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NANO HERBAL MEDICINES: A REVIEW

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ABSTRACT

Plants and herbs have been used since long for curative/ healing purposes of human ailments. According to the World Health Organization, 80% of people in developing countries depend on traditional medicinal practices to meet and/or supplement their basic health needs due to the enormous diversity of structures of medicinal plants, their chemical composition, popular uses and fewer side effects. Herbal medicines have been widely adaptable since ancient time, especially in India because of their better therapeutic value for various diseases (like curcumin, periwinkle, reseveratol, quercetin etc.) with lesser side effects as compare to conventional medicines along with their easy metabolization into the body. Nanotechnology is a novel approach for phytopharmaceuticals to deliver the components in a sustained manner in the form of nano sized novel drug delivery carriers (like nanopartices, liposomes, dendrimers, ethosomes, nanoemulsion, micelles, micro emulsions, quantum dots etc.) which is considerable importance to improves bioavailability, patient compliance and other constrains of herbal medicines by bypassing all the barriers like deterioration of drug due to acidic pH, liver metabolism, toxic effects etc.

KEYWORDS: Herbal medicine, Nanotechnology, Nano sized novel drug delivery system

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INTRODUCTION

The future of medicine is rooted in the past. In the past, almost all the medicines were from the plants and the plant being man's only chemist for ages [1]. Plants and herbs have been used since long for curative/ healing purposes of human ailments in different cultures like China, Egypt, Africa, America and India in the form of crude extracts prepared in different solvent systems [2, 3].

According to the World Health Organization, 80% of people in developing countries depend on traditional medicinal practices to meet and/or supplement their basic health needs due to the enormous diversity of structures of medicinal plants, their chemical composition, popular uses and fewer side effects. Currently, despite marketing and encouragement from the pharmaceutical industry during the development of allopathic medicines, a large segment of the population in many countries continues to utilize complementary practices for their health care derived from medicinal plants [18].

There are lots of drugs that have their vast side effects to the body. For instance, taxol has about all kinds of side effects such as neurotoxicity, nephrotoxicity, allergic, cardiotoxicity [28]. There is impressive success with herbal remedies like curcumin, periwinkle etc in cancer. Various new and lethal diseases such as cancers, cardiovascular disease, diabetes, rheumatism and AIDS, are difficult to treat and bring the challenges for the scientists. These types of diseases require innovative effectual drugs and efficient delivery systems delivering the drugs [19].

Advantages of Herbal Drugs over Conventional Allopathic Drugs [5, 21, 22 & 23]

The use of herbal remedies over conventional drugs is more advantageous because of:

- ✓ Insufficient availability of costly allopathic drugs,
- ✓ Severe side effects and multi drug resistance problem in conventional drugs
- ✓ Cost effective.
- ✓ Easy metabolization of herbal drugs in the body.
- ✓ Having capability of treating various disease conditions with low side effects.

Constrains of Conventional Herbal Drug Formulations

Though herbal medicines are considered as dependable and affordable therapeutics, but the effectiveness of many species of herbal medicines relies on the release of biologically active constituents of the plants and herbs [3, 4]. The majority of the active components of plants and herbs are associated with some problems *viz*. rapid release of the herbal drug, unknown toxicity, low solubility, poor bioavailability and low absorption of drug to the site of action, deterioration and metabolization of many herbal constituents in the acidic pH of stomach and liver respectively resulting in the low therapeutic responses of the conventional herbal formulations [3, 5, 15, 19, 21, 25].

Due to these obstacles their standardization and quality control were also not an easy task [3, 16, 17]. To overcome these obstacles of herbal medicines; modern phytopharmaceuticals research solves the scientific needs for herbal medicines as in modern medicine, which gives way for developing novel phytoformulations as nanosized herbal formulations (viz., liposomes, polymeric nano-particles, nano-emulsion, nanospheres, solid lipid nanoparticles) with the use of nanotechnology which might be capable to strengthen the improving bioactivity action of herbal medicines and also eliminate the inadequacies of conventional herbal formulations [4, 5, 6].

