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NANOPARTICLES: POTENTIAL IN CANCER THERAPY

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ABSTRACT

Nanoscience is an emerging field that deals with interactions between molecules, cells and engineered substances such as molecular fragments, atoms and molecules. In terms of size constraints, the National Nanotechnology Initiative (NNI) defines nanotechnology in dimensions of roughly 1 to 100 nanometers (nm),1 but in boarder range it can be extended up to 1000 nm. Particles that fall within this range appear to be optimal for achieving a number of important tasks as nano-carriers, including the alteration of a drug's reactivity, strength, electrical properties, and ultimately, its behavior in vivo. Nanoparticles for the purpose of drug delivery are defined as submicron (< 1μm) colloidal particles. This definition includes monolithic nanoparticles (nanospheres) in which the drug is adsorbed, dissolved, or dispersed throughout the matrix and nanocapsules in which the drug is confined to an aqueous or oily core surrounded by a shell-like wall. Alternatively, the drug can be covalently attached to the surface or into the matrix. This review deals with the formulation approaches of nanoparticles and the potential use in the cancer therapy.

Key Words: Nanoparticles, Cancer, Nanotechnology, Nanomedicine

INTRODUCTION

Nanoscience is an emerging field that deals with interactions between molecules, cells and engineered substances such as molecular fragments, atoms and molecules. In terms of size constraints, the National Nanotechnology Initiative (NNI) defines nanotechnology in dimensions of roughly 1 to 100 nanometers (nm),1 but in boarder range it can be extended up to 1000 nm. Particles that fall within this range appear to be optimal for achieving a number of important tasks as nano-carriers, including the alteration of a drug's reactivity, strength, electrical properties, and ultimately, its behavior in vivo[1-3] .

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There is great interest in developing new nanodelivery systems for drugs that are already on the market, especially cancer therapeutics. Ideally, nanodelivery systems will allow for more specific targeting of the drug, thereby improving efficacy and minimizing side effects. By using nanotechnology in drug design and delivery, researchers are trying to push nanomedicine to be able to deliver the drug to the targeted tissue, release the drug at a controlled rate, be a biodegradable drug delivery system, and to be able to escape from degradation processes of the body. The prefix 'nano' derives from Greek word for 'dwarf'. Nanoparticles can range in size from 1 to 100 nm. One nanometer (nm) is equal to one billionth of a meter (1 nm = 10-9 m). This progressive continuous influx of novel technology platforms lead the potential to a positively healthcare impact at various important levels like detection of molecular changes responsible for disease pathogenesis, imaging and diagnosis of various diseases, drug delivery, multifunctional systems for combined therapeutic and diagnostic applications, vehicles to report the in vivo efficacy of a therapeutic agent and nanoscale enabling technologies which will accelerate scientific discovery and basic research.

Nanoparticles can enter into smallest capillary vessels due to their ultra-tiny volume size and avoid rapid clearance by phagocytes, so that, their duration in the blood stream is greatly prolonged. They can penetrate cell and tissue gaps to arrive at the target organs. They are able to show controlled release properties due to their biodegradability, pH, ion and temperature sensibility of materials. Presently, nanoparticles have been widely used to deliver antibiotics, anticancer agents, radiological agents, vaccines, proteins, polypeptides, antibodies, genes, and so on. Over the years, nanoparticle-based drug delivery and imaging systems have shown huge potential in biological, medical, pathological, and pharmaceutical applications.[2-4]

Nanoparticles for the purpose of drug delivery are defined as submicron (< 1μm) colloidal particles. This definition includes monolithic nanoparticles (nanospheres) in which the drug is adsorbed, dissolved, or dispersed throughout the matrix and nanocapsules in which the drug is confined to an aqueous or oily core surrounded by a shell-like wall. Alternatively, the drug can be covalently attached to the surface or into the matrix.[2]

CHARACTERISTICS OF NANOPARTICLES [5]

1. These are the small particles containing dispersed drug and having a diameter of approx 200 nm to 500 nm.
2. They are colloidal drug delivery system.
3. Nanoparticles can be target drugs to liver spleen and tumors cells
4. Because of their small size they can be injected by i.v route.
5. Nanoparticles are prepared using non toxic, biodegradable polymer.
6. Nanoparticles release the drug by diffusion or by combination of both.
7. They are having large surface area of the material,which dominates the contribution made by small bulk of the material.
8. The high surface area to volume ratio of nanoparticles provides a tremendous driving force for diffusion, especially at elevated temperatures.

