Review Article

Novel Drug Delivery System: Nanoparticulate System

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ABSTRACT

Nanotechnology is a tiny science. Design characterization, production and applications of structures, devices and systems by controlling shape and size at nanometer scale is refers to nanotechnology. Nanotechnology can be used to achieve better therapeutic action, better bioavailability and better patient compliance. The use of nanotechnology in medicine and more specifically drug delivery is set to spread rapidly. Currently many substances are under investigation for drug delivery and more specifically for cancer therapy. Interestingly pharmaceutical sciences are using nanoparticles to reduce toxicity and side effects of drugs. Nanoparticles are being used for diverse purposes, from medical treatments, using in various branches of industry production such as solar and oxide fuel batteries for energy storage, to wide incorporation into diverse materials of everyday use such as cosmetics or clothes, optical devices, catalytic, bactericidal, electronic, sensor technology, biological labeling. With these nanoparticles the specific targeting to various cells or exists which are responsible for cellular internalization and cellular uptake. To improve the pharmacokinetic and pharmacodynamics activity of the drug medication system like nanoparticles has made a break through by means of physical application. By means of targeted drug delivery system the targeted drug delivery will be achieved quickly. To maintain a controlled and sustain the rate of drug exposure on the site of action nanoparticles are used. That's the reason why the nanotechnology became as the most advanced in the field of medicine by maintaining the therapeutic activity .

Keywords: Nanotechnology, Drug delivery system, Targeting, Drug release.

INTRODUCTION

The word "Nano" has been used in last decade is ever increasing application to different fields of knowledge. Nanoscience, Nanotechnology, Nanomaterials are only few of nano containing terms used frequently in scientific reports in popular books, in newspapers that have been familiar to wide public, Non experts. Nanoparticles are defined as particulate dispersions or solid particles with a size in the range of 10-1000nm. The drug is dissolved, entrapped, encapsulated or attached to a nanoparticle matrix. Depending upon the method of preparation, nanoparticles, nanospheres or nanocapsules can be obtained. Nanocapsules are systems in which the drug is confined to a cavity surrounded by a unique polymer membrane, while nanospheres are matrix systems in which the drug is physically and uniformly dispersed. In recent years, biodegradable polymeric nanoparticles, particularly those coated with hydrophilic polymer such as polyethylene glycol) (PEG) known as long-circulating particles, have been used as potential drug delivery devices because of their ability to circulate for a prolonged period time target a particular organ, as carriers of DNA in gene therapy, and their ability to deliver proteins, peptides and genes.

Although the definition identifies nanoparticles as having dimensions below 0.1 µm or 100 nm, especially in the area of drug delivery relatively large (size >100 nm) nanoparticles may be needed for loading a sufficient amount of drug into the particles. In addition, for drug delivery not only engineered particles may be used as carrier, but also the drug itself may be formulated at a nanoscale, and then function as its own "carrier" The composition of the engineered nanoparticles may vary. Source materials may be of biological origin like phospholipids, lipids, lactic acid, dextran, chitosan, or have more "chemical" characteristics like various polymers, carbon, silica, and metals. The interaction with cells for some of the biological components like phospholipids will be quite different compared to the non-biological components such as metals like iron or cadmium. Especially in the area of engineered nanoparticles of polymer origin there is a vast area of possibilities for the chemical composition.

Although solid NPs may be used for drug targeting, when reaching the intended diseased site in the body the drug carried needs to be released. So, for drug delivery biodegradable nanoparticle formulations are needed as it is the intention to transport and release the drug in order to be effective. However, model studies to the behavior of nanoparticles have largely been conducted with non-degradable particles.

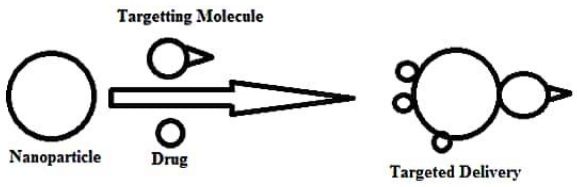

Figure 1: Nanoparticle Targeting

History of Nanoparticles [1, 2]

Although nanoparticles are associated with modern science, they have a long history. Nanoparticles were used by artisans as far back as Rome in the fourth century in the famous Lycurgus cup made of dichroic glass as well as the ninth century in Mesopotamia for creating a glittering effect on the surface of pots. In modern times pottery from Middle Ages and Renaissance

Ultrafine nanoparticles were defined synonymously during the 1970s and 80s were underway in USA and Japan, during the 1990s before the National Nanotechnology Initiative was launched in the USA, the new name, "nanoparticle."