Nano Sized Novel Drug Delivery Systems for Herbal Remedies

From past two decades, nanotechnology is exploited for efficacious drug delivery and tissue-specific targeting of drug [6, 16]. Nanocarriers applying to herbal remedies will carry optimum amount of the drug to their site of action bypassing all the barriers such as acidic pH of stomach, liver metabolism and increase the prolonged circulation of the drug into the blood due to their small size [7]. Improved drug delivery techniques help in minimizing toxic effects and achieving enhanced effectiveness which is beneficial for the patients [5]. Most of the research is intended for treatment against the cancer disease, a number of applications of nanomedicine to other ailments is also being worked on (like infective endocardisis, coronary artery diseases etc.) [20]. **Figure 1** shows the clinical purposes and the therapeutic potential of most specific and well-known herbal remedies [19].

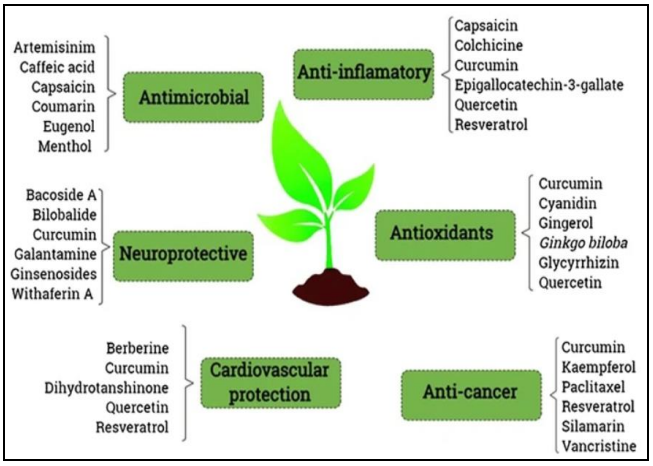

Figure 1: Some Natural Compounds Extracted from Herbal Plants Used in Nanomedicine [20]

Herbal remedies were selected as feasible drug candidate for delivery through a nano delivery system because of the following properties:

- ✓ Effective chloroform, petrol, acetone, and methanolic extracts are available which may not be suitable for delivery as such.
- ✓ These are the bulk drugs, so dose reduction is intended.
- ✓ Prevention of deterioration of herbal compounds under acidic conditions.
- ✓ Patient non-compliance due to large doses and less effectiveness with the available formulations.
- ✓ Currently marketed formulations lack target specificity for various chronic diseases.
- ✓ Some other side effects are associated with currently modern formulations. Various modern medicines are causing side effects and not able to effectively treat many of the common health conditions with increased incidences of drug resistance [6].

Sources of Nanoparticles from Herbal Plants

Nanoparticles of various size and shape have been synthesized from different parts of plant like stem, root, leaves, fruit, seed etc.

Advantages of Nano – sized Herbal Drugs [5, 6, 7, 10, 23, 25]

Nano–sized Herbal remedies were selected as feasible drug candidate for delivery through a because of the following properties:

1. Nanosized delivery appears to be able for site-specific targeting of herbal medicines to enhance their selectivity, solubility, delivery, safety, and effectiveness.
2. Delivering the drug in small particle size enhances the entire surface area of the drugs therefore allocating quicker dissolution in the blood.
3. Nano - sized herbal drug delivery systems are designed to achieve a continuous delivery of drugs due to controlled therapeutic blood levels instead of oscillating blood levels.
4. Shows EPR (enhanced permeation and retention) effect.
5. Novel nanotechnology has shown improved patient compliance due to reduced frequency of dosing and the reduction of the total dose of drug administered.
6. They appear to be able to deliver high concentrations of drugs to disease sites because of their unique size and high loading capacities.
7. Exhibits passive targeting to the disease site of action without the addition of any particular ligand moiety.
8. Incorporation of nano sized novel drug delivery technology to herbal or plant actives minimizes the drug degradation or pre-systemic metabolism and serious side effects.
9. Increase entrapment efficiency and skin penetration by improving the precutaneous permeation.
10. Improve the product stability.

