A review on herbal drug loaded into pharmaceutical carrier techniques and its evaluation process

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Abstract

Background: The herbal drug is molded in nanocarriers to boost growing interest in a pharmaceutical era for various fields in sort to amplify therapeutic worth. Nowadays, a promising interest has been developed in nanotechnology using herbal medicines as core material to provoke its activity on the target site.

Main body: By administering herbal medicine in the nano-size form, there are chances for improving the bioavailability, binding receptor selectivity due to higher active surface energy thereby enhancing the effectiveness and safety of the active entity. In the last few decades, formulations with nano-sized herbal active ingredients have emerged as nano-phytomedicines owing to its wide range of interest and effectiveness because of its unique nature. Nanonized drug delivery structure of herbal drug has an approaching outlook for getting bigger the doings and overcome problems associated with plant medicine. The current review will focus on nanoparticles, herbal drug-loading techniques, herbal nanoformulations, and applications in various fields.

Conclusion: We conclude that by formulating herbal drug in nanocarriers would be a promising guide for the progress of core remedy and will act as a promising proposal for many pathological conditions.

Keywords: Nanoformulations, Herbal drug-loading technique, Application

Background

Nano-size particle or nanoparticle is a spacious class of materials that enclose particulate substance which has not as much of 100 nm in size [1]. It is a well-known field of research of this century and it has a wide range of revolutionary developments in the field of nanotechnology such as treatment, monitoring, diagnosis, and control of biological systems.

Nanoparticles or nanomaterials have gained prominent advancements in nanotechnology due to their tunable physiochemical and biological performance over their counterparts [2]. The major drawbacks of conventional are nonspecific, lack of solubility, and inability to enter inside the cells which offer a great opportunity for nanoparticles to play significant roles.

Herbal medicines have been extensively used in the region of the world since antique times. In India herbal medicines or traditional system of medicines such as Siddha and Ayurveda use herbal preparations [3]. Nowadays, herbal drugs dwell in a leading position in the pharmaceutical industry as their effects are known and side effects are very negligible. Moreover, the herbal drug has a symmetrical way of interest to fabricate nanoparticles compared to synthetic drugs [4]. Even though the herbal drug has enormous pharmacological actions toward many diseases, it has been shown an only limited effect on the human biological system due to their less kinetic performance such as low absorption, inability to cross lipid membrane, high molecular size and weight, or poorly absorbed, resulting in a reduction of bioavailability and efficacy over the biological system [5]. Moreover, some of the extracts are not used clinically because of the abovementioned hinders. To overcome such

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related issues, carriers have been used as an alternative approach to amend and improve the kinetic and dynamic parts of a drug molecule on a biological system.

In recent decades, an herbal drug with nanocarriers has received a lot of attention with enthusiasm because of its future potential and its unique properties making these materials indispensable in many areas of human activity. So nano herbal systems have a promising prospect for raising the activity and overcoming the dilemma allied with plant remedy.

The major necessitate of the herbal drug has nanocarriers is before to reaching into the bloodstream the activity of drugs will be ruined in the highly acidic pH of the stomach or might to metabolized by the liver [6, 7]. Because of these short of optimal amount on the affected region, there will be no means to be evidence for the therapeutic effect of the drug, so to progress the bioavailability and therapeutic activity of the herbal drug molecule on the affected region and to prevent the drug from the acidic environment, the drug has been formulated using carriers.

Nanoparticles are classified based on many forms, such as based on materials, based on size, based on surface, and based on shapes [8]. Example based on coating materials and ligand anchor over the nanoparticles and based on the use for the study purpose the classification of nanoparticles will be represented (Fig. 1).

Nanocarriers or nanostructure systems can be broadly divided into organic and inorganic. The physiochemical properties of these carriers can be tuned by altering their composition or dimension [7]. Nanocarriers’ application to herbal remedies will provide more surface area and enhanced solubility, bioavailability, and facilitate exact drug targeting which is an endeavor to release a drug molecule over a particulate area of the system for a prolonged period to elicit a response on diseased tissue.

Nanocarriers are important to deliver a potent drug on the needed region in our body to elicit a potent pharmacological reaction. Nanocarriers are classified based on carrier materials’ used, such as organic and inorganic carriers [9]; those carriers are chosen to carry the active drug based on the kinetic property of the moiety (Fig. 2).

