

INTEGRATION OF NANOTECHNOLOGY AND HERBAL MEDICINE: THERAPEUTIC POTENTIAL FOR IMPROVEMENT OF HEALTH CARE

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Abstract: Herbal medicine represents one of the oldest forms of medical practice since ancient times, which is still used around the world and includes the use of herbal medicines for preventive or therapeutic purposes. On the other hand, nanomedicine represents a new scientific field that uses nanotechnology, the manipulation of materials on the nanoscale (1 - 100 nm), for the diagnosis, treatment and prevention of diseases at the molecular level. Although these two disciplines are very different at first glance, their integration could unlock the full therapeutic potential of phytotherapy by enabling innovative approaches to improve the bioavailability and efficacy of herbal medicines through targeted and controlled delivery, allowing to overcome its current limitations and reduce side effects. This paper explores the importance of implementing nanotechnology in herbal medicine, emphasizing its potential impact on health care. Also, the techniques of encapsulating herbal medicines into nanomedicines, various herbal nanoformulations and application and modes of action, are presented. In conclusion, continued research in this area is considered a key factor in unlocking the full potential of nanomedicine application in herbal medicine. Such research drives innovation, as well as personalized approaches to therapy and advances healthcare, which could pave the way for a healthier and more sustainable future.

Keywords: herbal medicine, nanomedicine, nanoformulations, bioavailability.

1. INTRODUCTION

Herbal medicine and nanomedicine represent two different, but interconnected medical fields that have an extremely high potential for improving medical interventions and health care [1,2].

Herbal medicine or phytotherapy is one of the oldest forms of medical practice that has been an integral part of traditional healing practices in different cultures around the world for centuries. For many people, herbal medicine represents the starting point for prevention, therapy and help with various health disorders, especially chronic ones, and forms an integrated part of the health system. Even today, medi-

cine could not be imagined without herbal medicine. According to WHO estimates, about 80% of the world's population uses herbal medicine in primary health care [1-4]. Herbal medicine involves the use of herbal medicinal preparations and natural compounds, such as natural herbal extracts, herbal teas, essential oils and other herbal formulations, with the aim of improving health, alleviating disease symptoms and supporting the healing process. Due to its importance, with the advent of modern medicine, numerous researches were carried out in the field of application of herbal medicinal preparations. This confirmed the effectiveness of many herbal medi-

cines and discovered many pharmacologically active components of plant origin, which were isolated and represent the forerunner of many medicines that are still used today in modern, evidence-based medicine (aspirin, morphine, paclitaxel, camptothecin, podophyllotoxin, vincristine, vinblastine, etc.) [5,6].

On the other hand, with the development of science, a new scientific field appeared, nanotechnology, which found its application in various areas of human activity, including medicine. Nanomedicine represents a revolutionary technology that finds its wide application in various segments of treatment, monitoring, diagnostics and control of biological systems. Thus, nanomedicine is a modern discipline that refers to the application of nanotechnology in the medical field, including herbal medicine, and which uses nanoscale materials for the diagnosis, treatment and prevention of diseases at the molecular level. A key feature of nanomedicine lies in the nanometer scale, which typically ranges from 1 to 100 nm. Nanoparticles, the building blocks in nanomedicine, can be engineered to have specific shapes, sizes, and surface properties, and to exhibit unique and adaptive properties compared to classical materials, thus enabling improvement of the pharmacokinetic and pharmacodynamic properties of a drug with precise control over targeted delivery [7-9].

Both nanomedicine and herbal medicine offer unique advantages, but also face specific challenges and limitations. However, when combined, they have the potential to create a synergistic approach that can improve therapeutic outcomes and address some of the existing limitations [3,10]. The therapeutic approach in modern medicine implies the use of high-quality, harmless and effective medicines, including herbal medicines. Herbal medicinal preparations contain numerous pharmacologically active components, which both, isolated and synergistically, can have a significant therapeutic potential. However, very often their physicochemical properties, such as poor solubility, size of particles, reduced ability to absorb, sensitivity to an acidic environment etc, represent limiting factors of their bioavailability and effectiveness in the biological systems, which is why their therapeutic effect can be significantly reduced or even absent. The integration of nanomedicine with herbal medicine may offer a solution to these challenges. Using the unique properties of nanoparticles, plant com-

pounds can be encapsulated within nanocarriers, thereby overcoming limitations and opening up new possibilities. Herbal formulations with nanoparticles provide improved stability and bioavailability, targeted delivery, controlled release of active compounds, the possibility of synergistically combining different compounds, as well as standardization of herbal medicines. In this way, the optimization of therapeutic efficiency is achieved with the reduction of side effects and it is possible to personalize the therapy for the needs of the patient based on his individual characteristics, that is, specific genetic factors and the state of the disease [10-13].