Goal or need of nanoparticles [3, 4]

1. Designing nanoparticles as a delivery system are to control particle size, surface properties and release of pharmacologically active agents in order to achieve the site-specific action of the drug at the therapeutically optimal rate and dose regimen.
2. Though liposomes are also been used but potential carriers with unique advantages including protecting drugs from degradation, targeting to site of action and reduction toxicity or side effects, their applications are limited due to instability, low drug encapsulation efficiency, leakage of water soluble drug

Advantages of Nanoparticles [1, 3, 4]

Nanoparticle offers numerous advantages in drug delivery system. These advantages include, but are not limited:

1. Nanoparticles have many significant advantage over conventional and traditional drug delivery system
2. Particle size and surface characteristics of nanoparticles can be easily manipulated to achieve both passive and active drug targeting after parenteral administration.
3. In the tiny areas of body nanoparticles shows better drug delivery as compare to other dosage form and target to a particular cell type or receptor.
4. As a targeted drug carrier nanoparticles reduce drug toxicity and enhance efficient drug distribution
5. By using polymers drug release form nanoparticles can be modified which makes polymeric nanoparticle an ideal drug delivery system for cancer therapy, vaccines, contraceptives and antibiotics.
6. They control and sustain release of the drug during the transportation and at the site of localization, altering organ distribution of the drug and subsequent clearance of the drug so as to achieve increase in drug therapeutic efficacy and reduction in side effects.
7. Controlled release and particle degradation characteristics can be readily modulated by the choice of matrix constituents.
8. Drug loading is relatively high and drugs can be incorporated into the systems without any chemical reaction; this is an important factor for preserving the drug activity.
9. The system can be used for various routes of administration including oral, nasal, parenteral, intra-ocular etc

Limitations of Nanoparticles [1, 3, 4]

1. Altered physical properties leads to particle-particle aggregation, making physical handling of nanoparticles difficult in liquid and dry forms due to smaller particle size and larger surface area.
2. Smaller particle size and large surface area makes them very reactive in the cellular environment.
3. Small particle size results in limited drug loading and burst release. These problems should be sorted down before they are used clinically and made commercially available.

According to the size of nanoparticles, it's Clearence and applications are depended. The following table tells us about the particle size relative to its clearance and applications

Table 1: Particle size relative to its clearence

Particle size (based on rigid sphere)	Nanomedicine Applications
<10 nm	Rapidly cleared through extravasation or renal clearence
10-20 nm	Detection, imaging, potential to cross blood brain barrier (BBB)
20-100 nm	Drug, gene delivery, cancer therapy, sites of inflammation (optimal range to escape physiological barriers; high circulation potential , reduced filtration by liver and spleen)
100-200 nm	Drug, gene delivery (high potential for prolonged circulation)
200 nm^{-1} µm	Generally cleared by the spleen
>1µm	Usually opsonized and accumulate in liver and spleen, cleared from circulation almost immediately

Classification of Nanoparticles: [3, 4]

- Labile Nanoparticles: Liposomes, micelles, polymers, nanoemulsions etc.
- Insoluble Nanoparticles: TiO_2, SiO_2, fullerens, quantum dots, carbon lattices, nanotubes etc.

- One dimensional Nanomaterial: Nanowire and nanotube.
- Two dimensional Nanomaterials: Self assembled monolayer film.

Figure 2: Various shapes and types of nanoparticles

Classification of Nanoparticles based on the composition[5]

1. Metal based nanoparticles
   - Metal nanoparticles (Ag, Fe, Zn, Cu)
   - Metal oxides nanoparticles (TiO_2, ZnO, MoO_3)
   - Binary oxides nanoparticles (Bi_2O_3, CeO_2, CrO_2)
2. Carbon based Nanoparticles
   - Fullerness
   - MWCNT
   - SWCNT
3. Nanocomposites
   - Ceramic matrix nanoparticles (Al_2O_3, TiO_2, SiO_2)
   - Metal matrix nanoparticles (Co/Cr, Fe. Cr/ Al_2O_3, Fe.MgO)
   - Polymer matrix nanoparticles (Polymer/ TiO_2, Polymer/CNT)
4. Dendrimers (Nanosized nanoparticles)
5. Quantum dots (CdSe, CsTe, ZnSe, ZnS)

Properties of nanoparticles [6, 7, 8]

The outstanding importance of nanoparticles and nano structured systems can be ascribed to:

1. Particle size bioavailability in water non soluble substances can be transported as nanoparticles in an organism of human beings (application in life sciences)

2. Large specific surface area strong surface area effects (e.g. reactivity, high energy of surface area, adsorption, higher solubility, lower melting point etc.)