Common nanoformulation systems loaded with herbal active ingredients
Nanotechnology is one of the input novel drug delivery methods under examination, with nanoformulation attention to have a wide variety of benefits in contrast with conventional preparations of plant constituents, which include improved permeability, solubility, bioavailability, therapeutic action, stability [10, 11], enhanced allocation within tissues, and persistent delivery.

Over the past decades, various nanotechnology-based systems such as the following:

1. Polymeric nanoparticles
2. Solid lipid nanoparticle
3. Magnetic nanoparticles
4. Metal and inorganic nanoparticles
5. Quantum dots
6. Polymeric micelles
7. Phospholipids micelles
8. Colloidal nano-liposomes
9. Dendrimers are being available in the pursuit to improve aqueous solubility and drug delivery to the pathological site [12].
10. Metal-organic framework (MOF) nanoparticles (zeolitic imidazolate framework) are essentials to form strong interaction between drugs to increase the drug-loading efficacy. The nanoparticle based on metal-organic framework can comprehensively enhance the immunotherapy of various therapeutic agents [13, 14].
11. Micelle carrier, the stable micelles, may exhibit improved photothermal efficiency toward cancer cells for both in vitro and in vivo studies [15].

Nanotechnology for herbal drug (Anticancer Res. 2016, 35, 15821614) have reported by loading herbal active entities in the above carriers is therapeutically effectual against several human conditions [16], owing to its anti-inflammatory, antioxidant, antibacterial, anticancer, wound healing properties, etc. [17] compared to conventional form.

Nanoparticles with different morphologies. 0-D, 1-D, and 2-D are the different dimensions of nanoparticles, mesoporous [18], liposomes, and micelle and are entirely made up of lipids, and there spherical structures are amphiphilic compound; the dendrimer is branched-type compound. Polymeric nanoparticles and hydrogels are completely made by natural and synthetic polymers; they are usually more stable in nature (Fig. 3).

Main text
Herbal drug loading
Herbal drugs are becoming more popular in the modern world for their application to cure a variety of diseases with less toxic effects and better therapeutic effects [19]. On the other hand, a few limitations of herbal extracts are unstable in highly acidic pH, high first-pass metabolism, etc. [20], may lead to drug level below the therapeutic concentration in the blood resulting in less or no therapeutic effect [21]. To abolish such effects, the herbal drugs are loaded into the novel carriers to minimize drug degradation and severe side effects by the accrual of drugs to the non-targeted area [22] (Fig. 4).

Phytoconstituent-loaded nanoparticles were formulated by the following steps; initially, the phytoconstituents have to extract from the plant and then have been formulating into nanomaterial-loaded phytoconstituents, then this has been promoting pharmacological effect in the desired form [23].

Techniques for loading nanoparticles
1. Hot homogenization technique
2. Cold homogenization technique
3. High-pressure homogenization method
4. Complex coacervation method
5. Coprecipitation method, self-assembly methods
6. The salting out method, supercritical fluid method
7. Nanoprecipitation method or solvent displacement method
8. The solvent emulsification diffusion method

Hot homogenization
This process will take place in the presence of a higher temperature than the melting point of the lipid [24, 25]. The pre-emulsion will form when the drug is loaded with melted lipids in the presence of a hot aqueous solution of surfactants. Finally, the nanoparticles will be formed.

Cold homogenization technique
In this approach, the drug is melted in the lipid melt, and quickly cooled using cryogenic systems like liquid nitrogen or ice nitrogen. Then make it into dispersing powder form using powder mill. Then homogenize at room temperature or below to get a nanoparticle (Fig. 5).

Example: hot and cold homogenization techniques were mostly used to prepare lipid-based nanoparticles formulation.

Solvent emulsification diffusion method
The method involves the preparation of an o/w emulsion, oil phase contains polymer in presence of organic solvent and aqueous phase contain stabilizer [26], which are emulsified using a high shear mixer, followed by adding up of water to provoke the diffusion of organic solvent, thus consequential in development of nanoparticles (Fig. 6). Example: breviscapine liposomes for CVS disease, cyclosporine-loaded sodium alginate glycolate technique, and doxorubicin-loaded nanosphere or nanocapsules [27]
Complex coacervation method
This is a spontaneous phase-separation process of two liquid phases in colloidal systems, which results in the interaction of two oppositely charged polyelectrolytes upon mixing in an aqueous solution.