In this paper, we explore and present the potential and achievements in the integrated application of nanomedicine and herbal medicine. Through the synergy of these two areas, we aim to shed light on the transformative impact this integration could have on modern healthcare and pave the way for safer, more efficient and personalized treatment options. As research in this area continues to advance, nanotechnology is expected to play an increasingly important role in advancing modern medicine.

2. TYPES OF NANOFORMULATIONS USED IN HERBAL MEDICINE

The application of nanotechnologies in herbal medicine involves the use of different types of nanoparticles that are used as carriers for the encapsulation of herbal compounds or preparations, with each type of nanoparticle offering different advantages in terms of drug delivery, stability and release characteristics. Some of the common types of nanoparticles used in herbal nanomedicine (Figure 1) are:

(a) **liposomes** - spherical vesicles composed of lipid bilayers; they are biocompatible and have a hydrophilic outer surface and a hydrophobic inner layer, making them ideal carriers for both hydrophilic and hydrophobic plant compounds; they can encapsulate plant extracts within their lipid bilayers, protecting the active compounds from degradation and improving its stability; offer versatility in size and surface modification, enabling controlled drug release and targeted delivery to specific cells or tissues;

(b) **nanoemulsions** - mixtures of immiscible liquids (usually oil and water – O/W or W/O) stabilized by an emulsifying agent, that consists of tiny droplets of size typically ranges from 20 to 200 nm;

(c) **polymer nanoparticles** - particles made of synthetic or natural polymers; the choice of polymer affects the release rate and degradation characteristics of nanoparticles, which affects the duration of drug release and therapeutic effects; they offer excellent biocompatibility, stability and the ability to modify, depending on the needs;

(d) **solid lipid nanoparticles (SLN)** and **nanostuctured lipid carriers (NLC)** - nanoparticles similar to liposomes, which contain solid lipids or a mixture of solid and liquid lipids; they can effectively encapsulate lipophilic plant compounds and provide controlled and prolonged drug release; offer improved stability during storage and transport compared to conventional liposomes;

(e) **nanocrystals** - crystalline particles of submicron size; can improve the dissolution rate of herbal compounds, increasing absorption and bioavailability; they are particularly useful for herbal compounds with limited water solubility, solving one of the main challenges in herbal medicine;

(f) **dendrimers** - branched macromolecules with a well-defined, compact and organized structure, which makes them suitable for encapsulating herbal compounds with a high drug loading capacity; can be modified on the surface to improve stability, biocompatibility and targeted delivery of herbal medicines; their multivalent surface enables functionalization with ligands for targeted drug delivery, increasing the potential for personalized therapy;

(g) **albumin nanoparticles** - derived from the natural albumin protein; they offer good biocompatibility and are easily modified for targeted drug delivery; are used to encapsulate plant compounds and improve their stability and bioavailability; they can accumulate at tumor sites due to the effect of improved permeability and retention, which makes them suitable for the delivery of herbal compounds in cancer therapy;

(h) **metal and inorganic nanoparticles** - nanoparticles composed of metallic elements or inorganic components; possess specific physico-chemical properties thanks to their small size; some of the most common are metal nanoparticles, quantum dots, silica nanoparticles, magnetic nanoparticles (nanoparticles with magnetic properties, usually composed of materials with magnetic properties such as iron, cobalt or nickel, coated with biocom-

patible materials), then metal oxide nanoparticles, carbon nanotubes, etc; due to potential toxic effects, insufficient stability and biocompatibility, special caution is required when formulating and using these nanoparticles;

(i) **polymer micelles** - nanoparticles composed of hydrophobic and hydrophilic polymer chains; they are often used because they can encapsulate hydrophobic drugs within their hydrophobic core, and enable efficient and targeted transport to target tissues or cells, thereby increasing the bioavailability of the drug and reducing side effects;

(j) **phospholipid micelles** - nanoparticles composed of phospholipids representing amphiphilic molecules composed of a hydrophilic head and a hydrophobic tail; in aqueous solution they spontaneously form micelles composed of a hydrophobic core and a hydrophilic shell; they can encapsulate hydrophobic drugs inside the core, improving the solubility and stability, and the therapeutic efficiency of drugs that are poorly soluble in water;

(k) **“MOF” nanoparticles** (metal-organic framework, MOF) - nanoparticles consisting of combined metal ions or clusters with organic ligands to create a strong crystalline structure; porous structure and favorable properties such as large surface area, variable pore size, strong interactions and other specific physico-chemical properties, enable encapsulation of various drugs and controlled drug release in target tissues;

(l) **hydrogel** - a three-dimensional network of hydrophilic polymers that can absorb and retain a significant amount of water within its structure, giving it a gel-like consistency; due to their unique properties, including high water content, biocompatibility and tunable mechanical properties, hydrogels can serve as delivery systems for herbal medicines by encapsulating them within their three-dimensional structure and gradually releasing them over time, providing long-lasting therapeutic effects.

