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CLINICAL APPLICATIONS OF NANOPARTICLES IN CANCER AND FUTURE PERSPECTIVES

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ABSTRACT

Nanoparticles are ultra-thin highly fine particles as having one structural measurement of less than 100nm, constructed them similar in size to sub cellular structures, including biological macromolecules or cell organelles thereby enable their organized inclusion into biological systems. Nanoparticles can innate activate immune systems and activate anti-cancer immune response. One of the top therapeutic methods in the treatment and diagnosis of cancer is nanotherapy. Most advanced progress has been made in the improvement of new agents in the treatment of cancer and novel drug delivery technologies. Nanocarriers have huge potential to enter tumour directly by provided that API in the tumor sites within specific time. Targeted Nanocarriers imaging particles give an innovative paradigm in cancer imaging teqniques which enables premature detection of cancer as well as handling monitoring at the molecular/cellular stage. In future, nanotechnology must achieve priority due to reduced side effects introducing new sources of nanoparticles.

KEYWORDS

Cancer, Therapies, Nanocarriers, Micro, Targeted, Nanocrystals and Tumour.

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INTRODUCTION

Cancer has escalated the mortality rate during the last decades. Chemotherapy is the first-line therapy for tumor eradication in most cases. However, the multifunctional nanoparticles serve as a lifesaving tool for treatment of cancer[1]. The mortality rate among Americans is estimated as 606,800 in 2019, relatively to about 1700 deaths per day[2]. Chemotherapy is no longer successful treatment in terms of precise targeting and reducing side effects. On the contrary, Nanotechnology provides

versatility in improving the specificity to the target site, increasing efficacy and reducing potential harmful effects. It has altered the fortune of tumour cells through early detection, diagnosis and improved therapy[3]. Targeted drug delivery and controlled drug release rate can be achieved by the development of novel nanosized drug delivery systems[4]. The ideal properties of nanocarriers include improve blood circulation time, promptly intracellular release of the drug, to facilitate uptake of cancer cells and enrichment in neoplasms[5]. Therefore, multifunctional nanoparticles have been introduced to optimize therapy such as gold core silica nanoparticles coated with poly-2-ethyl oxazoline and β-cyclodextrin[6]. This review will briefly discuss the current status of novel nanoparticles in cancer therapy and their likelihood in the forthcoming years.

FUNCTION OF IDEAL NANOCARRIERS

Nanocarriers have great potential to target tumour directly by providing API in the tumor sites. The small size of nanoparticles facilitates passage through the epithelia of GIT and micro capillaries, resulting in improved bioavailability and enhanced therapeutic outcomes[7].

TYPES OF NANOPARTICLES

Magnetic nanoparticles

These nanoparticles possess great biocompatibility characteristics due to the presence of a solid magnetic core, ferrite and an iron oxide. Recently, magnetic nanoparticles are known for many biomedical applications such as cancer therapy, magnetic resonance imaging and drug delivery. Metal ions for instance zinc, cobalt and manganese have profound influence in optimizing the potential of Magnetic nanoparticles to kill tumor[8]. Nowadays, super paramagnetic iron oxide nanoparticles (SPIONs) are being widely used in tumour eradication[9]. SPIONs exhibit remarkable stability, biocompatibility and high magnetic susceptibility. Hyperthermia includes the production of high temperature such as 113ºF to suppress tumor growth and kill cancer cells. The development of magnetic biomaterials like SPIONs produces hyper thermic reactions to treat osteosarcoma. Furthermore, SPIONs may act as a controllable source of heat, in exchanging the magnetic fields, thus controlling the production of consistent temperature in the tumor. Due to the rapid change of magnetic polarity, mild hyperthermia may induce deep in the neoplasm and prevent cancer[10].

Gold nanoparticles

Gold nanoparticles can be easily modified into controllable shape and size. They are used for various purposes such as treatment of cancers, genomics, wound healing, immunoassays and optical equipment. AUNPs are used in hepatic cancer as a drug and gene carrier[11]. Functional AuNP's are conjugated with antibodies, bioactive ligands or drugs to eradicate tumor. Recent studies determined that the clove phytochemicals coated with gold nanoparticles can inhibit 50% cell death at 330ppm. However, clove extract (without gold nanoparticles) inhibited 30% cell death at 330ppm to treat prostate cancer[12]. Therefore, it is preferable to design novelnanoparticles conjugated with various bioactive agents.

