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Nanoparticles Use in Cancer Therapy

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Abstract: *Cancer is one of the major causes of mortality worldwide and advanced techniques for therapy are urgently needed. According to huge studies and the best use of nanoparticles for cancer treatment the nanoparticle is play a consequent role as a drug delivery system. Nanoparticles generally divided into 3 major parts inorganics, organic, hybrid. Due to their small structure, they effectively deliver drug and achieve EPR effect. Among these gold nanoparticles are found successful agent for cancer therapy. Mesoporous Silica Nano-particle become novel and promising drug delivery vehicle. carbon nanotubes quantum dots, organic nanoparticles and hybrid nanoparticles also play a important role in cancer therapy. This review highlights mainly the different types of Nanoparticles in cancer therapy their synthesis and targeting atsite*

Keywords: Nano Particle, Inorganic and Organic Nanoparticle, Gold Nanoparticles, Liposomes, Quantum Dots, Np in Cancer Therapy, Carbon Nanotubes, Mesoporous Silica Nanoparticle, Polymeric Nanoparticle, Polymeric Micelles, Dendrimers, Hybrid Nanoparticles, Testing, Passive and Active Targeting

I. INTRODUCTION

The nanoparticles are less in diameter. Can't see by naked eyes particle size Nano particles exhibit their unique properties for cancer treatment. Nanoparticles as a drug delivery vehicle were first advancement in the late 1960s by sister and co-workers in the previous 1970s. The Hydrogels they are made up of water-insoluble acrylamide and potassium acrylate nanoparticles were prepared. Sheffield et al. advancement in a process for production of radiolabelled albumin particle for in nuclear medicine. wider et al incorporated magnetic particles into thenanoparticles for targeting of these particles by means of magnetic field.

Nanoparticles are of 3 types as follows: -

- Inorganic nanoparticles: -
- Gold nanoparticles: -
- Mesoporous Silica nanoparticles: -

Organic nanoparticles are tiny synthesis of collecting of molecules or polymers Such as polymeric, liposome, and virus like particle. Inorganic nanoparticles are innocuous, water loving, biomaterials used in a medical device, constant compared to organic material. Such as gold, nanoparticles, Having pores of a size between 2 and 50 manometers of silica nanoparticles. Hybrid nanoparticles are a type of materials that mostly formed from several different components has at least one dimension to the nanoscale. that's made up of two or more inorganic compounds, or two or more organic compounds. Active targeting best uses the expression of surface receptors on cancer cells by act targeting ligands that can bind to receptors. Passive targeting of NPs is highly developed by the increase permeability and retention effect which best use increase the vascular permeability and weakened lymphatic drainage of cancer cells and make it possible NPs to targeting cancer cells. Nanoparticles have been proven to be useful as drug delivery vehicle. many uses for nanoparticles drug delivery systems exist, including gene therapy, cancer therapy, AIDs therapy and radiations. Cosmetic manufacturers use nanoscale size ingredients to provide better UV protection, deeper skin penetration, long-lasting effects, increased colour, finish quality, and many more. lymphoscintigraphic studies, sentinel lymph node mapping, blood pool imaging, and protein-losing gastroenteropathy.

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Inorganic nanoparticle

Inorganic nano-particle contains metal or non-metal element, or take the form of an oxide, hydroxide, chalcogenide or phosphate compound. There are four types of inorganic based nano particles i.e. gold nanoparticles, mesoporous silica nano particles, copper nanoparticles, carbon nanotubes magnetic nanoparticles, quantum dots. Using inorganic nano-particle as co-delivery carriers to make necessary nanoparticle modification for efficient and successful co-delivery two or more physical and chemical modification can be used. FDA and EMA have only approved another as a drug delivery system for limited anticancer therapy for prostate and pancreatic cancer. None of the inorganic nanoparticles for have been approved for co-delivery because they have not yet crossed the first clinical stages. Recently gold and mesoporous silica nanoparticles are receiving greatest attention in various experimentation and development.

Gold nanoparticles

Gold nanoparticles are newly found as successful agent for cancer therapy they are investigated as drug carrier photothermal agent contrast agent and radiosensitizers. Gold nanoparticles are discovered in 19th century by Michel faraday. AuNPs are less toxic and can enter tumor cells via enhanced permeability and retention (EPR) effect. AuNPs are easy to synthesize, cost-effective, have a large surface-to-volume ratio, penetrate the biological tissues, and have inherent biocompatibility. In past couple of decades AuNPs were surface functionalized by various molecules such as peptide, folates, ligands and antibiotics for target delivery at local tumor sites.

