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NANOPARTICLES: A NOVEL DRUG DELIVERY FOR CANCER THERAPY

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ABSTRACT

The word nano comes from Greek νᾶνος,which means"dwarf".[1] Having particles of size 1 billionth of a meter (<100 nm).The main advantage is that at this size range, nano-particles having a maximum surface:volume ratio, which makes them appropriate for surface functionlization and incorporation of a chemotherapeutic load.[2] In last years different types of nano-particle technologies developed for cancer treatment to improve the therapeutic efficacy and safety for anticancer drugs.[3] Nano technology has the potential to major change the early diagnosis, treatment, and monitoring the progress of the disease.By using nano-techniques the possibility to work at the same scale of several biological processes, cellular mechanisms, and organic molecules. The nano particle like nano-meters and nano-tubes, technologies could be used to administer drugs more precisely.this techniques target specific cells in a patient suffering from cancer or other life-threatening conditions. This review paper describes the role of multi-functional nano-particle in diagnosis and treatment of different types of cancer.[4]

KEYWORDS: Nanoparticles, Drug delivery, Cancer treatment.

INTRODUCTION

Various techniques are getting developed to treat the cancer in last few decades. The new technology like Chimeric antigen receptor T cells are T cells becoming the new era of treating the lymphoma. Cancer continues to be one of the most difficult global healthcare problems. Although there is a large library of drugsthat can be used in cancer treatment, the problem is selectively killing all the cancer cells while reducing collateraltoxicity to healthy cells. There are several biological barriers to effective drug delivery in cancer such as renal, hepatic,or immune clearance. Nanoparticles loaded with drugs can be designed to overcome these biological barriers toimprove efficacy while reducing morbidity.[5] Combined therapy of two or more drugs promotes synergism among the different drugs againstcancer cells and suppresses drug resistance through distinct mechanisms of action. Nanoparticle drug delivery, onthe other hand, enhances therapeutic effectiveness and reduces side effects of the drug payloads by improving theirpharmacokinetics.[6]

Cell recognizing ability of nanoparticles by various strategies having unique identifying properties that distinguish them from previous anticancer therapies. specific drug delivery by nanoparticles inside the cells illustratingmany successful researches and nanoparticles remove the side effects of conventional therapies with tailored cancer treatment. Polymeric nanoparticle, Dendrimer, Nanoshell, Dendrimer, Polymer micelletypes of nanoparticle used in treating various types of cancer.[7]

Applications Of Nanoparticles In Treatment Of Different Types Of Cancer

Lung Cancers

Virus Nanoparticles can be used for a treatment of lung cancer Generally virus having two type Mammalian and Plant Virus having size range of 20-400 nm. Plant virus-based nanoparticles have been shown to be effective for cancer treatment. The genetic material of the virus is protected by the protein coating known as capsid.the virus capsid nano-particles are non-replicated and non-infectious.This virus capsid has the capacity to withstand extreme temperature, pH, and harsh chemicals. Plant virus nanoparticles can be functionalized so that they can be preferentially taken up by cancer cells. Computational modeling can help design plant virus nanoparticles to be carriers for anticancer drugs. Synthetic (organic) Nanoparticles Polymer Nanoparticles (PNS)-USFDA has approved PLGA Poly (lactic-co-glycolic) acid (PLGA), Nanoparticles which are more effective against carcinoma cells the amended into a formulation that shows the good tumor suppressor, biomolecule to A549 lung cancer cell. PLGA is more suitable for the target delivery and it has more circulation

time in the bloodstream and less renal clearance.[8]

Hongli Y et alconducted a study on Paclitaxel Loaded Core Shell Magnetic Nanoparticles and Cold Atmospheric Plasma Inhibit Non Small Cell Lung Cancer Growth and this study. They have concluded from vitro study that PTX-loaded nanoparticles and CAP inhibited the growth of A549 cells more effectively than when each was used individually. CAP could induce the PTX-loaded nanoparticles in tumor cells to increase the effective drug concentration to a level that might be conducive to reduce drug resistance. The combination of PTX-encapsulated nanoparticles and CAP provides a promising tool for the development of a new non-small cell lung cancer treatment strategy.

