

Article

Application of Nanotechnology on Herbal Drug formulation: A Review

Shahnawaz Ahmed¹, Susheel Kumar²

^{1,2} Scientists Institute for Industrial Research and Toxicology Ghaziabad U.P.

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Corresponding Author:

Shahnawaz Ahmed, Scientists Institute for Industrial Research and Toxicology Ghaziabad U.P.

E-mail Id:

susheelmom@gmail.com

Orcid Id:

orcid.org/0000-0001-8679-7804

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A B S T R A C T

Since ancient times Herbal drugs have been extensively castoff all over the globe and have been recognized by medical doctors and patients for their better therapeutic value as compared with contemporary medicines as they have fewer adverse effects. To deliver the components Phytotherapeutics need a scientific approach in a prolonged manner to increase patient compliance and avoid repeated administration. This can be reached by manipulative Novel Drug Delivery Systems (NDDS) for herbal ingredients. Novel drug delivery scheme advance the therapeutic value by dipping toxicity and cumulative the bioavailability and reduce the repeated administration to overwhelmed non-compliance. Individual such novel technique is nanotechnology to raise the animation and overpowering trouble which are associated with medicines which are primarily existing in plants. Nano technology and its Nano-sized drug delivery classifications of planted drugs have a sturdy and tenable future. Henceforth, integration of the nanocarriers as a NDDS in the outdated medicine system is essential to struggle more long-lasting diseases like diabetes, cancer, asthma and others.

This can be achieved by designing Novel Drug Delivery Systems (NDDS) for herbal constituents. NDDSs not only reduce the repeated administration to overcome non-compliance, but also help to increase the therapeutic value by reducing toxicity and increasing the bioavailability. One such novel approach is nanotechnology. Nano-sized drug delivery systems of herbal drugs have a potential future for enhancing the activity and overcoming problems related with plant medicines. Hence, addition of the nanocarriers as a NDDS in the outmoded medicine system is essential to conflict more chronic diseases like asthma, diabetes, cancer, and others.

Keywords: Herbal Drugs, Nanotechnology, Novel Drug Delivery Systems

Introduction

The herbal remediation have many constituents that all work simultaneously against the diseases.¹ Phytotherapeutics essential a scientific approach to deliver the mechanisms in a sustained manner to intensification patient compliance and avoid repeated administration (Ansari et al 2012). It

can be possible by make a novel drug delivery systems (NDDSs) for plants and its essential. Novel drug delivery system will reduce the repeated administration to overcome non-compliance and also make a street to growth the therapeutic value by decreasing toxicity and growing the bioavailability, and so on.^{2,3}

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Integration of the herbal extracts into novel formulation systems have certain additional recompenses, such as their bulk give medicine to and less preoccupation and bioavailability can be stunned which is one of the chief problematic existence confronted day to day, mostly by the pharmaceutical corporations.

Nanomedicine are lately referred by nanotechnology for treatment, diagnosis and monitoring the biological system. Since nanotechnology is a field of functional art and technology it purposes to advance strategies and dosage methods in the range of 1 to 100 nm. The nanocarriers have been made of substance like synthetic biodegradable, polysaccharides polymers and lipids. They are safe to use.

As all the apparatuses make available synergistic action and therefore improve the therapeutic value, the action of herbal drugs be contingent on complete function of dissimilar active constituents. They are all associated to each other hence active components play an important role. However, most of the herbal formulation having more or less insoluble nature leading to lesser bioavailability and greater systemic approval requiring repeated administration or higher dose, which makes the preparation as a destitute candidate for therapeutic use. In phyto-formulation research, manufacture nano dosage types (Polymeric Nanoparticles [Nanospheres and Nanocapsules], Liposomes, Proliposomes, Solid Lipid Nanoparticles [SLNs], Nanoemulsion, etc.) has outsized amount of plus opinions for herbal formulations, plus development of solubility bioavailability, pharmacological activity, protection from toxicity, with development of stability, sustained delivery, fortification from physical and chemical degradation, cultivating tissue macrophages distribution etc. Hence, amalgamation of the nanocarriers as a NDDS in the traditional medicine system is necessary to counter more chronic ailments like diabetes, cancer, asthma and others.¹ There is a range of herbal nanoparticles delivery system has been summarized in Table 1.

