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Research Article

NANOPARTICLES: CLASSIFICATION, FABRICATION TECHNOLOGIES AND DRUG DELIVERY APPROACHES

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ABSTRACT

The purpose of this review article is to reflect the emerging importance of nanotechnology with emphasis on nanoparticles with a current research of scientific interest in biomedical, pharmaceutical, optical, biosensors and electronic areas. Nanoparticles are particles having a size range of 1 and 100 nanometers, defined as a small object behaving as a complete unit with respect to the drug transport and theraputic properties. Nanotechnology employing nanoparticles can be applied to any field of medicine, energy, electronics, manufacturing and materials, food agriculture, textiles, environment, renewable energy, quantum computers, UV protection and industrial catalysts. The nanoparticles are generally classified into the organic, inorganic and carbon based particles. Nanoparticles offer more effective and convinent routes of administration and used for drug delivery for treatment of cancer, diabeties, asthama and so on.

INTRODUCTION

Nanotechnology is a science that deals with matter at a scale of 1 billionth of a meter (i.e. 10 − 9 m = Nanoparticles are the most fundamental component in the manufacture of nanostructures and are much smaller than the world of everyday objects described in Newton's laws of motion, but larger than an atom or a simple molecule that is governed by quantum mechanics.1 nm) and is also a study of the manipulation of matter at the atomic and molecular scales.

Nanotechnologies are now commonly considered to have the ability to bring benefits to fields as diverse as drug creation, water decontamination, information and communication technology, and the manufacture of stronger and lighter materials. Nanotechnologies include the production and processing of nanometre-scale materials, either by scaling from a single group of atoms or by refining or reducing bulk materials.

Advantages of Nanoparticles

- ✓ Increased bioavailability
- ✓ Dose proportionality
- ✓ Decreased toxicity
- ✓ Smaller dosage form (i.e., smaller tablet)
- ✓ Stable dosage forms of drugs which are either unstable or have unacceptably lowbioavailability in non-nanoparticulate dosage forms.

Improved surface area of the active agent results in a faster breakdown of the active agent in an anaqueous environment, such as the human body. Faster breakdown is usually linked to higher bioavailability, lower doses of medications, lower toxicity.

Classification of Nanoparticles

Nanoparticles can be classified as follows

- ✓ Dimensions
- ✓ Based on carbon

Classification of Nanoparticles based on Dimensions

Nanoparticles can be classified on the basis of dimensions as

- ✓ one,
- ✓ two &
- ✓ three dimensions.

One Dimension Nanoparticles (1D NP's)

The term 'nano' has been allocated to refer to number 10-9, which means one billionth of any unit resulting in the creation of 1D NP as a thin film that has been used for decades in electronics, chemistry, pharmaceuticals and engineering[24]. Thin films or monolayers range from 1-100 nm in size due to the growing importance of NP in research and development and have a broad variety of possible applications in the field of electrical, optoelectronic, nanoscale LEDs, storage systems,

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chemical and biological sensors, fibre-optic systems, magneto-optic systems and optical devices. 1D NP has a significant effect on the development of nanowires, nanotubes, nanotubes, nanotubes, nanotubes and hierarchical nanostructures.

Two Dimension Nanoparticles (2D NP's)

2D nanostructures have two dimensions beyond the nanoscale range with specific shape-dependent characteristics and subsequent use as building blocks for the main components of nanodevices.2D nanostructures have been investigated and their potential applications in the field of sensors, photocatalysts, nanocontainers, nanoreactors and 2D structure models of other materials have been developed.

Nanostructures which exhibit 2D structure include

Carbon Nanotubes (CNT's)

CNTs are smooth cylindrical hollow fibers composed of a single sheet of pure graphite with a hexagonal network of carbon atoms, 1 nm in diameter and 100 nm in length, and are highly lightweight when hollow. Carbon nanotubes are solid, and nanotubes can be bent easily, and when released, they can jump back to their original form, but they didn't crack. Nanotubes exhibit in various shapes and structures, varying in length, thickness and number of layers, but the characteristics of nanotubes depend on the graphene surface.

