

# NANO HERBAL FORMULATION: A NEW APPROACH OF MEDICINAL PLANTS AND THEIR THERAPEUTIC MODALITIES

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## Abstract

Modern medicine has made a significant contribution to humanity's ability to combat a wide range of infectious illnesses. People have shifted their focus back to natural remedies since traditional medication has a reputation for having a plethora of side effects, many of which are mild to nonexistent. The use of herbal remedies to treat infectious illnesses has been around since the beginning of time and has been shown to be a viable option. However, their limited bioavailability and solubility limit their practical use. More effective options have been found in the form of plant-based nanoparticles, which have been shown to boost bioavailability and solubility of herbal medications. For this review, nanotechnology systems will be highlighted as a new drug delivery method for herbal medicines to increase the therapeutic benefits and bioavailability of naturally occurring medications. Also discussed are how to make herbal

nanoparticle formulation, their structure and how to employ herbs in conjunction with nanoparticles. It is expected that this comprehensive study of biomedical science will serve as a springboard for new research and applications in the field. PubMed, Google Scholar, and Medline were used to gather information.

**Keywords:** Nanomedicines, Medicinal Plants, Infectious disease, Nanoparticles herbal formulations.

## 1. Introduction

In practically every illness, herbal remedies have been used to treat human ailments for years. Traditional medications have fewer negative effects than synthetic ones, which is why we have the option to utilize them in the modern day [1-2]. Food and medicine have always relied on plants, which are a natural source of healing. In fact, instead of focusing on reducing the number of illnesses, researchers are once again turning their attention to alternative remedies. Primarily in underdeveloped nations, 80 percent of the world's population currently relies on herbal medicines for primary health care. However, there are certain limitations to these herbal treatments because to problems with stability and low lipid solubility [3-5]. The primary duty of the herbal medication maker is to ensure the long-term preservation and safe use of the herbal medicines by patients. Only a small percentage of the injected dosage reaches the target location in most conventional medications, and the rest is wasted. Abstract Modern medicine has made a significant contribution to humanity's ability to combat a wide range of infectious illnesses. People have shifted their focus back to natural remedies since traditional medication has a reputation for having a plethora of side effects, many of which are mild to nonexistent. The use of herbal remedies to treat infectious illnesses has been around since the beginning of time and has been shown to be a viable option. However, their limited bioavailability and solubility limit their practical use. More effective options have been found in the form of plant-based nanoparticles, which have been shown to boost bioavailability and solubility of herbal medications. For this review, nanotechnology systems will be highlighted as a new drug delivery method for herbal medicines to increase the therapeutic benefits and bioavailability of naturally occurring medications. Also discussed are how to make herbal nanoparticle formulation, their structure and how to employ herbs in conjunction with nanoparticles. It is expected that this comprehensive study of biomedical science will serve as a springboard for new research and applications in the field. According to the physiochemical and metabolic properties, 2 is diffused throughout the body, resulting in a poor therapeutic effect [6-7].

Herbal medications need to have their stability profiles established since they include several active ingredients. Having a steady Phyto formulation gives the patient additional peace of mind [8]. Most medicinal plant species rely heavily on the supply of active components for their effectiveness. Tannins, flavonoids, and terpenoids found in herbal medicinal extracts are very water-soluble but cannot permeate the lipid membranes of cells, resulting in decreased absorption and a reduced bioavailability and efficacy. Some extracts aren't used in practice because of these disadvantages [9]. Phytomedicines have created new medication delivery

strategies to address these issues. In addition to vesicular delivery methods like liposomes, ethosomes, phytosomes, and transferosomes, herbal innovators in drug delivery are also developing particulate delivery systems including micro pellets, nanoparticles, and micro- and nano-emulsions. Assimilation into these drug delivery systems has improved the stability, bioavailability, and toxicity reduction of several natural drugs [10]. While standard dosages of herbal medicines are still available on the market, various new delivery methods, including nanoparticles, are being developed to improve their therapeutic benefits and efficacy. The use of herbal remedies has seen a substantial uptick in recent years due to advances in nanotechnology [11]. Nanoparticles are regarded to be one of the most effective medication delivery techniques [12]. The use of herbal medications in combination with nanotechnology has long been advocated. Using nanostructured methods, herbal extracts may be made more effective while reducing dosage and adverse effects and increasing activity. Treatment may be prolonged by using nanotechnology to deliver active substances at a high concentration to the desired location of action [9].

