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INFLUENCE OF NANOTECHNOLOGY ON HERBAL DRUGS

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ABSTRACT

Herbs have been a surviving unit since we were born on this planet. Currently, they are the most probed topic in the food industry or pharmacotherapy due to their multidimensional approach where one herb targets various diseases and proffers a wide range of health benefits. Herbal remedies and natural products are being used to cure the diseases. Unlike widely used allopathic system, the herbal remedies have thousands of constituents that all work simultaneously against the diseases. Phyto therapeutics need a scientific approach to deliver the components in a sustained manner to increase patient compliance and avoid repeated administration. Nano-sized drug delivery systems of herbal drugs have a potential future for enhancing the activity and overcoming problems associated with plant medicines.

KEYWORDS: Herbal Drugs, nanotechnology, formulation technology of nanoparticles.

1. INTRODUCTION

Herbal medicines are increasingly popular throughout the world and have promising potential to provide treatment, maintain and improve health, as well as prevent and treat several diseases because they are considered safe compared to modern conventional medicines and are more economical. However, most of these biologically active phytochemical constituents have limitations; namely, their absorption and distribution are low, and the target specificity of phytochemicals is generally low, which results in low bioavailability, resulting in decreased biological activity.(Ansari S. H. et,al., 2012) In addition, the large doses are required to produce the activity of these phytochemical compounds, also some of these phytochemical compounds are sensitive to acidic conditions and have low stability phytochemical compounds. (Neha Singh et, al., 2023)

Nanotechnology-based delivery systems function as drug carriers that can overcome the various limitations that herbal medicines face, including increasing the bioavailability and bioactivity of phytochemicals. (Rinku Y. Patil et, al., 2018) The approach using nanotechnology can be a promising innovative technology that is applied to phytochemical constituents, increasing the phytotherapy efficiency of herbal medicines. The development of an efficient and safe drug delivery system is the goal of various researchers. Recent developments in the field of nanotechnology have led to renewed interest in herbal medicinal formulations. Several delivery systems approach, such as phytosomes, solid lipid nanoparticles (SLN), nanos- structured lipid carriers (NLC), polymeric nanoparticles, nano emulsions, etc., have been proposed. (Yadav D. et, al., 2011)

Nanoparticles have been used to modify and improve the pharmacokinetic properties of different drugs, so the nanotechnology approach is expected to increase the bioavailability and bioactivity of herbal medicines. This article review aims to provide an overview of the latest advances in the development of nanotechnology-based herbal drug formulations that increases herbal activity. (Ansari S.H. et, al., 2012)

2. NANOTECHNOLOGY

The nanoscale system has a particle diameter of 0.1 µm, otherwise known as a submicrometer. This provides several advantages regarding various aspects, including the route of administration and increased therapeutic effects, which makes this nanotechnology more developed and widely studied by researchers. Many studies have combined herbal medicine with nanotechnology because nano-sized systems can increase activity, reduce dosages, and minimize side effects. Herbal medicines using nanotechnology-based delivery systems have great potential and unique properties, such as being able to convert less soluble, poorly absorbed, unstable substances into promising drugs. (Ansari S.H. et, al., 2012)

Therefore, nanotechnology-based delivery systems represent a promising prospect for enhancing herbal activity and overcoming the dilemmas associated with herbal medicine.

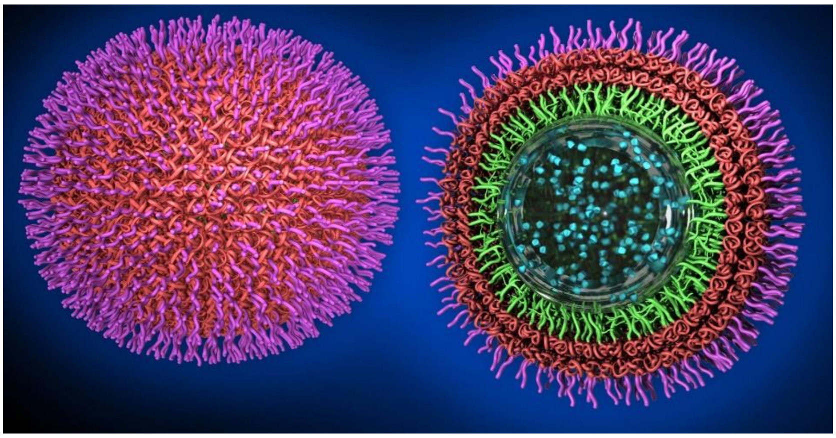

Figure 1: Nanoparticles.