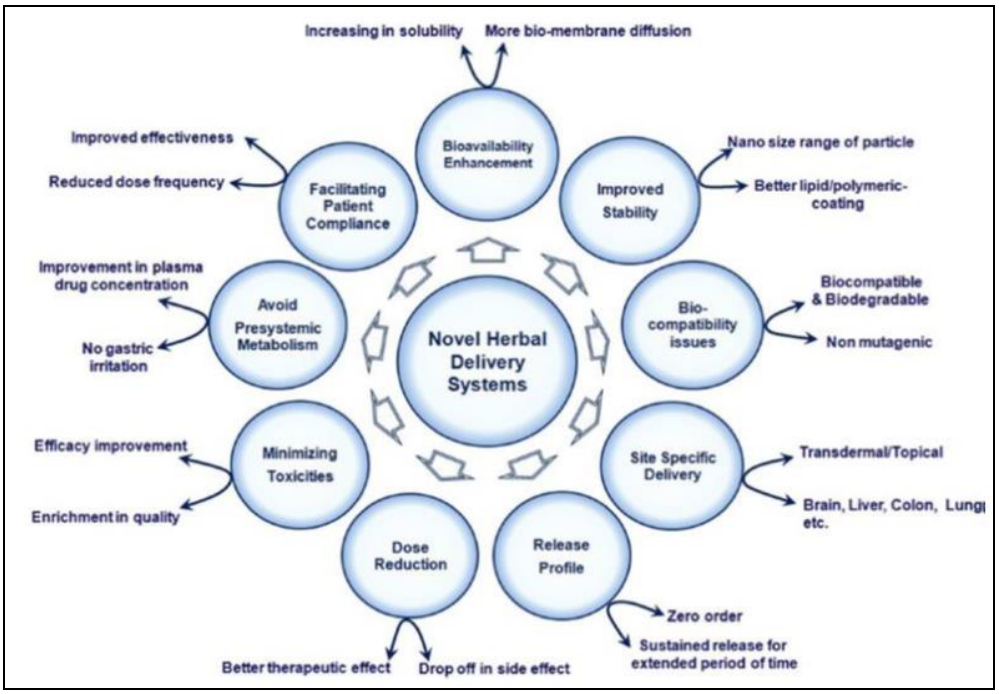

Figure 2: Salient Features of Novel Herbal Drug Delivery System

Prospective Approach of Nano-Sized Novel Drug Delivery Carriers in Herbal Formulations [4, 5, 6, 28, 29, 30]

- ✓ Nanoparticles (Polymeric nanoparticles, Solid lipid nanoparticles, Magnetic nanoparticles, Metal and inorganic nanoparticles)
- ✓ Colloidal nano-liposomes
- ✓ Polymeric micelles
- ✓ Phospholipids micelles
- ✓ Niosomes
- ✓ Phytosomes
- ✓ Microsphres
- ✓ Emulsions
- ✓ Ethosomes
- ✓ Transferosomes
- ✓ Quantum dots
- ✓ Dendrimers