Liang C et al developed a GE11-modified liposomes for non-small cell lung cancer targeting: preparation, ex vitro and in vivo evaluation in this research they have formulated doxorubicin-loaded liposomes containing GE11. cytotoxic effect of doxorubicin-loaded liposomes on A549 cells was closely related to GE11 density, and liposomes containing 10% GE11 showed the highest tumor killing activity. Modified GE11 liposomes could increase accumulation and prolong retention of the liposome at the tumor site. And it may be a promising carrier for delivery of therapeutic drugs in NSCLC.

Breast Cancer

Liposomes can be used to treat breast cancer. Also Dendrimers used as contrast factor in MRI and can be the assisting factor to clear pathologic procedures.using nanobodies could decrease the metastasis of cancer cells of breast glands in rats.by making specific nanobodies of the two surface receptors, cancer can be diagnosed and treated[9].Vineela P et al conducted a study on Inhalable Pirfenidone Liposomes for Non-Small Cell Lung Cancer Treatment.they have concluded that PFD-loaded liposomes while being inhalable, present a potential treatment strategy for NSCLC. The results from scratch cell migration, and colony formation assays revealed that PFD-loaded liposomes were more effective in reducing cellular interaction, migration, and single-cell tumor development, as compared to plain drug, which makes it suitable to be considered as an alternative for repurposing PFD for lung cancer.

Multifunctional Nanotherapy for colon cancer

Qixiong Z, Fuzhong Z, et al proposed a site-specific, combination nanotherapy strategy for targeted treatment of CAC by the oral route. They have developed a combination nanotherapy strategy for targeted treatment of colorectal cancer by an oral route. Their results explains that that anticancer nanotherapies derived from intrinsic anti-inflammatory nanocarriers are promising for targeted treatment of inflammation-associated tumors by simultaneously normalizing inflammatory microenvironment.[10] Kai L et al prepared 5-FU-loaded HA-conjugated SiNPs to target the colon cancer cells. In this study, they have showed the specific binding and intracellular accumulation of targeted nanoparticles based on HA surface modifications in colon carcinoma cells.Their study showed that conjugation of HA to SiNPs could result in enhanced uptake of 5-FU through CD44-mediated endocytosis uptake and could result in significant antitumor efficacy. Thus, 5-FU/HSNP could be a promising drug delivery system for colon cancer therapy.

Nanoparticles for Treatment of ColorectalCancer

Jun Xconcluded that the an immune-stimulating UCNP-based PDT strategy in combination with CTLA-4 checkpoint blockade to effectively destroy primary tumors under light exposure, inhibit distant tumors that can hardly be reached by light, and prevent tumor reoccurrence via the immune memory effect. PDT with UCNP-Ce6-R837 in combination with the cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) checkpoint blockade not only shows excellent efficacy in eliminating tumors exposed to the NIR laser but also results in strong antitumor immunities to inhibit the growth of distant tumors left behind after PDT treatment.

Colorectal cancer (CRC) is the third leadin cause of cancer death the U.S. and additionallythe third widely diagnosed cancer in the world.Combined anticancer therapies loaded in NPs focolon cancer therapy Combination of Drug-loaded Nanostructures inthe treatment of CRC shows potential to enhancelocal drug concentration, improving chemotherapyand tumor-targeting. Anita *et al*. examinedthe anticancer effects of curcumin/5-fluorouracil loaded thiolated chitosan nanoparticles on colon cancer cell line (HT29). Nanostructures of Cur-TCS and 5-FUTCS, which are sensitive to pH, were also compared as freely used, and had2 and 3-fold increase in anticancer effects. The amount of necessary dose to view a specific cytotoxic effect was also reduced Payjakata *et al.* designed pH-sensitive polymer nanostructures which carries curcumin. In this process, the drug encapsulation efficiency was 72% and the particle size less than 130 nm. These nanostructures could be used to reduce thedose of curcumin to inhibit colon cancer as well as increasing the cellular uptake of curcumin.[11]

Targeted nanoparticles for pediatric leukemia therapy

The two major forms of leukemia, acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML), account for about one-third of the malignancies diagnosed in children. nanoparticles with an emphasis on high density lipoprotein-based drug delivery systems to examine their potential role(s) in the enhanced treatment of children with leukemia.