Advantages of herbal nanoparticle delivery system

1. Shows EPR (enhanced permeation and retention) effect i.e., enhanced permeation through the barriers because of the small size and retention due to poor lymphatic drainage such in tumour.
2. Exhibits passive targeting to the disease site of action without the addition of any ligand moiety.
3. Decrease in the side effects.
4. Decrease in the dose of the drug formulation.
5. Nanoparticulate system delivers the herbal formulation directly to the site of action.
6. Increased efficacy and therapeutic index.
7. Increased stability via encapsulation.
8. Improved pharmacokinetic effect. (Yadav D, et, al., 2011)

Classification of Nanoparticles

1. Labile Nanoparticles: Liposomes, micelles, polymers, nano emulsions etc.

2· Insoluble Nanoparticles: TiO2, SiO2, fullerene, quantum dots, carbon lattices, nanotubes

3· One dimensional nanomaterial: Nanowire and nanotube

4· Two-dimensional nanomaterial: Self assembled monolayer film. (Alakh N Sahu et, al., 2013)

Techniques are used for the preparation of above nano pharmaceuticals

1. Complex coacervation method

This is a spontaneous phase separation process of two liquid phases in colloidal systems, which results due to the interaction of two oppositely charged polyelectrolytes upon mixing in an aqueous solution. It mainly includes three steps-

1. Formation of three immiscible chemical phases.
2. Depositing the liquid polymer coating upon the core material.
3. Rigidizing the coating.(Rinku Y. Patil et, al., 2018)

2. Co-precipitation method

This method is a modification of the complex coacervation method for the preparation of nano scale core-shell particles. This method has been reported to provide good dispersion stability to poorly water-soluble drugs. (Rinku Y. Patil et, al., 2018)

3. Salting-out method

This method is based on the solubility of a non-electrolyte in water is decreased upon addition of an electrolyte. Acetone is selected as water miscible solvent because of its solublizing properties and its well-known separation from aqueous solution by salting out method with electrolytes. The diffusion of acetone from the droplets is the most imp step. This diffusion which takes place on dilution with excess water, can generate interfacial turbulence leading to polymer aggregation in the form of nanoparticles.

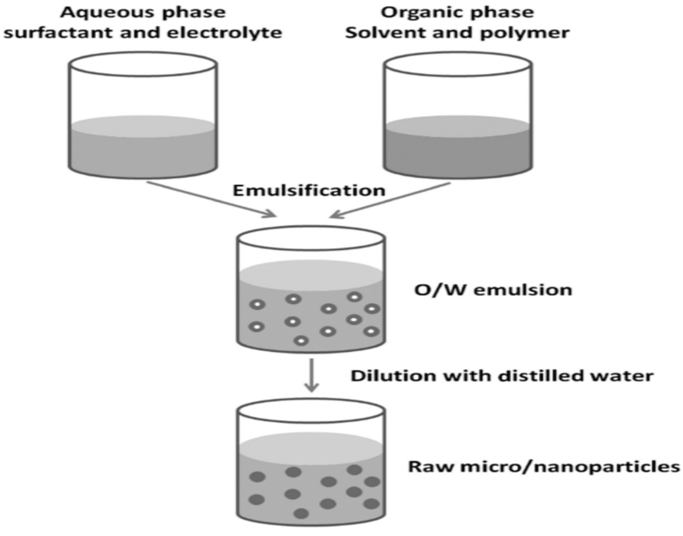

Figure 2: Diagrammatic representation of Salting out method.

4. Nanoprecipitation method or solvent displacement method

As biodegradable nanoparticles meet with increasing interest for drug delivery applications, a series of investigations were carried out to understand the mechanism of the formation of drug loaded nanoparticles using the solvent displacement method. This method is based on interfacial deposition of a polymer after displacement of a semipolar solvent miscible with water from a lipophilic solution, thereby resulting in a decrease in the interfacial tension between the two phases, which increases the surface area with a subsequent formation of small droplets of organic solvent even without any mechanical stirring. (Rinku Y. Patil et, al., 2018)

5. Solvent emulsification–diffusion method

The method involves preparation of an o/w emulsion using oil phase containing polymer like PLGA and oil in an organic solvent which is emulsified with the aqueous phase containing stabilizer in high shear mixer followed by addition of water to induce the diffusion of organic solvent, thus resulting in formation of nanoparticles.