Each type of nanoparticle provides unique characteristics that can be tailored to the specific properties of herbal compounds, enabling improved bioavailability and drug delivery and better therapeutic outcomes in herbal medicine. The choice of nanoparticles depends on factors such as the nature of the herbal compound, the desired release profile and the targeted site of action [1,6,14-16].

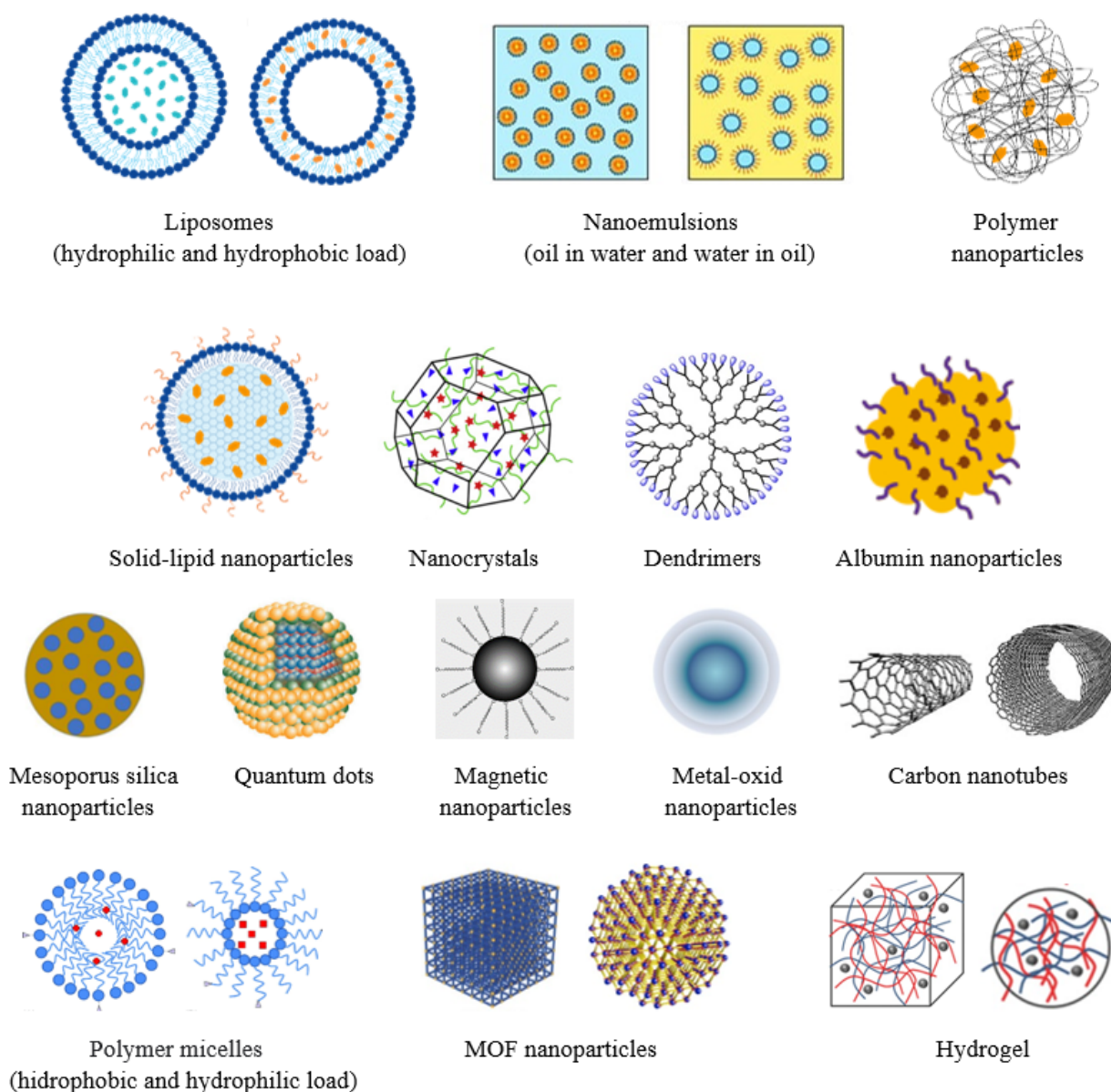


Figure 1. Types of nanoparticles used in herbal medicine

Depending on the type, nanoparticles can be of different shapes, each with its own unique properties and applications. The shape of nanoparticles can significantly influence their physicochemical and biological characteristics. The most common shapes of nanoparticles are: spherical, rod-shaped, cubic, octahedral, triangular, tetrahedral, star-shaped, branched, hollow, dendritic and similar (Figure 1). The choice of nanoparticle shape depends on the desired properties and application. Researchers are constantly looking for ways to synthesize and design nanoparticles of specific shapes and types to optimize their performance [14-16].