AuNPs were attached to chemotherapeutic drugs and drug-loaded stimuli-sensitive polymeric nanoparticles for stimuli-responsive drug release. Targeted delivery of AuNPs to the tumor site, stimuli-responsive drug release, biocompatibility, improved stability, and solubility of drugs loaded on AuNPs are suitable candidates for cancer theragnostic with reduced morbidity and mortality risks. AuNPs also generate heat when exposed to NIR laser light, which makes them suitable for the photothermal treatment of cancer. In addition, AuNPs have are nonimmunogenic by nature. AuNPs are used in cancer diagnosis by magnetic resonance imaging, Photoacoustic imaging, Positron emission tomography imaging, Fluorescence imaging.

Mesoporous Silica Nanoparticles

Synthesis of monodispersed silica particles involves a soul-gel method that was reported for the first time by Stöber et al. in 1968. Such method involves the hydrolysis of tetra alkyl silicates in an alcohol and water solution using ammonia as a catalyst, to originate non-porous silica particles that can be engineered to possess sizes in the range of a few nanometres to some microns.Mesoporous silica nanoparticles (MSNs) have become apparent as a promising and novel drug vehicle due to their unique mesoporous structure that preserving a level of chemical stability, surface functionality and biocompatibility ensure the controlled release, and target drug delivery of a variety of drug molecules.Mesoporous nanoparticles have a solid framework with porous structure and large surface area, which allow the attachment of different functional group for targeted the drug moiety to a particular site. Chemically, MSNs have honeycomb-like structure and active surface.Surgery, radiotherapy, chemotherapy or their combination are still the most used therapeutic approaches used for cancer therapy.

NP in cancer therapy

NPs with a diameter range of 10 to 100 nm are generally considered suitable for cancer therapy, as they can effectively deliver drug and achieve enhanced permeability and retention (EPR) effect. Their size should not be less than 10nm Because smaller particles easily leaked from the normal vasculature. If they are larger then 100nm they easily get cleared from circulation by phagocytes. The drug loaded formulation that release Higer Dose of drug for prolonged period of time completely inhibit the growth of tumor cells. Many times, chemotherapy fails to cure cancer because some tumor cell develop Resistance to multiple anticancer Drugs. The EPR lbp, while useful for targeting newly vascularized tissues, can be undesirable if it reduces the half-life of the nanodrug. An efficient way to reduce this effect is to cover the nanoparticle with a layer of PEG. This procedure is a technology customized under the name STEALTH®.PEG is a special polymer use to cover NPs Because it is FDA approved, water soluble, have low immune response and biocompatible. NPs are generally engineered in such way that they only bind with cancer cells not to neigh boring healthy cells. They generally enter into tumor cells and goes towards very Centre of the cells. These n

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nanoparticle's fuses with endosome which is part of digestive system of the cell. There is acidic medium present in endosome where nanoparticles release drugs. In this way drug spread all over the cell and affects cell.

Carbon Nanotubes

Carbon nanotubes (CNTs) are cylindrical molecules that consist of rolled-up sheets of single-layer carbon atoms (graphene). They can be single-walled (SWCNT) with a diameter of less than 1 nanometer (nm) or multi-walled (MWCNT), consisting of several concentrically interlinked nanotubes, with diameters reaching more than 100 nm.Carbon nanotubes (CNTs) are among the most interesting nano vectors currently under investigation. Functionalized CNTs have shown great promise as novel delivery systems based on their ability to cross biological barrierCNTs that are not explored therapeutically, we can begin to learn lessons and determine design parameters to be implemented in the development of CNT constructs for cancer therapy.Moreover, it is also becoming apparent that chemically functionalized CNTs and those suspensions exhibiting best aqueous dispersibility and stability in physiological environments can allow development in biomedical applications.