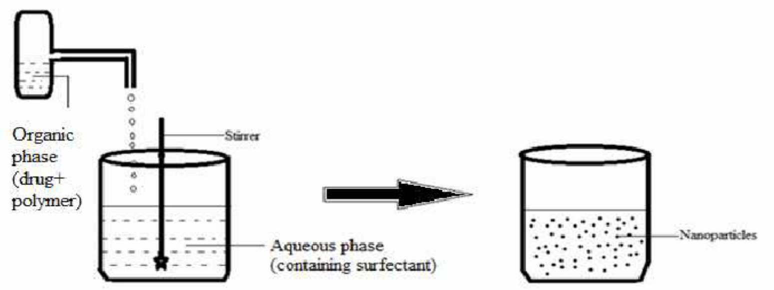

Figure 3: Diagrammatic representation of Solvent emulsification–diffusion method.

6. Supercritical fluid methods

A supercritical fluid (SCFs) can either be a liquid or gas and used above its thermodynamic critical point of temperature and pressure.(Ansari S.H. et, al., 2012) The most used SCFs are carbon dioxide. Particles that have the smooth surfaces, small particle size and distribution and free flowing can be obtained with SCF techniques. Rapid Expansion of Supercritical Solutions (RESS), Supercritical Anti Solvent (SAS) and Particles from Gas Saturated Solutions (PGSS) are three groups of processes which lead to the production of fine and monodisperse powder.

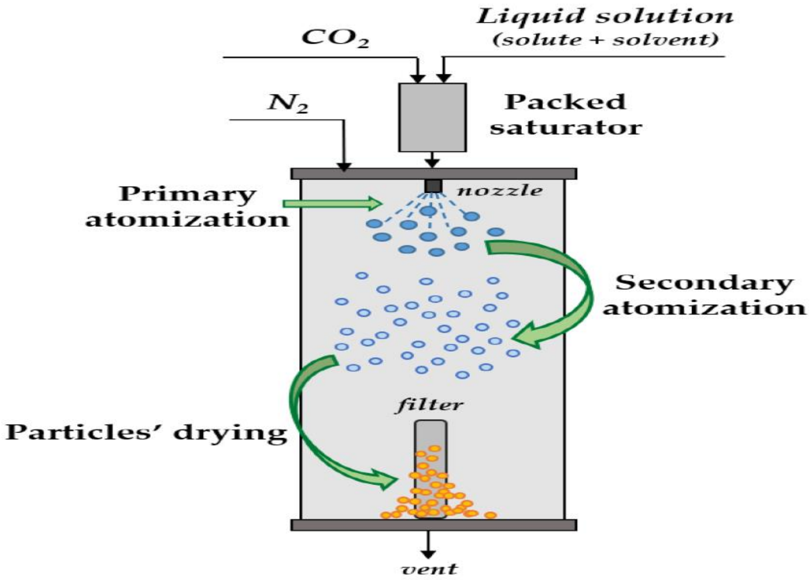

Figure 4: Supercritical fluid methods.

7. High-pressure homogenization method

In this method, the lipid is pushed with high pressure (100 to 2000 bar) through a very high shear stress, which results in disruption of particles down to the submicrometer or nanometer range. High-pressure homogenization method is a very reliable and powerful technique for the large-scale production of nano structured lipid carriers, lipid drug conjugate, SLNs, and parenteral emulsions. (Rinku Y. Patil et, al., 2018)

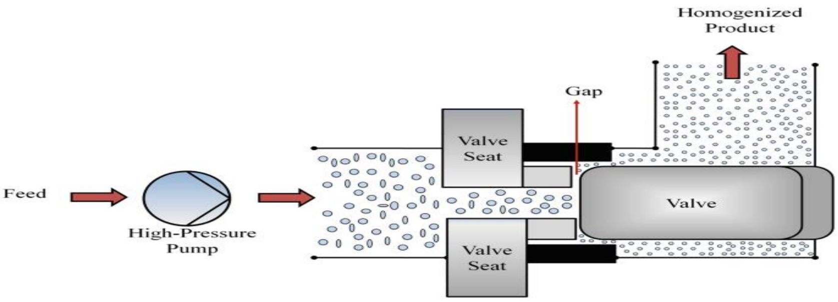

Figure 5: High-pressure homogenization method.

8. Self-assembly methods

Self-assembly is the physical process wherein pre-existing disordered components, atoms, or molecules organize themselves into regulated nanoscale structures by physical or chemical reactions without any contribution from any external source.