ADVANTAGES

The following are among the important technological advantages of nanoparticles as drug carriers:

1. High stability (i.e., long shelf life);
2. High carrier capacity (i.e., many drug molecules can be incorporated in the particle matrix)
3. Feasibility of incorporation of both hydrophilic and hydrophobic substances.
4. Feasibility of variable routes of administration, including oral administration and inhalation. These carriers can also be designed to enable controlled (sustained) drug release from the matrix.
5. They are having larger surface area enabling absorption,by passing the first metabolism and extending a sustained release pool of the drug material.
6. The properties of nanoparticles enable improvement of drug bioavailability and reduction of the dosing frequency, and may resolve the problem of nonadherence to prescribed therapy, which is one of the major obstacles in the control of TB epidemics.

METHODS OF PREPARATION

1. Emulsification Solvent Evaporation

The most common method used for the preparation of solid, polymeric nanoparticles is the emulsification–solvent evaporation technique.[6-8]

- The preparation of particles by the classical method follows the general protocol of dissolving the polymer in a water immiscible, volatile organic solvent which is then emulsified with an aqueous phase to stabilise the system.
- The organic solvent is then evaporated inducing the formation of polymer particles from the organic phase droplets.
- The solvent evaporation method was described by Niwa et al and has since been widely used to prepare particles from a range of polymeric materials, particularly PLA and PLGA .
- This technique has been successful for encapsulating hydrophobic drugs. However, results for incorporation of hydrophilic bioactive agents have been poor.
- A modification of this procedure has led to the protocol favoured for encapsulating hydrophilic compounds and proteins viz., the double or multiple emulsion technique. First, a hydrophilic drug and a stabilizer are dissolved in water. The primary emulsion is prepared by dispersing the aqueous phase into an organic solvent containing a dissolved polymer. This is then reemulsified in an outer aqueous phase also containing stabilizer [9].

- From here, the procedure for obtaining the nanoparticles is similar to the single emulsion technique for solvent removal.
- The main problem with trying to encapsulate a hydrophilic molecule like a protein or peptide-drug is the rapid diffusion of the molecule into the outer aqueous phase during the emulsification.[10]

Several parameters can influence the properties of the particles produced, these parameters include:[6,9]

- nature of polymer
- polymer molecular weight
- nature of organic phase
- polymer concentration in the organic phase
- volume ratio of organic: aqueous phase
- nature of surfactant
- surfactant concentration and molecular weight
- stirring speed.
  - The main drawback of this method, besides the problem of preparing particles which are sub 200 nm in diameter is the need for the removal of excipients post production. Any residual organic solvents will have toxicological implications.
  - In addition the excess surfactant used is difficult to remove.
  - Another limitation is that surfactant must be present for preparation of nanoparticles in order to stabilize the system. Particles therefore cannot be produced naked and then post adsorbed with a surfactant. polyvinyl alcohol (PVA) is most frequently used as a stabilizing emulsifier to fabricate nanoparticles. However, PVA has some problems in that it remains at the surface of the nanoparticles and is difficult to remove subsequently. It is known that PVA existing on the surface of nanoparticles changes biodegradability, biodistribution, particle cellular uptake, and drug-release behaviour [10,11].