History and Development

The foundation of concept of modern drug development remains rooted in traditional medicine and therapies.^{4,5} Plants and dissimilar parts of plants (like leaf, root, stem) had been used for medicinal purposes long before verified history in different parts of the world like ancient China, Africa, America, Egypt and India. Availability of Chemical analysis first started in the early 19th century which started the extraction and alteration of herbal constituents.^{4,6} Owing lack of scientific justification and processing difficulties, herbal items we're not restrained for expansion as novel formulations such as standardization, extraction, and proof of identity of specific drug constituents in complex polyherbal systems. Though, modern phytopharmaceuticals research paved the path for technical requirements for herbal drugs as in modern formulations, also underwritten in unindustrialized novel know-hows of formulations such as nanoparticles, micro-emulsions, matrix systems, solid dispersions, liposomes, SLNs, and so on. Nanomicellar system,⁷ nanotubes,⁸ and colloidal nanogels have been established for curcumin to be used alone as well as in grouping with other chemotherapeutic agents like paclitaxel.^{1,29}

Requirement For “Nano Carriers” For “Herbal Remedies

Before reaching of drugs to the plasma, many constituents of the herbal drugs get denatured in the highly acidic medium of the gastric juice and other constituents might be metabolized by the liver. As the result optimum amount of the herbal drugs may not reach the blood. If the constituents do not reach in the most favorable quantity to the infected site at “minimum effective level,” then there will be no medium to confirm the therapeutic effect of the preparation. Applying Nanocarriers of herbal remedies avail calculated amount of the drug to their site of action

Table 1. Some Herbal Drug Nanoparticles

Formulation	Active Ingredients	Biological Activity	Method of Preparation
Curcuminoids Solid-Lipid Nanoparticles	Curcuminoids	Anticancer And Antioxidant	Micro-Emulsion Technique ^{1,21}
Glycyrrhizin Acid Loaded Nanoparticles	Glycyrrhizin Acid	Anti-Inflammatory Antihypertensive	Rotary-Evaporated Film Ultra Sonication Method ^{1,22}
Nanoparticles Of CuscutaChinensis	Flavonoids And Lignans	Heptoprotective And Antioxidant Effect	Nanosuspension Method ^{1,23}
Taxel- Loaded Nanoparticles	Taxel	Anticancer	Emulsion Solvent Evaporation Method ^{1,24}
ArtemisininNanocapsules	Artemisinin	Anticancer	Self Assembly Procedure ^{1,25}
CPT Encapsulated Nanoparticles	Camptothecin	Anticancer	Dialysis Method ^{1,26}
Berberine Loaded Nanoparticles	Berberin	Anticancer	Ionic Gelation Method ^{1,27}

bypassing all the hurdles such as acidic pH of stomach, liver metabolism and increase the extended circulation of the medicine into the blood due to their tiny size.^{1,9}

Since of the subsequent possessions Herbal preparations were designated as adequate drug candidate for distribution over a nano delivery system:

- These are the wholesale drugs so dose lessening is suggested.
- Operative petrol, acetone, chloroform and methanolic extracts are obtainable which may not be suitable for delivery as such.
- For numerous chronic diseases advertised preparations lack target specificity.
- Patient's refusal due to large doses and less usefulness with the current formulations.
- Numerous other side effects are linked with presently marketed formulations.

Strategies of Nanotechnology

Because of the following advantages nano-sized delivery system was preferred:

- Their unique size and high loading capacities as they look as if to be gifted to deliver high concentrations of drugs to disease sites.¹ Assigning quicker dissolution in the blood, nanoparticles deliver the drug in the smaller size that upsurges the whole superficial area of the drugs.
- The concentration of drugs persevere at the site of action for the longer phases.¹
- Since of the smaller size and retention capacity (due to poor lymphatic drainage) such in tumor shows EPR (enhanced permeation and retention) effect¹
- Deprived of the addition of any specific ligand moiety they exhibition passive targeting to the disease site of action.
- They lower the chances of side effects.¹
- They decreases the dose amount of the drug formulation.¹

Techniques

The techniques usually applied for the formulation are:

High-Pressure Homogenization Method

In this technique, the lipid is propelled with high pressure (100 to 2 000 bar) through a very high shear stress, which causes disruption of particles down to the submicrometer or nanometer range. High-pressure homogenization technique is a very unfailing and powerful process for the large-scale building of nanostructured lipid carriers, SLNs, lipid drug conjugate and parenteral emulsions.^{10,11}

Complex Coacervation Method

Complex coacervation method a spontaneous phase

partition practice of two liquid phases in colloidal systems, which outcome by the interference of two oppositely emotional polyelectrolytes upon blending in an aqueous solution.¹⁰

Co-precipitation method

This process is an alteration of the complex coacervation method for the formulation of nanoscale core-shell particles. This technique has been proved to afford good dispersion stability to inadequately water-soluble drugs.¹⁰