Nanotechnology-based goods are estimated to generate \$1 trillion in worldwide sales by 2015. The Chinese and Indian governments have also shown an interest in nanotechnology. The governments of India and Australia have pledged a combined donation of \$20 million to kickstart the Australia-India Science Research Funding Program. It was estimated that the worldwide market for nanomedicines was \$63.8 billion in 2010 and \$72.8 billion in 2011, respectively, by BCC Research [13].

Although nanoparticles may be manufactured from a variety of biological systems, plants biosynthesized from carbon dioxide are the most suitable. The use of plant material makes the whole process environmentally friendly [14].

Nanotechnology has the potential to solve many of the problems associated with herbal formulations. Nano-dosage versions of herbal medications provide a lot of advantages, according to herbal drug researchers. Controlled administration, enhanced bioavailability, stability, and solubility, as well as decreased toxicity and an increase in tissue macrophage dispensation are all benefits of this formulation [6]. As a result of their unique size and higher carrying capacity, nano dosage form delivery systems are the ideal option because of their ability of distributing large quantities to the desired places [15].

When it comes to nanomaterials, they may be found in a range of sizes ranging from 1 to 100 nanometers and are made up of synthetic or natural polymers and other smaller structures. It is dissolved, compressed, or linked to nanoparticle formations. Nano capsules and nanospheres may be made from nanoparticles using several production methods. The medicine is contained in a hollow surrounded by a polymer membrane in nano capsules [16]. Whereas, in nano-spheres, the medication is clearly visible and uniformly dispersed. The nano-carriers are safe to use since they are made from non-toxic components such as synthetic biodegradable polymers, polysaccharides, and lipids [17].

One of the most common uses of Nanocarriers is to transport other materials like drugs, such as a vaccine. A variety of materials and biological components, including as polymers, micelles, liposomes, and other components, are utilised as nanocarriers. Nanocarriers are now used to carry drugs, and their unique features suggest that they might be useful in chemotherapy in the future. Nanocarriers may deliver hydrophobic and hydrophilic preparations throughout the body due to the use of a variety of nano substances [18]. Because water makes up the majority of the human body, nanoparticles provide the primary therapeutic effects necessary to effectively deliver water-insoluble medicines to people. Micelles may store both water-soluble and insoluble medicines depending on the alignment of the phospholipids in the micelles [19].

## **2. Methods and Materials Nanotechnology and a new medication delivery mechanism for natural medicines are both required**

As a result of the stomach's very acidic pH, medicines are broken down into several components before they can enter the bloodstream, where they are then transported to the liver to be processed. This means that not enough of the medicine is absorbed into the bloodstream. In order to show a therapeutic effect from a medicine, it must be delivered to the site of action at the "lowest possible extent" necessary. Because of their tiny size, herbal nanomedicines that employ carrier methods reach their intended location in the proper quantity by overcoming all obstacles such as the acidic pH of the stomach and the liver's metabolism [15, 20].

Because of the following qualities, the nano delivery system selects herbal medicines as practical medication extranets for delivery through this technology:

- Herbal extracts, such as chloroform, petrol, acetone, and methanolic extracts, are readily available, but they are not ideal for delivery in the current state of affairs.
- Because the medicine in question is available in bulk forms, it is designed to lower the quantity of the drug administered. For a variety of chronic conditions, the formulations currently on the market lack target specificity.
- At present, herbal formulations accessible in market have certain linked negative effects.
- Greater doses of medicine and worse effectiveness with currently marketed formulations prompting the patient's complaints [21].