2. Interfacial Polymer Deposition (IPD) Method

- The technique involves addition of polymer, dissolved in a water miscible solvent (usually acetone) into an aqueous non solvent under stirring. [11-14]
- The non-solvent is usually an aqueous surfactant or drug solution without surfactant. The rapid diffusion of solvent into the aqueous phase causes a decrease in the interfacial tension between the two phases which, together with the increased interfacial surface area created by the turbulence, results in the formation of small droplets of organic solvent without the need for high shear mechanical stirring. [13]
- The solvent then diffuses further into the aqueous phase and water concurrently diffuses into the solvent droplets, resulting in the formation of polymer particles from the droplets. Particles are stabilised by a layer of polymer deposited at the interface.
- Thus, polymer properties may alter the physicochemical properties at the interface as explained in the Marangoni effect [12].
- Decreased miscibility of organic solvents with water is associated with an increase in their resultant interfacial tension and thus increases the size of the particles. The higher the viscosity of the organic phase, the greater the surface tension and hence the size of the particles. An increase in molecular weight of polymers is associated with a decrease in the number of end carboxyl groups and hence lowers the zeta potential of the resulting particles.
- Additives present in the formulation may also significantly affect this surface charge. Carla et al studied PLA nanocapsules in the presence and absence of lecithin. PLA with high molecular weight (109 and 251 kDa) yielded poorly stable nanocapsules larger in size and susceptible to aggregation.
- In the presence of lecithin, polymer charges were masked and zeta potential was determined by amount of lecithin present on the outer surface either mixed with or surrounding the polymer film [14].
- The presence of surfactant in the system acts as a stabilizer to prevent coalescence of the droplets. However Fessi et al reported that particles could be prepared using his method, in presence of water alone as the aqueous phase. Paclitaxel and mPEG-PLGA nanoparticles prepared without surfactant exhibited a smaller size and higher encapsulation efficiency. Surfactants like PVA were important to form nanoparticles in a technique like emulsification as here they prevent coalescence of newly formed droplets.

- However, Pluronic F-68 like surfactants may be added to improve steric stability of particles produced by the IPD method but are not primarily responsible for formation of particles [13,14].
- A distinct advantage of the IPD method is that there are no residual solvents left in the system, which is important from a toxicological point of view.
- Another advantage, from the viewpoint of using particles as a drug carrier, is that the particles produced are in the nanometer size range. Fessi et al prepared particles below 200 nm, and PLGA particles have been prepared which are sub 100 nm. In addition, the samples exhibit low polydispersity and the preparation of particles in the absence of surfactant allows the effect of post adsorption of surfactants. In particular, the in vivo behaviour of the coated and uncoated particles can be compared in order to determine the role of coating surfactant in preventing particle recognition by the Mononuclear Phagocytic System (MPS).

3. Spray Drying

- In the classical spray drying technique the polymer and drug are dissolved in an organic solvent and sprayed through a fine nozzle. Solid, spherical particles form on the immediate evaporation of the solvent.
- High temperatures are generally employed in this process, which can create problems, particularly in the encapsulation of peptides, and proteins that are easily denatured. Spray drying produces particles that are in the micrometer size range and hence will not be considered further here.

4. Salting Out

- Bindschaedler and co workers patented this technique in 1988 [15]. The technique involves the preparation of particles by an emulsification technique but avoids the use of chlorinated solvents.
- In brief, a saturated salt solution containing a stabilizing agent such as PVA is added under stirring to an acetone solution of the polymer. An o/w emulsion forms as the salt prevents the water and acetone mixing. Sufficient water is then added to allow the acetone to diffuse into the external aqueous phase and induce particle formation.
- Allemann et al used this technique to prepare Savoxepine nanoparticles. From the perspective of drug encapsulation, this method is most appropriate for water insoluble compounds, although the loading of water-soluble compounds can be improved by techniques such as altering the pH of the aqueous phase [16,17].
- Salts permeate biological systems and are crucial for life. However, salts also affect the stability of proteins. It has been reported since many years that neutral salts perturb various protein structures in ways that go well beyond simple, nonspecific charge effects [15,16].

