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A Study of Nanoparticles in Herbal Drugs

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Abstract:

In the world, Herbal medicine is undoubtedly the oldest system and widely used of medical science since ancient times and it's recognized by physicians and patients for their therapeutic value as they have fewer adverse effects as compared with other modern medicines. This drug is used for the purpose to cure the disease and it have hundreds and thousands of constituents that all work together against the diseases. In the market, most conventional pharmacognostical or pharmaceuticals products play a crucial role, they are rooted from natural products (NPs) and their derivatives with herbal products. For converting botanical materials into medicines, the herbal drug technology is used and it's important for quality control with proper integration of modern scientific techniques and traditional knowledge is important. The new pharmacognosy play an important role that includes all the features of drugs development and discovery, where biotechnology-driven applications. In this paper, discuss about the herbal drug, nanoparticles of herbal drug and its technology.

Keywords: *Herbal Drugs, Nanoparticles, Pharmaceutical Science*

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Introduction

Herbal medicine is the oldest drug of health care known to mankind and it is an essential part of the development of modern civilization. This medicine plant-based formulation is based to alleviate diseases and these formulations are faced the most important challenges because of their lack of evaluation. This evaluation is necessary for the quality and purity of the herbal product. For every plant medicine, it is very important to establish a system of evaluation in the market, since the scope for variation in different batches of medicine is massive (Khan *et.al* 2012).

From plant origin, use of indigenous drugs forms a major part of complementary and alternative medicine/traditional medicine (CAM/TM). For herbal medicine, exist world market that includes herbal products and raw materials have been estimated to have an annual growth rate between 5 and 15%. At the US, total global herbal drug market is estimated at $62 billion and by the year 2050, is expected to grow to the US $5 trillion. One of the major segments of the traditional system of medicine is an herbal formulation that contributes enormously to the positive health of an individual (Joshi *et.al*, 2004).

Medicinal plants are now getting more attention than ever because they have the potential of providing large benefits to society or indeed to all mankind, especially in the line of medicine. By reducing the toxicity and side effects of drugs at the same time, herbal treatment helps to increase the therapeutic value that it also increase the biodiversity. Nanotechnology plays a great role in this approach and the use of nanotechnology in herbal medicine and more specifically in drug delivery is set to spread rapidly. For enhancing the activity, nano herbal drug delivery systems (NDDS) have a potential future and overcoming the problems associated by medicinal plants. To treat the dangerous disease like cancer, diabetes etc. to helping the herbal nano-carries. For the development of novel formulations, herbal medicines were not considered due to lack of scientific justification and processing difficulties but scientific needs of herbal medicines (such as determination of pharmacokinetics, site of action, mechanism of action, accurate dose required etc.) can be solved by modern phytopharmaceutical research that to be incorporated in novel drug delivery system such as solid dispersions, solid lipid nanoparticles, nanoparticles, liposomes, micro-emulsions and so on. With enhanced efficacy, the herbal drugs can be utilized in a better form by incorporating them into modern dosage forms. By designing novel drug delivery systems, this can be achieved for herbal constituents (Yadav *et.al* 2011).

Within local or regional healing practices, naturally occurring drugs which are the traditional herbal medicine that is plant-derived substances with negligible or no industrial processing that have been used to treat illness. In global health debates, traditional herbal medicines are getting significant attention.

Table 1: Existing Traditional Medicinal Systems in Different Countries (Banerjee and Mitra, 2012)

Country	The traditional system of medicine
India	Ayurveda, Siddha
China	Chinese Herbal medicine
Japan	Kampo
Korea	Hanbang
Pakistan	Indusynunic
Middle East	Islamic, Unani
Europe	Aromatherapy, homeopathy, botanicals, and herbalism
USA, Australia	Western Herbal medicine
Africa	Many traditional medicine systems used by various tribes like Muti, Ifa etc. and made operational by sangomas or inyangas, traditional healers etc.

