REVIEW ARTICLE

A New Arena of Herbal Nanotechnology

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Abstract

Herbal drugs have been used since ancient times due to their renowned therapeutic efficacy and safety parameters. Today, people are shifting more frequently from synthetic substances to herbal compounds for drug-related needs. The major problems with phytocompounds are their limited aqueous solubility, degradation in acidic pH, etc. The answer to this came with the recent developments in nanotechnology, which allow the creation of nanoparticles with enormous potential as drug delivery systems due to their reduced size up to the nanoscale. Drugs undergoing nanoscale transformations have distinctive properties, such as enhanced drug efficacy, extended circulation, improved drug localization, and increased solubility. Herein, a new era of nano-phytomedicine has been discussed that ensures the delivery of bioactive compounds and diagnostics to a target site by exploiting various carriers. The review also summarizes the processes for the synthesis of nanoparticles and their characterization parameters, with the pivotal role of nanotechnology in recent applications exploiting novel phytoconstituents.

Key words: Herbal drugs, nanoparticles, nano-phytomedicine, nanotechnology, target site

INTRODUCTION

Natural resources serve as a cornerstone of medicine and have been employed for curing numerous ailments since ancient times. People around the world not only have a special understanding of the natural resources on which they rely, but they also possess incredible botanical knowledge. About 85% of the world's population has access to these traditional medicines for their medical requirements.[1]

The ancient texts have confirmed the use of phytoconstituents or herbs as a source of medicines in India, Egypt, China, Rome, Greece, and Syria from around 5000 years ago. Even though traditional medicines incorporating phytocompounds have been used for eons before the invention of modern pharmaceuticals. The assertion by the WHO in 2003 still represents the applicability of this therapeutic approach in today's era.[2]

The Indian science of herbal medicines known as "Ayurveda" has also contributed majorly by dealing with herbal pharmaceuticals and herbo-mineral preparations, though such treatments require standardized herbal preparations with constant quality and clearly identified ingredients to be successful.[3] Hence, it becomes crucial to maintain the safety, quality, and efficacy of herbal drug components so as to prevent the major health issues.

Several conventional drugs were created from plant materials a century ago, and still, most of them are being used as an effective medication. Willow bark, opium poppy, and cinchona bark, which are used to make aspirin, morphine, and quinine respectively, are few amidst the countless examples of botanical medicines.[4]

However, the underlying problem with herbal medicines is their poorkinetic performance which reduces the drug's bioavailability and effectiveness. The previous studies have assured that incorporating these herbal drugs or phytoconstituents with nanotechnology helps in enhancing the solubility and bioavailability, with providing the better effectiveness.[5] The concept of size reduction is renowned and as old as "Charak Samhita" which explains the concept of "Bhasmas" an oldest dosage form, employing the metal and herbs in nanoparticles range for therapeutic purpose.[6] This review starts with a brief description of types of nanoparticles with the potential mechanism behind their cellular entry. Later, different literatures on herbal nanoparticles with a detailed iteration of current achievements and challenges have been elaborated.

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HERBAL NANOTECHNOLOGY

Herbal preparations are being used in India since ancient time and now, they are spreading all over and are at forefront in the pharmaceutical sector, due to their well-versed therapeutic effects and minimal adverse effects.[7] Even in "Ayurveda" drugs are being prepared from ages either using herbs or they are herbo-mineral preparation having gold, silver, zinc, etc. However, as the treatments require standardized herbal preparations with constant quality and clearly identified ingredients to be successful.[8] Polyherbal systems, due to unsubstantiated scientific data and processing challenges, like absence of any standardization procedures, vigorous extraction and difficulty in identification of specific medicinal components were long ignored.

Despite the fact that herbal medicines have powerful pharmacological effects for a wide range of diseases, they are not that effective due to poor solubility and large molecular weights. Increased systemic clearance also necessitates their more frequent administration or a greater dose, which disqualifies the herbal medication for therapeutic usage.[9]

Modern research resolves these scientific needs for herbal medicines by opening the door to the creation of innovative formulations where herbal compounds can be incorporated as nanoparticles, SLNs, and so on. Such as with the development of colloidal nanogels, nanotubes, and nanomicellar systems, curcumin can now be utilized both on its own and in conjunction with other chemotherapy drugs like paclitaxel. This explains the increased demand of novel drug delivery systems to acquire desired therapeutics effect.[10] Figure 1 highlights the continuous evolvement of nanotechnology from ancient to modern era.