3. Change of electronic properties quantum effects of particles < 10 nm, importance for electronic and optoelectronic application

Approaches to Nanoscale structures [6]

1. Driving force for particle growth

Gibbs energy minimization by reducing the surface/volume ratio.

Surface energy increases quadratically, but volume energy decreases cubically.

Very small particles (rc) are highly reactive, due to their high chemical potential.

2. Stabilization of small colloidal particles

Electrostatic- Surface Charging

Thermodynamic- Surface Complexation (Modification)

Static- Adsorption of polymer molecules by the surface

Approaches of Nanotechnology: [3, 9, 10]

Nano carriers

Nanocarriers are the substances used to entrap the herbal drug to prolong the drug circulation in the blood and to reach the drug at the specific site by bypassing all the barriers. Commonly used nanocarriers include micelles, polymers, carbon-based materials, liposomes and other substances. Different types of nanomaterial being used in nanocarriers allows for hydrophobic and hydrophilic drugs to be delivered throughout the body

Polymeric Nanoparticles

Nanoparticles refer to colloidal systems with particle size ranging from 10 to 1000 nm. Nanoparticles have several advantages including solubility enhancement, bioavailability enhancement, efficacy enhancement, dose reduction and improved absorption of herbal medicines compared to traditional herbal dosage forms

Ceramic Nanoparticles

Ceramic nanoparticles are inorganic systems with porous characteristics that have recently emerged as drug vehicles. The biocompatible ceramic nanoparticles such as silica 30, Titania and alumina can be used in cancer therapy

Metallic Nanoparticles

Metallic particles such as iron oxide nanoparticles (15–60 nm) generally comprise super paramagnetic agents that can be coated with dextran, phospholipids or other compounds to inhibit aggregation and enhance stability. These particles are used as passive or active targeting agents.

Solid Lipid Nanoparticles

Solid lipid Nanoparticles (SLNs) are colloidal carrier systems, developed in the early 1990s, that combine the advantages of other colloidal systems (such as emulsions, liposomes, and polymeric nanoparticles) for drug delivery, while avoiding, or minimizing, some of their drawbacks. SLNs have higher physicochemical stability, offer better

protection against degradation of labile drugs and can also be produced on a large scale. The solid matrixes of lipid particles protect the drug from degradation. When system is produced, crystallization occurs leading to low drug encapsulation efficiency and drug release.

Liposomes

Liposomes are nanoparticles comprising lipid bilayer membranes surrounding an aqueous interior. It improves the efficacy and safety of the drug molecule, the hydrophilic drug gets acquired in aqueous phase whereas the hydrophobic drug gets acquired in the lipid phase.

Proliposomes

Although liposomes have many advantages, there are some problems like sedimentation, aggregation, fusion, hydrolysis, oxidation etc. In order to overcome these problems a novel method for liposome production has been reported, namely Proliposomes. Proliposomes are dry, free flowing particles that immediately form liposomal suspension in contact with water. Solid properties of liposomes help resolve the stability problems of liposomes.

Carbon Nanomaterials

Carbon nanomaterials include Fullerenes and Nanotubes. Fullerenes with a polygonal structure made up exclusively of 60 carbon atoms. Nanotubes have been one of the most extensively used types of nanoparticles because of their high electrical conductivity and excellent strength.

Quantum Dots

Quantum dots are nanoparticles made of semiconductor materials with fluorescent properties quantum dots must be covered with other materials allowing dispersion and preventing leaking of the toxic heavy metals. Quantum dots bind themselves to proteins unique to cancer cells, literally bringing tumors to light

Microemulsion and Nanoemulsion

Microemulsion is a system of oil, water and amphiphile which is thermodynamically stable. Amongst all it is considered to be an ideal alternative for oral delivery of poorly water soluble drug. It has several advantages like ease of preparation, low viscosity, and enhanced stability, increased dissolution of lipophilic drugs, thermodynamic stability, and bioavailability improvement. Nanoemulsion is also formulated to decrease the particle size and increase the efficacy.

Toxicity of Nanoparticles [3]

Nanoparticles are known for their effective drug delivery with more efficacy of the drug at the targeted site but at the same time due to use of intentionally engineered nanoparticles in the high tech industries can make them toxic to at the same time.