Traditional herbal medicine plays an important role in China in the strategy to contain and treat severe acute respiratory syndrome (SARS). Traditional herbal medicine is used by the African populations at 8% and the worldwide annual market for these products approaches US$ 60 billion.in global health, much traditional herbal medicine research will play a critical role. In traditional herbal medicines, China, India, Nigeria, the United States of America (USA) and WHO have all made substantial research (Tilburt and Kaptchuk, 2008).

When techniques were developed to produce a synthetic replacement for many of the medicines by arranging the pharmaceutical companies that had been derived from the forest. New pioneering or indigenous therapies are developed by the pharmaceutical efforts which are also developed the uniqueness of plant-based drugs (herbal remedies). In the pharmaceutical organizations, wide-range in structural diversity and

spacious series of pharmacological and pharmacognostical activities contained by the natural product. In the market, several of the most significant SNPs and their derived active components are present of pharmaceuticals industries that include lovastatin (anticholesterolemic), cyclosporine-A, doxorubicin (anti-cancer), paclitaxel, streptomycin, tacrolimus (immunosuppressive), erythromycin and amphotericin-B (fungicidal). From the plants, many drugs had been extracted as their active components for tearing various disease such as Atropine, Quinine, Colchicine, Asprin, Digoxin, Salbutamol, Bromelain and Morphin etc (Yadav *et.al* 2011).

The activity of herbal medicines depends on the overall function of a variety of active components, as all the constituents provide synergists action and thus enhance the therapeutic value. Each function plays an important role which is related to each other that possesses the insoluble character which is leading to lower bioavailability and increase systematic clearance necessitating repeated administration or higher dose, which makes the drug as a poor candidate for therapeutic use. Nano-dosage forms (Polymeric Nanoparticles) are developed in phyto-formulation research that includes Liposome, Solid Liquid Nanoparticles (SLNs), Proliposomes which has greater number of advantages for herbal drugs that are enhancement of bioavailability and solubility, enhancement of pharmacological activity, protection from toxicity, improving tissue macrophages distribution, enhancement of stability, protection from physical and chemical degradation and sustained delivery etc. For enhancing the activity and overcoming problems that linked with plant medicines, nano-sized drug delivery systems (NDDSs) of herbal drugs have potential future. In traditional medicine system, integration of the nano-carries as an NDDS that is essential to conflict more chronic disease such as cancer, asthma, diabetes and so on (Ansari, Islam, and Sameen, 2016).

The scientist has been developed various herbal nanoparticles delivery systems that are as follows:

Table 2: Various Herbal Drug Nanoparticles (Sachan and Gupta, 2015; Yadav, 2011; Ansari, Islam, and Sameen, 2016)

Formulations	Active Ingredients	Biological Activity	Method of Preparation
Curcuminoids solid lipid nanoparticles	Curcuminoids	Anticancer and antioxidant	Micro-emulsion technique
Berberine-loaded nanoparticles	Berberine	Anticancer	Ionic gelation method
CPT-encapsulated nanoparticles	Camptothecin	Anticancer	Dialysis method
Artemisinin nanocapsules	Artemisinin	Anticancer	Self-assembly procedure
Taxel-loaded nanoparticles	Taxel	Anticancer	Emulsion solvent evaporation method
Nanoparticles of Cuscuta Chinensis	Flavonoids a lignans	Hepatoprotective and antioxidant effects	Nano-suspension method
Glycyrrhizic acid-loaded nanoparticles	Glycyrrhizic acid	Anti-inflammatory, antihypertensive	Rotary-evaporated filmultrasonication method