5. Supercritical fluid expansion method (RESS)

- Recently the field of supercritical fluids has been investigated as an approach to the preparation of sub micron sized particles [18]. The rapid expansion of supercritical solutions consists in saturating a supercritical fluid with the substrate(s), then depressurizing this solution through a heated nozzle into a low pressure chamber in order to cause an extremely rapid nucleation of the substrate(s) in form of very small particles or fibres, or films when the jet is directed against a surface that are collected from the gaseous stream.
- The major merits of these processes include: production of organicsolvent free particles, mild operating temperatures for processing biological materials, and easier micro-encapsulation of drugs for controlled release of the therapeutic agents [19].
- Unfortunately, none of these techniques can produce small protein particles in the sub-micron range less than 300 nm having a very narrow size distribution.
- Fine particles of model compounds cholesterol acetate (CA), griseofulvin (GF), and megestrol acetate (MA) were produced by extraction of the internal phase of oil-in-water emulsions using supercritical carbon dioxide [20].

6. Complex Coacervation

- Complex coacervation is a phase separation process that spontaneously occurs when two oppositely charged polyelectrolytes are mixed in an aqueous solution. Compared to other methods, this process can be performed entirely in an aqueous solution and at low temperature and thus has a better

chance to preserve activity of the encapsulated substances.

- The colloidal particles produced are in the nanometer or micrometer scale depending on the substrates or the processing parameters used for example; pH, ionic strength and polyelectrolyte concentrations [19,20].
- The major drawback of this technique is that complex coacervates have low drug loading efficiency and poor stability. Therefore, crosslinking of the complex by chemical reagents such as toxic glutaraldehyde is necessary. Jiang B et al have reported a modified method called 'coprecipitation' where they chose positively charged and water-soluble Dextran as a coating layer [14].
- The process included precipitation of negatively charged Ibuprofen in a supersaturated solution and deposition of Dextran onto the precipitated Ibuprofen particles through electrostatic interaction.

FORMULATION OF NANOPARTICLES

The principle parameters of nanoparticles are their shape (including aspect ratios where appropriate), size, and the morphological sub-structure of the substance.[21,22]

Nanoparticles can be formulated as:

1. An aerosol (mostly solid or liquid phase in air)
2. A suspension (mostly solid in liquids) or
3. An emulsion (two liquid phases).

In the presence of chemical agents (surfactants), the surface and interfacial properties may be modified. Indirectly such agents can stabilise against coagulation or aggregation by conserving particle charge and by modifying the outmost layer of the particle. Depending on the growth history and the lifetime of a nanoparticle, very complex compositions, possibly with complex mixtures of adsorbates, have to be expected. In the typical history of a combustion nanoparticle, for example, many different agents are prone to condensation on the particle while it cools down and is exposed to different ambient atmospheres. Complex surface chemical processes are to be expected and have been identified only for a small number of particulate model systems. At the nanoparticle - liquid interface, polyelectrolytes have been utilised to modify surface properties and the interactions between particles and their environment. They have been used in a wide range of technologies, including adhesion, lubrication, stabilization, and controlled flocculation of colloidal dispersions.[22-25]

At some point between the Angstrom level and the micrometre scale, the simple picture of a nanoparticle as a ball or droplet changes. Both physical and chemical properties are derived from atomic and molecular origin in a complex way. For example the electronic and optical properties and the chemical reactivity of small clusters are completely different from the better known property of each component in the bulk or at extended surfaces. Complex quantum mechanical models are required to predict the evolution of such properties with particle size, and typically very well defined conditions are needed to compare experiments and theoretical predictions.

Applications of nanoparticles[25-28]

A list of some of the applications of nanoparticles to biology or medicine is given below:

1. Fluorescent biological labels
2. Drug and gene delivery
3. Bio detection of pathogens
4. Detection of proteins
5. Probing of DNA structure
6. Tissue engineering
7. Tumour destruction via heating (hyperthermia)
8. Separation and purification of biological molecules and cells.
9. MRI contrast enhancement
10. Phagokinetic studies

Nanoparticle-Based Targeted Delivery Systems in Cancer Treatment:[28-39]

The nano-range dimensions imbue nanoparticles with advantageous unique physical properties that facilitate immense possibilities in cancer therapeutics. Several new nanotechnologies, mostly based on nanoparticles, can facilitate delivering anticancer and imaging agents to kill cancerous cells in cancer therapy and cancer diagnosis respectively.