CNTs are of several forms but typically classified as either single walled (SWNT) or multi-walled nanotubes (MWNT) where carbon nanotubes combine with their remarkable properties. SWNT can be formed by rolling a one-atom-thick graphite sheet into a smooth ring, while MWNT consists of several rolled graphite layers MWNT is known for its unique mechanical properties, strength, optical and thermal properties.

Three Dimension Nanoparticles (3D NP's)

The behavior of nanoparticles depends heavily on the sizes, shapes, dimensions and morphologies that are key factors for the efficiency and application of nanostructures and their similarity, and 3D NP's interest in research and medical science has grown over the last 10 years. Due to its broad range of applications in the field of catalysis, magnetic material, electrode material for batteries, transport of reactants and drugs, 3D nanoparticles are an important material.

Nanostructures which exhibit 3D structure can be categorised as

Structure of Nanoparticle

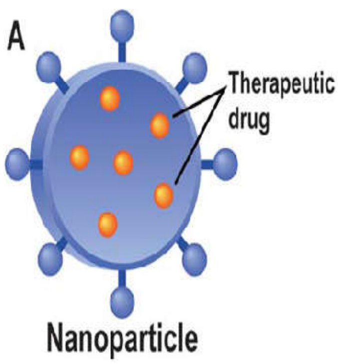
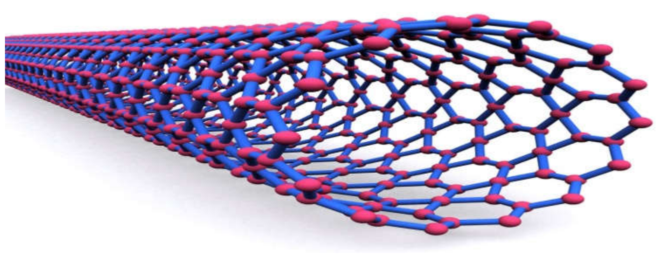


Figure-1



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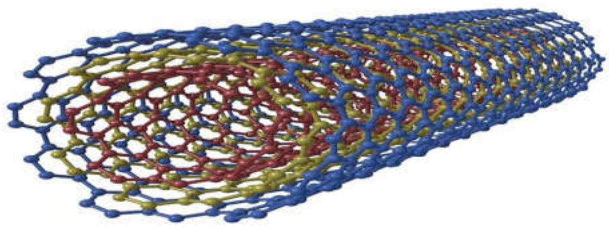

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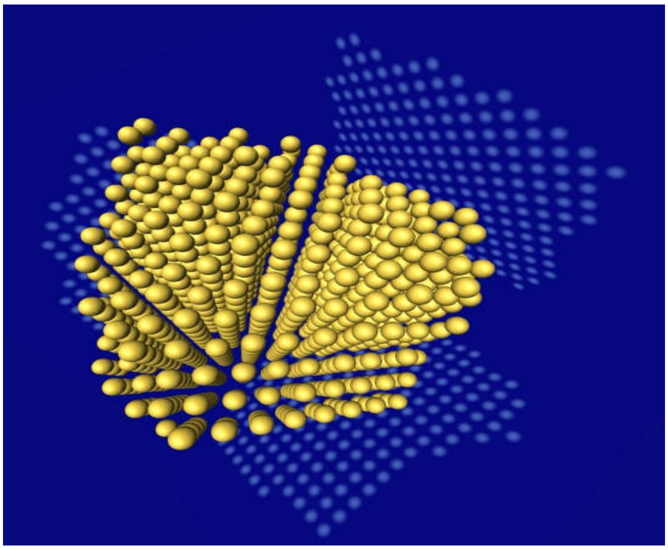