Nanotechnology is been applied in the medical sciences trying to achieve personalized medicine, however the same properties which make the nanoparticle as the attractive in drug delivery may contribute to the toxicological profile of nanoparticles in biological system In fact, the smaller particles are, the more the surface area they have per unit mass; and this property makes nanoparticles very reactive in the cellular environment. Therefore, any intrinsic toxicity of the particle surface will be enhanced. The respiratory system, blood, central nervous system (CNS), gastrointestinal (GI) tract and skin have been shown to be targeted by nanoparticles. A typical urban atmosphere contains approximately 107 particles/cm3 of air that is less than 300nm in diameter. Carbon in elemental form is a major component of these particles and the size of these particles is a determinant of their ability to cause systemic cardiovascular effects. Indeed, fine and ultrafine particulate matter (from 0.1 to 2.5 mm in mass median aerodynamic diameter) that can more easily access the vasculature via inhalation are linked to cardiovascular dysfunctions, particularly in subjects with preexisting vascular diseases.

Preparation of Nanoparticles [3, 4, 9]

Nanoparticles have been usually prepared by three methods:

1) Dispersion of preformed polymers
2) Ionic gelation or coacervation of hydrophilic polymers
3) Polymerization of monomers

1. **Dispersion of preformed polymers**

Usually Nanoparticles are dispersed in the continuous phase. The following are the dispersed systems

Dispersed phase	Continuous phase			
	Gaseous		Liquid	Solid
Gaseous			bubbles	Porous solids, xerogels, cryogels, aerogels
Liquid	aerosol	fog	emulsion microemulsion	Porous solids with liquids hydrogels, alcogels
Solid	aerosol	smoke	nanoparticles	composite material

Figure 3: Dispersed systems

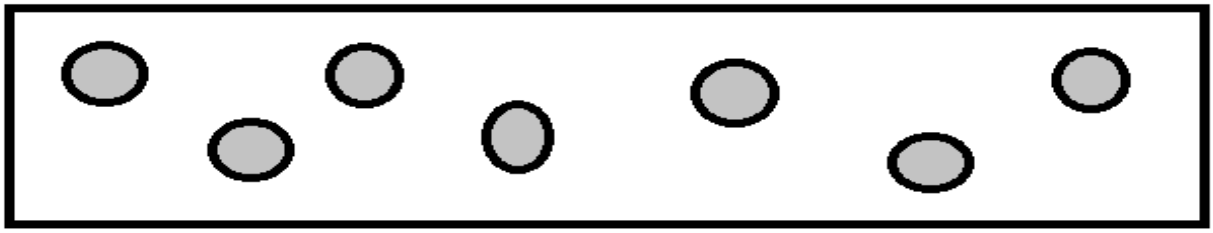

Figure 4: Dispersion of nanoparticles in continuous phase

Solvent Evaporation

Solvent evaporation is been done in two steps, In 1st step take a mixture of polymer and aqueous solution containing surfactant and Emulsifying agent and in 2nd step evaporation of solvent inducing polymer precipitation. Polymer and hydrophilic organic solvent is been emulsified in the aqueous solution. Organic solvent is been evaporated by continous stirring. Nanoparticles are collected by ultracentrifugation and washed with distilled water to remove stabilizer residue or free drug and lyophilized for storage. Modification is known as solvent evaporation or high pressure emulsification subjected to homogenization at high pressure followed by stirring to remove the organic solvent. Size of nanoparticles is been controlled by stirring rate, amount of dispersing agent, viscosity of organic and aqueous phase and temperature.

Solvent emulsification / Solvent diffusion

It is been developed from solvent evaporation. In this water miscible solvent and organic solvent are been used as an oil phase. Interfacial turbulence is generated during spontaneous diffusion leads to small particles. Smaller particle size can be achieved by increasing the concentration of water miscible solvent.

Double emulsion and evaporation method

The emulsion and evaporation method suffer from the limitation of poor entrapment of hydrophilic drugs .Therefore to encapsulate hydrophilic drug the double emulsion technique is employed, which involves the addition of aqueous drug solutions to organic polymer solution under vigorous stirring to form w/o emulsions. W/O emulsion is added into second aqueous phase with continuous stirring to form the w/o/w emulsion. The emulsion then subjected to solvent removal by evaporation and nanoparticles can be isolated by centrifugation at high speed, nanoparticles formed are first washed before lyophilisation. In this method the amount of hydrophilic drug to be incorporated, the concentration of stabilizer used, the polymer concentration, the volume of aqueous phase are the variables that affect the characterization of nanoparticles

Salting out

Separation of water miscible solvent from an aqueous solution via salting out effect. Polymer and drug in the solvent are emulsified into an aqueous gel containing salting out agent and colloidal stabilizer is been used lead to formation of O/W emulsion. O/W emulsion is diluted with water to enhance diffusion of solvent in aqueous solution. Stirring rate, internal/external phase ratio, concentration of polymer, type of electrolyte can be varied in the process.

