NOVEL APPROACH: HERBAL REMEDIES AND NATURAL PRODUCTS IN PHARMACEUTICAL SCIENCE AS NANO DRUG DELIVERY SYSTEMS

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Abstract

Herbal remedies and natural products are being used for an ancient time to cure the diseases. Unlike the existing allopathic system, the herbal remedies have hundreds and thousands of constituents that all work together against the diseases. Natural products produced by the organisms such as fungi, bacteria, animals and plants act as biologically active agents. Mostly, the conventional pharmaceuticals or pharmacognostical products in the market are rooted from natural products and their derivatives with herbal products playing pivotal role. All over the world, the research on these herbal remedies has been carried out in the different fields for instance pharmaceutical chemistry, pharmacognosy, pharmacology and clinical therapeutics. Incorporation of these herbal extracts into novel formulation systems in order to have added advantages and to overcome their bulk dosing and less absorption which is the major problem being faced, enticing the attention of major pharmaceutical corporations. ‘Nanotechnology’ is the new emerging technology in the drug discovery and it has the property of self targeting in the sense that without the attachment of a specific ligand, these can be used for targeting, due to their distinctively small size, at the infected pathological areas. Some of such formulations are already present in the market and many
more are expected to come by 2020 after their success in ongoing clinical trials. In this review, this new approach is escalating the interest of number of scientists to improve and to accelerate the joint drug discovery and development of novel nano delivery systems for herbal extracts.

**Keywords:** Natural products, Herbal remedies, Nanotechnology and Drug Delivery System, Pharmaceutical Science.

**Introduction**

Natural products (NPs) that are isolated from the plants are known as ‘herbal remedies’ and these are the traditional medicinal systems that are being followed for the last few decades. Practically, herbal remedies have the date back long history to the existence of the human civilization. New medicines are being developed and will be developed gradually by the scientists through the different ways. But always ancient or herbal remedies and NPs have been the roots of these medicines and will be the main source of the medicines and therapeutics in the future. In ancient time before the arrival of high throughput screening concerned to drug discovery; 90-95% drug materials were NPs. Information on source of new drugs nearby 1981-2007 specify that approximately half of the drugs are based on the NPs. It has been proved that NPs are more voluntarily absorbed than synthetic drugs. NPs drug discovery will be more sanctified specialized and occupy prudent use of ancient and modern therapeutic expertise in a harmonizing behavior so that utmost payback can be built up to the patients and the community. The pharmaceutical companies were laid when techniques were developed to produce synthetic replacement for many of the medicines that had been derived from the forests. Now the pharmaceutical efforts are cracking to developing the new pioneering or indigenous therapies and development the uniqueness of plants based drugs (herbal remedies). NPs have extensively predictable for their wide-ranging structural diversity as well as their spacious series of pharmacological and pharmacognostical activities in the pharmaceutical organizations. Several of the most significant NPs and their derived active components present in the market today’s pharmaceuticals industries are paclitaxol, doxorubicin (anti-cancer), lovastatin (anticholesterolemic), erythromycin, streptomycin, rafamycin (antibiotic), cyclosporine-A and tacrolimus (immunosuppressive), and amphotericin-B (fungicidal). Actually, in
the context of conventional pharmaceuticals, they have their existence from herbal remedies. Many drugs had been extracted from the plants as their active components for treating various diseases such as Asprin, Salbutamol, Digoxin, Quinine, Morphin, Atropine, Colchicine, Bromelain etc. [6] Morphine is isolated as a first drug by Sertturner from the plant Opium popy (Papaver somniferum) as a painkiller. Quinine extracted from the cinchona tree (Cinchona officinalis) that is used to treat malaria and aspirin isolated from willow bark for treatment of fever. [7] Most of the plants and formulations have explored the potential to cure cancer and inflammation such as Curcumin, Triphala, Pomegranate, Kalonji, Sariva etc. [8]