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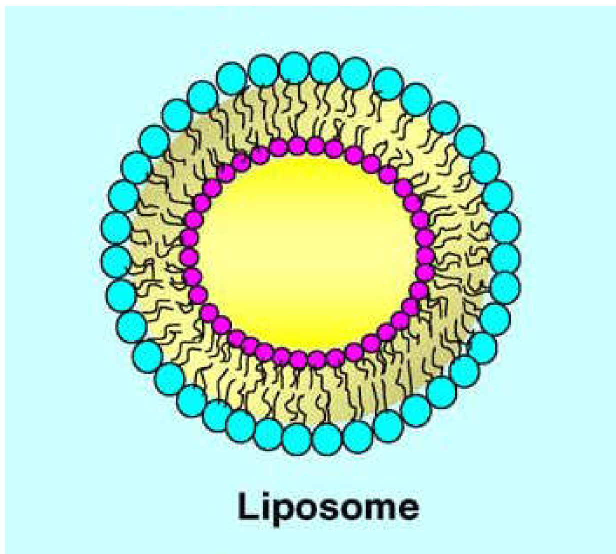

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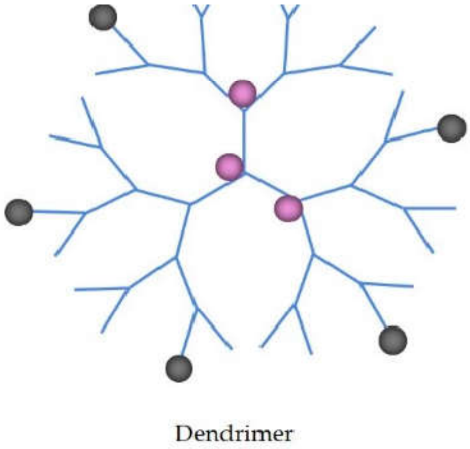

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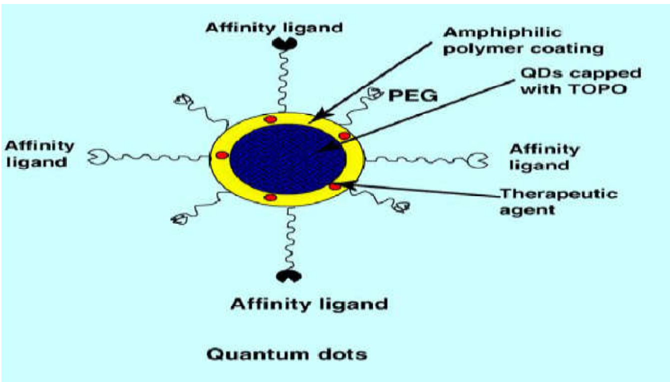

Figure-7

Fullerenes

Fullerenes are known by various names such as Carbon 60 Buckminsterfullerene Buckytubes and Buckyonions and Buckyballs. Carbon 60 is a hollow spherical cage composed of 20 hexagonal rings and 12 pentagonal rings with 28 to more than 100 carbon atoms resembling a soccer ball. Fullerenes exhibit unusual physical properties as they can be subjected to intense pressure and recover their original shape when the pressure is removed. These have an important use as lubricants, data storage and medical applications to bring biologically active molecules.

Classification of Nanoparticles based on Carbon

The nanoparticles are generally classified into the organic, inorganic and carbon based.

Organic nanoparticles

Dendrimers, rats, liposomes, ferritin, etc. are generally known as organic nanoparticles or polymers. Such nanoparticles are biodegradable, non-toxic, and certain particles, such as micelles and liposomes, have a hollow core often known as nanocapsules and are prone to thermal and electromagnetic radiation, such as heat and light. Those specific features make them the perfect alternative for the delivery of medicines. The drug carrying power, its stability and distribution mechanisms, whether trapped or adsorbed, determine their area of application and their effectiveness in addition to their usual characteristics such as scale, structure, surface morphology, etc.

Organic nanoparticles are most commonly used in the biomedical field, such as the drug delivery system, because they are effective and can also be injected into different sections of the body that is also known because targeted drug delivery.

Liposomes

As closed spherical vesicles, liposomes consist of a lipid bilayer that encapsulates an aqueous step in the storage of drugs. With the size (90150 nm) slightly larger than the standard concept (≤100 nm), liposomes do not constitute novel nanotechnology, but a significant portion of them are related to nanotechnology research. Forming lipid bilayers by hydrophobic activity, liposomes are considered to be excellent sites for the delivery of hydrophobic and hydrophilic drugs.