9. Emulsion-Solvent Evaporation Method

Emulsification-solvent evaporation involves two steps. The first step requires emulsification of the polymer solution into an aqueous phase. During the second step polymer solvent is evaporated, inducing polymer precipitation as nanospheres. The nano particles are collected by ultracentrifugation and washed with distilled water to remove stabilizer residue or any free drug and lyophilized for storage. Modification of this method is known as high pressure emulsification and solvent evaporation method. This method involves preparation of a emulsion which is then subjected to homogenization under high pressure followed by overall stirring to remove organic solvent. (Ansari S.H. et, al., 2012)

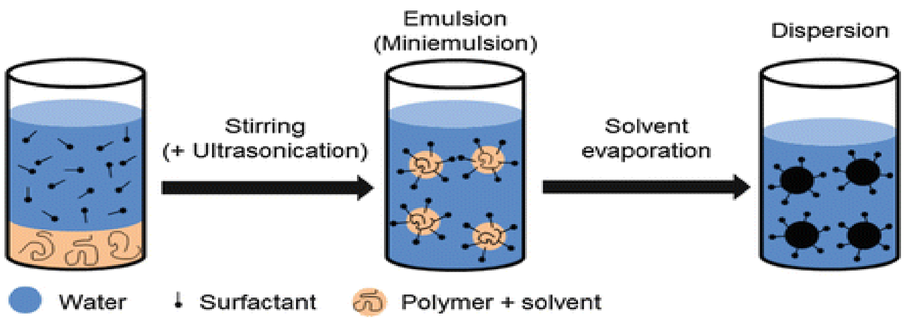

Figure 6: Emulsion-Solvent Evaporation Method.

10. Double Emulsion and Evaporation Method

The emulsion and evaporation method have limitation of poor entrapment of hydrophilic drugs. Therefore, to encapsulate hydrophilic drug the double emulsion technique is employed, which involves the addition of aqueous drug solutions to organic polymer solution under vigorous stirring to form w/o emulsions. This w/o emulsion is added into second aqueous phase with continuous stirring to form the w/o/w emulsion. The emulsion then subjected to solvent removal by evaporation and nano particles can be isolated by centrifugation at high speed. The formed nanoparticles must be thoroughly washed before lyophilisation. In this method the amount of hydrophilic drug to be incorporated, the concentration of stabilizer used, the polymer concentration, the volume of aqueous phase are the variables that affect the characterization of nano particles.

Table 1: Herbal Drug Nanoparticles.

Sr. No.	Formulations	Active ingredients	Biological activity	Method of preparation	Benefit of formulation
1.	Berberine-loaded nanoparticles	Berberine	Anti-neoplastic activity	Ionic gelation method.	H-Pylori growth inhibition
2.	Curcuminoids solid lipid nanoparticles	Curcuminoids	Antitumor, antioxidant, antiamylodin, antiplatelet aggregation and anti-inflammatory, antimalarial.	Micro-emulsion technique.	-increase in activity -Enhanced stability of curcuminoids
3.	Artemisinin nano capsules	Artemisinin	Anticancer	Self-assembly procedure.	- achieving prolonged drug release through self-assembly of polyelectroytes on natural drug crystals. - controlled release
4.	Nanoparticles of cuscuta chinensis	Flavonoids and lignans	-Hepatoprotective and antioxidant effects -Used to improve sexual function, prevent senescence and regulate the immune system. Some studies showed anticancer, antiageing and immune-stimulatory effects.	Nanosuspension method.	Enhanced solubility
5.	Quercetin Nanoparticles-	Quercetin	antioxidant, anti-proliferative, antitumor, antibacterial	nano participation technique	- improve the bioavailability

Advanced techniques for identification and characterization of nano herbal medicine

1. High performance Liquid chromatography (HPLC)

Preparative and analytical HPLC are widely used in pharmaceutical industry for isolating and purification of herbal compounds. Vasicine, the major bioactive alkaloid of *Adhatoda vasica*, was estimated by HPLC in two polyherbal drug formulations- *Shereeshadi Kashaya* and Yastyadivati, and its content was found to be 18.1 mg/100 g in *Shereeshadi Kashaya* and 0.7 mg/100g in Yastyadivati. Standardization of the *Triphala* (an antioxidant-rich herbal formulation) mixture of *Emblica officinalis*, *Terminalia chebula* and *Terminalia belerica* in equal proportions has been reported by HPLC method by using the RP18 column with an acidic mobile phase. (Rinku Y. Patil et, al., 2018)