The well-organized pharmaceutical corporations have produced evidence supported NPs and herbal remedies that are being extensively utilized in the assorted organizations, accordingly the pharmacopoeial guiding principles. [9, 10] These have reasonably well thought-out records, and additional far-reaching accounts that can be analyzed using various modern scientific methods to segregate and sanitize the products and in analytical systems to establish structures, for their further draw on in the present pharmaceuticals. More recently, the scientists have their interest in analytically and systematically incisive of the NPs and herbal remedies into novel drug delivery systems for being the key stride of many diseases such solid tumors, diabetes, asthma, inflammation, brain disorder and so on. [11]

A drug delivery system for a therapeutic negotiator is glowing sustained for fragile equilibrium between its therapeutic efficacy and unfavorable side effects as well as toxicity during the administration in a diseased state. These sorts of drug delivery systems can be attained by controlled drug delivery systems that transport the drugs at the spot of action in the preferred quantity. [12] The bioavailability of the drug is 100% when the drug is administered intravenously. Hence, for enhancing the bioavailability of the drugs, there should be novel drug delivery systems and those can protect the drug from the other distractions of the body such acidic pH, reticuloendothelial system, metabolic process. [13] This type of new systems such as nano carriers are unique come up to the drug delivery systems that speak to the drawbacks of the conventional drug delivery systems. These drawbacks compelled to the scientists to propose nano carriers as a novel drug delivery approaches that assert to pioneer essential alteration to the systems drugs put forth their proceedings. Due to the small size and broad surface
area ‘Nanotechnology’ is a novel drug strategy in drug discovery. The several scientists are being used of appropriate molecular weight polymers and lipids in the manufacturing of the nano carriers for novel drug delivery system. Hence, use of herbal remedies in a novel drug delivery system will enhance the improvement in the use of herbal remedies that will come forth to treat the various chronological diseases.

**NPs for drugs development**

Natural products (NPs) engage in recreation the imperative part in the drug discovery progression for all miniature and chronic disease areas from beginning to end this century afar. There are some drugs from NPs that have been discovered and in development recently such as salinosporamide, dolastain, curacin, turbomycin, vancomycin, cryptophicin, platensimycin, stichloroside, platencin, theopalauamide. [14] NPs are characteristically derived secondary metabolites, isolated from organisms (such as bacteria, fungi, protozoans, animals and plants) in response to peripheral stimuli i.e. nutritional alters, infection, inflammation and other chronic diseases. [15] Something like 35% of the most-selling drugs present in the market is the NPs or their derivatives. [15] In pre-developed civilization and industrialized society, plants consequent NPs were utilized with indigenous populations as therapies intended for numerous diseases seriating from infection to tumors. The medicinal herbal remedies are several of oldest medicines and their growing utilization in modern existence is evidence of a public attention in having alternatives to conventional medicine. NPs have some intricacies versus modern drugs. NPs have a major disadvantage that they take long time to progress from NPs assay to knowing its structures in the drug discovery development led by the progress of programmed high throughput screening versus synthetic drugs for the structure is already known. [16] Medicinal chemists always say that NPs are ‘dreadful ducklings’ due to their unpleasant texture such as structural complexity, multiple hydroxyl moieties, ketones and chiral centers. In the recent years, to overcome these problems, a new stage of the pharmaceutical has been emerged as a combinatorial chemistry making promise of new intensity of chemical diversities. Combinatorial chemistry has achieved significant accomplishment in specific drug discovery strategies such as HIV protease inhibitors. Combinatorial chemistry and NPs can show vital roles in an extremely competitive drug discovery chemistry curriculum. Moreover,
combinatorial chemistry strategies have improved traditional medicinal in the biochemical and physiological sciences. [17] Plants extracts that are the part of NPs have found the biologically active through various testing and identifications in today’s high-throughput screening environment. Herbal medicines persist to be a foremost market in U.S. and other country pharmacies and make up a multi-billion dollar industry.