## **3. Techniques for preparation of nanoparticles**

Many methods have been developed to synthesize nanoparticles. Depending on the formulation's demands, these processes fall into one of two main categories: polymerization reaction or direct polymerization [22]. Emulsion and interfacial polymerization are two more types of polymerizations. Emulsion polymerization is further divided into organic and aqueous polymerization based on the continuous phase. It is possible to create nanoparticles from previously produced or natural polymers, as well as from macromolecules that have been desolate. Nebulization procedures are now used to create these polymeric structures [23].

### **3.1 Preparation of polymeric nanoparticles for medication delivery**

Polymeric nanoparticles may be made in a variety of ways, depending on the demands of the application and the kind of medicine that has to be compressed [23]. Nanoparticles contain a wide range of bioactive chemicals and are widely employed in the development of nanomedicines. Nanoparticles made of biodegradable polymers have been shown to be a viable method of delivering drugs. Biocompatibility, subcellular size, and a precise/constant discharge characteristic are all features of these nanoparticles [24]. Other advantages include being non-thrombogenic in blood, nonvirulent, noninflammatory, not susceptible to provoke an immunological response, not producing activation of neutrophils, biodegradable, and suited to various particles such as medications, proteins, nucleic acids, and peptides [25].

### **3.2 Herbal nano tablets**

Tablets containing herbal nanoparticles are increasingly being used by people in impoverished countries who lack access to safe drinking water. The herbal nano pills are made using Brahmi (*Bacopamonniera*) extract and a porcelain disc coated with silver or copper nanoparticles and submerged in water. It can sterilize water within the container for around six months. Nanoparticles containing herbal medications are utilised to deliver pharmaceuticals in a precise and targeted manner. The anticancer benefits of Bhasmas layered nano herbal tablets have been documented [27]. It's simple to utilize nano coffee energy pills to make energy beverages at home. Vitamin C, Vitamin B6 B12 B5, niacin, Guarana seed extract, Folate, Chromium, caffeine (from herbal sources), glucuronolactone, Columbian roasted coffee bean, Taurine, and leaf extracts of green tea [10] are the active ingredients employed in these beverages. Silver nanoparticles were synthesized biologically utilizing *Piliostigma thonningii* water base leaf extract and employed in the sanitization of laboratory roused waste water, according to research.

## **4. Nanotechnology-based compositions of herbal medications**

The active phytocomponents or systemized extracts of nano herbal medicines are manufactured. Through the use of nanotechnology, the given medicine gains in efficacy and bioavailability. Additionally, nano herbal compositions lessen the negative effects and virulency of the medications supplied [28].

### **4.1 Curcumin Nano formulations**

turmeric (*Curcuma longa*) contains the active ingredient curcumin, which has been shown to have several health advantages. Many studies and tests have shown the pharmacokinetics, protection, and usefulness of this component in human diseases [29]. The low water solubility and high solubility of organic molecules in curcumin makes it less bioavailable. Curcumin's rapid metabolism reduces its bioavailability even more. Due to all of these challenges, a superior version of curcumin has been developed that provides all of the benefits while also being more operationally exact and bioavailable. This problem has been handled by using tiny curcumin particles crushed in an oil-filled hollow sheath. Increased absorption and bioavailability of curcumin, which is fat soluble, are two of the benefits of this tiny particle compression.

Curcumin has been shown in several studies to have antioxidant, antitumor, antiarthritic, and anti-inflammatory properties in vitro and on animals. Curcumin entangled nanoparticles have been shown to increase oral bioavailability by around a factor of nine in comparison to curcumin with piperine as an absorption stimulant [30].

#### **4.2 Bhasma Nano-herbal medicine**

They are a unique preparation of dried herbal juices or decoctions and widely recommended for the treatment of various long-term conditions. Bhasma purification and subsequent reactivity with various minerals and/or herbal extracts are necessary before ash can be called Bhasma; it is described as an ash that is obtained after combustion. Bhasma has a wide range of beneficial benefits on health, including the maintenance of adequate alkalinity, which is essential for good health, as well as the reduction of acid-damaging effects. Because Bhasma does not metabolize, it breaks down heavy metals in the body without releasing any harmful byproducts [28].