Delivery of herbal compound through nano delivery system is chosen due to the qualities offered by nanoparticles such as unique size, higher loading efficiency, delivering high concentrations of drug to target site, obviating the obstacles including pH variations, small size ensuring slower rate of metabolism with increased duration of the drug's blood circulation, possibility of amalgamating the nanomedicine, and imaging techniques.[11,12]

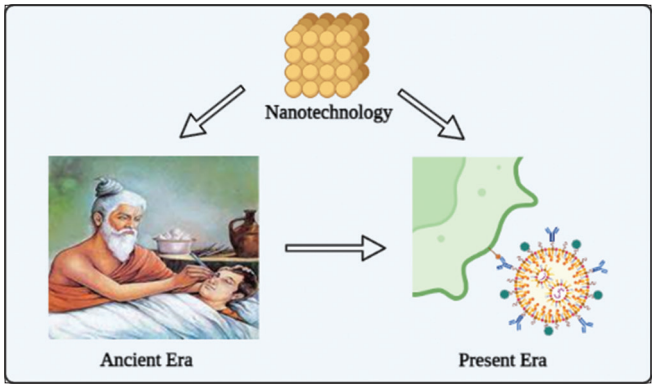

Figure 1: Paradigm shift in nanotechnology from ancient to present era

NANOPARTICLES

Nanoparticles are tiny particles existing among 1–100 nm size and can be comprised of carbon, metal, metal oxides, or organic material. The nanoparticles often show distinct physical, chemical, and biological features at nanoscale comparing its counterpart particles at higher scales. Increased chemical reactivity or stability, increased surface area to volume ratio, better mechanical strength, and other factors all contribute to this phenomenon. These attributes of nanoparticles are helpful in a wide range of applications.[14] Some of the advantages of nanoparticles are illustrated in Figure 2.

Types of herbal nanoparticles

Nanoparticles are broadly classified according to their composition as follows [Figure 3]:

Organic nanoparticles

This category includes nanoparticles composed of polymers, lipids, proteins, carbohydrates, and other organic substances. Nanospheres, dendrimers, liposomes, micelles etc. are some of the most well-known instances of this class.[15,16] These can be further categorized as:

i. Polymeric nanoparticles: These nanoparticles are made up of numerous natural or synthetic polymers, facilitating many different conceivable shapes and properties. As they are biocompatible and have straightforward formulation parameters, they may be formulated by controlling various NP characteristics for effective delivery systems. Two most prevalent types of polymeric NPs are nanocapsules which consist cavities wrapped by a polymeric membrane or shell and nanospheres.[17]
ii. Lipid-based Nanoparticles: Majority of lipid-based NPs are spherical structures made up of at least one lipid bilayer encircling at least one interior aqueous compartment.[18]

Carbon-based nanoparticles

NPs formed only from carbon atoms fall under the category of "carbon-based NPs." Fullerenes, carbon nanotubes, and quantum dots are prominent representatives of this class.[19,20]

Inorganic nanoparticles

This category consists of NPs which are not comprised of carbon or organic components. The common instances of this include semiconductor NPs, metal NPs, and ceramic NPs. These are made entirely of metal precursors, hence can be either monometallic, bimetallic, or polymetallic. Inorganic minerals such as gold, iron, and silica have been employed for the creation of nanostructured materials utilized for drug delivery and imaging applications.[21]