Quantum dots

Quantum dots (QDs) are semiconductor particles a few nanometres in size, having optical and electronic properties that differ from those of larger particles as a result of quantum mechanics. They are a central topic in nanotechnology and materials science. QDs have a higher potential to degrade than conventional optical imaging tests, allowing them to track cell measurements for a longer time and give fresh information on subatomic collaborations. There is a great significance of QDs in the treatment and diagnosis of many malignancies: Apart from the benefits, this study discusses the features, mechanism of action, different schemes of QDs, function of QDs in early diagnosis, tumor imaging (in vitro and in vivo), targeted drug administration, photodynamic therapy, and so on. In addition, cytotoxicity studies of QDs in cancer therapy are being pursued. Several studies used Quantum dots to develop in vitro fluorescent images of human malignant cells from melanoma, ovarian, breast, pancreatic, glioblastoma, ovarian epidermoid, lung, hepatocellular, and adenocarcinoma cancers.

Organic nanoparticles

Organic nanoparticles are small particles made of aggregated molecules or polymers. These materials are of broad interest owing to ease of fabrication and wide range of aggregated structures that can be achieved. Organic nanoparticles (NPs) are present in the nature and also, they form part of many industrial products. There are many types of organic nanoparticles: - tA polymeric nanoparticle, liposomes, c micelles, d dendrimers, and e solid lipid nanoparticles.

Polymeric nanoparticles

Polymeric nanoparticles (NPs) are particles within the size range from 1 to 1000 nm and can be loaded with active compounds entrapped within or surface-adsorbed onto the polymeric core. Polymeric nanoparticles being used in cancer chemotherapy have significant advantages compared to the conventional drug in terms of controlled mode of action, different administration methods to the tumor site, both organic and inorganic drug delivery. The use of PNPs showed potential, which facilitates targeting of cancer cells, demonstrating its efficacy to enhance local drug concentration and improving chemotherapy. Polymeric NPs have shown their capability to manipulate particles, target malignant tissues, control the release of drugs, and minimize the uptake of the drug by normal cells. Besides, they may enhance the treatment efficacy of chemotherapy medicine and reduce their toxic effects.

Liposomes

Liposomes are small artificial vesicles of spherical shape that can be created from cholesterol and natural non-toxic phospholipids. Liposomes are used for drug delivery due to their unique properties. In fact, they can contain a wide variety of hydrophilic and hydrophobic diagnostic or therapeutic agents, providing a larger drug payload per particle and protecting the encapsulated agents from metabolic processes. Liposomes overcome the limitations of conventional chemotherapy by improving the bioavailability and stability of the drug molecules and minimizing side effects by site-

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specific targeted delivery of the drugs. Liposome-mediated immunotherapy can be potentially used to mediate efficient delivery to target sites and provoke robust immune responses. Since the tumor immunity plays such an important role in tumor development, progression, and metastasis, it offers opportunities for liposomes to improve the efficiency of cancer treatment.

Polymeric micelles: -

Polymeric micelles are nanoscopic core/shell structures formed by amphiphilic block copolymers.Polymeric micelles are formed from self-aggregation of amphiphilic block/graft co-polymers with the hydrophobic part of the polymer on the inside (core) and hydrophilic on the outside (shell).In drug delivery, PM are classified under the "Nano carriers". A polymeric micelle usually consists of several hundred block copolymers and has a diameter of about 20-50 nm. Polymeric micelles are extensively utilized in pre-clinical studies for delivering poorly soluble chemotherapeutic agents in cancer. Their nano-size enables them to accumulate to the tumor microenvironment via the Enhanced Permeability and Retention (EPR) effect. Moreover, the stimuli-sensitive breakdown provides the micelles an effective means to deliver the therapeutic cargo effectively.

Dendrimers: -

Dendrimers are highly ordered, branched polymeric molecules. Synonymous terms for dendrimer include arborols and cascade molecules. Typically, dendrimers are symmetric about the core, and often adopt a spherical three-dimensional morphology. Dendrimers are used for their unique properties as carriers of other molecular structures, in order to improve the activity and efficiency of an active drug molecule and also to reduce its toxicity. Examples of several types of dendrimers include those which have immense applications in drug delivery including poly(amidoamine) (PAMAM) dendrimers, poly (propylene imine) (PPI) dendrimers, polyether-copolyester (PEPE) dendrimers, PEGylated dendrimers, peptide dendrimers, etc. Dendrimers are successfully explored for the delivery of anticancer drug as well as for theragnostic applications in cancer therapy. Dendrimer improve the solubility of poorly soluble anti-neoplastic drugs. Multiple functional groups are present on outer surface of dendrimers, which can be used to attach vector devices for targeting to particular site in the body. Presence of numerous peripheral functional groups on dendrimers is responsible for tumor cell-specific delivery.