Nanotechnology in the form of Bhasma is the earliest of its kind. Bhasma has been around for a long time, but nanomedicine is a newer invention that uses metal to synthesis active ingredients from basic materials. Some herbal juice and a specific medicine are often used in all of these operations, which need periodic burning and crushing. Due of its small size, it modified its fundamental features. Different instruments and methodologies, such as AFM (atomic force microscopy) and scanning electron microscope [27], determine the particle's size to be 56 nm.

#### **4.3 Nano-herbal formulation of Aloe vera extract**

Aloe vera extract is often used in the manufacture of several skin care products. It is aloe vera extracts that are found in most of the cream or lotion compositions used to treat dermatitis and other skin conditions such as dryness and psoriasis. Aloe vera extract is not able to pass the stratum corneum, according to current studies in Japan. Aloe vera extract cannot permeate the skin because aloe vera is a hydrophilic substance and the stratum corneum consists of high protein cells and intracellular lipid domains, which function as an impenetrable barrier for it. Increasing the amount of extract applied to the skin may help, but it might also create irritation. Liposomes containing Aloe vera extract from soybean lecithin were examined in this work. Using human skin fibroblasts and epidermal keratinocytes, produced Aloe vera with liposomes was able to demonstrate its ability to penetrate the skin in vitro. Their diameter is less than 200 nm. According to the findings, liposomes containing Aloe vera proliferate at a far greater rate than when the plant is not encapsulated at all. The collagenase production was also boosted by 23% when liposomal aloe vera extract was used instead of extracts without encapsulation [31].

#### **4.4 Tanshinone IIA Nano-herbal formulation**

Danshen (*Salvia miltiorrhiza*), a well-known traditional Chinese medicine, has a significant amount of the active ingredient tanshinone IIA (TA). Most of its therapeutic benefits are limited because of the drug's poor water solubility and poor suspension. Nano emulsions of TA are used to address this problem. It was shown that nano emulsions of the drug TA were able to release more of the drug in vitro than when they were used alone. Researchers found that employing TA

nano emulsions, at various doses and times, increased the cell death of T24 human bladder cancer cells by 103.4 times [32].

#### **4.5 Artemisia annua Nano-herbal capsules Formulations**

The active ingredient in *Artemisia annua*, an Asteraceae plant with a solitary stem and an annual cultivation cycle, is Artemisinin [33]. Antimalarial properties are among its many therapeutic benefits. Lower pharmacokinetic properties and a shorter half-life limit its therapeutic applicability. Nanotechnology was able to alleviate this problem by creating artemisinin coated in nanoparticles. Aqueous solutions include nano capsules, which are dispersed more precisely and more evenly. Nano capsules of artemisinin were more hydrophilic than artemisinin alone [34]. Anticancer activity has also been shown by these formulations, which release a steady supply of the medication.

#### **4.6 Berberine Nano-herbal medicine**

Berberine is an isoquinoline alkaloid that may be found in nature. Many therapeutic plants contain this alkaloid in various portions, including the roots, rhizome, and stem bark. [36] Berberine has a remarkable ability to cure a wide range of physical illnesses. There have been several studies showing that berberine is an excellent anti-inflammatory and cancer-fighting agent [37]. Human malignant brain tumors, esophageal cancer, leukemia, and colon cancer cells were all shown to be significantly inhibited or killed by berberine [38]. Because of this, it was recommended to create berberine nanoparticles following encapsulation in order to facilitate the drug distribution [39].