**Herbal remedies**

Overall, traditional medicines are sum of the awareness, and practice based on hypothesis, beliefs, and experiences imaginative to various cultures. They used in the upholding of good health as well as in the diagnosis, and progress or curing of physical and mental disease. Traditional medicines include herbal, Ayurveda, Siddha medicine, Unani, ancient Iranian medicine, Islamic medicine, traditional Chinese medicine, acupuncture, Muti, Ifá, and other medical knowledge and practices all over the globe. [18] These medicines are primary health care requirement of up to 80% of the population of Asian and African countries. These are often called complementary and alternative medicine when implemented of its traditional culture outside. Actually improper utilization of traditional medicines or practices can show dangerous effects. Hence more research is required to ascertain the efficacy and safety of the medicinal plants used in traditional system as suggested by WHO. [19] Ethnomedicine, ethnobotany, and medical anthropology are hub obedience for study of traditional medicinal system. Herbal medicines include herbal materials, preparations and products that have as active ingredients, parts of plants or other plant materials or combinations. Their use is well recognized and extensively accredited to be safe and effective, and accepted by national authorities.

Herbal drugs constitute found in major contribution to all the officially renowned systems such as Ayurveda, Yoga, Unani, Siddha, Homeopathy and Naturopathy. Herbal remedies are medicinal plants that contain as active ingredients plant materials such as juices, gums, fatty oils, essential oils and many other substances of these. They also include crude plant material such as leaves, fruit, seed, bark, root, stem, or other parts of the plants entirely or fragmented by using different local methods of different countries like extraction, purification, fractionation etc. [20] These preparations made by steeping or heating herbal materials in some beverages such as alcohol, honey and
others. People use herbal remedies regularly, as spices, home-remedies, health foods as well as self-medication. The many non-allopathic practitioners have trained in the medical colleges of their particular coordination of health and registered with the official councils which supervise professionalism. These systems lead to the rational and organized formation of pathogenesis and diagnosis, which provide also as determinant for therapy.

There are many herbal remedies have been utilized globally, for instance, Indian Aloe \[21\] is widely used in India for dermato-cosmetic, medicinal and nutraceutical purposes along with the potential as antiaging are still untouched. Adhatoda vasica \[22, 23\] has been extensively recognized for cough and its significance in bleeding disorders and tuberculosis is available. Actually, all foods work as functional foods rather than supplements. Many medicinal herbal remedies and dietary elements having practical aspects are spices such as onion, garlic, mustard, red chilli, turmeric, clove, cinnamon, saffron, curry leaf, fenugreek and ginger. \[24\] Many medicinal herbs possess antitumor potential such as Bixa orellana and others like amla, wheat grass, soybean and Garcinia cambogia etc. \[25\]

**How do herbal remedies work?**

Many people have realized that herbal remedy consumers have well nutrias body for ages. Herbal remedies are produced from renewable sources of raw materials by ecofriendly practices and will convey economic opulence to the sufficient emergent of these raw materials. Herbalist’s attention is always towards to stumble on the underlying reason of a disease rather than treat the individual symptoms. Pharmaceutical cure the individual symptoms quite than dealing with the emphasize health issue itself. Herbal remedies are extracted from plants parts such as leaves, petals and roots and are a composite mixture of a number of different active ingredients. The body is organized by individual parts that necessitate working altogether. Treating a patient whole body system must work. The idea of herbal ’synergy’ elucidates that the complex mixture of hundreds or thousands of constituents of a plant extract all work together to treat a disease. \[26\] This is one of the several reasons that herbal remedies are preferential over manufactured ones.

An antiasthma drug ephedrine was first isolated from the plant Ephedra that was used to treat chest complaints in traditional medicines. Ephedrine has the side effect of increasing the blood pressure. Herbalists spotted that in the
complex mixture of the numerous active ingredients in the plant, there is one of its constituent that lowers blood pressure itself.