Example: coacervation or ionic gelation method has been focused for the preparation of nanoparticles using biodegradable hydrophilic polymers such as chitosan, sodium alginate, and gelatin [28]. This method has been used for the preparation of chitosan nanoparticles.

Coprecipitation method
This method is an amendment of the composite coacervation method for the preparation of nano-size particles [29]. This method has been reported to afford good dispersal stability to feebly water-soluble drugs.

Salting out method
This method is based on the event that the solubility of a non-electrolyte in water is decreased in the lead adding up of an electrolyte [30].

Example: nanospheres are formulated by salting out method, initially in a solvent, polymer and drug are dissolved which is consequently containing the salting out agent [31] (electrolytes), most commonly, this technique uses for heat sensitive substances.

Supercritical fluid extraction of emulsion
Supercritical fluid extraction of emulsion (Int.J.nanomed, 2017, 12, 2689) has been prepared through solid lipid nanoparticles using supercritical CO₂. This technique uses supercritical fluid for removing the solvent from o/w emulsion [32, 33]. The supercritical anti-solvent precipitation can serve as a substitute for supercritical fluid extraction of emulsions (Fig. 7).
**Nanoprecipitation method or solvent displacement method**
This method is based on interfacial accrual of a polymer after dislocation of a semi-polar solvent miscible with water from a lipophilic solution, thereby ensuing in a dwindle in the interfacial tension between the two phases [34, 35], which increase the shell area with a consequent configuration of small droplets of organic solvent even devoid of any mechanical stirring.

Example: for most of the poorly soluble drugs, nanoprecipitation method is well suited. By adjusting preparation parameters, nanosphere size and drug release can be controlled effectively.

**Mechanism of cellular uptake of nanoparticles and their effect on drug delivery**

In the field of diagnosis and treatment in contemporary medicine, nanoparticles (NPs) are an important novelty. They are drug delivery systems on the nanometer scale, whose uptake mechanisms and routes of internalization differ, depending on their properties. For successful treatment, it is crucially important to understand the interplay between uptake mechanisms and NP properties [36]. In this article, mechanisms of NP uptake and the subsequent intracellular events are presented. NPS can enter cells via phagocytotic or non-phagocytotic pathways (clathrin-mediated endocytosis, caveolae-mediated endocytosis, macropinocytosis, and other endocytotic pathways). The route of internalization determines the site of drug release, which can be in the acidic and enzyme-rich environment of lysosomes, or NPS avoid this compartment and release drugs in the cytosol or another organelle. This process can be controlled by a careful selection of NP ingredients and precise design of their physicochemical properties (size, shape, surface properties). Phagocytosis is generally undesirable, since its main purpose is the elimination of foreign materials from the body, and therefore the drug taken up in this way is usually lost. To avoid this internalization mechanism, the particles should be small showing a hydrophilic surface [37]. However, the most successful approach is to attach ligands to the NP surface, which governs the uptake through non-phagocytotic mechanisms. Knowledge about cellular uptake mechanisms is crucial for predicting drug delivery to the target site in the cell since it can lead to better stability of NPs and preserved biological activity of labile drugs.

The nanoparticles were mostly internalized into the cells by clathrin and caveolae independent and dependent endocytosis pathway [38]. The dependent pathway is involved in cell signaling and regulation of membrane proteins, lipids, and fatty acid.

The interdependent pathway is involved in the utilization of growth hormone, extracellular fluid, GPI-linked protein, and interleukins-2.

Mostly, those pathways were utilized for internalization of micron-sized nanoparticles which are not feasible to be taken up into the cells [39, 40]. The nanoparticles can enter by macropinocytosis or phagocytosis process. In macropinocytosis, all dissolved particles in the extracellular fluid are taken into the endocytic vesicle, despite the presence of their precise receptors, making the process a form of nonspecific bulk fluid uptake.