Salting-out method

This process is based on the phenomenon that the solubility of a non-electrolyte in water is reduced upon accumulation of an electrolyte.¹⁰

Nanoprecipitation method or solvent displacement method

This method is works on interfacial deposition of a polymer after dislocation of a semipolar solvent miscible with water from a lipophilic solution, thus resulting in a reduction in the interfacial tension among the two phases, which enlarges the surface area with a succeeding arrangement of tiny droplets of organic solvent even without any mechanical stirring.^{10,12}

Solvent emulsification–diffusion method

The technique engages in preparation of an o/w emulsion with the help of oil phase containing polymer and oil in an organic solvent, which is emulsified with the aqueous phase, containing stabilizer, in high shear mixer, go after by adding of water to induce the transmission of organic solvent, thus resultant in creation of nanoparticles.[10]

Supercritical fluid methods

In this method a supercritical fluid (SCFs) can either be a liquid or gas and used above its thermodynamic critical point of temperature and pressure. This method used to prepare submicrometer-sized and nano-sized formulations. Generally use carbon dioxide and water in (SCFs) [10,13]

Self-assembly methods

Self-assembly is the physical method in which pre-existing disarranged constituents, atoms, or particles establish themselves into synchronized nanoscale configurations by physical or chemical reactions deprived of the help from any external source.¹⁰

Types of Nanopharmaceuticals

- Colloidal nano-liposomes
- Dendrimers
- Phospholipids micelles
- Polymeric nanoparticles
- Polymeric micelles
- Magnetic nanoparticles

- Metal and inorganic nanoparticles
- Quantum dots
- Solid lipid nanoparticles

Recent Progress

Recently, pharmaceutical researchers have reallocated their focus on designing a perfect drug delivery system for herbal drugs using today's scientific advancement. *Cuscuta chinensis* is a frequently used traditional ancient Chinese medicine to nurture the liver and kidney. Due to the reduced water solubility of its major formulations such as flavonoids and lignans, its absorption upon oral administration could be inadequate. So, the nanoparticles for the same were industrialized.^{1,14} A newest study of polylactic acid nanoparticles of lipophilic anticancer herb drug (Cucurbitacins and Curcuminoids) applying a precipitation technique have been developed.^{1,15} Work has also been in advance in the emerging and describing of SLNs for the traditional Chinese drug for their targeted delivery and adequate bioavailability and efficiency.^{1,16} In the recent years, nanostructured carrier mechanisms like, SLNs, polymeric micelles, polymeric nanoparticles, liposomes, nanoemulsions, etc. have been examined for their potential to distribute anticancer drugs by oral route.^{1,17,18} furthermore, the oral route recommends great potential for delivery of cytotoxic agents and therefore the awareness has focused on the formulation of oral chemotherapy in oncology.^{1,19,20}

Issues of Toxicity

Although nanopharmaceuticals may potential various never-ending opportunities in the field of drug delivery for the diagnosis and management of various diseases, their safety should not be unnoticed.¹⁰

The change in the structural properties and physicochemical of engineered nano-sized matters with a reduced in size could be accountable for a number of material interactions that could lead to toxicological ill consequences. At present, researchers must accept that it is still very early in the toxicological assessment for nanomaterials and nanomedicine, and there are only few data on the safety and toxicity.

Future Prospective

The research has been going on herbal treatment and natural products all over the globe. The formulations of herbal remedies in the drug delivery system in a number of institutes and research centers are being carried out at fundamentals and clinical trial levels. The only necessity is to build up the better schemes for the proper delivery of such drugs at the sites of action and in the whole body in the doses which will not compromise with the present treatment. Something that would not only heal the patients from side effects like toxicity and hypersensitive reactions

but also will intensify the patient's vigor internally is very much beneficial. In the close future, the beginning of herbal nanoparticles for cancer drug delivery may also fascinate some active exploration organizations and possibly create attention-grabbing outcomes.

Therefore, using "herbal medication" in the nanocarriers will amplify its strength for the treatment of a variety of chronic ailments and health benefits. Numerous efficacious examples with experienced evidences are present among us in the direction of nano investigation. Herbal remedies are also effective properties of advantageous ingredients holding antioxidants and constituents that can be made use in purposeful foods and supplements.²⁸ This type of collaborative experimentation and researches among the old-style "Herbal remedies" and newer approaches of modern drug delivery system, i.e., "Nanotechnology" has established the fascinating therapies to the pharmaceutical in near future that will improve health of community. It is predicted that the operative and respected significance of the natural products and herbal remedies being applied with the nanocarriers will improve the significance of existing drug delivery systems.¹

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