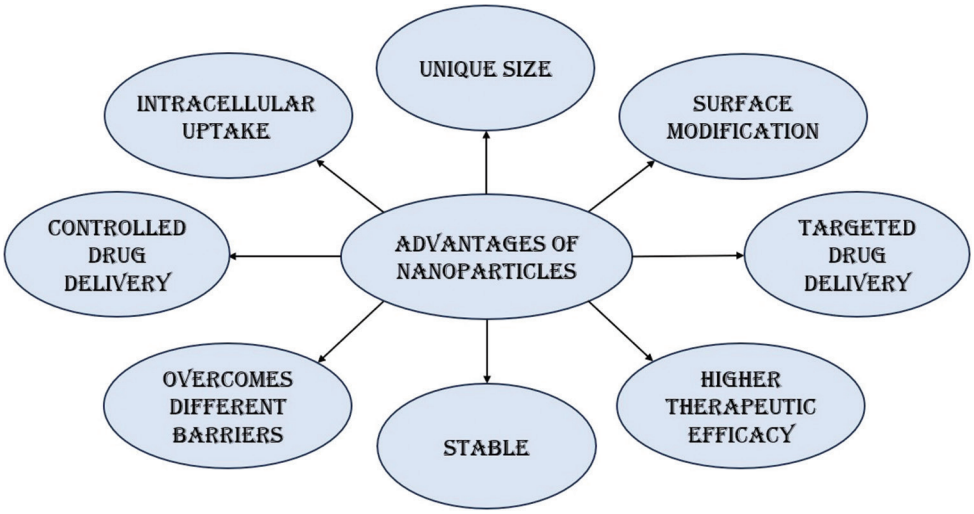

Figure 2: Advantages of nanoparticles[13,14]

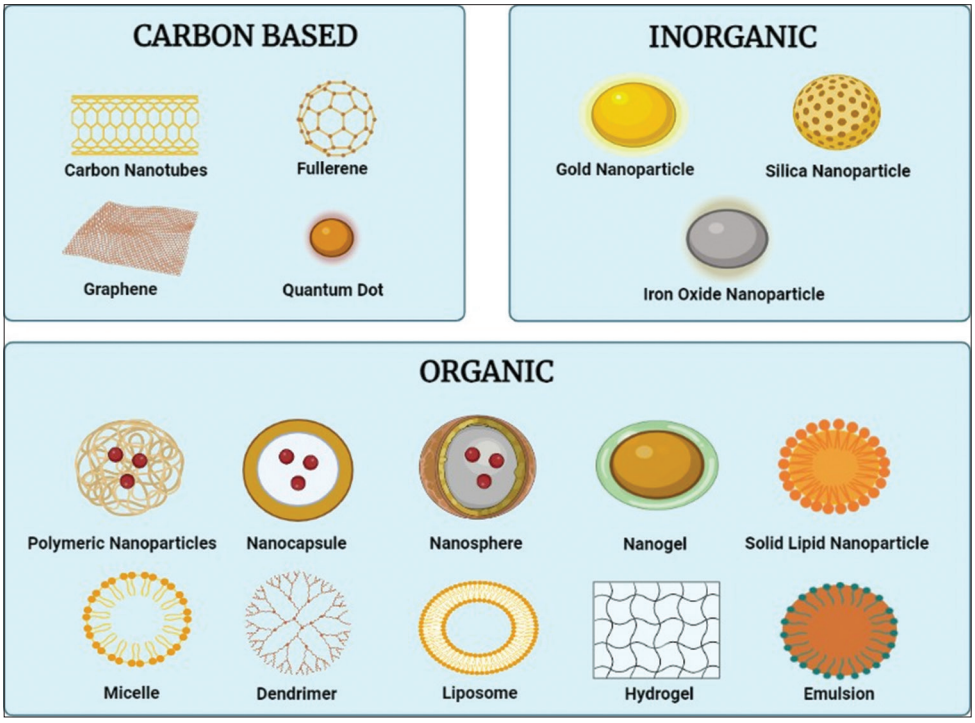

Figure 3: Classification of nanoparticles

Cellular uptake mechanism of nanoparticles

On reaching the exterior of cell, nanoparticles get cellular entry through endocytosis. This starts with opsonization in which complement proteins and immunoglobulins attach to NPs and are identified and get adhered to phagocytes using precise ligand-receptor interactions. This initiates a signaling cascade leading to activation of actin assembly, development of cell surface extensions, and the eventual engulfment and ingestion of particles, resulting in the formation of a "phagosome." Figure 4 illustrates the phagocytic process for cellular entry of nanoparticles. Depending on the type of cell and particle surface, the mentioned processes may persist from few minutes to hours. This process includes the Fc, complement, and other receptors such as mannose/fructose receptors.[22,23] The physiochemical characteristics of nanoparticles which control the uptake by the phagocytic pathway are described as:

a. Receptors: The type of receptors involved affects the precise mechanism of phagocytosis and subsequent events; for instance, phagocytosis depending on the Fc receptor produces pro-inflammatory mediators, but phagocytosis dependent on the complement receptor does not. Therefore, related receptors influence NPs' toxicity (i.e., inflammatory response) as well as their delivery of NPs.[23]
b. Particle size: In general, phagocytes are more effective in capturing bigger particles. For example, larger

particles definitely exhibited increased phagocytic absorption when incubated with human mononuclear cells while using radio-labeled albumin NPs of about 200–1500 nm.[24]

c. Shape: In addition, it was shown that shape had a significant impact on how well NPs were taken up by the cells. Arnida *et al*. evaluated in their study about the cellular absorption of PEGylated gold nanorods and nanospheres following a 6-h incubation with murine macrophages. Nanospheres accumulated more than gold nanorods, but less so. These results provided an explanation for the *in vivo* portion of the study, which showed that gold nanorods had longer circulation than nanospheres after being injected into animals with ovarian tumors.[25,26]

d. Surface properties: Surface characteristics influence opsonization and interactions with cellular membrane receptors and this is another crucial factor regulating the uptake of NPs by phagocytes. For instance, cellular absorption may be altered by functionalizing NPs with sterically shielding polymers such as hydrophilic PEG.[27] Opsonization of PEGylated NPs can be resisted by reducing or blocking protein adsorption to their surface.

Synthesis of herbal nanoparticle

Several methods are available for preparing nanoparticles, broadly they are based on two approaches: bottom-up and top-down approach. Both the approaches with methods have been discussed in earlier section with illustration in Figure 5.

Bottom-up approach

Bottom-up method of making nanoparticles involves creating nanostructures from smaller building blocks such as atoms, molecules, or clusters. As the process continued, the physical forces operating at the nanoscale joined small, stable units into bigger ones. The methodology primarily relies on self-assembly principle and usually employs in chemical production of nanoparticle.[28] Some commonly used techniques are

Emulsion polymerization

The most popular technique for creating nanoparticles is emulsion polymerization. While employing aqueous continuous phase, surfactants or emulsifiers are not required because the monomer gets dissolved in anaqueous media as continuous phase. Here, the monomer in continuous phase strikes an initiator molecule, which could be an ion or a free radical, the reaction is said to have initiated. Alternatively, polymerization begins whenever a starting molecule or potent radiations interacts with the dissolved monomers in the aqueous phase. Before or after the polymerization reaction has ended, phases might separate and solid particles can form. Example: Polymethylmethacrylate nanoparticles can be generated using polymerization method, exempting the emulsifiers, and are ideal adjuvants for vaccinations.[29]