**Herbal in pharmaceutical science**

Herbal medicines are a paradigm of the precision that is furnished us by nature to stay alive. Pharmaceuticals are an instance of humans wish for reproduce and develop ahead what nature has offered us. Pharmaceuticals have a tendency to alter the physiology though herbal remedies effort with the body. Estimation by the global market survey, it is found that traditional medicine market is scaling up at the rate of 7 – 15% cent annually.\textsuperscript{[27]} The worldwide herbal market is worth US 60 billion dollars cause of the affluent and varied herbal sources in counties.\textsuperscript{[4]} Plants are attracting the attention of the scientists as significant resources of new drugs to drawbacks of the multi drug resistance, toxic effects of modern drugs and chronic diseases that have no curable drugs. 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.\textsuperscript{[28]} There is impressive success with herbal remedies like curcumin, periwinkle etc in cancer. Hence researches on herbal remedies have carried out in the various fields like pharmacognosy, chemistry, pharmacology and clinical therapeutics. 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. \textbf{[Table 1]} shows the clinical purposes and the therapeutic potential of most specific and well known herbal remedies with scientific name.

\textbf{Table 1: Some herbal remedies with scientific name with their therapeutic action.}

<table>
<thead>
<tr>
<th>Common name</th>
<th>Botanical name</th>
<th>Main therapeutic potential</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aloe</td>
<td>Aloe vera</td>
<td>Antidiabetic</td>
<td>[29]</td>
</tr>
<tr>
<td>Amlaki</td>
<td>Phyllanthus emblica</td>
<td>Rasayna</td>
<td>[30]</td>
</tr>
<tr>
<td>Aswagandha</td>
<td>Withania somnifera</td>
<td>Immuomodulatry</td>
<td>[31]</td>
</tr>
<tr>
<td>Bilva</td>
<td>Aegle mermelos</td>
<td>Antidiarrhoeal</td>
<td>[32]</td>
</tr>
<tr>
<td><strong>Dadima</strong></td>
<td><em>Punica granatum</em></td>
<td>Antidiarrhoeal</td>
<td>[33]</td>
</tr>
<tr>
<td><strong>Eranda</strong></td>
<td><em>Ricinus communis</em></td>
<td>Heptoprotective</td>
<td>[34]</td>
</tr>
<tr>
<td><strong>Haldi</strong></td>
<td><em>Curcuma longa</em></td>
<td>Antimicrobial</td>
<td>[35]</td>
</tr>
<tr>
<td><strong>Haritaki</strong></td>
<td><em>Terminalia chebula</em></td>
<td>Hypolipidemic</td>
<td>[36]</td>
</tr>
<tr>
<td><strong>Indian Kino Tree</strong></td>
<td><em>Pterocarpus marsupium</em></td>
<td>Antiinflammatory</td>
<td>[37]</td>
</tr>
<tr>
<td><strong>Manjishtha</strong></td>
<td><em>Rubia cordifolia</em></td>
<td>Antioxidant</td>
<td>[38]</td>
</tr>
<tr>
<td><strong>Malabar Nut Tree</strong></td>
<td><em>Adhatoda vasica</em></td>
<td>Antituberculosis, Haemostatic</td>
<td>[39, 40]</td>
</tr>
<tr>
<td><strong>Shunth</strong></td>
<td><em>Zingiber officinale</em></td>
<td>Antiemetic</td>
<td>[41]</td>
</tr>
<tr>
<td><strong>Tulasi</strong></td>
<td><em>Ocimum sanctum</em></td>
<td>Anticancer</td>
<td>[42, 43]</td>
</tr>
<tr>
<td><strong>Kalonji</strong></td>
<td><em>Nigella sativa</em></td>
<td>Antibacterial Antipyretic</td>
<td>[44, 45]</td>
</tr>
</tbody>
</table>