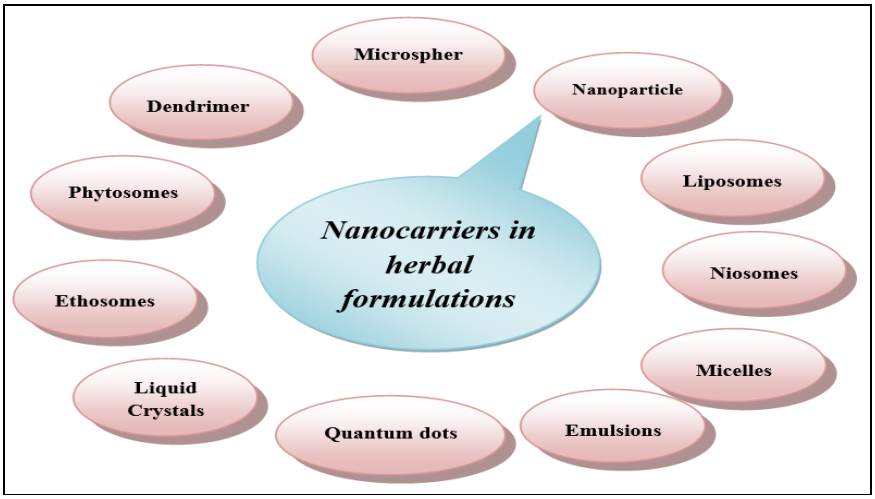

Figure 3: Novel Drug Delivery Carriers in Herbal Formulations [4, 5, 6, 29, 30]

Table 1: Recent Developments of Plant Actives and Extracts

Type of nano preparation		Active Phytoconstituents	Clinical Significance	Pharmacological activity	Method of preparation
Nanoparticles	Berberine loaded Nanoparticles	Berberine	Sustained drug release	Anticancer	Ionic gelation Method[10]
	Curcuminoids solid lipid nanoparticles	Curcuminoids	Improve the bioavailability	Anticancer and antioxidant	Micro-emulsion technique [8]
	Glycyrrhizic acid-loaded nanoparticles	Glycyrrhizic acid	Improve the bioavailability	Anti-inflammatory, Antihypertensive	Rotary-evaporated Film ultrasonication [7]
	Artemisinin Nanocapsules	Artemisinin	Sustained drug release	Anticancer	Self-assembly [7]
	Triptolideloaded Solid lipid Nanoparticles	Triptolide	Decreasing the toxicity	Anti-inflammatory	Emulsification ultrasound [10]
	Cuscuta Chinesis nanoparticles	Ethanolic extract	Improve water solubility	Anticancer, immune stimulatory and antihepatotoxic	Emulsification[10]
Liposomes	Liposomes encapsulated silymarin	Silymarin	Improve bioavailability	Hepatoprotective	Reverse evaporation technique [10]
	Paclitaxel liposome	Paclitaxel	High entrapment efficiency and pH sensitive	Anticancer	Thin film hydration method [5]
	Curcumin liposome	Curcumin	Long circulating and high entrapment efficiency	Anticancer	Ethanol injection method [9]
	Quercetin liposomes	Quercetin	Reduced dose and enhanced penetration in BBB	Antioxidant and anticancer	Reverse evaporation technique [5]
	Usnea acid liposomes	Usnea acid	Increased solubility and localization	Antimcrobial	Hydration of a thin lipid film with sonication [10]
	Vincristine liposomes	Vincristine Bisindole	Overcome Neurotoxicity problems and other side effects	Broad spectrum anticancer activity against lung and prostate cancer	sonication method [10]
	Colchicine liposomes	Colchicine	Enhance skin accumulation and prolong release	Antigout	Rotary evaporation sonication method [5]
	Capsaicin Liposome	Capsaicin	Increase in skin permeation as well as prolongation of duration of action	Analgesic	Reverse evaporation technique [11]
	Nux vomica Liposome	Alkaloid	High encapsulation efficiency improved stability in blood, and relative low price	Anti-tumor, Analgesic	liposomes composed of hydrogenated soybean phosphatidylcholine (HSPC) and soybean