In particular, liposomes have a large persistence in the blood. It enables the efficient delivery of drugs to target tissues. All lipids have all fatty acid chain lengths, different head sizes and different melting temperatures. Commercial liposomes have already been licensed by the US FDA. A common example is doxorubicin capsulated liposomes (Doxil), which has a good antitumor effect against a wide variety of cancers.

Dendrimers

Dendrimers are a new class of polymeric materials which are highly branched, star-shaped macromolecules with nanometric dimensions.These differ from one another due to the various shapes and sizes of drimers with shielded interior cores with possible applications in both biological and material sciences, including drug delivery, gene transfection, catalysis, energy processing, photoactivity, molecular weight and size determination, rheology adjustment, and nanoscale science and technology.Dendrimers may be synthesized by divergent or converging approaches.

Quantum Dots (QD's)

Quantum dots are small particles or nanocrystals of semiconductor material ranging from 2 to 10 nm in diameters that show specific electronic properties and optical applications due to their vivid, pure colors and their ability to emit rainbow colors coupled with their high performance, longer lifespans and high extinction coefficient.

QDs can be prepared using various techniques including colloidal synthesis, manufacturing process or electrochemical techniques most widely used by cadmium selenide (CdSe), cadmium telluride (CdTe), indium phosphide (InP) and indium arsenide (InAs). QDs made up of two main shell and core sections where the shell and core were rendered using zinc sulphide (ZnS) CdSe, CdTe, InP or InAs.QDs are also small dots of (CdSe) ZnS. The small bits, that is. QDs can be applied anywhere in the body to biomedical applications in various areas of medical imaging, biosensors, drug delivery, DNA testing and target particular proteins or cells.

Inorganic nanoparticles

Inorganic nanoparticles are non-carbon particles. Nanoparticles based on metal and metal oxide are commonly known as inorganic nanoparticles.

Fabrication Technologies

A number of high-value-added nanotechnologies have recently been developed. Nanomaterials include the creation and use of structures and devices with organizational characteristics on an intermediate scale between individual atoms and less than 100 nm, where novel properties occur relative to bulk materials.

This implies the ability to create custom nanostructures and the different properties of the functions by manipulating them at the molecular level. Nanoparticles are one of the most important subgroups of nanomaterials since the manufacture of nanoparticles is an integral component of nanotechnology. Assembling nanoparticles and associated structures is also the most common way to produce nanostructured materials and build up bulk nanomaterials. Complete metal nanoparticle work began in the 1970s. It has been shown in this work that the melting point is decreased by the reduction of the metallic particle to the nanolevel.This is theoretically shown to increase the proportion of the surface area in the entire volume and to become unstable by reducing it to nanoscale. This is the plasmonic surface effect of gold and silver nanoparticles, resulting in red colors in goThat is, since the era of quantum mechanics, people have been using nanotechnology and nanoparticles. The history of nanoparticle metal is the oldest in nanotechnology.ld nanoparticle dispersions of glass and yellow colors for silver nanoparticle dispersions.

Bottom-up method

The simple or constructive approach is to build up material from atom to cluster to nanoparticle. Sol-gel, spinning, chemical vapor deposition (CVD), pyrolysis and biosynthesis are the most widely used bottom-up methods for nanoparticle development.

Sol-gel

Sol – a colloidal solution of solids suspended in a liquid form. A gel – a rigid macromolecule dissolved in a solvent. Sol-gel is the most preferred bottom-up method due to its simplicity and as most of the nanoparticles can be synthesised from this method. It is a wet-chemical process containing a chemical solution acting as a precursor for an integrated system of discrete particles.Metal oxides and chlorides are widely used precursors in the sol-gel cycle. The precursor is then distributed in the host liquid either by shaking, stirring or sounding, and the resulting solution comprises liquid and solid phases. The phase separation is carried out in order to extract nanoparticles by different methods, such as sedimentation, filtration, centrifugation and moisture, which are further extracted by drying.