There are many successful companies in India, such as Himalaya Drug Company (HDC), Emami, Aswini, Ayur, Dabur, Cholayil Pharma, etc., that have patented their herbal and ayurvedic products in India and abroad. There is need for major efforts to assurance a steady and adequate quality of herbal remedies. Reproducible therapeutic results can get by selecting the plant material and a standardized manufacturing process and the concentration of the ingredients should be constant. Preparation of the herbal remedies should be standardized to hold the sufficient amount of the active constituents. Standardization of the drugs that is essential for drugs development start from analysis of raw materials for validation, extractive values, and chromatographic reports to production of quality materials, microscopic estimation, and heavy metal detection.

**Drug delivery system (DDS)**

Contemporary therapies treat particular diseases by making goal accurately to the affected region inside the body and carrying the drug to that site. Drug delivery system is the manner by which all that is made feasible. “DDS is the process that administers an optimum quantity of the concerned drug to the patient in the manner such that it acts suddenly at the exact ‘site of action’ after arriving there. Improvement in the drug delivery system is required to
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optimization of the pharmacological action of the drug and to overcome the toxic side effects in vivo. In recent years, competition for drug development has been highly increased in which the quality of the drugs and the time taken from assay to development are fundamental and essential factors in the success of a company, due to the demand on NPs agenda to compete with synthetic chemicals has increased to a large extent. So, how can NPs and Herbal introduce to DDS? Different scientists will find various routes, but these are the challenges. There is an answer to this question, a combination of approaches that are novel drug delivery systems can be manifested as nanoparticles drug delivery.

Nanotechnology as a novel drug delivery strategy

Drug delivery system fetched a novel drug delivery system, a novel approach to overcome the drawbacks of the traditional drug delivery systems. The treatment of the chronic diseases such as cancer using targeted drug delivery nanoparticles is the latest achievement in the pharmaceutical drug delivery field. The term ‘nanotechnology’ was derived by Greek word “nanos” that means “dwarf”. Nano device and nano strategy are one billionth of a meter or $10^{-9}$ m. Nanotechnology clumps of atoms, molecules, and molecular fragments into extremely small particles between 1 and 100 nm and puts forward to the interactions of molecular level matters and engineered materials characteristically.

In recent years there is vast advancement has been done by the scientists to modify the backdrop of the pharmaceutical industries for the predictable future. The number of the drugs in the pipeline of the pharmaceutical companies will come off patent in next few years. The nanoparticles work specifically as-

1) To deliver the drug in the small particle size that enhances the entire surface area of the drugs allocating quicker dissolution in the blood.

2) Drug delivery system is targeted in a specific manner.

3) Permeation of the drugs across epithelial and endothelial barriers.

4) To deliver the drugs at sites of action.

5) Combined therapy of the two different modalities or drugs.
6) Detection of the infected sites through the drug delivery combining with imaging modalities.

The nanoparticles have come forward as the capable approach in drug delivery systems for the well-organized delivery of drugs utilized in the treatment of various diseases such as cancer by crossing the reticuloendothelial system, enhanced permeability and retention effect and tumor-specific targeting. These novel strategies are well-organized in the specific manner that these are free in the body and acts selectively at the pharmacological sites. To formulate a novel nanoparticle drug delivery system, the following physiochemical parameters are essential i.e. temperature, pH, monomer concentration, ionic strength as well as surface charge, particle size and molecular weight. There are different types of the nanoparticles in NPs and Herbal drugs development that are going through the researches.