#### **4.7 Centella asiatica Herbal nanoparticles**

An ingredient known as "Gotu Kola" (*Centella asiatica* (L.)) is a natural brain tonic. Enzyme inhibition, total neuroprotection, and oxidative stress reduction are some of the strategies it uses to protect the brain against the effects of Alzheimer's disease, Parkinson's disease, and other conditions. Because of its neuroprotective properties, it is indicated as a developing natural medication [40]. In vitro callus extracts of *C. asiatica* (L.) were used to produce silver nanoparticles from the leaf extract. The antimicrobial properties of these nanoparticles were astounding [41]. Many studies have shown that *C. asiatica* (L.) possesses a variety of medicinal properties, including anxiolytic, anti-nervousness, and antioxidant properties. It is also used to treat leprosy, alopecia and other skin diseases; cancer; fever; allergies; and syphilis [42-45]. *C. asiatica* extract has strong biological qualities, but its practical use is limited since it is physically unstable. Powdered extracts are more hygroscopic than liquid extracts. It was necessary to create nanoparticles that contained the extract and kept it safe from exposure to moisture from the air. *C. asiatica* extract was used to make chitosan-alginate nanoparticles. *C. asiatica* was more stable in these formulations than in its extract alone [46].

#### **4.8 Celastrol Herbal nanoparticles**

To treat autoimmune diseases, the root extract of *Trypterygium wilfordii* Hook F contains considerable amounts of the anti-inflammatory drug celastrol, also known as tripterine [47]. Celastraceae is the family to which *Trypterygium wilfordii* Hook F belongs. Also known as

"Thunder of God Vine," it has been used for centuries in Chinese medicine to treat rheumatoid arthritis [48]. Celastrol's lower water solubility limits its medicinal use. These nanoparticles were made and examined in vitro for anticancer activity, and they were shown to significantly reduce the growth of human retinoblastoma cells when given at certain doses and times. Their ability to stop the progression of retinoblastoma in a mouse xenograft model shows that they are a viable treatment option in lieu of chemotherapy for the disease [49].

#### **4.9. Murva Herbal nanoparticles**

Many bioactive compounds are found in *Maerua oblongifolia*, a plant of the family Capparaceae. Murva, a potent phytochemical derived from *Maerua oblongifolia*, has long been used in traditional medicine to treat a wide range of ailments. Murva is said to have a powerful ability to treat anaemia, fever, stomach ailments, diabetes, typhoid, UTIs, and cough [50,51]. But its water solubility and bioavailability limit its practical use. Nanoparticles are used to increase solubility and bioavailability of the drug [19]. Natural plant medications may be stabilised and bioavailable by a variety of approaches. Among the many ways, nanomaterials-based medication delivery systems have become the most popular and modern. Chitosan nanoparticles are incorporated into Murva via an ionic gelation process, and their particle size is smaller than 650 nm. These nano preparations showed a modest and consistent discharge in an in vitro testing. Murva can be taken orally on a regular basis using these nano formulations, which have been shown to increase its and bioavailability [19].

#### **4.10. Genistein Herbal nanoparticles**

Soybean and other legumes are rich in genistein, an isoflavone that is derived from dried meals. Phytoestrogen [52,53] and antioxidant [54] are two of the properties it has. Osteoporosis, heart disease, breast and uterine cancers were also shown to be reduced [55,56]. Due to a lack of bioavailability and water solubility it is not as useful as it may be. Thus, the genistein nanoparticles have to be synthesized to improve its water solubility and bioavailability. Nanoprecipitation was used to create genistein nanoparticles [57]. Genestein nanoparticles have a larger bioavailability (241.8 percent) than genistein alone, according to a recent study [58].

#### **4.11. Danshen (*Salvia miltiorrhiza*) Herbal nanoparticles**

Danshen (*Salvia miltiorrhiza*), a classic chinese medication, has promising uses in the therapies for coronary heart disease [59]. It is a dried root of *Salvia miltiorrhiza*, a plant of Lamiaceae family. It is frequently utilized as treatments for increasing circulation and healing blood stasis. Danshen has extensive uses in the treatment of coronary cardiovascular disease, cerebrovascular diseases and hyperlipidemia [60-61]. However, in addition to possessing such a magnificent benefit, this natural medicine has a major drawback of delayed pharmacological action. *Salvia miltiorrhiza* nanoparticles demonstrate stronger antioxidant activity and the discharge was faster than the conventionally powered medicines [62]. Phospholipids complex packed nanoparticles similarly demonstrated better oral bioavailability than the standard samples [63].