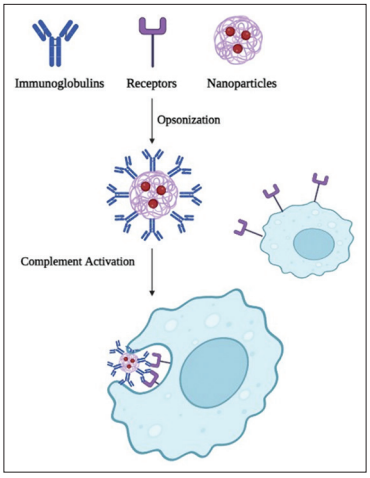

Figure 4: Cellular entry of nanoparticles through phagocytosis

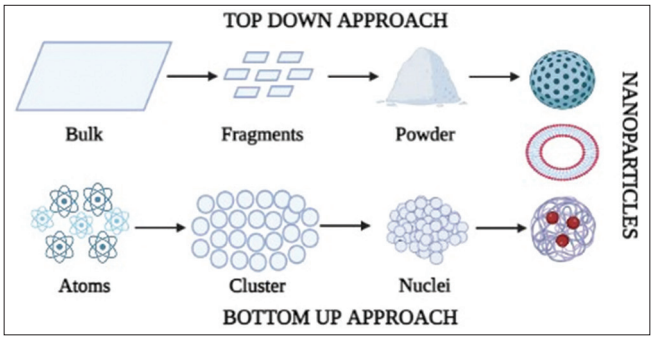

Figure 5: Approaches for synthesis of nanoparticles

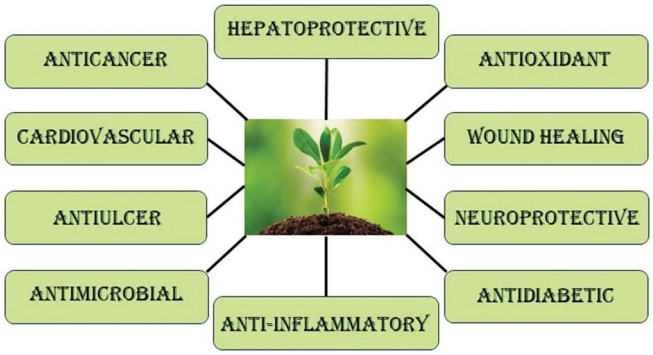

Figure 6: Applications of herbal nanotechnology

Interfacial polycondensation

This included a hydrophobic monomer like phthaloyldichloride, and a hydrophilic one, such as diethylenetriamine, to create polymeric nanoparticles with or without surfactant. The prepared nanoparticles are of 500 nm or smaller. Another modified form of method involved the polyurethane polymer and poly (ether urethane) copolymers as drug carriers for α-tocopherol. Polyurethane and poly(ether urethane) nanocapsules are produced by the interfacial interaction of two monomers.[30]

Sol-gel synthesis

This is an example of wet chemical technique that is frequently employed to create metal-oxide-based nanoparticles. During

the process, the liquid precursor is transformed into a sol, which gets converted into a gel-like structure. The process begins with hydrolyzing the metal oxide in water or with alcohol, so as to create a sol followed by condensation which results in the formation of porous structures with increased viscosity. Continual polycondensation alters the material's structure, properties, and porosity. Aging causes the porosity to decrease and the distance between colloidal particles to widen. The gel is dried after age by expelling water and organic solvents from it. Finally, calcination helps in creating nanoparticles.[31,32]

Chemical vapor deposition (CVD)

This method is mostly employed for the development of carbon-based nanoparticles like nanotubes. CVD enables the production of inorganic nano-metric layers on the surface of 3D substrates. The volatile precursor is first introduced by a carrier gas into the reactor chamber followed by adherence of the precursor vapor on the surface of substrate and finally intermediate products are formed. Finally, the breakdown of intermediates on substrate results in nucleation and development of the solid layer/grains.[33,34]

Spray pyrolysis method

In this technique, precursor solution having solvent like water and a solute typically containing a metal and a non-metal element is transformed into a spray of tiny droplets. The solvent vaporizes and the solute precipitates when the droplets are subsequently placed in a heated environment. The final particles are formed by a chemical decomposition, provided that the procedure is conducted at high temperature. Depending on the conditions used during procedure, particles created may be empty or completely filled.[35]

Reverse micelle methods

Another significant method for creating desired nanomaterials of varying size is reverse micelle method. Reverse micelles are aqueous domains dispersed in a continuous oil phase to form a microemulsion. These are formed in w/o emulsion, where the hydrophilic region is oriented towards an aqueous core. For creating nanomaterials, this core acts as nanoreactor, thereby serving as an aqueous reservoir.[34] Groo *et al*. developed reverse micelle-lipid nanocapsules using plectasin derivate AP138, where prepared LNCs showed high loading efficiency with sufficient antimicrobial activity.[36]

Top down approach

The most recent nanotechnology research focuses on nanosizing plant extracts and offers a variety of benefits. Herbal extracts are employed in a variety of ways to create nanoparticles using any of the following methods:

High-pressure homogenization method

The drug-dispersed lipid is subjected to a high shear stress and high pressure (100–2000 bar), which causes disruption of particles down to the submicrometer or nanometer range. The large-scale manufacturing of SLNs, parenteral emulsions, lipid drug conjugates, and nano-shaped lipid carriers can be accomplished using the high-pressure homogenization approach.[37] Both hot or cold homogenization approaches can be used to obtain submicron sized particles. In hot homogenization process, temperature is kept greater than lipid's melting point and when the drug is loaded with molten lipids and heated aqueous solution of surfactants, it results in pre-emulsion that eventually develops nanoparticles. The method has the disadvantage of drug being dispersed in aqueous phase with temperature-dependent drug degradation. Cold homogenization came in existence to overcome this. This method involves melting the medication in a lipid melt and quickly cooling it with a cryogenic system, such as liquid nitrogen or dry ice followed by milling the powder to turn it into a dispersed powder form.[38] Nanoparticle can be obtained by homogenizing the mixture at room temperature.