**Polymeric Nanoparticles**

Polymeric nanoparticles are polymeric colloidal spheres that are very small in size ($10^{-9}$ m.) and have ability to entrap the drug within the matrix or adsorb or conjugate at their surface. The release of the drug from the nanoparticles occurs through the diffusion and erosion from the matrix. Those particles that adsorb the drug on the surface show the fast release of the drug from other particles those entrap the drug. Both natural and synthetic polymers take part in the formulations. Polymers that are being used in the pattern are categorized in biodegradable and non-biodegradable polymers. Biodegradable polymers have persuaded the attention of the scientists because they degrade in the body and do not have any further toxicity. The dextran, gelatin and chitosan are naturally derived polymers and synthetic polymers poly(esters), poly(anhydrides), poly(amides) that have been broadly considered and studied.

Polymeric micelles are the point of attraction for the scientists from many years due to their controlled properties and pharmacological characteristics. They are amphiphilic, the inner core is hydrophobic and the outer shell is hydrophilic and manufactured by assembling the both hydrophobic and hydrophilic groups are placed in the water. Hydrophobic core is capable of solubilizing lipophilic materials and a hydrophilic shell allocates between the hydrophobic core and external aqueous environment [fig 1]. The hydrophilic shells prevent recognition from the
immune system and raise the longevity of the drug into the blood. Micelles are 20-100 nm in size and low polydispersity index. These have lower critical micellar concentration (CMC) and have higher stability. Generally, the hydrophilic shell consists of poly ethylene oxide, poly ethylene glycol. Taxol has been productively encapsulated up to 40% using a PEG–poly (ortho ester)–PEG block copolymer micelle.\[54\]

**Fig 1 Polymeric micelle with Drug**

**Liposomes and Lipid-Based Systems**

Liposomes are small area as bubble that has hydrophilic head and hydrophobic tail such as phospolipid. Lipids are also formulated into water in a well-organized manner, hydrophilic tails aggregate forming a core and hydrophilic head freely towards the external environment.\[55\] Hydrophilic end attracts towards the water. These clusters are called liposomes. There are three type of lipids investigated for the drug delivery system i.e. cationic, anionic and neutral. There are number of drugs with liposomal formulations that have been tested for the control release such as for the delivery of proteins that have shown the reduced side effects. There uses in cancer disease have been studied
Liposomes have some problems like interaction with body’s own lipoproteins, partial accessibility due to this the formulation becomes quite expensive at large scale.

**Solid Lipid Nanoparticles**

Solid lipid nanoparticles (SLN) have the 50-1000 nm particle size [fig 2]. SLN are particulate systems includes biodegradable physiological lipids and stabilizers. These are melting emulsified nanoparticles based on solid lipids at room temperature. SLN were prepared of Mitoxantrone for breast cancer and its lymphnodes metastatases.

Tetracaine, etomidate and prednisolone were also incorporated by high pressure homogenization of aqueous surfactant solutions. Tetracaine and Etomidate SLN have shown the 100% burst drug release in a minute that was endorsed to the drug improvement in the shell of the particles. Prednisolone-SLN showed reverse result, a long release for 5 weeks period. There are some other methods that comprise microemulsion, and precipitation.

![Fig 2 Solid lipid Nanoparticle (SLNP)](image)

**Dendrimers**

Dendrimers are spheroid or globular nanostructures of polymeric materials. They are highly branched, monodisperse nanoparticles that bind the drug at the surface or entrap within their inner cores. There is a unique property of branching around the inner space that has huge effect on physical and chemical properties [fig 3]. Preparations of these particles are either by divergent or convergent methods. The size grows linearly while the number of surface groups put in. They have very low polydispersity index and ranging dimension increment by stepwise from 1-10 nm. The performance and individual properties of dendrimers can be at variance deeply
from their linear complements. Due to very low polydispersity of Dendrimers, they contribute to their efficacy as drug delivery strategy.

To formulate the Dendrimers, the polymers are selective that have an alliance between the polymer and the drug. In a study, Dendrimers have been formulated having hydrophilic shell of poly ethylene glycol (PEG) in which Indomethacin has been loaded that show very slow release of the drug i.e. in 25 hours in the comparison of a controlled system, loaded into cellulose and release in 4 hours. \(^\text{[63]}\) Incorporated 5-Fluorouracil has been entrapped into poly (amidoamine) dendrimers additional with mPEG-500. \(^\text{[64]}\) Release was observed for PEGylated and non-PEGylated formulations by incubating together, PEGylated formulation took more time than non-PEGylated.