#### 4.12. Cuscuta Herbal Nanoparticles

Dodder plant, amarbel, and akashabela are common names for the parasitic *Cuscuta reflexa*, a member of the family Convolvulaceae. It is often referred to as a "wonder plant" [64]. Flavanoids and lignins make up the bulk of this plant's composition. Anticancerous [65], ageing [66], and immunological stimulatory effects are all found in this product [67]. Since it has a poor solubility, oral administration is limited. Nanoprecipitated *Cuscuta chinensis* nanoparticles have been produced [68]. It is well known that *C. chinensis*, another *Cuscuta* species with the same name, is a well-known substitute for the true herbal medication, *C. reflexa* [69]. To further preserve liver function and reduce free radical damage, the extract and its nanoparticles of the Chinese ginseng are used in conjunction [12].

#### 4.13. Quercetin Herbal Nanoparticles

Plant parts of *Spohora japonica* L. (mainly bark and leaf) that have been air dried produce the flavonoid Quercetin, which belongs to the Fabaceae family. In terms of antioxidant activity, quercetin is superior than ascorbyl and trolox, two other well-known antioxidants. Additionally, it has anticancer and antiviral effects [70,71]. Although it has a wide range of pharmacological properties, its use in the biomedical sector is limited owing to its low water solubility and stability, which results in poor bioavailability [72]. An improvement in the bioavailability of quercetin has been shown by combining quercetin with superparamagnetic iron oxide nanoparticles (SPION). According to the findings of the research, these nanoparticles attach to particular proteins and inhibit brain cell death, hence improving memory and cognition in humans. Quercetin might be enhanced by SPIONs as a result, which could lead to better learning and memory [73].

#### 4.14. Paclitaxel Herbal Nanoparticles

An active ingredient found in *Taxus brevifolia* Nutt. bark is called Paclitaxel. The taxaceae family includes this plant, which possesses anticancer effects. As a result of its higher lattice energy, it has a lower water solubility (0.7-30 g/ml-1). As a result, paclitaxel's antitumor efficacy was enhanced when it was incorporated into nanoparticles [74,75]. Nano-precipitation and sequential simplex optimization methods were used to manufacture paclitaxel-loaded nanoparticles [76,77]. Improved drug stability, consistent drug discharge, and increased bioavailability may be achieved by using paclitaxel nanoparticles [12].

### 6. Future perspectives

There are numerous anti-cancer properties in many herbal medicines, and nanoparticle formulations have already piqued the interest of researchers. Nano-phytomedicines, on the other hand, still need to be studied more in order to aid in cancer treatment. Antioxidant properties and a wide range of health advantages are also provided by the herbal medications. New pharmaceutical options will be created by combining traditional medicines with nanotechnology, which is a combination that has been studied for decades. In order to develop products that are both safe and dependable, additional study into the physicochemical, biological, and pharmacotoxicological aspects of nano-phytomedicines is required. As a potential treatment for a

wide range of ailments, the use of nanoparticles in conjunction with medicinal plants might be revolutionary. The nano phytomedicines will be future-generation remedies to alleviate the side effects. Innovative studies, ongoing efforts, a large variety of applications, and the promotion of nano phytomedicines will undoubtedly elevate the status quo of life.

## 6. Conclusion

For herbal medications, nanoparticles serve an important role in combating the difficulties of decreased bioavailability and less water solubility. Research on herbal medications and treatments is taking place all over the globe. Additionally, the side effects of herbal medicines have been examined. Many techniques have been devised to address these challenges, but nanotechnology has emerged as one of the most promising. It enhances the herbal medications' bioavailability, stability, and water solubility. There is no doubt that nano-phytomedicines have shown exceptional abilities to cure and increase the therapeutic efficiency of herbal medications. Nano-phytomedicines listed above have all shown dramatically improved efficacy. To reduce the risk of adverse effects, they are boosting the therapeutic uses of many herbal treatments while simultaneously decreasing the therapeutic dose of herbal medicines.

## Conflict of interest

Authors declare no conflict of interest regarding this article.

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