Emulsion diffusion

This is another widely used method to prepare nanoparticles. The encapsulating polymer is dissolved in a partially water-miscible solvent (such as propylene carbonate, benzyl alcohol), and saturated with water to ensure the initial thermodynamic equilibrium of both liquids. Subsequently, the polymer-water saturated solvent phase is emulsified in an aqueous solution containing stabilizer, leading to solvent diffusion to the external phase and the formation of nanospheres or nanocapsules, according to the oil-to-polymer ratio. Finally, the solvent is eliminated by evaporation or filtration, according to its boiling point.

Supercritical fluid technology

The above mention conventional methods offers excessive use of organic solvents which is hazardous to the environment as well as to physiological system Therefore, there is an urgent requirement of suitable technology which avoid the usage of organic solvents or any other ingredient hazardous to health. Since supercritical fluids are environmentally safe, therefore, the supercritical fluid technology has been investigated as an alternative to prepare biodegradable micro- and nanoparticles. Supercritical fluids are those fluids which are at a temperature above its critical temperature remains in a single phase regardless of pressure CO_2 (SC CO_2) is the most widely used supercritical fluid because of its mild critical conditions, non-flammability, low price and nontoxicity. Among the various processing techniques involving supercritical fluids, supercritical anti-solvent (SAS) and rapid expansion of critical solution (RESS) are the most common one. In former process a liquid solvent (methanol) is selected on the basis of it's completely miscibility with the supercritical fluid (SC CO 2). This is done to dissolve the solute to be micronized at the process conditions. Since the solute is insoluble in the supercritical fluid, the extract of the liquid solvent by supercritical fluid leads to the instantaneous precipitation of the solute, results in the formation of nanoparticles. In later process called as RESS, solute is dissolved in a supercritical fluid such as supercritical methanol and then the solution is rapidly expanded through a small nozzle

into a region lower pressure. This dramatically affects the solvent power of supercritical fluids which is ultimately decreases and the solute eventually precipitates. RESS and its modified process have been used for the product of polymeric nanoparticles.

Ionic gelation or coacervation of hydrophilic polymers

Methods such as ionic gelation can be used for preparing hydrophilic polymer based nanoparticles. Calvo and co-workers developed method for preparing chitosan based nanoparticles by ionic gelation method. In this method two different aqueous phases are prepared for polymer [chitosan, a di-block co-polymer ethylene oxide or propylene oxide (PEO-PPO)] and the other is for polyanion sodium tripolyphosphate. This method is based on the strong electrostatic interaction between positively charged amino group of chitosan and negative charged tripolyphosphate to form coacervates with a size in the range of nanometer. Existence of strong electrostatic interaction between two aqueous phases leads to the formation of coacervates. In contrast ionic gelation involves the material undergoing transition from liquid to gel due to ionic interaction conditions at room temperature.

Polymerization method

This method involves polymerization of monomers to form nanoparticles in an aqueous solution. In polymerization drug is incorporated at two different stages (either by being dissolved in the polymerization medium or by adsorption onto the nanoparticles after polymerization completed). Ultracentrifugation can be used to purify nanoparticle suspension by removing various stabilizers and surfactants employed for polymerization, followed by the re-suspension of particles in an isotonic surfactant-free medium. This technique is reported for making poly (alkylcyanoacrylate) or polybutylcyanoacrylate nanoparticles. Desirable size of nanocapsule can be achieved by optimization of concentration of the surfactants and stabilizers.

Separation of nanoparticles [11]

Purification by filtration

Spectrum's KrosFlo Research II*i* System and filter modules were purchased from Spectrum labs and were used following manufacturer's instructions. Briefly, 10 mL of polymersomes at a polymer concentration of 10 mg/mL were diluted to 50 mL with PBS. The dilute polymersome solution was aliquoted into polystyrene sample tubes and attached to the KrosFlo research system with a 50 nm hollow fibre filter module. The filtration was started with the flow rate of 2 mL/minute. After the retained volume was reduced to 2 mL it was diluted to 50 mL and the process was repeated. To concentrate polymersome samples, a hollow fibre module with pores of 10 kDa was utilized.