Nanoparticle size between 25 and 50 nm is required for the finest endocytosis and intracellular localization. Steps detailing the cytosolic delivery of therapeutic agents via nanoparticle carriers [41]
(1) Cellular organization of nanoparticles
(2) Internalization of nanoparticles using endocytosis
(3) Endosomal break away from nanoparticles or
(4) Lysosomal deprivation of nanoparticle
(5) Therapeutic agent generously diffuses into the cytoplasm.
(6) Cytoplasmic transfer of therapeutic moiety to intentional organelle
(7) Exocytosis of nanoparticles

**Phagocytosis of nanoparticles**

Usually, initiated by opsonization, opsonins such as immunoglobulins, complement proteins, or other blood proteins (e.g., laminin and fibronectin) are adsorbed onto the nanoparticle surface. Opsonized nanoparticles are then accepted by, and attach to phagocytes via specific ligand-receptor interactions. This initializes a signaling surge that can activate actin assembly, the formation of cell surface extensions, and successive engulfing and internalization of particles, forming what is known as a “phagosome.”

Therefore, mentioned events take between 30 min to several hours, depending on cell type and the nature of the particle surface. Phagocyte receptors concerned in this process contain Fc receptors and complement receptors (Fig. 8).

Nanoparticles initially form a complex by binding with immunoglobulins, and that process is called opsonization [42]. Then the complex formation binds with phagocyte which is named as complement activation process. The engulfment of the activated complex by phagocyte is called phagocytosis.

Nanoparticles are classified into organic, inorganic, and carbon-based nanoparticles. The examples for organic nanoparticles are dendrimers, liposomes, and micelles. The examples for carbon-based nanoparticles are graphene and fullerene. The example for inorganic nanoparticles is further divided into metal-based and metal oxide-based forms (Fig. 9).

**Herbal formulations**

Herbal remedies were chosen as feasible drug molecule for delivery through nanocarriers as a promising delivery system [43]; the main reasons for the popularity of herbal medicines are as follows (Table 1):

1. Deliver in high concentration may increase the unique size and high loading capacities
2. May persist at the site for a longer time
3. May have fewer side effects
4. May decrease the dose of the drug formulation

As per the World Health Organization (WHO), in developing countries, around 80% of the world populations at present utilize herbal medicine for primary healthcare. Presently, the scientific community is focused on the study associated with the bioactive compounds, its chemical composition, and pharmacological potential of a variety of plant species, to fabricate pioneering active ingredients that present moderately minor side effects than existing molecule [58].

The number of synthetic molecules that are essentially marketed is departing on diminishing day by day and thus investigate on the creation of the natural-based active compounds are again approaching to the attention in spite of its hurdles [59].

Several drugs that also possess natural therapeutic agents in their composition are already available commercially; their applications and names are as follows [46]: malaria treatment (Artemotil derived from...
Artemisia annua, a traditional Chinese medicine plant) and cancer treatment (paclitaxel and its analogs derived from the Taxus brevifolia plant; vinblastine and vincristine extracted from Catharanthus roseus; liver disease (silymarin from Silybum marianum)).

In the last few decades, substantial notice has been focused on the progress of herbal drug in a novel drug delivery system [60, 61]. The novel carriers should preferably accomplish two prerequisites.

1. Should transport the drug directly based on the necessity of the body throughout treatment

2. Should discharge the active moiety of the herbal drug at the spot of action

**Evaluation of nanoparticles**

**X-ray powder diffraction (XRD)**

A rapid systematic method used for phase detection of the crystalline material and can endow with information on unit cell measurement and atomic spacing [62]. The X-ray is produced by cathode ray tube, potable to fabricate monochromatic radiation, collimated to on purpose, and projected toward the sample [63].