Ionic gelation method

The ionic gelation approach was used to create chitosan nanoparticles initially by Calvo *et al*. in 1997.[39] This technique depends on electrostatic interaction among the negatively charged polyanion group like tripolyphosphate and the amine group of chitosan. Chitosan is first solubilized in acetic acid with or without poloxamer, a stabilizer that can be mixed in chitosan solution prior or later the addition of polyanion. Following the addition of a polyanion or anionic polymer, nanoparticles develop at room temperature using mechanical stirrer.[40]

Emulsion solvent diffusion method

The process depends on partial miscibility of an organic solvent with water creating an o/w emulsion, where the oil phase contains a polymer in organic solvent and the aqueous phase contains a stabilizer such as poloxamer,[41] which are then emulsified using a high shear mixer. Next, water is added to cause the organic solvent to diffuse, which leads to the formation of nanoparticles.

Solvent displacement/nanoprecipitation method

In this process, polymers, drugs, and lipophilic surfactants are dissolved in semipolar solvents like ethanol or acetone followed by injecting it in stabilizer-containing aqueous solution which is being stirred magnetically, thereby producing the nanoparticles by rapid diffusion of solvent. The suspensions are subsequently processed under lower pressure to remove the solvent. The rates at which the organic phase is added to the aqueous phase have an impact on particle size. With increasing the mixing rates of both the phases, a decrease in particle size and drug entrapment was noticed.[42]

Emulsion-solvent evaporation method

Most popular technique for creating nanoparticles is emulsion solvent evaporation, which is a two-step process. Initially, the polymeric solution needs to be emulsified into an aqueous phase followed by the evaporation of solvent resulting in the precipitation of polymer as nanospheres. The nanoparticles are obtained using ultracentrifugation, freed from any remaining drugs or stabilizers, and then lyophilized for storage.[43]

Table 1: Techniques for characterization of herbal nanoparticles

Morphological characterization		
Scanning Electron microscopy	Examination of surface morphology with direct visualization	[50,51]
TEM electron microscopy	To find out the interior structure of NP's	[51,52]
CryoTEM	Preserves the morphology, allows sample visualization in unmodified state	[51,52]
Nuclear magnetic resonance	Qualitative nature and size, physicochemical state of the inside constituents of NP's	[53]
Dynamic light scattering	For analyzing the size and polydispersity index	[53]
Atomic force microscopy	Allows 3D visualization of individual particles and groups of particles, Surface hydrophobicity study	[54,55]
X-ray photoelectron spectroscopy	Identification of specific chemical groups on the surface	[56]
Structural and chemical characterization		
X-ray diffraction analysis	Analyses crystalline or polycrystalline nature and phase analysis	[57]
FTIR	Characterizes organic materials such as lipid structure by determining the chemical composition or functionalization of NPs	[58]
Zeta Potential Analyzer	Determines the surface charge of NPs	[58]
Thermal characterization		
Differential scanning calorimetry	Can be used for determining the measure melting point, crystallization points, structural-phase transition points, latent heat capacity, heat of fusion, and oxidative stability	[58]
Differential thermal analysis	Used to characterize phase diagrams and transition temperatures and also to assess melting points, thermal stability, and oxidative stability	[58]
Thermogravimetric analysis	Thermal stability of materials	[53,58]
Others		
UV Spectroscopy or HPLC	Drug loading, drug entrapment, or drug release study	[59]

Salting-out method

This approach is based on the idea that the solubility of a non-electrolyte in water decreases with adding the electrolyte. Because of its solubilization properties and well-versed ability of separating from aqueous solution on adding electrolytes during salting out procedure, acetone is used as a water-miscible solvent. The salting out agents usually calcium chloride and magnesium chloride, or non-electrolytes, like sucrose and a colloidal stabilizer, like PVP or HEC, are added after the polymer and drug have first been dissolved in a solvent. The production of nanospheres is induced by diluting this oil/water emulsion with an adequate amount of water to improve solvent diffusion into the aqueous phase.[44,45]