Liposomes

Liposomes are small artificial spherical vesicles composed of non-toxic phospholipids and cholesterol, which selfassociate into bilayers to encapsulate drugs, genes and other biomolecules on aqueous interior. Liposomes are within the size-range of 25 nm to 10 µm, depending on their preparation method various therapeutic agent loaded liposomes are being tested extensively as targeted delivery for

fighting against cancers. Liposomes of certain sizes, typically less than 400 nm, can rapidly penetrate tumor sites from the blood, but are kept in the blood stream by the endothelial wall in healthy tissue vasculature Liposomes use over expressions of perforation in cancer nanovusculature to produce effective therapeutic concentrations of anticancer agents at the tumor site. They have ability to limit and / or reduce some common side-effects like nausea, headache, vomiting, and hair loss. Several kinds of nanoscale liposomes, which are widely employed in cancer therapeutics.[28,29]

Polymeric Micelles

Polymeric micelles, actually supramolecular, selfassemblies of block copolymers, are spherical, colloidal nanoscale particles with unique core-shell structure.The inner core of polymeric micelles serves as a nanocontainer for hydrophobic molecules surrounded by an outer shell of hydrophilic flexible tethered strands of polymers. For the formation of polymeric micelles, drugs can be partitioned in the hydrophobic core and the micelle core acts as a drug reservoir. The outer hydrophilic layer forms a stable dispersion in aqueous media, which can be administered intravenously. Polymeric micelles have demonstrated high durability in the blood stream and effective tumor accumulation after their systemic administration. To support prolonged systemic circulation, polymeric micelles are designed to be biocompatible and thermodynamically stable in physiological solution21. The better thermodynamic stability of polymeric micelles indicates low critical micelle concentration (CMC), which prevents in vitro rapid dissolution. They are currently recognized as one of the most promising nanocarrier system for drug and gene delivery in the treatment of cancers. Polymeric micelle-based anticancer drug delivery has several benefits over other anticancer drug delivery systems like drug solubility, prolonged half-lives, efficient drug loading without any chemical modification of the parent drug, evading defenses, selective accumulation at the tumor site, and lower toxicity. They might show a tumor-infiltrating ability as well as controlled release of drugs, which is likely to be important for the complete eradication of tumor mass. Like liposomes, polymeric micelles can be modified using piloting ligand molecules for targeted delivery to specific cancer cells and pH-sensitive drugbinding linkers can be added for controlled drug delivery. Multifunctional polymeric micelles may be designed and developed to facilitate simultaneous drug delivery and related imaging in cancer therapeutics.[29,30]

Nanosystems

Novel nanosystems can be programmed to alter their structure and properties during the drug delivery process, providing more efficient extra- and intra-cellular delivery of encapsulated anticancer agents. This is achieved by molecular sensors that respond to physical and / or biological stimuli, including changes in pH, enzymes, temperature or red-ox potential. Biological drugs can be delivered with programmed nanosystems including DNA, SiRNA and other nucleic acids.[30]

Nanoshells

Nanoshells are another attractive platform for cancer diagnosis and cancer therapy. They are mainly metal based nanoparticles. Nanoshells have a core of silica with a top layer of gold..

By changing the thickness of the gold layer, the alteration in optical absorption properties of these nanoshells is possible when radiated with near-IR laser. The near–IR laser illuminates the tissue and the light will be absorbed by nanoshells to generate intense heat. Thus, nanoshells get active to destroy only the cancerous cells and tumors thermally without damaging the surrounding healthy cells. Antibodies and/or therapeutic anticancer agents can be attached to their surfaces, enabling those nanoshells to target cancerous cells or tumors8. The gold nanoshellantibody complex can be used to ablate breast cancer cells. Gold nanoshells have been used in rapid immunoassays, capable of detecting analyte within complex biological media without any sample preparation. Aggregation of antibody-nanoshell conjugates with extinction spectra in the near-IR is monitored spectroscopically in the presence of analyte.[30-33]

Fullerene-based Derivatives

Fullerene-based derivatives are recently proposed in nanopharmaceutical formulations and have found various applications in cancer therapy. They are crystalline particles in form of carbon atoms. The most abundant form of fullerenes is Buckminster fullerenes (C 60) with 60 carbon atoms and arranged in a spherical structure with truncated icosahedron shape, resembles that of a soccer ball (bucky ball), which contains 20 hexagons and 12 pentagons.