![Fig.3 Highly branched Dendrimer](image)

**Fig.3 Highly branched Dendrimer**

**Nanotechnology for Herbal and NPs**

Herbal medicines have been widely used all over the world since ancient times and have been documented by physicians and patients for their improved therapeutic value as they have smaller number of adverse effects as compared with modern medicines. However, phytotherapeutics needs a scientific approach to deliver the components in a sustained manner to increase patient compliance and avoid repeated administration. This can be achieved by designing novel drug delivery systems for herbal constituents. Novel drug delivery systems 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, and so on. Recently, pharmaceutical scientists have shifted their
focus to designing a drug delivery system for herbal medicines using a scientific approach. For a long time herbal medicines were not considered for development as novel formulations owing to lack of scientific justification and processing difficulties, such as standardization, extraction and identification of individual drug components in complex polyherbal systems. However, modern phytopharmaceutical research solves the scientific needs for herbal medicines as in modern medicine, which gives way for developing novel formulations such as nanoparticles, microemulsions, matrix systems, solid dispersions, liposomes, solid lipid nanoparticles, and so on. This article summarizes various drug delivery technologies for herbal actives, which are gaining more attention for better therapeutic response.

Nanomicellar system [65] nanotubes [66] and colloidal nanogels have been developed for curcumin to be used alone as well as in combination with other chemotherapeutic agents like paclitaxel.

*Cuscuta chinensis* is a commonly used traditional Chinese medicine to nourish the liver and kidney. Due to the poor water solubility of its major constituents such as flavonoids and lignans, its absorption upon oral administration could be limited. So, the nanoparticles for the same were developed. [67]

A recent experimental study of polylactic acid (PLA) nanoparticles of lipophilic anti-cancer herb drug (Cucurbitacins and Curcuminoids) using a precipitation method have been developed. [68]

Work has also been carried out in the development and characterization of solid lipid nanoparticles for the traditional Chinese medicine for their targeted delivery and increased bioavailability and efficacy. [57]. In the recent years, nanostructured carrier system like polymeric nanoparticles, liposomes, solid lipid nanoparticles, polymeric micelles, nanoemulsions, etc., have been investigated for their potential to deliver anticancer drugs by oral route [69, 70]. Moreover, the oral route offers great potential for delivery of cytotoxic agents and therefore the attention has focussed on the development of oral chemotherapy in oncology [71-73]. Scientists have developed many types of nanoparticles for development of herbal drugs [Table 2].
Table-2: Some Herbal drug nanoparticles.

<table>
<thead>
<tr>
<th>Formulations</th>
<th>Active ingredients</th>
<th>Biological activity</th>
<th>Method of preparation</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Curcuminoids solid lipid nanoparticles</td>
<td>Curcuminoids</td>
<td>Anticancer and antioxidant</td>
<td>Micro-emulsion technique</td>
<td>[74]</td>
</tr>
<tr>
<td>Berberine-loaded nanoparticles</td>
<td>Berberine</td>
<td>Anticancer</td>
<td>Ionic gelation method</td>
<td>[75]</td>
</tr>
<tr>
<td>CPT-encapsulated nanoparticles</td>
<td>Camptothecin</td>
<td>Anticancer</td>
<td>Dialysis method</td>
<td>[76]</td>
</tr>
<tr>
<td>Artemisinin nanocapsules</td>
<td>Artemisinin</td>
<td>Anticancer</td>
<td>Self-assembly procedure</td>
<td>[77]</td>
</tr>
<tr>
<td>Taxel-loaded nanoparticles</td>
<td>Taxel</td>
<td>Anticancer</td>
<td>Emulsion solvent evaporation method</td>
<td>[78]</td>
</tr>
<tr>
<td>Nanoparticles of Cuscuta chinensis</td>
<td>Flavonoids and lignans</td>
<td>Hepatoprotective and antioxidant</td>
<td>Nanosuspension method</td>
<td>[79]</td>
</tr>
<tr>
<td>Glycyrrhizic acid-loaded nanoparticles</td>
<td>Glycyrrhizic acid</td>
<td>Anti-inflammatory, antihypertensive</td>
<td>Rotary-evaporated filmultrasonication method</td>
<td>[80]</td>
</tr>
</tbody>
</table>