**Table 1 Herbal formulations**

| S.no | Formulations                                      | Active ingredients          | Function                                |
|------|---------------------------------------------------|----------------------------|-----------------------------------------|
| 1    | Curcuminoid solid lipid nanoparticles             | Curcuminoids               | Anticancer and antioxidant [44]         |
| 2    | Artemisinin nanocapsules                          | Artemisinin                | Anticancer [45]                         |
| 3    | Berberine-loaded nanoparticles                    | Berberine                  | Anticancer [46]                         |
| 4    | Silybin nanoemulsions                             | Silybin                    | Hepatoprotective [47]                  |
| 5    | Rutin-alginate-chitosan microcapsules             | Rutin                      | Cardiovascular disease [48]            |
| 6    | Camptothecin-loaded microsphere                   | Camptothecin               | Anticancer [49, 50]                    |
| 7    | Docetaxel submicron emulsion                      | Docetaxel                  | Anticancer activity [51]               |
| 8    | Curcuma-phospholipid complex                      | Curcumin                   | Anticancer [52]                         |
| 9    | Gugulipid proniosome gel                          | Gugulin                    | Anti-liver toxicity [53]               |
| 10   | Chitosan nanoparticles of *Camellia sinensis*     | Catechins                  | Antiviral, anti-inflammatory [54]       |
| 11   | Naringenin nanoparticles                          | Naringenin                 | Hepatoprotective [55]                  |
| 12   | Tetrandrine-loaded nano-aggregates                | Tetrandrine                | Rheumatoid arthritis, psoriasis [44]   |
| 13   | Curcumin-loaded PLGA nanosphere                   | Curcuminoids               | Antiplatelet, antioxidant [56]          |
| 14   | Quercetin microemulsion                           | Quercetin                  | Anti-parasitic, anti-angiogenic [57]    |
Thermogravimetric analysis/differential thermal analyzer
Thermogravimetric analysis (TGA) is a thermal analysis method which deals with the weight change in a substance as a utility of temperature and time, in a prescribed environment [64]. It is appropriate for use with all types of solid materials, including organic or inorganic materials.

Differential thermal analysis is a calorimetric technique, soundtrack the temperature, and heat surge related to thermal transitions in a substance [65]. This enables stage transitions to be resolute (e.g., melting point, glass transition temperature, crystallization). Thermogravimetric analysis (TGA) is a type of testing performed on samples that determines changes in weight about change in temperature.

Particle size, polydispersity index
The particle size and polydispersity index of materials can be analyzed by a dynamic light scattering method at a set angle and optimized temperature. This method is used to reveal the surface charge and physical stability of the formulation.

Transmission electron microscopy (TEM)
The structural surface and shape of carriers and the formulation can be easily investigated by transmission electron microscopy [66]. First, the samples should be diluted with distilled water then place a drop on a 200 mesh carbon film covered copper grid and further stained with a suitable staining solution. Dry the sample and analyze the shape.

Dynamic light scattering
It is the fastest method for determining the particle size. Commonly used for the size determination in colloidal particles in the nano and submicron range particles. The dynamic light scattering can also use for the determination of particle size distribution.

Nuclear magnetic resonance
Nuclear magnetic resonance is used for the estimation of both the qualitative nature and size of nanoparticle measurement. NMR can provide data about the physicochemical state of the constituent inside the nanoparticles.

Determination of encapsulation efficiency and recovery
The study aims to determine the encapsulation efficiency of the drug into the carrier. The sample was diluted with an organic solvent and sonicated in an ultrasonic bath for 30 min to extract drug. The resulted mixture was centrifuged for 10 min at suitable rpm and analyzed by HPLC or UV.

Stability studies
The common and conventional techniques by which stability of nanoparticle can be analyzed are as follows:
1. Transmission electron microscopy (TEM)
2. Dynamic light scattering
3. UV-visible spectroscopy (UV-Vis)
4. Zeta potential

UV-visible spectroscopy
A sample is placed between a light source and a photodetector [67]. The intensity of a beam of UV-visible light is calculated before and after the transitory through the sample. These measurements are compared at every wavelength to specify the sample’s wavelength-dependent spectrum. The data is classically plotted as absorbance as a function of wavelength.

Surface plasmon resonance
Every nanoparticle has its unique resonance absorption wavelength. The resonance condition is established when the frequency of light photons matches the natural frequency of surface electrons, oscillating against the restoring force of positive nuclei [68]. At the nanometer scale, particles put on view property are not inherent in individual atoms or to those in the bulk substance. The optical properties of nanoparticles are distinctly reliant on particle size and interpretable medium. When the nanoparticles move toward each other, they agglomerate owing to pH change, finally, UV can be used to learn the agglomeration of the particle.