Spinning

The synthesis of nanoparticles by spinning is achieved by a spinning disk reactor (SDR). It includes a spinning disk within a chamber / reactor where physical parameters such as temperature can be monitored. Generally, the reactor is filled with nitrogen or other inert gases, which extract oxygen within the reactor and prevent chemical reactions.The disk is rotated at different speeds where the liquid, i.e. the precursor and the water are pumped in. The rotating cycle allows the atoms or molecules to bind together and is precipitated, collected and dried. Various operating parameters such as liquid flow rate, disk rotation speed, liquid / precursor ratio, feed position, disk surface, etc. Determines the properties of the SDR-synthesized nanoparticles.

Chemical Vapour Deposition (CVD)

Chemical vapor deposition is the deposition of a thin layer of gaseous reactants to a substrate. Deposition is carried out in a reaction chamber at room temperature by the mixture of gas molecules. A chemical reaction occurs when the hot substrate comes into contact with the combined material. This reaction produces a thin film of the substance on the surface of the substrate that is recovered and used. The substrate temperature is a factor that affects the CVD. The advantages of CVD are very clean, uniform, hard and solid nanoparticles. The drawbacks of CVD are the specifications of special equipment and the gaseous by-products are highly toxic.

Pyrolysis

Pyrolysis is the most commonly used method for large-scale nanoparticle production in industries. It requires the burning of a precursor with a flame. The precursor is either a liquid or a gas that is pumped into the furnace at high pressure through a small hole where it burns. The combustion or by-product gasses are then treated as air for the recovery of nanoparticles**.** Some of the furnaces use laser and plasma instead of flame to achieve high temperatures for fast evaporation. The advantages of pyrolysis are simple, efficient, cost-effective and continuous processes with high yields.

Biosynthesis

Biosynthesis is a renewable and environmentally sustainable approach to the synthesis of non-toxic and biodegradable nanoparticles. Biosynthesis uses bacteria, plant extracts, fungi, etc. along with precursors to produce nanoparticles instead of traditional chemicals for bioreduction and capping purposes. Biosynthesized nanoparticles have special and improved properties that make their way into biomedical applications.

Top-down method

Top-down or destructive approach is to reduce bulk content to nano-scale particles. Mechanical milling, nanolithography, laser ablation, sputtering and thermal decomposition are some of the most commonly used methods of nanoparticle synthesis.

Mechanical milling

Of the various top-down methods, mechanical milling is the most commonly used for the processing of various nanoparticles. Mechanical milling is used for milling and post-analysis of nanoparticles during synthesis, where various elements are milled in an inert atmosphere.The effect factors in mechanical milling are plastic deformation, which leads to a particle shape, fracture leads to a reduction in particle size and cold-welding leads to an increase in particle size.

Nanolithography

Nanolithography is a study of the manufacture of nanometric scale structures with a minimum of one dimension in the range of 1 to 100 nm. There are various nanolithographic processes such as optical, electron beam, multiphoton, nanoprint and lithography scanning. Generally, lithography is the method of printing the appropriate shape or structure on a light sensitive material that selectively extracts a portion of the material to create the desired shape and structure. The key advantage of nanolithography is that it is generated from a single nanoparticle to a cluster of the desired shape and size. The drawbacks are the need for sophisticated equipment and the associated costs.

Laser ablation

Laser Ablation Synthesis in Solution (LASIS) is a common method for the production of nanoparticles from different solvents. The irradiation of a metal dissolved in a liquid solution by a laser beam condenses a plasma plume that creates nanoparticles. It is a robust top-down approach that offers an alternative to traditional metal-based chemical reduction to metal-based nanoparticle synthesis. As LASiS provides a stable synthesis of nanoparticles in organic solvents and water that does not require any stabilizing agent or chemicals, it is a 'natural' process.

Sputtering

Sputtering is the accumulation of nanoparticles on the surface by ejecting particles from the surface by colliding with ions. Sputtering is typically a deposition of thin layers of nanoparticles accompanied by annealing. The thickness of the coating, the temperature and length of the annealing, the form of substrate, etc. shall determine the shape and size of the nanoparticles.

Thermal decomposition

Thermal decomposition is an endothermic chemical decomposition created by heat that breaks down the chemical bonds in the compound. The exact temperature at which the element is chemically decomposed is the temperature of the decomposition. The nanoparticles are produced by decomposing the metal at specific temperatures undergoing a chemical reaction producing secondary products.