Leukemia/lymphoma therapeutics via lipoprotein-based drugdeliverysystems

Vitols et al. found that leukemic cells with monocyte differentia- tion expressed an elevated low density lipoprotein (LDL) receptor Subsequently, Vitols et al.

established that human leukemia cells were avidly taking up LDL and thus proposed lipoproteins as potential drug transporting vehicles for selective leukemia ther-apeutics More recently, Masquelier et al. attempted to use LDL as a vehicle for delivering chemotherapeutic agents to leukemia cells. The targeted therapy via the rHDL nanoparticles is anticipated to limit the toxicity of drugs during therapy, via a novel drug delivery model with desirable physical characteristics and out- standing selective targeting potential toward malignant cells and tissues .Additionally, the rHDL delivery systemhas a potential to reposition a variety of approved drugs that proved to have limited applicability due to poor solubility and excessive peripheral toxicity. This approach could be most economical and profitable, in contrast with conventional and very costly drug and target-screening strategies.[12]

Silver nanoparticlesin Dalton's lymphoma

Muthu Irulappan SriramSelvaraj et al study shows theefficacy of biologically synthesized silver nanoparticles (AgNPs) as an antitumor agent using Dalton'slymphoma ascites (DLA) cell lines in vitro and in vivo. The AgNPs showed dose-dependentcytotoxicity against DLA cells through activation of the caspase 3 enzyme, leading to inductionof apoptosis which was further confirmed through resulting nuclear fragmentation. The present study explores the potential antitumor activity of biologically synthesized AgNP in a DLA tumor system in vitro by activation of the caspase 3 enzyme which is known to have a potent inhibitory effect on disease progression in a mouse model, leading to a potent restorative effect in the treated tumor mice near to normal by reducing tumor volume and weight gain. These drug delivery systems are mainly developed according to their ability to differentiate between malignant and nonmalignant cells, making them a promising alternative to existing drugs. a study of the exact mechanism by which AgNPs inhibit signaling cascades responsible for the development and progression of the disease would be a tremendous breakthrough in the field of nanomedicine.[13]

Nanotechnology for the treatment of melanoma skin cancer:

Malignant melanoma (MM) or simply melanoma, is a malignancy of pigment production cells (melanocytes), localized primarily on skin.The incidence of MM has been increasing in the last, especially in light skin people population exposed to excesive solar radiation. Malignant melanoma (MM) or simply melanoma, is a malignancy of pigment production cells (melanocytes), localized primarily on skin. The incidence of MM has been increasing in the last, especially in light skin people population exposed to excesive solar radiation. The most important exogen factor is ultraviolet radiation, particularly intermittent exposition to sunlightMalignant melanoma (MM) or simply melanoma, is a malignancy of pigment production cells (melanocytes), localized primarily on skin.The incidence of MM has been increasing in the last, especially in light skin people population exposed to excesive solar radiation. The most important exogen factor is ultraviolet radiation, particularly intermittent exposition to sunlight.[14]

Active targeting nanotechnology involves conjugation of ligands such as peptides, antibodies, sugars, aptamers, or other small molecules to nanoparticles allowing the homing of the drug to the target site (Ojea-Jimenez et al. 2013). An ideal ligand–receptor should be selected to target the nanoparticles only to the malignant cells, avoiding the health cells. Some antibodies that we can mention for targeting melanoma cells are trastuzumab, rituximab, and bevacizumab, which are all approved by the FDA. Although antibodies have been used to direct the carriers in a site-specific manner, there are some limitations such as the high cost, the challenges of production in large scale, as well as the complex and large structure of monoclonal antibodies (Li et al. 2010). Particularly in the case of melanoma, other ligands can be harnessed for active targeting. Over the last few years, a significant progress has been done regarding the active targeting field, however, though it is still needed to specific molecular targetexpressed by melanoma cells. This can be the breaking point to the development of more efficient drug delivery system (DDS).[15]