Need for Nano-Sized Delivery System for Herbal Remedies

In human, animal, plants, and microorganisms, pharmaceutical drug discovery acquired an immense increment although together with natural products pharmacologists, biochemists, chemistry, and microbiologists commenced unraveling the chemistry of natural progressions. Many elements of herbal drugs will be damaged in highly acidic pH of the stomach and by the liver, other elements might be metabolized before reaching to the blood. It gives a

result that may not reach to the blood of optimum quantity of herbal drug that means do not reach to the infected area by the exact amount of the drug. At 'minimum effective level', the drug does not reach in an optimum amount to the infected area due to which not show the therapeutic effect of the drug. The optimum amount of drug is carried by the nano carriers that is applying to herbal remedies to their site of action by passing all barriers such as liver metabolism, acidic pH of the stomach and increase the prolonged circulation of the drug into the blood due to their small size. In the traditional medicine system, incorporation of the nano carriers as an NDDS that is essential to conflict more chronic disease like cancer, asthma, diabetes and so on.

The drawbacks of traditional herbal drug delivery systems overcome by the nano-sized herbal delivery system that was selected. It contains some reasons that are as follows:

- To improve the selectivity, effectiveness, drug delivery, and safety by using the nanoparticles that can be used to target the herbal medicine and it reduces doses and increase patient compliance.
- To increase the herbal drug solubility by using nanoparticles and help to localize the drug in a specific site thus resulting in better efficacy.
- To deliver high concentrations of drugs to disease sites by appearing of nanoparticles because of their unique size and high loading capacities.
- In small particles size, delivering the drug that helps the entire surface area of the drugs, therefore, assigning quicker dissolution in the blood.
- It shows Enhanced Permeation and Retention (EPR) effect.
- Decrease the side effects.
- To the disease site of action, exhibits passive targeting without the addition of any particular ligand moiety (Ansari, Islam, and Sameen, 2016; Sachan and Gupta, 2015).

Types of Nano-pharmaceuticals

Polymeric Nanoparticles

With particle size, nanoparticles refer to colloidal systems ranging from 10 to 1000nm. Polymeric colloidal spheres refer to as the polymeric nanoparticles that are very small in size (10^{-9}m) and at their surface, it has the ability to entrap the drug within the matrix or adsorb or conjugate. From the matrix, the release of drug from nanoparticles that occur through the diffusion and erosion. On the surface, some particles adsorb the drug that shows the fast release of drug from other particles. In the formulation, both natural and synthetic polymers take part and in the pattern form, polymers are used that are categorized into two parts biodegradable and non-biodegradable polymers. The biodegradable polymer is degraded into the body and does not have any further toxicity. The natural polymers are dextran, gelatin, and chitosan and synthetic polymers are poly (anhydrides), poly (esters), poly (amides).

For many years, polymeric micelles are the point of attraction for many scientists due to which control their property and pharmacological characteristics. Polymeric micelles are amphiphilic, the inner core is hydrophobic and the outer shell is hydrophilic and manufactured by assembling both hydrophilic groups are placed in the water. The solubilizing lipophilic material is capable for hydrophobic core and between the hydrophobic core and external aqueous environment that is allocated for a hydrophilic shell. From immune system, hydrophilic shells are prevented and raise the longevity of the drug into the blood. These micelles are 20-100nm in size and low polydispersity index and it also contains lower critical micellar concentration (CMC) and higher stability. Poly ethylene oxide, poly ethylene glycol consist of the hydrophilic shell (Sachan and Gupta, 2015; Yadav *et al.*, 2011).

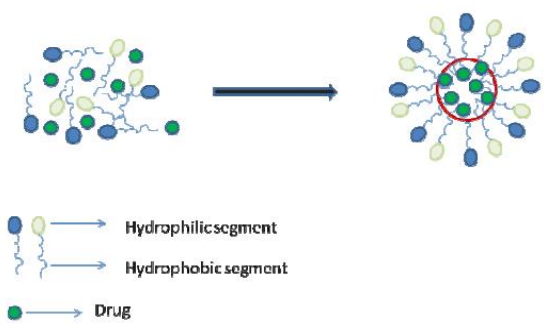

Figure 1: Polymeric Micelle with Drug

Metallic Nanoparticles

Iron oxide nanoparticles (15-60 nm) are metallic particles that consist of super paramagnetic agents coated with phospholipids, dextran or other compounds which inhibits aggregation and increase the stability and used as an active and passive targeting agents. Nano-sized metals are described by metal nanoparticles with the dimension (length, width, and thickness) range between 1-100nm. For preparing metallic nanoparticles, consists of various liquid phase methods such as sol-gel, chemical reduction and reversed micelle. With spherical shaped and size are

continuously produced the Nobel metal nanoparticles by using chemical reduction methods.