			of phospholipids of the novel liposomes		phosphatidylcholine (SPC) containing the total alkaloids from seed of Strychnos nux-vomica[10]
	Garlicin Liposome	Flavanoid And diallylsulfide and trisulfide	Increase efficiency	Anti-oxidant	Revers-phase evaporation Method[10]
	Green tea extract noisome				
	Withania somnifera niosome	Withanolide	Improve penetration	Antioxidant	Solvent injection method [11]
microsphere	Zedoary oil Microsphere	Zedoary oil	Sustained release and Higher bioavailability	Hepatoprotective	Quasi-emulsion–solvent diffusion method[14]
	Quercetin Microspheres	Quercetin	Significantly decreases the dose size	Anticancer	Solvent Evaporation[14]
	Cynara scolymus microspheres	Cynara scolymus extract	Controlled release of neutraceuticals	Nutritional Supplement	Spray-drying[14]
	Rutin-alginate-chitosan microcapsules	Rutin	Sustained release action	Cardiovascular and cerebrovascular diseases	Complex-coacervation method[14]
emulsion	Docetaxel submicron emulsion	Docetaxel	Improve residence time	Anticancer	High pressure Homogenization Method [9]
	Berberine nanoemulsion	Berberine	Improve residence time and absorption	Anticancer	Drawing ternary phase diagram[9]
	Silybin nanoemulsion	Silybin	Sustained release formulation	Hepatoprotective	Emulsification method[9]
	Quercetin Microemulsion	Quercetin	epidermis	Antioxidant	High speed Homogenization method [9]
transferosome	Capsaicin Transferosomes	Capsaicin	Increase skin penetration	Analgesic [5]	High shear dispersion technique
	Colchicine Transferosomes	Colchicine	Increase skin penetration	Antigout [5]	Hand shaking method
	Vincristine Transferosomes	Vincristine	Increase entrapment efficiency	Anticancer [5]	By using lecithin and sodium deoxycholate in 70/20 ratio
Phytosomes	Ginkgo biloba Phytosomes	Flavonoids	Flavonoids of GBP stabilize the ROS	Cardioprotective, antioxidant activity	Phospholipids complexation [9]
	Subcutaneous Silybin Phytosome	Flavonoids	Absorption of silybin phytosome from silybin is approximately seven times greater	Hepatoprotective , antioxidant	Silybin-phospholipid complexation [9]
	Ginseng Phytosome	Ginsenosides	Increase absorption	Nutraceutical, Immunomodulator	Phospholipids Complexation [9]
	Curcumin Phytosomes	Curcumin	Increase bioavailability	Antioxidant, Anticancer	Curcumin–phospholipid Complexation [9]
Ethosomes	glycyrrhizinate ethosome	Glycrrhizic acid	Increases of in Vitro percutaneous permeation and significantly enhanced inflammatory activity	Anti-inflammatory	Antisolvent dispersion method [27]
	Triptolid ethosome	Diterpene triepoxide	high entrapment efficiency, good percutaneous permeability	Anti-inflammatory	Combining filmingre hydration method ultrasonic method [28]
	Podophyllotoxin ethosomes	Etoposide and Teniposide	Higher entrapment efficiency and enhance its therapeutic effect	Purgative, antirheumatic, antiviral and antitumor	Solvent dispersion method [29]
	Sesbania Ethosome	Leucocyanidin and cyanidin	Enhance Trans-dermal permeation	Anti-microbial	Solvent dispersion method [10]

CONCLUSION AND FUTURE PROSPECTS

This review gives information about the conventional methods of drug delivery and currently available some medicines have certain limitations in the progress of efficacious herbal drug development. Nano – sized Novel drug delivery system in herbals offer prospective approaches in this area in terms of nano formulation developed for herbal remedies. Nanosized novel drug delivery systems for herbal drugs will significantly enhance the biological activity of the herbal remedies, improved solubility, bioavailability, reduced toxicity, controlled release delivery, effectiveness with dose reduction.

The application of modern nanotechnology collaboration with these remedies will serve as a very useful tool in terms of *in-vivo* and *in-vitro* targeted drug delivery, sustained delivery by improving the pharmacokinetic profile of herbal drugs for future. However, significant challenges in the development of novel herbal preparations include the trial of novel methods to control the incompatibility of nanocarrier material. In spite of this, there is also a need for careful and elaborate toxicological studies of various multifunctional nano deliveries system to fulfil several biological and therapeutic responses.

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CONFLICT OF INTEREST

None

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