Purification by centrifugation

The initial step of polymersome purification by size involved removal of micelles from the solution using the KrosFlow filtration system. The polymersomes were centrifuged at 500 Rotational Centrifugal Force (RCF) for 20 minutes. The resulting pellet was removed and resuspended in PBS. This fraction contained the largest aggregate fraction. The supernatant was then re-centrifuged at 2000 RCF for20 minutes and the pellet was removed and re-suspended, constituting fraction 1. This was repeated with further20-minute centrifugations at 5000, 10000, 15000 and 20000 RCF.

Purification by GPC

For separation of polymersomes by GPC, micelles and aggregates were removed as described above and the remaining polymersome solution was concentrated to approximately 200 µ L using a500 kDa MicroKros filter module. The solution was then placed in a glass liquid chromatography column containing Sepharose 4B. The fractions were collected in a 96-well plate. Dynamic Light Scattering (DLS) measurements were performed on a Zetasizer Nano ZS (Malvern Ltd.) as described previously

Purification by density gradient centrifugation

Density gradient centrifugation was performed using

Solutions of 5, 10, 15, 20, and 25% w/v sucrose dissolved in PBS. Aliquots of 200 µ L of each solution were carefully layered one on the top of each other in the order from the densest to the least dense within a 1.5 mL microcentrifuge tube, while avoiding mixing between the layers. Finally, 150 µ L of the solution containing a mixture of rhodamine-labelled vesicles of different shapes (spheres and tubes) prepared by film rehydration was deposited at the top of the sucrose layers and the microcentrifuge tube was centrifuged at 20000 RCF for 2 hours. After centrifugation, 20 µ L of solution from each layer was collected and analysed by Transmission Electron Microscopy (TEM).

Characterization of Nanoparticles [1, 3, 4, 9]

Nanoparticles are generally characterized by their size, morphology and surface charge, using such advanced microscopic techniques as scanning electron microscopy (SEM), transmission electron microscopy (TEM) and atomic force microscopy (AFM). The particle size can be very important to determine the toxicity. Surface charge tells about the polymer dispersion, redispersibility, and physical stability.

Particle size

Particle size distribution and morphology are the most important parameters of characterization of nanoparticles. Morphology and size are measured by electron microscopy. It has been found that particle size affects the drug release. Smaller particles offer larger surface area, Polymer degradation can also be affected by

the particle size. For instance, the degradation rate was found to increase with increasing particle size in vitro

DLS (Dynamic light scattering), AFM (Atomic force microscopy), TEM (Transmission electron microscopy), SEM (Scanning electron microscopy) are been used for the measurement of different particles of nanoparticles.

Particle Shape

SEM characterizes the nanosuspension before going for evaluation; the nanosuspension is lyophilized to form solid particles. The solid particles are coated with platinum alloy using a sputter coater.

Surface Charge

The nature and intensity of the surface charge of nanoparticles is very important as it determines their interaction with the biological environment as well as their electrostatic interaction with bioactive compounds. The colloidal stability is analyzed through zeta potential of nanoparticles. This potential is an indirect measure of the surface charge. The measurement of the zeta potential allows for predictions about the storage stability of colloidal dispersion. High zeta potential values, either positive or negative, should be achieved in order to ensure stability and avoid aggregation of the Particles, it also creates information regarding the nature of the substance.

Surface hydrophobicity

Surface hydrophobicity can be determined by several techniques such as hydrophobic interaction chromatography, biphasic partitioning, adsorption of probes, contact angle measurements etc. Recently, several sophisticated analytical techniques are reported in literature for surface analysis of nanoparticles. X – Ray photon correlation spectroscopy permits the identification of specific chemical groups on the surface of nanoparticles

Drug Release

A central reason for pursuing nanotechnology is to deliver drugs, hence understanding the manner and extent to which the drug molecules are released is important The drug loading of then nanoparticles is generally defined as the amount of drug bound per mass of polymer (usually moles of drug per mg polymer or mg drug per mg polymer); it could also be given as percentage relative to the polymer. The following methods for the determination of the *in vitro* release have been used:

1. Side by side diffusion cells with artificial or biological membranes

2. Dialysis bag diffusion technique

3. Reverse dialysis sac technique

4. Ultracentrifugation

5. Ultra-filtration (Centrifugal) technique

The dialysis technique is generally preferred10. Various researchers have proposed different methods with one common strategy of using synthetic membrane bag with specified porosity to hold the sample. The bag containing the sample is immersed in the recipient fluid, which is stirred at a specified rpm. The samples are withdrawn at regular intervals and are analyzed for the drug content

Drug Entrapment Efficiency

The nanoparticles were separated from the aqueous medium by ultracentrifugation at 10,000 rpm for 30 min at 50C. Then the resulting supernatant solution was decanted and dispersed into phosphate buffer saline pH 7.4. Thus the procedure was repeated twice to remove the unentrapped drug molecules completely. The amount of drug entrapped in the nanoparticles was determined as the difference between the total amount of drug used to prepare the nanoparticles and the amount of drug present in the aqueous medium.