Due to characteristic features, metal nanoparticles are widely used and these features such as large surface enhance provides specific electronic structure between molecular and metallic states and process a large number of low coordination sites. It can be used in gene and radionuclide delivery, therapeutic drug, radio frequency method for the catabolism of tumors through hyperthermia, magnetic separation of labeled cells and other biological entities and contrast enhancement agents for magnetic resonance imaging (Chakraborty, Shivakumar and Ramachadndran, 2016; Sachan and Gupta, 2015).

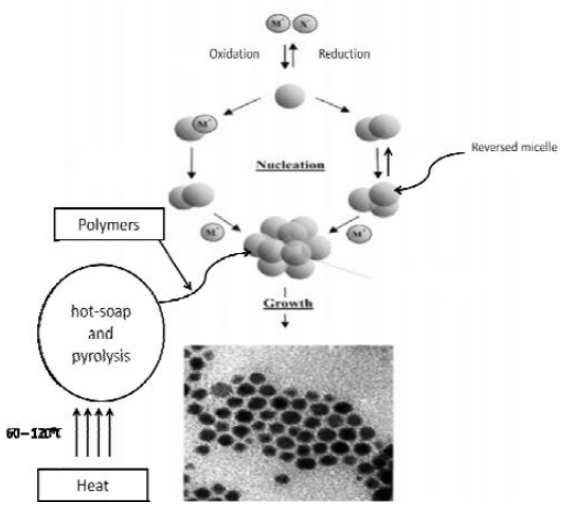

Figure 2: Preparation of Metallic Nanoparticles

Solid-Liquid Nanoparticles (SLN)

Solid-liquid nanoparticles are developed in the early 1990s that are the colloidal carrier systems which combine the advantages of other colloidal systems (such as liposomes, emulsions, and polymeric nanoparticles) for drug delivery but it minimizing or avoiding some their drawbacks. SLNs are produced on a large scale that has higher physicochemical stability and gives protection against degradation of labile drugs. It contains the particle size 50-1000 nm and includes biodegradable physiological lipids and stabilizers. At room temperature, SLNs are based on solid lipids that are melting emulsified nanoparticles. Mitoxantrone is prepared by using the SLN for breast cancer and its lymph nodes metastases. By high-pressure homogenization, tetracaine, etomidate, and prednisolone were also integrated of aqueous surfactant solutions. 100% burst drug which was endorsed to improve in the shell of particles contained in the tetracaine and etomidate SLN that release in a minute but prednisolone SLN shoed the reverse result of both drug (Sachan and Gupta, 2015; Yadav *et.al*, 2011).

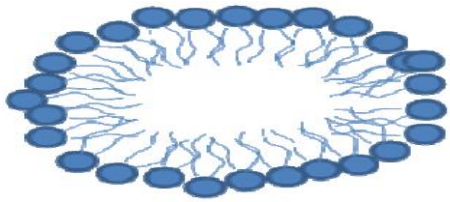

Figure 3: Solid-Liquid Nanoparticles (SLNs)

Magnetic Nanoparticles

With the number of different compositions and phases, magnetic nanoparticles have been synthesized that includes pure metals like copper, nickel and iron, metal alloys such as CoPt, FePt. The magnetic particle size of approximately 3 nm by using magnetic nanoparticles that can be obtained. Combustion synthesis, microemulsion, colloidal method, sonochemistry, thermal decomposition, solvothermal, coprecipitation and hydrothermal method are various methods that have been used in magnetic nanoparticles. In bio separation, magnetic nanoparticles have some key applications where the conjugated of target biomolecules and with specific receptors, magnetic nanoparticles are functionalized, forms complexes and by applied magnetic field can be easily attracted and extracted from the pristine mixture. For bioseparation, it provides the convenient and time-saving approach as compared to the conventional method such as filtration and centrifugation. This technology can also be used in magnetic resonance imaging, biosensing, and hyperthermia and drug delivery (Chakraborty, Shivakumar and Ramachandran, 2016).