3. TECHNIQUES FOR FORMULATION OF NANOPARTICLES WITH HERBAL MEDICINES

Encapsulation of plant compounds within nanoparticles requires precise engineering and formulation techniques to ensure stability and efficacy of the nanomedicine. Several methods are used for encapsulation, each with its own advantages for different types of plant compounds and desired nanoparticle characteristics. Some of the common techniques used to encapsulate herbal compounds inside nanoparticles:

1. Hot homogenization technique: nanoparticles are formed at a temperature higher than the melting point of lipids by mixing the herbal medicine with dissolved lipids in the presence of a hot aqueous surfactant solution.

2. Cold homogenization technique: the herbal medicine is mixed with melted lipids, after which it is rapidly cooled by cryogenic systems, such as liquid nitrogen, and then ground into powder using a specialized mill and homogenized at room or lower temperature.

3. High pressure homogenization technique: a mechanical process used to reduce particle size by dispersing materials and creating uniform mixtures; implies exposure of the mixture of substances to high pressures and pushing through the narrow openings of the homogenizer, which leads to a reduction in the size of the particles; the process can be repeated several times to achieve the desired particle size reduction and uniformity; the effectiveness of the method depends on factors such as pressure, flow rate, number of passes through the homogenizer and the design of the homogenization chamber, and it is very important to control these parameters in order to achieve the desired results, while avoiding excessive energy input and potential damage to sensitive materials.

4. Solvent emulsification/evaporation technique: plant compounds and a suitable polymer (e.g. poly(lactic-co-glycolic acid), poly(lactic-co-glycolic acid), PLGA) are dissolved in an organic solvent and added to the aqueous phase containing a stabilizer to form a primary oil-in-water (U/W) emulsion, and then the mixture is stirred vigorously to evaporate the organic solvent, resulting in the formation of nanoparticles that encapsulate the herbal compounds; nanoparticle size and drug release characteristics can be controlled by adjusting the parameters of the emulsification process; examples are ciclosporin-loaded sodium alginate glycolate; nanoparticles or nanocapsules filled with doxorubicin and others.

5. Nanoprecipitation technique: involves dissolving plant compounds and a suitable polymer or lipid in a common solvent, which is then rapidly injected into the insoluble material, leading to the precipitation of nanoparticles encapsulating the plant compounds; suitable for poorly soluble drugs.

6. Ultrasonic nanoparticle formation: this technique uses sonication to form nanoparticles from a solution containing plant compounds and a polymer; sonication breaks the solution into smaller droplets, leading to the formation of nanoparticles as the solvent evaporates; enables the formulation of nanoparticles with narrow size distribution and uniformity.

7. Double emulsion/solvent evaporation technique: used when herbal compounds must be encapsulated inside nanoparticles surrounded by a polymer shell (core-shell structure); double emulsion method; a water-in-oil-in-water (W/U/W) or oil-in-water-in-oil (U/W/U) emulsion is formed, which enables the formation of a shell-core nanoparticle, where the core of the nanoparticle contains plant compounds, while the shell is composed of a polymer that provides stability and controlled release.

8. Supercritical fluid technology: supercritical carbon dioxide (scCO₂) is used as a solvent for the deposition of nanoparticles; plant compounds and polymer are dissolved in scCO₂, and rapid pressure reduction causes the formation of nanoparticles; enables the use of scCO₂ as a green solvent, minimizing the need for organic solvents.

9. Coacervation: involves the phase separation of two liquid phases in a colloidal system, in the presence of plant compounds, which leads to the interaction of two oppositely charged polyelectrolytes after mixing in an aqueous solution and the formation of nanoparticle aggregates, which are stabilized by cross-linking or other methods to form discrete nanoparticles which encapsulate herbal compounds; it is most often used to prepare nanoparticles using biodegradable hydrophilic polymers such as chitosan, sodium alginate and gelatin.