Other fullerenes are C70, C76, C78, C84, C86, C540. Fullerene cages are about 0.7 to 1.5 nm, in diameter and the cage structure of fullerene is ideal for attaching anticancer agents or even radiological agents to increase treatment efficacy for killing as well as diagnosis of cancerous cells. Their good stability make them unique candidates for safely delivering highly toxic substances to tumors. Both empty and metallofullerenes have low in vitro and in vivo cytotoxicity. Endohedral metallofullerenes have shown their potential application in diagnosis. Water solubilized forms of metallofullerenes are being used as magnetic resonance imaging (MRI) contrast agents, X-ray contrast agents, and

radiopharmaceuticals. The advantage of fullerene-based therapies over other targeted therapies is likely to be fullerene potential to carry multiple drug pay-loads such as taxol and other chemotherapeutic agents.[33-35]

Carbon Nanotubes (CNTs)

Carbon nanotubes consist of exclusively carbon atoms arranged in a series of condensed benzene rings rolled-up into tubular architecture .Carbon nanotubes belong to the family of fullerenes, the third allotropic form of carbon along with graphite and diamond, have been recently developed to use in cancer therapeutics. Tumor targeting carbon nanotubes have been synthesized covalently attaching multiple copies of tumor specific monoclonal antibodies (MABs), radiation ion chelates and various fluorescent probes. The surface of carbon nanotubes can be modified with proteins for cellular uptake. Then they are heated up upon absorbing near-IR light wave. When exposed to near-IR light carbon nanotubes quickly release excess energy as heat (~70ºC), which can kill cancerous cells. The approach of coating the surfaces of tiny carbon nanotubes with MABs is used towards developing a biosensor for breast cancer detection, by functionalizing the carbon nanotubes with antibodies that are specific to cell surface receptors of breast cancer cells. They often further potential of killing cancerous cells over a wide area that may serve the biological cell-signaling pathway, thus promoting cancer remission.[32-36]

Dendrimers

Dendrimers were first described by Vogtle et al. They are perfect monodisperse macromolecules with regular and highly branched 3-D architecture. Dendrimers consist of a series of chemical shells, namely an interior small core; interior layers (generations) composed of repeating units, radically attached to the interior core and exterior (terminal functionality) attached to the outermost interior generations. The emerging role of dendrimers for anticancer therapies and diagnostic imaging has highlighted the advantages of these well-defined materials as the newest class of macromolecular nanoscale delivery devices. Dendrimers used in drug delivery and imaging are usually 10 to 100 nm in diameter with multiple functional groups on their surfaces rendering them an ideal carrier systems for targeted drug delivery. Scientists and researchers have fashioned dendrimers into an effective and sophisticated anticancer therapy machines carrying 5 important chemical tools:

(i) a molecule designed to bind cancerous cells and tumors
(ii) fluorescence upon locating genetic mutations
(iii) to assist in imaging tumor shape using Xrays
(iv) carrying therapeutic agents released on demand signaling when cancerous cells are finally dead

Antibody-dendrimer conjugates have been used for radiolabelling with minimum loss of immunoreactivity. Research on dendrimer-based delivery applications shows that anti-PSMA antibody (J 591) when conjugated with a dendrimer containing fluorocrome, can be used for targeting prostate cancer and imaging. Again, the controlled surface modification followed by the conjugation of folate and fluoresin moieties on the surface of dendrimer, is shown to yield molecules capable of tumor targeting through folate receptor.[35-39]

Quantum Dots (QDs)