Quantum dots

QDs nanocrystals exhibit unique fluorescent and photo stability characteristics, broad spectrum of absorption, narrow-emission spectra, and adjustable size. They are suitable candidates for early detection of cancer biomarkers and cell labelling[13]. Multifunctional nanohybrids of QD with inorganic molecules, polymers, lipids, proteins, gold nanoparticles facilitate superior imaging and anticancer activity. Example of Inorganic nanocarriers is graphene derivates such as graphene oxide and graphene quantum dots. They possess high loading capacity and minimum toxicity[14].

Liposomes

Liposomes are spherical vesicles having an aqueous core enclosed by one or more belayed membranes. They are biocompatible, biodegradable and enable to entrap both hydrophilic and lipophilic molecule. Most widely used anticancer drugs are doxorubicin, daunorubicin andcytarabine[15]. In addition, positive surface coated liposomes were formulated to

increase the stability, controlled release and targeted therapy. Their surface can be easily modified to enhance the cellular uptake of the drugs. Modification helps to encapsulate various drugs with different nature, size and solubility[16]. These versatile characteristics make them potent carriers for drugs like anticancer, antibacterial, antiviral, insulin and plasmid DNA[17].

Polymeric nanoparticles

They are highly efficient in the incorporation of hydrophobic drugs. The polymeric coating provides sustained drug release, prevents degradation and increases the residence time of the drug[18]. They are obtained from natural polymers like chitosan, albumin, gelatine, and DNA or synthetic polymers like polyacrylate, polyacrylamide and polycaprolactone (PCL). They are coated with inorganic surfactants to minimize immunological responses and intermolecular interaction at the surface of chemical groups. Chitosan is cationic and soluble in water which makes it more biocompatible and less toxic. It is mostly used to deliver 5-fluorouracil in malignant tumor[19].

Porous silicon nanoparticles

They have excellent properties like large surface area, retained bioactivity of drug, uniform size, and large pore volume, biodegradable and biocompatible. They are enabling to escalate the bioavailability of anticancer drugs such as doxorubicin and paclitaxel[20]. Moreover, some organic molecules like platinum (IV) prodrug are conjugated on mesoporous nanoparticles for tumor ablation[21]. However, mesoporous silica has least drug storage capacity and irregular morphology which makes them low-grade nanocarrier. Therefore, hollow mesoporous nanoparticles have received great attention to rectify this issue. They contain mesoporous shell and a hollow cavity for drug storage. Not only increase the drug loading capacity, but also provide pH-responsive controlled release of a drug. Interestingly, pH in tumor cells is relatively higher than tissues and blood. To avoid this problem, these systems act as pH stimuli to control the drug release rate. Recent studies evaluated that MgAl hydrotalcite can be employed for the pH-responsive targeted treatment. With that in mind, MgAl-LDH is coated on the outer surface of HMS, encapsulated the 5-fluorouracil anticancer drug within the pores and cavities to facilitate pH-controlled targeted drug delivery system[21].

NANOCLUSTERSAS A THERANOSTIC AGENT

Nanoclusters are extensively used for dual mode photodynamic therapy and imaging to detect malignancies. Multiple tumor clusters in patients with colorectal, prostate, breast and lung cancer have increased the rate of mortality and reduced life span. This is why the use of nanoclusters promotes trapping and killing of specific tumors. For instance, CD44 and CD133 (stem-cell markers) reduce the re-occurrence of the tumor and eliminate it effectively.

Fluorescent nanoprobes attached with MUC1 antibody are the promising candidates for tumor detection. Tumor clusters are effectively trapped by using different techniques such as selectin. Selectin proteins bind to ligands present on the surface of tiny clusters to detect tumors during metastasis. It was evaluated that the combination of folate receptors and EpCAM on immunomagnetic nanospheres significantly increased the capture efficiency up to 75.75% in Lung adenocarcinoma patients[22].