Each of these techniques offers specific advantages in terms of adaptability, reproducibility and control of nanoparticle characteristics. The choice of encapsulation technique depends on the properties of the herbal compounds, the desired release profile and the application of nanomedicines. These encapsulation techniques play a key role in optimizing the delivery and therapeutic efficacy of herbal compounds and unlocking the potential of nanotechnology in herbal medicine [1,6,14,16-26].

4. CHALLENGES IN HERBAL MEDICINE AND THE ROLE OF NANOMEDICINE IN OVERCOMING THEM

Traditional herbal medicine, although it offers numerous benefits and has exceptional therapeutic importance, faces several issues and challenges that limit its full potential. Two of the most significant issues associated with traditional herbal medicine are low bioavailability and lack of targeted delivery of active medicinal substances. Many herbal compounds, although they have an exceptional therapeutic potential, *in vivo* systems they show poor bioavailability, which means that they are not absorbed enough in the body and thus cannot show their effectiveness in full.

On the other hand, herbal formulations that are most often used in traditional herbal medicine, such as herbal extracts, teas, decoctions etc, do not have the possibility of targeted delivery, which means that they do not selectively reach diseased tissues or organs. These issues of low bioavailability and lack of targeted delivery can significantly affect the efficacy and safety of herbal medicinals. Some specific factors that contribute to these problems include: complex chemical composition (herbal drugs usually consist of a complex mixture of bioactive compounds, which can vary significantly between different batches or preparations of the same plant, which presents a challenge to determine the specific bioactive compounds responsible for therapeutic effects and leads to variability in bioavailability), poor solubility (lipophilic volatile constituents of essential oils, many of which have shown significant biological activities, have limited solubility in biological fluids, making it difficult for the body to efficiently absorb and distribute them to target organs; this can lead to reduced absorption in the gastrointestinal tract, further contributing to low bioavailability), first-pass metabolism (some compounds, e.g. plant elagni tannins are intensively metabolized in the gastrointestinal tract, so despite the confirmed biological activity they cannot reach the receptor site in an unchanged form, and nanoformulations could be a way to overcome this problem), lack specificity (herbal drugs are usually not designed to target specific cells or tissues in the body, and as a result may lead to potential side effects), as well as variability in patient response (individual variability in metabolism and

genetic factors may also affect bioavailability and response to herbal medicines) [1,3,10,11,27].

To overcome these limitations associated with the traditional use of herbal medicines, contemporary research is focused on the integration of nanotechnology and herbal medicine. Nanomedicine offers solutions such as drug delivery systems based on nanoparticles that improve bioavailability, enable targeted delivery and provide controlled release of herbal compounds. By encapsulating herbal preparations and compounds in nanoparticles, researchers aim to improve the absorption and stability of bioactive compounds, leading to more effective and safer application of herbal therapy [11-14].

Nanomedicine can overcome these challenges by formulating drug delivery systems based on nanoparticles that can encapsulate plant compounds, protecting them from degradation in the gastrointestinal tract and increasing its stability. Nanoparticle encapsulation can protect the herbal medicine and prevent or reduce inactivation and first-pass metabolism, as nanoparticles protect herbal compounds from direct exposure to gastric juice and liver enzymes, increasing its stability during passage through the digestive system and ensuring that more of the compound reaches the bloodstream. Also, their small size and large surface area allow them to pass through biological barriers more easily, improving the absorption of plant compounds and increasing bioavailability. Nanoparticle encapsulation can improve the solubility of these compounds in biological fluids, allowing them to dissolve and distribute more easily after administration. This improved solubility results in increased absorption and bioavailability. Nanomedicines can be engineered to pass through some difficult-to-permeable biological barriers, such as the blood-brain barrier. This ability enables the targeted delivery of herbal compounds to previously inaccessible sites, expanding the scope of treatment for various diseases, including neurological disorders [13,17].

Furthermore, nanoparticles can be functionalized with ligands or antibodies that recognize specific receptors or markers on the surface of target cells. These ligands act as “keys” to enter the desired cells. This allows targeted delivery of herbal compounds to diseased tissues, reducing unwanted effects on healthy tissues. For example, nanoparticles can be functionalized with ligands that specifically bind to receptors

overexpressed on cancer cells, allowing selective delivery of herbal compounds to tumor sites [28,29].

Also, active targeting of nanoparticles to specific cells or tissues can enhance the accumulation of herbal compounds at the site of action, improving its therapeutic efficacy. This allows lower dosage while achieving the same therapeutic effect, which can minimize the risk of potential toxicity and side effects associated with high doses of herbal medicines [28,29].