Metal Nanoparticle Fabrication Method

The method of breakdown is a technique for crushing bulk metal by mechanical grinding (MG) or mechanical milling (MM). Nano-level regulation of the particle diameter is very difficult, although it is an simple technique. In addition, there is a problem with the fact that impurities are easily combined by rigorous and long-term milling, but the procedure is deemed inappropriate because plasticity is converted in the case of soft metals.

The buildup process is a procedure used to combine metallic atoms and has a number of variations. This approach is loosely divided into chemical and physical processes. Here, a key technique for nanoparticle paste for wiring is added.

Drug delivery approaches of Nano Particles

Therapeutic Application of Nanoparticles

For tumor-targeting drug delivery

Nanoparticles are an perfect alternative for anticancer drugs with improved selectivity and decreased side effects on tumor cells. Nanoparticles charged with drugs can be designed to perform more complex, cooperative targeting functions. Drug delivery systems based on nanoparticles surmount the pharmacokinetic drawbacks associated with traditional formulations. Nanoparticle induces targeted death of cells by interfering with the proliferation of over-expressed proteins. As compared to the drug solution, etoposide or paclitaxel lipid nanocapsules displayed a 4- to 40-fold higher efficacy in a culture of cancer cells. The nanoparticulate system was also found to satisfy appropriate concentrations of intracellular drugs. Nanoparticles were found to be helpful in the targeted delivery of oligonucleotides to cancer cells. Nanoparticles also show the Chemotherapy's ability to overcome multidrug resistance. Iron oxide nanoparticles were found to act as both magnetic and photothermal agents resulting in apoptosis-mediated complete cell death. Treatment with the magnetic mode used significantly reduced tumor growth, Both types of treatment culminated in complete tumor regression. Because of their smallness and ease of bioconjugation, gold nanoparticles functionalized exclusively to associate with biomolecules of interest, and thus emerged as candidates for targeting cancer cells while at the same time exhibiting low cytotoxicity. Because of their local, continuous and long-term therapeutic delivery, soil fibroin-derived curcumin nanoparticles have been found to be highly effective against breast cancer. Because of their ability to demonstrate extended circulation time in the blood and improved tumor aggregation, polymeric micelles provide an important delivery mechanism for poorly water soluble anticancer drugs.

For brain targeting drug delivery

The blood-brain barrier (BBB) is a basic, special, and protective boundary that regulates blood and neural tissue flow between homeostasis, ion, and molecules. The specific features are its relatively impermeable endothelial cells with close junctions, enzyme activity and active efflux Transportation systems. The BBB therefore poses serious challenges to the delivery of drugs into the brain. The use of formulating nanoparticles can target specific transportation processes, can improve drug transportation through the BBB, and can target appropriate brain regions for regenerative processes. To enter the brain was developed the novel system of apolipoprotein E-functionalized nanoparticles. The mechanism worked by improving the binding of endothelial cells to low-density lipoprotein receptors on the BBB. The program was found to be reliably robust and able to handle drugs faster and more precisely via the BBB. Brain-targeted pegylated immune nanoparticles can now be synthesized using peptidomimetic antibodies to the transcytosis receptor BBB. These allow the delivery of active drug trapped in the brain parenchyma possible without causing BBB permeability alteration.

For oral drug delivery

It is the most popular medication administration form with a higher patient acceptance level. It is however still connected to a variety of obstacles, such as stomach acid pH and digestive enzymes. The distribution of nanoparticles in this method occurs by transcytosis and intracellular absorption, and transportation occurs via the intestinal mucosa lining epithelial cells and Peyer's patches. Sharma *et al*. researched that wheat germ agglutinin coated lectin-functionalized polynanoparticles could be used via the oral as well as aerosol route as possible drug carriers for antituberculous drugs. Peptide-liganded nanoparticles that be used in the gastrointestinal tract for precise targeting. VB12-dextran nanoparticle conjugate was found to be a viable carrier for the delivery of oral insulin in animal diabetes models. Nanoparticles have been tested to provide an effective method for the oral delivery of water-insoluble drugs, such as rapamycin.