Quantum dots, semiconductor nanocrystals have emerged with promising applications for early detecting of cancers and determining the efficacy of tumor therapies. They are ranging from 2 to 10 nm in diameter and possessing unique tunable targeting properties. Quantum dots can be prepared from semiconductor materials by electrochemistry or by colloidal synthesis. The common quantum dots are cadmium selenide (CdSe), cadmium telluride (CdTe), indium phosphide (InP), indium arsenide (InAs) etc14. Depending on their size, they can excite at appropriate wavelengths. They can absorb white light and re-emit it within nanoseconds with different combinations of particles. Thus, various quantum dots can emit different fluorescent light (400 to 1350 nm). They are used as fluorescent probes in diagnostic imaging and therapeutics. But unfortunately, under some conditions, quantum dots become cytotoxic. Modification of quantum dots by PEG glycation and micelle encapsulation may limit cytotoxicity. Research on quantum dots is continuing to find biocompatible and effective quantum dots.[37,38]

Gold Nanoparticles (GNPs)

Gold nanoparticles have recently emerged as an attractive candidate in cancer therapy as targeted delivery systems. They have been also used as contrast agents in vitro based on their ability to scatter visible light. Gold nanoparticles exploit unique physical and chemical properties for transporting and unloading pharmaceuticals. They are inert and non-toxic and have shown to have 600 times more absorption in cancer cells than normal human cells. The ability of gold nanoparticles to bind strongly with various biological molecules has been utilized to target tumors by tagging. Researchers have developed gold nanoparticles-based ultra-sensitive detection systems for DNA and protein markers associated with many forms of cancers using these8.

It was demonstrated that systemically delivered gold nanoparticles-tumor necrosis factor (GNPTNF) accumulated in tumors in a subcutaneous model of colon cancer.[32-36]

Solid Lipid Nanoparticles (SLNs)

Solid lipid nanoparticles hold significant promise in cancer treatment. They are particles of submicron size (50 to 1000 nm) made from lipids that remain in a solid state at room as well as body temperature. Since early 1990's, a number of solid lipid nanoparticle-based systems for the
delivery of anticancer agents have been successfully formulated and tested. Various anticancer agents like doxorubicin, daunorubicin, idarubicin, pacltitaxel, camptothesins, etoposide, etc have been encapsulated using this nanotechnological approach. Several obstacles frequently encountered with anticancer agents, such as a high incidence of drug resistant tumor cells can be
partially overcome by delivering them using solid lipid nanoparticles.[33,34]

Nanowires

Nanowires are glowing silica wires in nanoscale, wrapped around single strand of human hairs. They are about five times smaller than virus and several times stronger than spider silk8. Nanowire based arrays have significant impact for early diagnosis of cancer, and cancer treatment. The nanowire-based delivery enables simultaneous detection of multiple analytes such as cancer biomarkers in a single chip, as well as fundamental kinetic studies for biomolecular reactions. Protein coated nanowires have potential applications in cancer imaging like prostate cancer, breast cancer and ovarian malignancies.[33,37]

Magnetic nanoparticles

Magnetic nanoparticles are able to target cancerous cells and have potential use in cancer therapeutics. Themagnetic effect of magnetic nanoparticles is due to super paramagnetic iron oxides, typically Fe2O3, and Fe3O4, which do not retain their magnetic property when removed
from the magnetic field. Their paramagnetic characteristics have made them good candidate the destruction of tumors in vivo through hypothermia. Polymer coating on the surface of magnetic nanoparticles prevents their cytotoxicity and allows them to move freely in the organism without any reaction or adhesion.[34,38]

CONCLUSION

In this review we have explored nanoparticles serving as agents of novel antineoplastic treatments We have witnessed the use of nanoparticulate technology in developing a new generation of more effective cancer therapies capable of overcoming the many biological, biophysical, and biomedical barriers that the body stages against conventional cancer therapies.. Their inherently small size and modifiability are allowing for innovative controlled and targeted techniques resulting in a drastic reduction in anticancer treatment side effects and increased antitumor efficacy. Combination nanoparticulate therapies have the potential to destroy cancers in their earliest stages in custom tailored treatments utilizing imaging to view treatment progress and success. Anticancer nanoparticulate technology is being developed with the goal to minimize side effects for nanoparticulate treatments by relying on nanoparticles that are perfectly engineered to attack cancer in a decisive manner with healthy tissues suffering no undesirable consequences at the initial stages of cancer cell development.

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