Drug Entrapment efficiency (%) = (Experimental drug loading/Theoretical drug loading) × 100

Applications of Nanoparticles [1, 3, 9, 10, 12, 13, 14]

Nanotechnology and NP in Cosmetics

Nano-emulsions are commonly used in certain cosmetic products, such as conditioners

or lotions, it's also been used in sunscreens in UV filters as the ingredients are used in nano form than in bulk form to make it transparent rather than making it white.

They are also used in breast creams, toothpaste, fullerness, haircare etc.

Nanotechnology in nutraceuticals

Nanotechnology platforms are widely being used to create delivery systems for nutraceuticals and bioactive natural products with poor water solubility.

Cancer Therapy

Photodynamic cancer therapy is based on the destruction of the cancer cells by laser generated atomic oxygen, which is cytotoxic. A greater quantity of a special dye that is used to generate the atomic oxygen is taken in by the cancer cells when compared with a healthy tissue. Hence, only the cancer cells are destroyed then exposed to a laser radiation. Unfortunately, the remaining dye molecules migrate to the skin and the eyes and make the patient very sensitive to the daylight exposure. This effect can last for up to six weeks. To avoid this side effect, the hydrophobic version of the dye molecule was enclosed inside a porous nanoparticle. The dye stayed trapped inside the Ormosil nanoparticle and did not spread to the other parts of the body. Enhancement of cell specificity by conjugating antibodies to carbon nanotubes with fluorescent or radiolabeling

Vaccine delivery

Conjugation with peptides may be used as vaccine delivery structures

Table 2: Characterization of nanoparticles

Parameter	Characterization method
Carrier-drug interaction	Differential scanning calorimetry
Charge determination	Laser Doppler Anemometry Zeta Potentiometer
Chemical analysis of surface	Static secondary ion mass spectrometry Sorptometer
Drug stability	Bioassay of drug extracted from Nanoparticles Chemical analysis of drug
Nanoparticle dispersion stability	Critical floculation temperature Atomic Force microscopy
Release profile	*In Vitro* characteristics under Physiologic and sink conditions
Surface Hydrophobicity	Rose Bengal (dye) binding Water contact angle measurement X-ray photoelectron spectroscopy

Gene delivery and Tissue engineering

The ability of nanotubes to transport DNA across cell membrane is used in studies involving gene therapy. During this therapy DNA can be attached to the tips of nanotubes or can be incorporated within the tubes.

Natural bone surface is quite often contains features that are about 100 nm across. If the surface of an artificial bone implant were left smooth, the body would try to reject it. Because of that smooth surface is likely to cause production of a fibrous tissue covering the surface of the implant. This layer reduces the bone-implant contact, which may result in loosening of the implant and further inflammation. It was demonstrated that by creating nano-sized features on the surface of the hip or knee prosthesis one could reduce the chances of rejection as well as to stimulate the production of osteoblasts. The osteoblasts are the cells responsible for the growth of the bone matrix and are found on the advancing surface of the developing bone. In the end this findings would allow to design a more durable and longer lasting hip or knee replacements and to reduce the chances of the implant getting loose.

Reduced toxicity and increases the efficacy

Carbon nanotubes enhance drug delivery, efficacy and reduces the toxicity as found in the case of Amphotericin B nanotubes. It has been found that Amphotericin B nanotubes has shown enhanced drug delivery to the interior of cells, increased antifungal efficacy and reduced toxicity to mammalian cells when compared to amphotericin B administration without nanotubes. Nanoparticles are also used for tumour targeting, Brain targeting, Reversion of multidrug resistance in tumour cells, Targeting of nanoparticles to epithelial cells in the GI tract using ligands

Gene silencing

Highly selective therapy is required for cancer therapy where tumor cells will be selectively modulated. In this case gene silencing has been done with small interfering RNA. This can be achieved by targeting functionalized single walled carbon nanotubes with siRNA to silence targeted gene expression in the targeted cell

Drug transport

Fullerenes are being investigated for drug transport of antiviral drugs, antibiotics and anticancer agents.

Stimulate host immune response and production of antibodies

Fullerenes are efficient in stimulating host immune response and production of fullerene specific antibodies.