Nanoparticles can also exploit the effect of enhanced permeability and retention (EPR effect), which is characteristic of tumor tissues and inflamed areas. The more porous vasculature in these regions allows nanoparticles to accumulate there, leading to passive targeting of specific diseased tissues and increasing the concentration of compounds at the site of action, improving therapeutic efficacy [30-32].

Nanoparticles can be engineered to provide controlled and sustained release of encapsulated plant compounds. This controlled release profile provides a stable and prolonged drug supply, maintaining therapeutic levels in the bloodstream for a prolonged period. Controlled release is particularly useful in chronic conditions, where sustained therapeutic effects are required to effectively control the disease, offering continuous treatment with reduced dosing frequency [33-34].

Furthermore, combining multiple herbal compounds within nanoparticles offers a promising approach to generate synergistic therapeutic effects. This enables the design of combination therapies, where synergistic interactions between different herbal compounds can be exploited to improve therapeutic efficacy. This strategy, often called combination therapy or polyherbal therapy, has also been practiced in traditional medicine systems for centuries. However, combination therapy using nanomedicine may offer superior advantages compared to single herbal drugs or combined traditional herbal medicinal preparations, as it can target multiple pathways or mechanisms involved in the disease process while optimizing and controlling the delivery and interaction of these compounds, leading to improved therapeutic outcome. For example, combining anti-inflammatory and antioxidant compounds in nanoparticles may provide a more comprehensive approach for managing conditions associated with oxidative stress. Also, combining multiple herbal compounds

can help minimize the development of drug resistance. As different compounds act on different aspects and mechanisms of the disease, the likelihood of one resistance mechanism becoming dominant decreases. Polyherbal nanoparticle formulations can exhibit broad-spectrum activities against various diseases or conditions. For example, a combination of antimicrobial and anti-inflammatory compounds can be effective against both infections and inflammatory responses. Furthermore, by combining herbal compounds with synergistic effects, it is possible to use lower doses of each compound, reducing the risk of potential side effects. Also, the possibility of combining several herbal compounds enables personalized approaches to medicine. Tailoring the nanoparticle formulation to include specific compounds based on an individual's health needs and genetics can improve treatment outcomes. Another example could be polyherbal nanoparticles with known anti-cancer properties for cancer therapy. Nanoparticles can be designed with ligands that actively target cancer cell receptors for increased uptake into diseased tissues. Each compound contributes to the inhibition of cancer cells through different mechanisms, such as arresting the cell cycle, inducing apoptosis, and inhibiting pathways that promote the development of cancer cells. Combining these compounds within nanoparticles and their synergistic action can lead to increased degradation of cancer cells and reduced toxicity to healthy tissues, improving the overall effectiveness of the therapy. In conclusion, the combination of multiple herbal compounds within nanoparticles represents a compelling approach to exploit the full potential of herbal medicine [35-38].

Another significant advantage of nanotechnology is that it allows the adaptation of nanomedicine to the individual characteristics of the patient. By adjusting the nanomedicine or combining several different herbal medicines in nanoparticles, a personalized herbal medicine can be obtained that enables action on specific genetic factors or disease states. Personalized nanomedicine can provide more optimal treatment results by taking into account individual variations in drug metabolism and response to therapy [39-41].

Overall, nanoparticle encapsulation offers a versatile and effective approach to improve the bio-availability of herbal compounds and therapeutic efficacy while reducing side effects. By addressing

the issues of solubility, stability and targeted delivery, nanotechnology enables more efficient absorption and utilization of plant compounds, increasing its therapeutic potential and expanding application in the treatment and management of diseases. By incorporating nanotechnology into herbal medicine, nanomedicine provides a systematic and technologically advanced approach to optimize the delivery and efficacy of herbal medicines. This integration not only improves the therapeutic effectiveness of herbal medicine, but also opens up new opportunities for personalized and targeted treatments, contributing to the improvement of patient treatment outcomes and the improvement of modern health practices.

5. SAFETY ASPECTS OF COMBINATING NANOMEDICINE AND HERBAL MEDICINE

Combining nanomedicine and herbal medicine provides numerous new opportunities for improving therapeutic efficacy. However, this also causes concern regarding the safety of its application. Addressing safety aspects is critical to ensure the successful introduction of these technologies into clinical practice. There are several key safety issues related to combining nanotechnology and herbal medicines, such as:

1. **Potential toxicity of nanoparticles.**

Nanoparticles themselves can exhibit a certain level of toxicity depending on size, composition, surface charge and other physicochemical properties. It is essential to thoroughly evaluate the biocompatibility and potential toxicity of nanoparticles used to encapsulate herbal compounds. Comprehensive preclinical studies should be conducted to evaluate the safety profiles of nanoparticles.