Leukemia

Leukemia is a type of hematopoietic stem/progenitor cell malignancy characterized by theaccumulation of immature cells in the blood and bone marrow. different types of nanocarriers, their capability in targeting leukemic cells.a proliferative e_ect on cancer cells when administered to children su_ering from acute lymphoblasticleukemia (ALL). According to this observation, he synthesized antagonists of folic acid that proved tobe e_ective in the treatment of this pathology.The investigated systems that enteredthe clinical trials are essentially represented by liposomes as they provide a prolonged lifetime of thedrug in the systemic circulation coupled with a slow steady release of their content. The latter propertyis particularly important in the treatment of leukemia as the combination of drugs having differentefects on the targeted cells is of paramount importance. It is well established that the maintenanceof proper molecular ratios between the administrated drugs at the site of action is crucial for thesuccess of the therapy. The slow release of the payload from the liposomal carriers guarantees theavailability of the administered drugs in the proper, intended ratio.[16]

Renal Cancer Drug Delivery

New nano-carriers are being constructed to target drugs to the glomerulus, mesangial cells and media fibroblasts. The cell surface receptor for folate is over expressed on the surface of kidney cancers/ malignancies. Folate-conjugated PEGylated cyanoacrylate nanoparticles have shown higher affinity for the folate receptor than free folate so they are going to be one of the most sought

after drug delivery system to renal cancer. Both PEGylated and Non-PEG, 85- 100 nm Nano-Liposomes loaded with Lurtotecan and Annamycin are also being tried for renal cell carcinoma.Carbon nano tubes have already been successfully used for hyperthermia treatment as well as drug delivery vehicle forrenal cancer.[17] active clinical practice with NPs in the fields of nephrology and urology. NPs have been deployed in renal imaging techniques and delivery of iron therapy with Ferumoxytol for CKD or ESRD patients who lack appropriate erythropoietin production. There exist active areas of research with NPs in animal models. Hypertensive and atherosclerotic rodents have shown major improvements in disease state with brief treatment periods. NPs are able to sensitize renal tumors to minimal invasive techniques such as RFA for improved cell necrosis. Magnetic assisted hemodialysis with toxin scavenging NPs shows promise in vitro of improved solute clearance in shorter dialysis sessions, which would greatly improve the quality of life of these patients.[18]

Ovarian cancer

Yao et al this comprehensive study consisted of: (1) the preparation and characterization testing of nanocarriers, (2) the slow-release effect verification in vitro and in vivo, (3) the tumor-targeting characteristics verification in vitro and in vivo, and (4) the antitumor effect verification in vitro and in vivo. All these results showed that the PTX-PEG-PLA-FA-NP nano-delivery system had improved hydrophilicity, slow-release effects, low toxicity, and tumor-targeting characteristics. More drugs could be delivered into tumor tissues selectively and accordinglyand the anti-tumor effect was enhanced significantly using this nano-delivery system. PTX-PEG-PLA-FA-NP-based therapy should be a promising new treatment strategy for ovarian cancer patients in the future[19].Multifunctionalpolymer micelles, including nanogels/magneticbased micelles, possess characteristics which couldimprove ovarian cancer therapy. These formulationshave capabilities of MRI visible targeting, targetedphotodynamic therapy, thermosensitive therapy andluminescence/near-infrared/multi-model imaging properties,which will allow tracking and monitoring ofnanoformulations and accumulated drug(s) at the tumorsite during the therapy procedures.[20] some nanoconstructs are used as novel therapeutic agents whether others are used as photosensitizers in photodynamic and photothermal therapy even to oral delivery of large molecules like DNA or protein they are being used as cassette. It is expected that 72 within the 2 or 3 years the human clinical trials of NPs will be started and within the 15-20 years' cancer will be fully curable by using the NPs.[21]