NPs have drawn increasing interest from every branch of medicine for their ability to deliver drugs in the optimum dosage range often resulting in increased therapeutic efficiency of the drugs, weakened side effects and improved patient compliance the development of hydrophilic NPs as drug carrier has represented over the last few years an important challenge. Among the different approaches, polyethylene oxide (PEO) and polylactic acid (PLA) NPs have been revealed as very promising system for the intravenous administration of drugs

Nanomedicines

Nano drugs, Medical devices, Tissue engineering

Chemical and Cosmetics Nanoscale chemicals and compounds, paints, coatings etc

Materials Nanoparticles, carbon nanotubes, biopolymers, points, coatings

As mentioned above, the fact that nanoparticles exist in the same size domain as proteins makes nanomaterials suitable for bio tagging or labelling. However, size is just one of many characteristics of nanoparticles that itself is rarely sufficient if one is to use nanoparticles as biological tags. In order to interact with biological target, a biological or molecular coating or layer acting as a bioinorganic interface should be attached to the nanoparticle. Examples of biological coatings may include antibodies, biopolymers like collagen, or monolayers of small molecules that make the nanoparticles biocompatible Nano-particle usually forms the core of nano-biomaterial. It can be used as a convenient surface

for molecular assembly, and may be composed of inorganic or polymeric materials

Environment and Energy

The use of nanoparticles is also be done in the water and air purification filters, fuel cells, photovoltaic

Military and Energy

Biosensors, weapons, sensory enhancement, Electronics Semiconductors chips, memory storage, photonica, and optoelectronics are done using nanoparticles

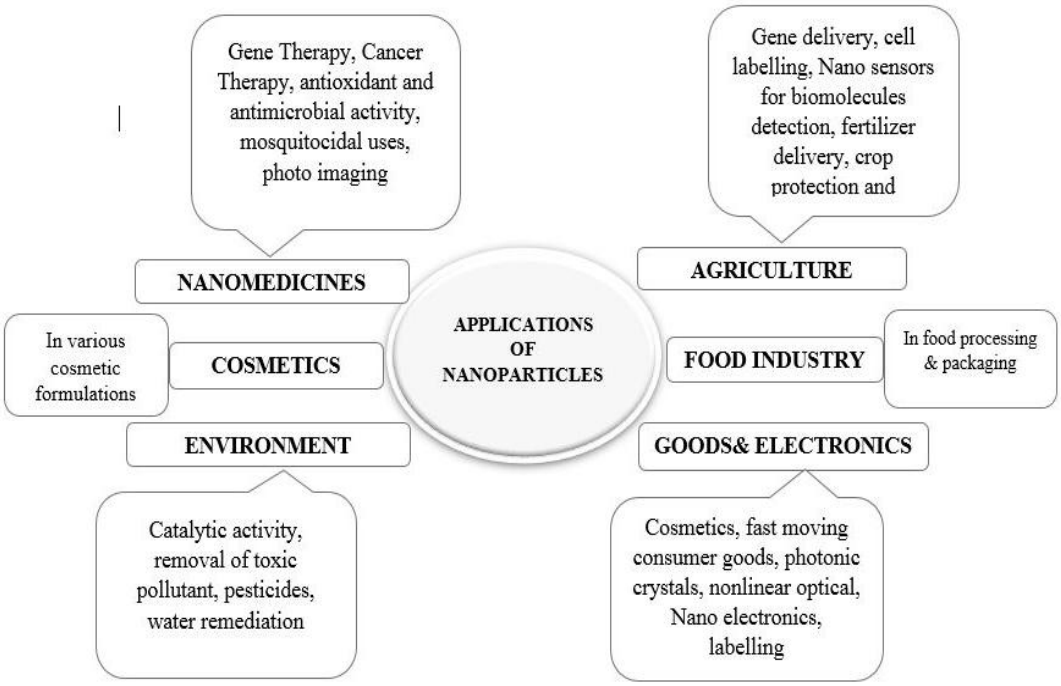

Figure 4: Applications of nanoparticles

CONCLUSION

The globalization of trade in market has brought about the different kind of herbal medicines by using nanotechnology as the effective and most promising drug delivery system with minimal side effects or toxicity and more efficacy. 'Nanotechnology' is been assigned as the most attractive therapy in the pharmaceutical field for the health of people. Increase in bioavailability, efficacy, solubility and permeability of the drugs in the body which are difficult to take orally can be achieved. A real therapeutic breakthrough can be achieved solely by carrying out painstaking studies in the field of nano-therapy. Using nanosystems in therapies of diseases may contribute to achieving an effective cancer treatment. Nanoparticles provide ingenious treatment by achieving targeted and controlled drug delivery system.

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