Supercritical fluid method

Development of green chemistry led to an increase in the popularity of supercritical fluid technology. A substance that does not condense or evaporate to form a liquid or gas when it is at a temperature and pressure above its critical temperature and pressure is termed as supercritical fluids. These fluids lack surface tension and exhibit qualities of both liquid and a gas. The most often used supercritical fluid is carbon dioxide. During the process, CO_2 gas is subjected to pressure and heat and transits from a liquid to a supercritical phase when it reaches the supercritical point. In this process, substance is solubilized in CO_2 and the mixture is sprayed through a nozzle to cause carbon dioxide solutions to expand quickly, causing the immediate production of nanoparticles.[46]

Complex coacervation method

In this technique, a polymeric solution is divided into two phases, one is colloid-rich dense coacervate phase and another is a supernatant having few colloids. In complex coacervation, oppositely charged colloids are combined due to electrostatic attraction with spontaneous liquid/liquid phase separation. This process requires mild conditions, hence can be useful for microencapsulation of living cells and labile molecules that cannot tolerate the harsh conditions such as heat and organic solvents.[47] Chitosan-DNA nanoparticles have been reported to form easily through coacervation between the positively charged amine groups on the chitosan and the negatively charged phosphate groups on the DNA.[48]

Coprecipitation method

The simplest technique of creating the inorganic and metal-based nanoparticles is coprecipitation. Iron oxide nanoparticles are well-known and the coprecipitation process is routinely used to create them. The species that produce the particles are often dissolved in an aqueous solution; in case of iron oxide nanoparticles, these species include $FeCl_3 \cdot 6H_2O$ and $FeCl_2 \cdot 4H_2O$. The nanoparticle preparation is caused by the precipitation, which is triggered by the addition of a base while stirring at room temperature in a non-oxidizing environment. The type of salt

and its ratio, temperature, pH, and ionic strength of reaction are the process variables that can control the final particles' colloidal characteristics[49] and hence can be used to treat numerous diseases as shown in Figure 6. Characterization is as crucial as preparation, hence some techniques for characterization of herbal nanoparticles are highlighted in Table 1.

Applications of herbal nanoparticle

The recent advancement in nanocarriers has facilitated in size reduction up to sub-microns level along with maximizing the solubility, bioavailability, and aiding in precise drug targeting. These nanocarriers whether it be biodegradable polymers, lipids, and polysaccharides contain lesser amount of drug in encapsulated form that also reduces the possible adverse effects. Such nanoparticles also have ability to target a specific organ which enhances selectivity, drug delivery, effectiveness, and safety and improving patient compliance.[60] Table 2 provides the literature about some of the herbal nanoparticles that have been explored by the researchers.

Problems encountered in herbal nanotechnology

Nanotechnology offers enormous advantages while delivering the herbal compounds such as increased solubility, bioavailability, pharmacological activity, and stability. Smaller dose, smaller size, etc., therefore promises an