Among different types of nanocrystals, carbon-based nanoparticles; particularly graphene oxide and reduced graphene oxide are used for targeted therapy, imaging, and detection of tumors. In a study, when rGO (reduced-graphene oxide) nanocrystals were loaded with Chlorine e6 and doxorubicin, improved targeted therapy was determined. On the other hand, GO-based nanocrystals functionalized with hyaluronic acid were shown to specifically target miR-21 and inhibited the development of tumor deep in the tissues. In another investigation, Graphene oxide alginate nanogels were loaded with Doxorubicin, showed improved activity against lung cancer.

Further, manganese ions inculcated with reduced graphene oxide nanoplatelets and functionalized

with iodine were used for MRI and CT applications. Additionally, the deposition of $MnFe_2O_4$ super paramagnetic iron oxide nanoparticles could produce $GO/MnFe_2O_4$ nanocrystals. These nanohybrids showed remarkable chemo-photo thermal effects on the tumor cells when encapsulated with DOX[23].

TARGETED THERAPY APPROACH IN THE CANCER TREATMENT

Nanoparticles have been extensively used in biomedical applications, particularly cancer. Multifunctional nanoparticles are used for early detection of malignant tumors and targeted tumor therapies.

TOXICITY OF METAL NANOPARTICLES

Among various nanoparticles, metal nanoparticles are most commonly known for their potential toxicity of tissues, organs and mammalian cells. It has been observed that small sized nanoparticles can easily penetrate through micro capillaries and affect the physiology of normal cells in the body.

Table No.1: Targeted Therapy Approach for Cancer

S.No	Nanoparticles based targeted therapy	Description	Application
1	miR-708	NPs prevent degradation of miR-708 from nucleases in the blood.	Malignant breast cancer
2	sTRAIL Plasmid DNA	LPD (Lipid protamine DNA) is used to encapsulate the sTRAIL Plasmid DNA to facilitate TAF targeting, resulting in the suppression of tumor.	Bladder cancer
3	FPPDH NPs	They are accumulated on the tumor surface and suppress tumor growth by dual-targeted therapy.	Liver cancer
4	MTO loaded iRGD-NP3	Directly target breast cancer cells (MCF-7)	Breast Cancer
5	PA/PtNPs (Phytic Acid coated platinum nanoparticles)	It suppresses tumor growth due to the accumulation of PA/PtNPs at the tumor site	Malignant Bone Tumor
6	Gold nanocore encapsulated Human serum albumin NPs)	It accumulates in the inflammatory sites, such as tissues or organs and effectively kills cancer cells.	Peritoneal cancer
7	Fe_3O_4-Au Hybrid NPs	Multifunctional nanoparticles, facilitate ablation of cancer cells	Breast Cancer, photodynamic therapy
8	PTX-loaded Gold NPs	It is coated with anti-EpCam- modified RBC membranes	Target 4T1 tumor cells
9	PEG-coated gold Nanoshells	Promote ablation of tumor	Colon cancer

Table No.2: Toxicity of Metal Nanoparticles

S.No	Nanoparticles	Toxicity	Mechanism
1	Silver and Copper Nanoparticles	Autonomic Denervation	Disruption of endothelial cell membrane by causing oxidative stress and increasing the free radical formation.
2	Gold Nanoparticles	Human Ha CaT keratinocytes	Trigger immunological responses, increases the expression of (IL-1), (IL-6) and TNF-α.
3	Silver Nanoparticles	Pericardial Edema Cardiac Arrhythmias	Increased production of ROS and down regulation of glutathione peroxidase genes causing damage to neurons.

CONCLUSION AND FUTURE PERSPECTIVE

It can be speculated that nanoparticles will have a great impact on cancer research, prevention and possible treatment solutions. Major advances are expected to enhance the targeted therapy and controlled release of a drug. With the use of multifunctional nanoparticles, tumor will detect at earliest stages allowing timely applied therapy. Nanotechnology will provide a versatile platform to extend the life span of cancer patients. On the other hand, serious adverse effects of nanoparticles are under consideration. What changes will bring after the application of nanotechnology in the field of cancer research, remains to be observed. However, nanoparticles will be in particular focus of scientists to improve healthcare system.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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