2. Interactions between nanomedicines and conventional medicines. Herbal compounds in the form of nanoparticles can interact with conventional medicines or other herbal compounds. These interactions may lead to unexpected effects, reduced efficacy or increased toxicity. Understanding the potential interactions of nanomedicines is crucial, especially for patients taking multiple medications or undergoing complex treatments and therapies.

3. Allergic reactions. Some individuals may be sensitive or allergic to specific plant compounds or nanoparticle components. Careful consideration of the patient's medical history and potential aller-

gens is necessary to avoid adverse reactions.

4. Long-term effects. Long-term exposure to nanoparticles requires evaluation to determine potential cumulative effects, chronic toxicity, or delayed adverse reactions. Long-term safety studies are necessary before considering chronic or maintenance therapy with nanomedicines.

5. Regulatory compliance. Nanomedicines must meet rigorous regulatory standards for quality, safety, and efficacy before they are approved for clinical use. The lack of specific guidelines for herbal nanomedicines can lead to uncertainty and delays in the regulatory process. Close collaboration between researchers, regulatory authorities and healthcare professionals is essential to ensure compliance and patient safety.

6. Quality control and standardization. Quality, consistency and standardization of plant extracts and nanoparticle formulations are crucial to ensure predictable and reliable therapeutic results. Appropriate quality control studies should be applied to avoid batch-to-batch variability and ensure product safety.

7. Biodistribution and excretion. Understanding the pharmacokinetics and bioavailability of herbal nanomedicines is essential for dosing, efficacy and safety. Nanoparticles can affect drug release and absorption, which can affect therapeutic outcomes and adverse events. Nanoparticles must be designed to minimize potential accumulation in non-targeted organs and tissues to avoid unwanted toxicity. Also, it is necessary that they can be excreted from the body unhindered after their action.

8. Ethical considerations. Ethical aspects, such as informed consent and patient autonomy, should be carefully considered when thinking about the application of nanomedicines in clinical practice.

9. Preclinical and clinical trials. Extensive preclinical trials, including in vitro and animal studies, are necessary to evaluate the safety and efficacy of combinations of nanomedicine and herbal medicine before proceeding to clinical trials. Clinical trials should include rigorous patient monitoring to assess safety and potential side effects, and follow established guidelines for conventional pharmaceuticals and drugs, while taking into account the specific characteristics of herbal nanomedicines. Evaluating and demonstrating efficacy through well-designed clinical trials can be challenging, especially for poly-

herbal nanoformulations. On the other hand, protecting intellectual property rights can be challenging due to the potential overlap of existing patents in nanotechnology and herbal medicine, so companies may face difficulties in patenting new combinations or formulations.

By taking these safety considerations into account and conducting thorough research, researchers and health care professionals can take advantage of combinations of nanomedicine and herbal medicines while mitigating potential risks. Collaboration between experts from different fields, including nanotechnology, pharmacology, toxicology, pharmacy, medicine and other, is essential to ensure a comprehensive understanding of safety aspects and to overcome these challenges. Developing specific guidelines for herbal nanomedicines and promoting interdisciplinary research can accelerate the regulatory approval and commercialization process. Open dialogue and knowledge sharing between stakeholders can foster a better understanding of the potential benefits and risks of using herbal nanomedicines, leading to greater confidence in these innovative therapies [42-48].

6. EXAMPLES OF COMBINATION OF NANOMEDICINE AND HERBAL MEDICINE IN MODERN PRACTICE

Herbal medicinal products based on nanotechnology have made a significant contribution to health care, revolutionizing the treatment and care of patients. Today, there is a large number of scientific researches dealing with the formulation of herbal nanomedicines, and we will mention only some of them that have already found its application in practice or are in the phase of intensive testing:

1. Doxil® (liposomal doxorubicin): Doxil® is a drug of doxorubicin encapsulated inside liposomes, which is used for chemotherapy. Liposomal encapsulation improves drug stability, reduces side effects and enhances its accumulation in tumor tissues through the EPR effect. Doxil® is used to treat various cancers, showing improved patient outcomes and reduced cardiotoxicity compared to conventional doxorubicin [49-51].

2. Abraxane® (nab®-paclitaxel): Abraxane® is a drug form of paclitaxel bound to albumin nanoparticles, which is used for chemotherapy. Albumin nanoparticles improve drug solubility and

targeted delivery to tumor cells. Abraxane® has shown increased efficacy and reduced side effects in the treatment of breast, lung and pancreatic cancer [52,53].

3. Nanoemulsion-based formulations: Nanoemulsions are nanoscale emulsions used to enhance and deliver lipophilic drugs and essential oils. These formulations improve the absorption and bioavailability of the active principles, allowing more effective treatment in conditions such as fungal infections and skin disorders [1,54-56].