Prostate cancer

The use of precision nanomedicine in prostate cancer has great potential as a novel approach to combat thelimitations of current therapies in both localized and metastatic disease settings.[21] McCarthy et al. showed that RALA/CMV-iNOS NPs reduced the proliferation of prostate cancer cells and systemic delivery may promote the survival of mice when they injected the nanoparticle into C57/BL6 mice intravenousl.IR780 (a near-infrared dye) and docetaxel (DTX) encapsulated human serum albumin NPs have highly self-accumulation properties and thereby used in the combination therapy with chemotherapy of photothermal and photodynamic therapy in the treatment of castration-resistant prostate cancer.[22]

In vivo, however, gold uptake into the cells was lower when animals were administered larger AuNPs resulting in the smaller AuNPs being more effective radiosensitizers invivo. It is likely that the smaller AuNP are more effective because of their ability to extravasate from the vasculature to bind and enter into tumor cells, which seemingly occurs less with the 19 nm AuNPs. It appears that smaller AuNPs resulted in lowerlevels of liver uptake and may lower off-target elemental toxicity of gold and/or radiation sensitivity to non-targeted tissuesFor in vivo radiotherapy, the enhancement isdependent on the amount of Au present in the tumor. With more AuNPs deposited in the tumor, higher radiation dose and therapy enhancement will be facilitated. Therefore, AuNPs with a smaller size are preferred since they have a higher tumor accumulation.8 Our observed tumor growth inhibition a□er radiation therapy agrees with this hypothesis, with the most signi□cant radiation therapy enhancement resulting from 2 nm.[23]

Liver Cancer

One of the most important types of liver cancer is hepatocellular carcinoma (HCC).HCC is the fifth most common cancer, and its correct diagnosis is very important. Forof nanoparticles are in medicine for organ imaging. Two methods of liver imaging areX-ray computed tomography (CT) and magnetic resonance imaging (MRI),[24] Chien-Hsun Wu et al concluded that SP94-modification of liposomal doxorubicin significantly improves therapeutic efficacy in human SK-HEP-1 tumor-bearing NOD.CB17-Prkdcscid/J mice, and significantly inhibits tumor cell viability, resulting in reduced tumor volumes and final average tumor weights compared with control nonspecific treatments. The rapid, massive, and specific accumulation of SP94-LD in tumor cells results in prominent tumor growth regression. These therapeutic outcomes confirm the key role of the tumor-specific binding and internalization of SP94-LD in achieving elevated local concentrations of chemotherapeutic agents inside tumors. These findings suggest a potential clinical benefit from SP94-targeted liposomal doxorubicin and liposomal vinorelbine combination therapy.[25]

Wejdan A et al prepared a cytochrome C combined pacitaxel loaded nanoparticles for the treatment Of liver cancer.the result from this study show that formulation of (PTX) pacitaxel into a nano-sized preparation increase the drug efficacy when compared with free Pacitaxel.this

nano-formulation may be helpful in the treatment of liver cancer.[26]

CONCLUSIONS

Nanotechnology in cancer treatment will bring significant advances in the treating and prevention of disease. Nanotechnology is the novel manufacturing technology of the 21st century which helps us to modify a various complex molecular techniques by manipulating matter on an atomic and molecular scale Future drug delivery system of nanotechnology is leading to the emergence of a new field called nanomedicine. Nanomedicine needs to overcome the challenges for its application, to improve the understanding of pathophysiologic basis of disease, bring more sophisticated diagnostic opportunities, and yield more effective therapies and preventive properties. Various nano systems in cancer therapy such as carbon nano tube, dendrimers, nano crystal, nano wire, nano shells etc. are given. The Implementation of in nano technology will cure the neuro degenerative disorders such as Parkinson's disease and Alzheimer's disease.

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