Table 2: Nanoparticles synthesized with herbal drugs

Herbal nanoparticles	Function (therapeutic category)	References
Silver nanoparticles of *Cuscutareflexa*	Hepatoprotective activity	[61]
Barbaloin loaded polydopamine-polylactide-TPGS (PLA-TPGS) nanoparticles	Gastric cancer	[62]
Podophyllotoxin solid lipid nanoparticles	Epidermal targeting	[63]
Artemisinin nanocapsule	Anticancer activity	[64]
Curcumin-loaded polymeric nanoparticle	Anticancer activity, antibacterial activity	[65,66]
Berberine-albumin nanoparticles	Alzheimer's disease	[67]
Turmeric extract-loaded PLGA nanoparticles	Antioxidant Activity	[68]
Copper nanoparticles of *Camellia Sinensis*	Breast Cancer	[69]
Lipid-polymer hybrid nanoparticles encapsulating β-sitosterol	Hepatotoxicity	[70]
Glycyrrhizic acid nanoparticles	Antiviral and anti-inflammatory activity	[71]
Gugulipid loaded proniosomal gel	Anti-inflammatory activity	[72]
Hispolon-loaded liquid crystalline nanoparticles	Hepatoprotective activity	[73]
Solid lipid nanoparticles of aloe-emodin	Anticancer activity	[74]
Resveratrol nanoemulsion	Dual-imaging agents, Alzheimer's disease	[75,76]
Nanoparticles of *Cuscuta Chinensis*	Hepatoprotective	[77]
Albumin nanoparticles of curcumin	Parkinson's Disease	[78]
Solid lipid nanoparticles of ginkgo biloba	Cytotoxicity and antibacterial activity	[79]
Gold nanoparticles of *Moringa Oleifera*	Hepatoprotective activity	[80]
Aloe vera-conjugated silver nanoparticles	Against multidrug-resistant pathogen	[81]
Chitosan nanoparticles of *Achillea Millefolium*	Antibacterial and Antiurolithiatic	[82]
Silver nanoparticles of *Ocimumgratissimum*	Acne Vulgaris	[83]
Cassia auriculata polymeric nanospheres	Hepatoprotective activity	[84]
Collagen nanoparticle-mediated brain delivery of silymarin	Neuroprotection	[85]
Solid lipid nanoparticles of hibiscus	Antidepressant Activity	[86]
Sustained release nanoparticles of naringin	Anti-inflammatory Activity	[87]
Quercetin microemulsion	Anti-parasitic, Anti-angiogenic	[88]
Fe_3O_4 magnetic nanoparticles coated with gallic acid	Anticancer activity	[89]
Silver nanoparticles of Silymarin	Hepatoprotective Effect	[90]
Tetrandrine-loaded nano-aggregates	Tissue Engineering	[91]
Rutin-liposome drug delivery	Antioxidant activity	[92]
Nanostructured lipid carriers of ellagic acid	Antioxidant activity	[93]
Nano-liposomes double-loaded with curcumin and tetrandrine	Hepatotoxicity and anti-tumor effects	[94]
Nanostructured lipid carriers of breviscapine	Cardiovascular disease	[95]

effective alternative treatment. Despite this fact, very few formulations are there in market which have passed the FDA approvals and made their way. This is because of the challenges that nanoparticles face during the formulation development. Current challenge in turning nanotechnology to treatment is due to trials that regulates how nanoparticles interact with biological systems. Some other potential risks associated with nanotechnology-based drug delivery systems that must be taken into account are higher cost of manufacturing, difficulty in clinical trials, problems in process scale-up, absence of regulatory guidelines, and the lack of safety and toxicity data of herbal formulations.[96]

The stability of the nanoparticles themselves is another difficulty for them. Because several nanoparticles have been demonstrated to leak following contact with blood components, the question of nanoparticles' capacity to retain medicines is becoming more important.[97] Major challenge with nanophytomedicine is their substantially increased prices which is due to raised production cost that serves as a barrier and limits the possibility of reaching these products to markets or the patients.[98] Another major issue with herbal constituents is toxicity and poor solubility profile. Taxol has exceptional anti-tumor effects, but its isolation is problematic and provides relatively low yields.[99] Initially, cremophor EL was used for enhancing the solubility of taxol but later, it was found to be toxic. This led to the conversion of taxol into nanoparticles using albumin. Such toxicity considerations need to be done carefully while developing nanoparticles with herbal compounds.[100]

Regulatory agencies like FDA and the European Therapies Agency evaluate nanoparticle-based medications on an individual basis using the standard benefit/risk analysis paradigm. There are not many criteria for judging nanomedicines because they are a unique class of medicinal ingredients or formulations.[101] Based solely on similarities in the findings of traditional pharmacokinetics and toxicity research, or even by simply comparing the composition of medical products, the bioequivalence between generic and novel nanomedicines may be impossible to predict.[102]

CONCLUSION

Since ancient times, herbal medicines have been extensively used around the world. Both doctors and patients have recognized their superior therapeutic efficacy due to the fact that they have less side effects than modern pharmaceuticals. By combining herbal compounds into novel dosage forms, they can be used in a more ethical manner with increased efficacy. Designing novel drug delivery systems such as nanoparticles for natural compounds can resolve may overcome the drawbacks linked with phytoconstituents, hence can aid to boost the therapeutic value by decreasing toxicity, enhancing bioavailability, etc. Literatures have confirmed the great success of nanoparticles and nanoformulation as drug delivery systems in and still offered a brighter outlook for a wide range of applications.

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