Zeta potential
Zeta potential is an assessment of the efficient electric charge on the nanoparticle’s surface, quantifying the charges. When a nanoparticle has a web surface charge, the charge is a screen by the concentration of ions of contradictory charges close to the nanoparticle surface [69]. These layers of oppositely charged ions move with the nanoparticle and collectively with the layer.

The magnitude of the zeta potential provides in sequence about particle stability. The higher the magnitude of potential exhibit amplified electrostatic revulsion and therefore amplified stability.

Transmission electron microscopy
TEM image provides the details about the size distribution and particle distribution of nanoparticles over the proposed shelf-life period.
Atomic force microscopy
By using this method can create a topological map of a sample and which is mainly based on the forces between the tip and the surface of the sample [70]. It is one of the most promising tools to obtain an ultrahigh-resolution of the particles.

In vitro release
In vitro release of herbal drug from the carrier was investigated using the dialysis bag method. Regenerate cellulose membranes were used to hold the carriers and permit the dispersal of the herbal drug into the discharge medium [71]. The drug-loaded carrier was deposited into the dialysis membrane and placed in release medium under optimized temperature and rpm [68]. A definite period interval samples were withdrawn and replaced with the same medium. Finally, the release was quantified by spectroscopy methods [72].

Acoustic methods
The technique determines the particle size by measuring the attenuation of sound waves and applying the physical equation [73]. The oscillating electric field twisted by the charged particle, progress under the direction of acoustic energy, which can be identified to afford information on the surface charge [74].

SEM
SEM micrographs have a large profundity of field acquiescent; they can give a characteristic three-dimensional appearance [75], useful for understanding the surface structure of a sample [76]. Under vacuum, electrons generated by a source are accelerated in a field gradient [77].

Applications
Application of nanomedicine in different field of biomedical research has been reported by Patravale et al. (Pharm Nanotec, 3(6), 293302) that the nanostructures and devices have various goals in a different field but the major core is to achieve the improved diagnosis, treatment, safety [78], and compatibility (Fig. 10, Table 2).

Application of nanoparticles in various fields such as tissue engineering, theranostics, targeted drug delivery, analytical, and imaging tool [88] (Table 3).

The herbal drug has a growing interest in the safety of drug and surgery when conventional medicines are failed to promote effective treatment for most of the common health conditions.

Future opportunities and challenges
Nanoparticles and nanoformulation have previously been useful as drug delivery systems with immense accomplishment, and nanoparticulate drug delivery systems have still a better perspective for countless applications. In recent years, nano herbal preparation emerging a high interest in various fields due to its amorous pharmacological activity. Nanotechnology enables drug delivery is notch forthcoming future in pharmaceutics.
| Nanoparticles types          | Application                                                                 |
|-----------------------------|-----------------------------------------------------------------------------|
| **Fullerenes**              |                                                                             |
|                             | Eg: berberine-loaded fullerene \( \text{C}_{60} \) for cancer (a molecule composed entirely of carbon \[79\]) |
|                             | 1. Fullerene \( \text{C}_{60} \)                                             |
|                             | 2. Metallofullerol \[31\]                                                   |
|                             | 3. Cationic, anionic, and amino acid-type fullerene                           |
| **Solid lipid nanoparticles (SLN)** |                                                                             |
|                             | Eg: curcumin-loaded solid lipid nanoparticles (mainly comprise lipids that are in solid phase) |
|                             | 1. Glycerol palmitostearate and cetyl palmitate \[80\]                       |
|                             | 2. Hyaluronic acid-coupled chitosan SLN                                     |
|                             | 3. Steric acid, soya                                                         |
| **Nanostructured lipid carriers** |                                                                             |
|                             | Eg: quercetin-loaded nanostructured lipid carrier (nanostructured lipid carriers are produced from a blend of solid and liquid lipid) \[81\] |
|                             | 1. Stearylamine and diacetyl phosphate                                        |