Novel drug delivery system ‘nano carriers’ for ‘Herbal remedies’ why?

Pharmaceutical drug discovery acquired a immense increment whilst together with natural products chemistry, pharmacologists, microbiologists and biochemists commenced to unravel the chemistry of natural progressions in human, animals, plants and microorganisms. Before reaching to the blood, many constituents of the herbal drugs will be smashed in the highly acidic pH of the stomach and other constituents might be metabolized by the liver. Resultant, the optimum quantity of the herbal drugs may not reach the blood that means the exact amount of the drug will not reach to infected area. If the drug doesn't reach in the optimum amount to the infected region at 'minimum effective level' then there will be no mean to show the therapeutic effect of the drug. Nano carriers
applying to herbal remedies will carry optimum amount of the drug to their site of action bypassing the all 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. [81] That is only the fundamental inspiration for using nanotechnology as a novel drug delivery system collaboratively with the herbal remedies. Hence integration the nano carriers as a novel drug delivery system in the traditional medicine system is essential to conflict more chronic diseases like asthma, diabetes, cancer and others. However, the research is still at a nascent stage and a long way from actually using the herbal remedy in various disease treatments.

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.

- Currently marketed formulations lack target specificity for various chronic diseases.

- Some other side effects are associated with currently marketed formulations.

- Patient non-compliance due to large doses and less effectiveness with the available formulations.

Nanosized delivery system was selected because of the following reasons:

- They appear to be able to deliver high concentrations of drugs to disease sites because of their unique size and high loading capacities.

- The concentration seems to persist at the sites for the longer periods.

- 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 tumor.

- Exhibits passive targeting to the disease site of action without the addition of any particular ligand moiety.

- Decrease in the side effects.

- Decrease in the dose of the drug formulation.
Future prospective

Herbal remedies have been used vastly by major part of the population for curing ailments. All over the world the research has been going on herbal remedies and NPs. The development of herbal remedies in the drug delivery system in a number of institutes is being carried out at basic and clinical trial levels. Though the herbal formulations are not expected to treat diseases properly but they can help in better management of diseases by the patient himself. It can improve the quality of life by giving nutritional supplement as well. The only requirement is to develop the better systems for the proper delivery of such drugs at the sites and in the whole body in the doses which will not compromise with the existing treatment. Toxicity & hypersensitivity reactions as associated with currently marketed i.v. formulations. Something, that would not only give relieve with such side effects but also will also increase the patient’s strength from inside are very much desirable. Nanotechnology is approaching new paradigm for drug delivery system by their unique small size and controlled release of the drug. Hence using ‘herbal remedy’ in the nano carriers will increase its potential for the treatment of various chronic diseases and health benefits. Many successful examples with experienced evidences are present among us in the direction of nano research. Herbal remedies are also prosperous resources of advantageous compounds holding antioxidants and constituents that can be made use in purposeful foods. This type of collaborative research among the traditional ‘Herbal remedies’ and newer approaches of modern drug delivery system i.e. ‘Nanotechnology’ has established the attractive therapies to the pharmaceutical in near future that will enhance health of people.

It is anticipated that the effectual and valuable relevance of the NPs and herbal remedies being applied with the nano carrier, will enhance the significance of existing drug delivery systems.

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