For transdermal drug delivery

Delivery of topical or transdermal drugs is a challenge, as the skin serves as a natural barrier to defense. The defensive feature of the skin is due to the corneum layer of the epidermal stratum. This layer also controls conveying compounds to the skin. The nanoparticles serve as a reservoir and transmit lipophilic drugs to the stratum corneum. Polymeric nanoparticles increase skin permeation adhesivity and length of the medication. Compared to the aqueous solution of the drugs, the gelatinpilocarpine hydrochloride (HCl) or hydrocortisone nanoparticles developed using a method of desolations showed sustained drug release.

For parenteral drug delivery

Parenteral formulations, mainly intravascular, provide a benefit from direct drug administration into the bloodstream and rapid drug action initiation. Also, it is useful as passive delivery of drugs to inflammatory sites. MiR-34a and siRNAs were studied to coformulate in GC4-targeted nanoparticles Two intravenous injections demonstrated an improved anticancer effect when given regularly. By increasing the amount of medication entering the target site, this technology increases the delivery of drugs to macrophages, thus minimizing therapeutic dosage and adverse effects. Nanocrystalline clofazimine was found to be equally effective in reducing bacterial loads in the liver, spleen, and lungs of infected mice following i.v., when given as liposomal clofazimine. Control. The single subcutaneous dose of three front-line antitubercular drugs Poly DL-lactide-co-glycolide nanoparticles resulted in persistent plasma levels of therapeutic drugs in the lungs and spleen. Also, the mean residence time and absolute drug bioavailability were found to be increased many times, suggesting a greater chemotherapeutic efficacy.

For pulmonary drug delivery

The potential advantage of the drug's direct delivery to the lungs is that it decreases systemic toxicity and can achieve higher concentration of drugs at the site of infection The route provides a high surface area and quick absorption due to high vascularization of the lungs, and another advantage is that it circumvents the first pass effect. Its low mass median aerodynamic diameter, an important parameter for particle deposition in the lungs, is a potential obstacle for pulmonary nanocarriers. Poly DL-lactide-co-glycolide nanoparticles of three frontline antitubercular drugs form a sound foundation for enhancing medication bioavailability and the the dosing frequency for improved pulmonary tuberculosis management. It has been studied that the pulmonary delivery by micro sprayer of solid lipid nanoparticles of amikacin decreased its side effects in the kidneys and extended the dosing intervals due to the continued release of drugs. Gelatin and poly (lactic-co-glycolic) acid plasmid DNA nanoparticles encoding a yellow fluorescent protein or rhodamine-conjugated erythropoietin for inhalation delivery improve the protein expression length .

For ocular drug delivery

Because of the tear video, blood-aqueous barrier, and blood-retinal barrier, oculary drug transport barriers face the challenge. Nanoparticles have the advantage of showing enhanced topical passage of large, poorly water-soluble molecules such as glucocorticoid and cyclosporine, and are useful in diseases associated with immune and vision-threatening conditions. We high the dosage of the drug and the duration of administration when combined with controlled drug delivery. These also reduce side effects and help in the drug's site-specific targeting. Drug-loaded polymeric nanoparticles give many beneficial biological properties such as biodegradability, nontoxicity, biocompatibility and mucoadhesivity. When used for the treatment of eye inflammation, cyclosporine A nanoparticles have been shown to be a useful solution due to enhanced eye retention and bioavailability.

CONCLUSION

Nanoparticles provide a wide variety of applications in different fields of science and technology and is a highly appealing forum for study and creative studies. The emergence of nanotechnology increased our understanding of new hope which would lead to significant medical and clinical research growth. We are focused on a future of promising manufacturing and manipulation of new nanomaterials to be produced for individual and multimodal applications including biosensors for therapeutic delivery and pharmaceutical bioimaging. Nanotechnology is also currently developing technologies for the preparation and synthesis of nanoparticles in batteries, coal liquefaction, carbon nanopowders, carbon nanoparticles, using easy and renewable methods.

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