Liver toxicity and diminished lipid peroxidation
Leukemia and bone cancer
HIV-reverse transcriptase and hepatitis C
Fungi and type 1 diabetes
Colorectal cancer
Gram-positive bacteria
Human immunodeficiency
Table 2 Application of different types of nanoparticles (Continued)

| Nanoparticles types | Application |
|---------------------|-------------|
| 2. DC-chol liposome  | Gene transfer in subcutaneous tumor |
| 3. Hydrogenated soy phosphatidylcholine, cholesterol, and di-stearoyl phosphatidylglycerol | Gram-negative bacteria |
| 4. Phosphatidylcholine, dynasan, and flurbiprofen | Sustained release of anti-inflammatory drug |
| 5. Fluticasone propionate, glyceryl palmitostearate and PEG | Topical cortico-therapy |

Nanoshells

Eg: Artemisinin nanoshells, Radix Salvia miltiorrhiza nanoshell
(Spherical core, surrounded by a shell or outer coating of a thin layer of another materials)

1. Silica coating of silver colloids
2. Gold nanoshell particles
3. Silver nanoshells, silica–silver core-shell particles
4. Nanoshell

Quantum dots

For measuring protein conformational changes, protein interaction, use in immune assay
In vivo animal imaging, lymph node mapping
Cell tracking and color imaging of liver cells

Superparamagnetic nanoparticles

For measuring protein conformational changes, protein interaction, use in immune assay
In vivo animal imaging, lymph node mapping
Cell tracking and color imaging of liver cells
**Table 2** Application of different types of nanoparticles (Continued)

| Nanoparticles types                                      | Application                                |
|-----------------------------------------------------------|--------------------------------------------|
| Eg: Hyaluronic acid-loaded superparamagnetic nanoparticles (molecules are those attracted to a magnetic field) | |  
| 1. Superparamagnetic iron oxide nanoparticles                      | Magnetic particle imaging                           |
| 2. Colloidal dispersion of superparamagnetic iron oxide nanoparticles | Magnetic fluid hyperthermia                         |
| 3. Superparamagnetic iron oxide nanoparticles coated with polyvinyl benzyl | Liver targeting MRI contrast agent             |
| Dendrimers                                                    |                                            |
| Eg: lactoferrin-tagged quantum dots (unimolecular, monodisperse, micellar nanostructures, around 20 nm in size) | |  
| 1. Polyamidoamine dendrimers                                   | Various bacteria                                |
| 2. Polylysine dendrimer                                         | Glaucoma                                      |
| 3. Pegylated lysine-based copolymeric dendrimer [87]             | Antifungal agent                               |
Table 3 Application of nanoparticles in various fields

| Nanoparticles                   | Application                                                                                                                                 |
|---------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|
| Drug delivery                   | Nanoparticle enhanced delivery of the drug to uptake by target cells                                                                          |
|                                 | Reduce the toxicity of free drug to non-target organs                                                                                       |
| Food                            | Improvement of food safety [89], enhancement of nutrition and flavor, longer shelf lives                                                  |
| Gene delivery                   | Enhancing the bioavailability of nutrients [90]                                                                                                |
|                                 | Efficiently introduce a gene of interest to express its encoded protein in a suitable host or host cell [92]                                   |
| Cancer treatment                | Maybe utilize to set in motion photosensitive therapeutic agent for application in cancer treatment [93, 94]                                  |
| Cosmetics                       | Sunscreen, lotions, etc.                                                                                                                     |
| Industrial engineering and chemical engineering | Nanoscale materials have been involved in window glass, sunglasses, car bumpers, paints, coatings, sports goods, explosives, propellants [95], etc. |
| Catalysis                       | Nanoparticles hold high exterior area that offers elevated catalytic activity [96]                                                             |
| Tissue engineering              | Repair of damaged tissues                                                                                                                   |
| Construction                    | Nanosilica is mixed with the normal concrete to improve the mechanical property and also improve durability [62]                              |
| Renewable energy and environmental remediation | Used to treat the surface water by disinfection, purification, and desalination [97–99]                                                      |

Abbreviations

GPI: G-protein-coupled receptor; HPLC: High-performance liquid chromatography; MRI: Magnetic resonance imaging; NP: Nanoparticles; NMR: Nuclear magnetic resonance; PEG: Polyethylene glycol; PLGA: Poly lactic glycolic acid; Qd: Quantum dots; SLN: Solid lipid nanoparticles; SEM: Scanning electron microscope; UV: Ultraviolet-visible light; WHO: World Health Organization

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