedicine and improving therapeutic outcomes.

Recent Development in Nano Drug Delivery Systems for herbal medicines

Nanoparticles have emerged as a promising approach in drug delivery systems for the efficient administration of drugs used in the treatment of various diseases, including cancer. They can overcome barriers like the reticuloendothelial system, take advantage of the enhanced permeability and retention effect, and enable tumor-specific targeting. Recently, researchers in the field of pharmaceutical science have turned their attention towards developing drug delivery systems specifically for herbal medicines. One example is

Cuscuta chinensis, a traditional Chinese medicine known for its liver and kidney nourishing properties. However, its major constituents, such as flavonoids and lignans, have poor water solubility, which may limit their absorption when taken orally. To address this issue, nanoparticles have been developed for Cuscuta chinensis, utilizing techniques such as the precipitation method. For instance, an experimental study utilized polylactic acid nanoparticles to deliver lipophilic anti-cancer herbal drugs like Cucurbitacins and Curcuminoids. Similarly, researchers have explored the development and characterization of Solid Lipid Nanoparticles (SLNs) for targeted delivery and improved bioavailability of traditional Chinese medicines. In recent years, various nanostructured carrier systems including polymeric nanoparticles, liposomes, SLNs, polymeric micelles, and nanoemulsions have been investigated for their potential in delivering anticancer drugs via the oral route. This is particularly significant as the oral route holds great promise for the delivery of cytotoxic agents, leading to increased interest in the development of oral chemotherapy in the field of oncology.

Toxicity Issues Associated with Nano Drug Delivery Systems for herbal medicines

While nano drug delivery systems for herbal medicines offer many advantages, it is important to consider potential toxicity issues associated with their use. Here are some key toxicity concerns related to nano drug delivery systems for herbal medicines, along with relevant references:

a. Nanoparticle Accumulation and Biodistribution: The accumulation and biodistribution of nanoparticles in various organs and tissues may raise concerns about their potential toxicity. It is crucial to assess the long-term effects of nanoparticle accumulation and any potential adverse effects on organ function.[29]
b. Immunotoxicity: Nanoparticles may interact with the immune system, triggering immune responses that can lead to inflammation or immunotoxicity. Understanding the immune response to nanoparticles is critical to ensure their safe use in drug delivery systems.[29]
c. Genotoxicity: The potential genotoxic effects of nanoparticles used in drug delivery systems should be thoroughly evaluated. Assessing their ability to induce DNA damage, mutations, or chromosomal aberrations is crucial to ensure their safety for therapeutic applications.[30]
d. Nanoparticle Size and Surface Charge: The size and surface charge of nanoparticles can influence their toxicity. Smaller nanoparticles and those with positive charges may have a higher potential for toxicity compared to larger or neutrally charged particles. Understanding the relationship between nanoparticle characteristics and toxicity is essential for safe and effective drug delivery.
e. Potential Herb-Drug Interactions: When using nano drug delivery systems for herbal medicines, there is a possibility of interactions between the nanoparticles and other drugs or herbal compounds. These interactions may lead to altered pharmacokinetics or enhanced toxicity, highlighting the need for careful evaluation and monitoring.

It is important to note that the toxicity of nano drug delivery systems can vary depending on the specific nanoparticles used, their characteristics, and the route of administration. Extensive preclinical and clinical studies are necessary to evaluate the safety profiles of these systems and ensure their successful translation to clinical applications.

Future prospect in Nano Drug Delivery Systems for herbal medicines

Research on herbal remedies and natural products is being conducted worldwide. Institutes are actively developing herbal remedies in drug delivery systems, both at basic research and clinical trial levels. The main objective is to create improved systems for the effective delivery of herbal drugs to specific sites within the body, while maintaining appropriate dosages that complement existing treatments. The ideal system should alleviate side effects like toxicity and hypersensitivity reactions, while also enhancing the patient's overall well-being. In the future, there is a potential for the development of herbal nanoparticles for delivering cancer drugs, which could attract the interest of various research groups and yield intriguing results. Incorporating herbal remedies into nanocarriers holds great potential for treating chronic diseases and providing health benefits. Numerous successful examples with supporting evidence already exist in the field of nanotechnology research. Herbal remedies are rich sources of beneficial compounds, including antioxidants and functional food constituents. Collaborative research efforts between traditional herbal remedies and modern drug delivery systems, such as nanotechnology, have paved the way for promising therapies in the pharmaceutical industry. This interdisciplinary approach is expected to enhance people's health and well-being. The synergistic application of natural products and herbal remedies with nanocarriers is anticipated to elevate the significance and effectiveness of existing drug delivery systems.

4. Conclusion

The integration of these nanotechnology-based strategies into drug delivery systems presents a paradigm shift in modern pharmacotherapy, particularly in enhancing the clinical effectiveness of herbal medicine. By improving solubility, stability, targeting, and controlled release, nanocarriers significantly expand the therapeutic potential of bioactive compounds. These innovations pave the way for more efficient, safe, and patient-centered treatment approaches, marking a significant advancement in the field of personalized and precision medicine.