2. High performance thin layer chromatography (HPTLC)

HPTLC is used for qualitative and quantitative phytochemical analysis of herbal drugs and formulations. Also, with the help of HPTLC several samples can be analysed simultaneously using a small quantity of mobile phase. Gallic acid, rutin and quercetin these are important active constituents of *Terminalia chebula* were estimated by HPTLC method. Glycoside (Jamboline), Tannin, Ellagic Acid and Gallic Acid are present in mother tincture of Syzygium Jambolanum was quantitatively evaluated in terms of stability, repeatability, accuracy and calibration by HPTLC. The HPTLC method gives accurate, faster and cost-effective quantitative control for the analysis of diosgenin. (Kharat A. et, al., 2014)

3. UPLC

Ultra-performance liquid chromatography (UPLC) was used to evaluate decocting-induced chemical transformations and chemical consistency between traditional and dispensing granule decoctions.

4. Liquid chromatography-Mass spectroscopy (LC-MS)

LC-MS has become method of choice in many stages of drug development.

LC-MS analysis of Amino glycosides showed that these drugs are highly soluble in water, exhibited low plasma protein binding, and were more than 90% excreted through the kidney. Further this technique helps in analysis of amino glycosides in plasma samples with ion pairing chromatography. The pharmacokinetic studies of Chinese medicinal herbs using LC-MS.

5. Gas chromatography - mass spectroscopy (GC-MS)

It is the system used for identification of large number of components present in natural and biological systems. The identification and quantification of chemical constituents present in polyherbal oil formulation (Megni) consisting of nine ingredients, mainly Myristica fragrans, Eucalyptus globulus, Gaultheria procumbens and Mentha piperita was analyzed by GC-MS method. Thirty-five volatile compounds were separated and identified. (Ansari S.H.et, al., 2012)

6. Capillary Electrophoresis

The methodology of CE was established to evaluate one herbal drug in terms of specificity, sensitivity and precision. Several CE studies dealing with herbal medicines have been reported and two kinds of medicinal compounds i.e. alkaloids and flavonoids have been studied extensively. Furthermore, the analysis time of the CE method was two times shorter than that in HPLC and solvent consumption was more than 100-fold less. The hyphenated CE instruments, such as CE-diode array detection, CE-MS and CE-NMR, have been utilized. Some Herbal Drug Nanoparticles with their method of preparation and application presented in Table1. (Kharat A. et, al., 2014)

Tools in Nanotechnology

A. Cantilever

Cantilever is a tiny bar anchored to one end can be engineered to bind to molecule associated with cancer. These molecules bind to alter DNA protein that present in cancer cell.

B. Nanopores

Nanopores allow DNA to pass through one strand at a time hence DNA sequencing can be made more efficiently. Thus shape, electrical property of each base on strand can be monitored. As these properties are unique for each of four bases that make up genetic code. The passage of DNA through a nanopore can be used to decipher the encoded information including error in code associated with cancer.

C. Fullerene

A fullerene is any molecule composed entirely of carbon, in the form of a hollow sphere, ellipsoid, or tube. Spherical fullerenes are also called buckyballs, and cylindrical ones are called carbon nanotubes or buckytubes. Fullerenes are similar in structure to graphite, which is composed of stacked graphene sheets of linked hexagonal rings; but they may also contain pentagonal (or sometimes heptagonal) rings. (Alakh N Sahu et, al., 2013)

D. Nanotubes

These are smaller than nanopores. Nanotubes are about half of the diameter of molecule DNA. It helps to exactly pinpoint location of changes in mutated region associated with physical shape of DNA can be traced.

E. Dendrimers

These are tree like macromolecules with branching reach out from central core. These branched macromolecules are constructed around a simple core unit. Dendrimers have a high degree of molecular uniformity, narrow molecular weight distribution, specific size and shape characteristics, and a highly functionalized terminal surface. (Alakh N Sahu et, al., 2013)

3. CONCLUSION

Nanotechnology is rapidly expanding and potentially beneficial field with tremendous implication for industry, medicine, and cosmetics. The combination of nanotechnology with traditional herbal medicine may provide a very useful tool in designing future herbal medicine with improved bioavailability profile and less toxicity. The connection between plant sciences and nanotechnology has the potential to develop an attractive symbiosis between green revolution and nanotechnology with realistic prospects for minimizing the application and generation of toxic chemicals that destroy living organisms.

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