4. Nanoparticles filled with curcumin, a bioactive compound isolated from the turmeric plant (*Curcuma longa* L), with strong anti-inflammatory and antioxidant properties. They showed improved solubility and stability compared to free curcumin. Studies have shown increased accumulation of curcumin in target cells in the form of nanoparticles, leading to enhanced therapeutic effects of curcumin [57-59].

5. Nanoparticles filled with resveratrol, a polyphenol compound found in grapes, berries and certain medicinal plants, which has antioxidant, anti-inflammatory and anti-cancer properties. Studies have shown an increased dissolution rate and improved bioavailability compared to free resveratrol. Also, they showed a sustained release profile, resulting in prolonged plasma concentrations and improved efficacy in suppressing tumor growth, as well as reduced toxicity compared to free resveratrol, indicating better safety and tolerability. All of the above leads to an improvement in the therapeutic efficacy of resveratrol, especially in cancer therapy [60,61].

These are just some of the herbal nanomedicines that find its application in modern therapy, but there is a much larger number of those that are in the testing phase and will find its application in future.

7. CONCLUSION

The integration of nanotechnology and herbal medicine has enormous potential to revolutionize health care and therapeutic approaches. Nanomedicine, with its cutting-edge advances in design and production of nanoparticles, has opened new horizons for improving the efficacy, bioavailability and targeted delivery of herbal compounds, while reducing the side effects of drugs. Combination of these two fields addresses critical challenges associated with traditional herbal medicine, including low bio-

availability and lack of precise delivery.

This paper explores the concept of nanomedicine and herbal medicine, emphasizing their individual importance as well as their combinations. The importance of their synergy is highlighted, showing how nanotechnology can overcome the limitations of herbal medicine by encapsulation in different types of nanoparticles. Examples of successful formulation of specific plant compounds into nanoparticles are given, showing improved therapeutic results.

The application of nanotechnology within herbal medicine also bridges the gap between traditional wisdom and modern scientific achievements and knowledge. This amalgamation has significant potential not only in targeted therapy but also in personalized medicine. However, challenges such as safety profiles, regulatory hurdles, and implementation must be addressed as the field progresses. The convergence of nanotechnology and herbal medicine requires multidisciplinary collaboration between researchers, clinicians, regulatory authorities and all industry stakeholders.

As ongoing research and clinical trials continue to develop, so do the prospects for this synergistic approach to take root in clinical practice. The potential impact on health care, patient outcomes and disease management is remarkable. Continued research and investment in these areas will undoubtedly shape the future of medicine, ushering in an era in which the wisdom of ancient healing practices aligns with the precision of modern technology to create a new paradigm of treatment.

8. LITERATURE

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ИНТЕГРАЦИЈА НАНОТЕХНОЛОГИЈЕ И ХЕРБАЛНЕ МЕДИЦИНЕ: ТЕРАПЕУТСКИ ПОТЕНЦИЈАЛ ЗА УНАПРЕЂЕЊЕ ЗДРАВСТВЕНЕ ЗАШТИТЕ

Сажетак: Хербална медицина представља један од најстаријих облика медицинске праксе још од античких времена, а која је и данас веома заступљена широм свијета и која подразумијева употребу биљних лијекова у превентивне или терапијске сврхе. С друге стране, наномедицина представља нову научну област која користи нанотехнологију, манипулацију материјалима на наноскали (1–100 nm), за дијагнозу, лијечење и превенцију болести на молекуларном нивоу. Иако су ове двије дисциплине на први поглед веома различите, њихова интеграција би могла откључати пуни терапијски потенцијал фитотерапије тако што би, омогућавајући иновативне приступе за побољшање биорасположивости и ефикасности биљних лијекова циљаном и контролисаном испоруком, омогућила да се превазиђу њена досадашња ограничења и да се смање нежељени ефекти. Овај рад истражује значај имплементације нанотехнологије у хербалној медицини, наглашавајући њен потенцијални утицај на здравствену заштиту. Такође, приказане су технике инкапсулирања хербалних љековитих принципа у нанолијекове, различите хербалне наноформулације, те њихова примјена и начини дјеловања. Закључно, наставак истраживања у овој области сматра се кључним за откључавање пуног потенцијала примјене наномедицине у биљној медицини. Таква истраживања подстичу иновације, као и персонализоване приступе терапији и унапређују здравствену заштиту, чиме би се могао утрти пут за здравију и одрживију будућност.

Кључне ријечи: хербална медицина, наномедицина, наноформулације, биорасположивост.

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