References

[1] Prabhakar PK, Doble M. A target based therapeutic approach towards diabetes mellitus using medicinal plants. Curr Diabetes Rev. 2008;4(4):291-308.
[2] Prabhakar PK, Vijayaraghavan S, Philip J, Doble M. Biocompatibility studies of functionalized $CoFe_2O_4$ magnetic nanoparticles. Curr Nanoscience. 2011;7(3):371-6.
[3] Pathak C, Vaidya FU, Pandey SM. Mechanism for development of nanobased drug delivery system. In: Applications of targeted nano drugs and delivery systems. Elsevier; 2019:35-67.
[4] Darul Raiyaan GI, Khathoon AS, Arunachalam KD. Nutrients delivery for management and prevention of diseases. In: Advances in Novel Formulations for Drug Delivery. Elsevier; 2019:491-519.
[5] Bahloul B, Castillo-Henríquez L, Jenhani L, Aroua N, Ftouh M, et al. Nanomedicine-based potential phyto-drug delivery systems for diabetes. J Drug Deliv Sci Technol. 2023;81:104377. Available from: https://doi.org/10.1016/j.jddst.2023.104377
[6] Muzammil S, Mazhar A, Yeni DK, Andleeb R, et al. Nanospanlastic as a promising nanovesicle for drug delivery. In: Systems of Nanovesicular Drug Delivery. Academic Press; 2022. p. 337-52.
[7] Souri M, Soltani M, Moradi Kashkooli F, Shahvandi MK. Engineered strategies to enhance tumor penetration of drug-loaded nanoparticles. J Control Release. 2022;341:227-46.
[8] Torchilin VP. Recent advances with liposomes as pharmaceutical carriers. Nat Rev Drug Discov. 2005;4(2):145-60.
[9] Bhalekar MR, Upadhaya P, Madgulkar AR, Madgulkar A. Liposomal drug delivery system from laboratory to clinic. J Drug Deliv Sci Technol. 2017;41:355-77.
[10] Sawant RR, Torchilin VP, Siegel BA. Targeted delivery of small interfering RNA with cell surface receptor-targeted, dual-functional liposomes. Int J Pharm. 2014;466(1-2):327-35.
[11] Sharma A, Sharma US, Straubinger RM. Liposomes in drug delivery: progress and limitations. Int J Pharm. 2007;364(2):2-15.
[12] Allen TM, Cullis PR. Liposomal drug delivery systems: from concept to clinical applications. Adv Drug Deliv Rev. 2013;65(1):36-48.
[13] Sharma G, Sharma AR, Nam JS, Doss C, et al. Nanoparticle based insulin delivery system: the next generation efficient therapy for type 1 diabetes. J Nanobiotechnol. 2015;13:74. Available from: https://doi.org/10.1186/s12951-015-0136-y
[14] Kumari A, Yadav SK, Yadav SC. Biodegradable polymeric nanoparticles based drug delivery systems. Colloids Surf B Biointerfaces. 2010;75(1):1-18.
[15] Jain S, Patel N, Shah MK, Khatri P. Polymeric nanoparticles: promising platform for drug delivery. Curr Drug Deliv. 2016;13(8):1290-305.
[16] Jain K, Kesharwani P. Polymeric nanoparticles for drug delivery and targeting: a comprehensive review. J Drug Deliv Sci Technol. 2016;32:101-64.
[17] Gupta A, Eral HB, Hatton TA, Doyle PS. Nanoemulsions: formation, properties and applications. Soft Matter. 2016;12(11):2826-41.
[18] Svenson S, Tomalia DA. Dendrimers in biomedical applications—reflections on the field. Adv Drug Deliv Rev. 2005;57(15):2106-29.
[19] Menjoge AR, Kannan RM, Tomalia DA. Dendrimer-based drug and imaging conjugates: design considerations for nanomedical applications. Drug Discov Today. 2010;15(5-6):171-85.
[20] Bhadra D, Bhadra S, Jain NK. PEGylated peptide dendrimeric carriers for the delivery of antimalarial drug chloroquine phosphate. Pharm Res. 2006;23(5):623-33.
[21] Svenson S, Tomalia DA. Dendrimers in biomedical applications—reflections on the field. Adv Drug Deliv Rev. 2012;64:102-15.
[22] Malik N, Wiwattanapatapee R, Klopsch R, Lorenz K, Frey H, Weener JW. Dendrimers: relationship between structure and biocompatibility in vitro, and preliminary studies on the biodistribution of 125I-labelled polyamidoamine dendrimers in vivo. J Control Release. 2000;65(1-2):133-48.
[23] Pantarotto D, Briand JP, Prato M. Translocation of bioactive peptides across cell membranes by carbon

nanotubes. Chem Commun (Camb). 2004;(1):16-7.
[24] Dreaden EC, Alkilany AM, Huang X, Murphy CJ, El-Sayed MA. The golden age: gold nanoparticles for biomedicine. Chem Soc Rev. 2012;41(7):2740-79.
[25] Lawrence MJ, Rees GD. Microemulsion-based media as novel drug delivery systems. Adv Drug Deliv Rev. 2012;64(Suppl):175-93.
[26] Li J, Mooney DJ. Designing hydrogels for controlled drug delivery. Nat Rev Mater. 2016;1:16071.
[27] Merisko-Liversidge E, Liversidge GG. Nanosizing for oral and parenteral drug delivery: a perspective on formulating poorly-water soluble compounds using wet media milling technology. Adv Drug Deliv Rev. 2011;63(6):427-40.
[28] Silva AL, Rosalia RA, Sazak A, Carstens MG, Ossendorp F, Oostendorp J. Protein encapsulation in biodegradable nanoparticles for antigen delivery: a review. J Control Release. 2015;217:154-63.
[29] Nel A, Xia T, Mädler L, Li N. Toxic potential of materials at the nanolevel. Science. 2006;311(5761):622-7.
[30] Magdolenova Z, Collins A, Kumar A, Dhawan A, Stone V, Dusinska M. Mechanisms of genotoxicity: a review of in vitro and in vivo studies with engineered nanoparticles. Nanotoxicology. 2014;8(3):233-78.