Hybrid nanoparticles: -

Hybrid nanomaterials are defined as unique chemical conjugates of organic and/or inorganic materials. That is, these are mixtures of two or more inorganic components, two or more organic components, or at least one of both types of components.There are three types of hybrid nanoparticles are as follows 1-Lipid-polymer hybrid NPs, 2-Organic-inorganic hybrid NPs.

a: - Liposome-silica hybrid b: Chitosan-carbon nanotubes hybrid 3-Cell membrane coated NPs a: Leukocyte membrane coated.

b: - Cancer cell membrane c: - coated Dual-membrane coated.

They possess several interesting properties that make them potential nanocarriers for anticancer drug delivery: -

(1) compositional and structural tunability allows for the fine tuning of physicochemical properties of the nanoparticles;

(2) highly porous and oriented structures accommodate efficient loading of diverse cargos.

(3) intrinsic biodegradability due to the relatively labile metal-ligand bonds.Lipid-polymer hybrid NPs, which consist of an inner polymeric core and a lipid shell, have been demonstrated to be a promising drug delivery platform in the treatment of pancreatic cancer, breast cancer, metastatic prostate cancer. This type of hybrid NPs combines the high biocompatibility of lipids with the structural integrity provided by polymer NPs, and are therefore capable of encapsulating both hydrophilic and hydrophobic drugs in order to achieve a better therapeutic effect.

TARGETING

Passive targeting: -

Passive targeting is achieved by embody the therapeutic agent into a macromolecule or nanoparticle that passively extend the target organ. In passive targeting, the drug's success is directly related to circulation time. This is achieved

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by clicking the nanoparticle with some sort of coating. Several substances can achieve this, with one of them being polyethylene glycol (PEG). By adding PEG to the surface of the nanoparticle, it is rendered hydrophilic, thus allowing water molecules to bind to the oxygen molecules on PEG via hydrogen bonding.

The result of this bond is a film of hydration around the nanoparticle which makes the substance antiphagocytic. The particles obtain this property due to the hydrophobic interactions that are natural to the reticuloendothelial system (RES), thus the drug-loaded nanoparticle is able to stay in circulation for a longer period of time. To work in conjunction with this mechanism of passive targeting, nanoparticles that are between 10 and 100 nanometres in size have been found to circulate systemically for longer periods of time.

Active Targeting: -

Active targeting of drug-loaded nanoparticles enhances the effects of passive targeting to make the nanoparticle more specific to a target site. There are several ways that active targeting can be accomplished. One way to actively target solely diseased tissue in the body is to know the nature of a receptor on the cell for which the drug will be targeted to. Researchers can then utilize cell-specific ligands that will allow the nanoparticle to bind specifically to the cell that has the complementary receptor. This form of active targeting was found to be successful when utilizing transferrin as the cell-specific ligand. The transferrin was conjugated to the nanoparticle to target tumor cells that possess transferrin-receptor mediated endocytosis mechanisms on their membrane. This means of targeting was found to increase uptake, as opposed to non-conjugated nanoparticles. Another cell-specific ligand is the RGD motif which binds to the integrin. This integrin is upregulated in tumor and activated endothelial cells. Conjugation of RGD to chemotherapeutic-loaded nanoparticles has been shown to increase cancer cell uptake in vitro and therapeutic efficacy in vivo. Active targeting can also be achieved by utilizing magneto liposomes, which usually serves as a contrast agent in magnetic resonance imaging. Thus, by grafting these liposomes with a desired drug to deliver to a region of the body, magnetic positioning could aid with this process. Furthermore, a nanoparticle could possess the capability to be activated by a trigger that is specific to the target site, such as utilizing materials that are pH responsive. Most of the body has a consistent, neutral pH. However, some areas of the body are naturally more acidic than others, and, thus, nanoparticles can take advantage of this ability by releasing the drug when it encounters a specific pH.

Another specific triggering mechanism is based on the redox potential.One of the side effects of tumors is hypoxia, which alters the redox potential in the vicinity of the tumor. By modifying the redox potential that triggers the payload release the vesicles can be selective to different types of tumors. By utilizing both passive and active targeting, a drug-loaded nanoparticle has a heightened advantage over a conventional drug. It is able to circulate throughout the body for an extended period of time until it is successfully attracted to its target through the use of cell-specific ligands, magnetic positioning, or pH responsive materials. Because of these advantages, side effects from conventional drugs will be largely reduced as a result of the drug-loaded.

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