Review of Literature

Joshi *et al.* 2004, concluded the botanical materials into medicines are converted by using the technology of herbal drug where the importance of standardization and quality control with the proper integration of techniques and knowledge. To standardize the botanical preparation by using the chromatographic techniques and marker compounds that has limitations because of their chemical complexity and variable sources. For authentication of plant species, widely used DNA techniques have been used that have medical importance. For improvement of curing the disease, development of new pharmacognosy with the development and discovery of new aspects of the drug.

Tilburt and Kaptchuk 2008, in traditional herbal medicine research, increasing the investment of Governments, international agencies, and corporations. For clinical to international traditional

herbal medicine research, applying the concepts in a comprehensive ethical framework. Scientific validity, social value, and favorable risk-benefit ratio are three key in which specific difficult questions arise for international herbal medicine research. In determining the concepts of scientific validity, social value and favorable risk-benefit ratio are significant challenges that across international research collaborations. In international herbal medicine, have ethical challenges that collaborative partnership including democratic deliberation which can and should be resolved.

Oyetayo 2008, in the last one decade in Nigeria, increasing the use of herbal remedies which would lead to the production of herbal products with bogus claims. The curing of microbial diseases by using the microbial quality and antibacterial properties with the efficacy of two Nigerian herbal remedies. To discover the herbal remedies that to be contaminated with microorganisms such as Bacillus coagulans, Basidiobotrytis species, Articulospora inflata, Bacillus subtilis, Bacillus cereus, Varicosporium species and Oedocephalum species. Killing rate disclose by analysis antibacterial that the herbal remedies had a bacteriostatic and not bacteriocidal effect.

Osemene, Ilori and Elujoba 2012, in this study, due to myriads, pharmaceutical research and development in herbal medicine are not fully developed in Nigeria. By applying the appropriate strategies, improvement of research and development process that can be highlighted by the respondents.

Khan *et al.* 2012, dictated that lack of complete evaluation have the most important challenges that are faced by herbal formulations and to ensure the quantity and quality of the herbal product, necessary the evaluation. Various parameters were tested for the evaluation of the capsule that containing the poly herbal crude drug. For finished products (hard gelatin capsule), using the formulation parameters and parameters that include disintegration time, uniformity of weighing and other quality control test were performed. For marker compounds, individual drugs, and finished product, using the HPTLC and DSC.

Pandey and Pandey 2014, stated that without the attachment of a specific ligand, nanotechnology has the property of self-targeting in the sense and due to their distinctively small size, it can be used for targeting at the infected pathological areas. Targeted drug delivery nanoparticles that is the latest achievement of nanotechnology used for the treatment of chronic disease like cancer. For bioavailability, using the application of nanotechnology methods to the improvement of herbal drugs by analyzing the relationship between nanotechnology and biological medicine. The development of non-herbal drugs with the application of nanotechnology of randomization of herbal drugs that possess high bioavailability which will open the new era for the discovery of herbal drug.

Conclusion

Herbal drugs have been more used to treat to all disease that has several problems such as poor bioavailability, instability, solubility, low oral absorption and unpredictable toxicity of herbal medicine. In worldwide, different kinds of herbal medicines are traded in a market that is derived from Indian herbs, Western herbs, Chinese herbs and Arabic herbs. In drug delivery system, development of herbal remedies in a number of institutes that have been carried out at basic and clinical trial levels. For cancer drug delivery, the concept of herbal nanoparticles may also be fascinating.

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