SELF ASSEMBLED RECYCLING NANOPARTICLES AS TARGETED DRUG DELIVERY SYSTEM IN MALIGNANCY: A REVIEW

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ABSTRACT

The development of more selective delivery systems for cancer diagnosis and chemotherapy is one of the most important goals of current anticancer research. This can provide insight for the engineering of nanoparticles and be extended to cancer therapy and diagnosis, so as to deliver multiple therapeutic agents and imaging probes at high local concentrations. By combining different hydrophobic moieties and hydrophilic polymer backbones, various self-assembled nanoparticles are prepared, and their *in vivo* distributions in tumor have been studied by radionuclide imaging technique. These polymers are characterized by easy processing and a reversal of polymerization at elevated temperatures while displaying properties similar to conventional polymers. Magnitude and pattern of tumoral distribution of self-assembled nanoparticles are influenced by several factors.

KEY WORDS: Self-assemblly, Re-cycling Nanoparticles, Tumor

INTRODUCTION

Various self-assembled nanoparticles as candidates to shuttle radionuclide and/or drugs into tumors and to investigate the mechanisms underlying the tumor targeting with self-assembled nanoparticles. Drug release applications the preparation of nanoparticles from biodegradable polymers e.g. polycaprolactone, PLA and PGA has been investigated, via strong dimerization of the (ureido-pyrimidinone) UPy moieties linear polymer chains are formed acting as conventional polymers. These polymers are characterized by easy processing and a reversal of polymerization at elevated temperatures while displaying properties similar to conventional polymers. Magnitude and pattern of tumoral distribution of self-assembled nanoparticles are influenced by several key factors—(i) *in vivo* colloidal stability: nanoparticles should maintain their intact nanostructures *in vivo* for a long period of time, (ii) particle size, (iii) intracellular uptake of nanoparticle: fast cellular uptake greatly facilitates the tumor targeting, (iv) tumor angiogenesis: pathological angiogenesis permits access of nanoparticles to tumors.

Self –assembled nanoparticles

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Self-assembly (SA) in the classic sense can be defined as the spontaneous and reversible organization of molecular units into ordered structures by non-covalent interactions. The first property of a self-assembled system that this definition suggests is the spontaneity of the self-assembly process: the interactions responsible for the formation of the self-assembled system act strictly on local level in the nanostructure builds itself.

In vivo tumor targeting and radionuclide imaging with self-assembled nanoparticles

In practice, gold nanoparticles are the most commonly used nanoparticles for diagnostics and drug delivery. Unique chemical properties of colloidal gold make promising targeted delivery approach for drugs. Gold and silica composite nanoparticles have been investigated as nanobullets for cancer. Researchers are also using magnetic nanoparticles for cancer drug delivery. In cancer therapy a major difficulty is to destroy tumor cells without harming the normal tissue. Self assembled nanopartical therapy, nevertheless damages healthy tissue which can not always be protected in the desired way in cancer chemotherapy and provides an opportunity for improved targeted drug delivery.

As tumor architecture causes nanoparticles to preferentially accumulate at the tumor site, their use as drug delivery vectors results in the localization of a greater amount of the drug load at the tumor site, their use as drug delivery vectors results in the localization of a greater amount of the drug load at the tumor site, thus improving cancer therapy and reducing the harmful

nonspecific side effects of chemotherapeutics. In addition, formulation of these nanoparticles with imaging contrast agents provides a very efficient system for cancer diagnostics.

Polymeric Nanoparticles (Nanospheres or Nanocapsules) as Drug Carriers

One of the major obstacles to drug efficacy is the nonspecific distribution of the biologically active compound after administration. They may be administered intravenously without any risk of embolization. Depending on the method used in the preparation of nanoparticles, either nanospheres or nanocapsules can be obtained. Nanospheres are matrix systems in which the drug is dispersed within the polymer throughout the particle. On the contrary, nanocapsules are vesicular systems, which are formed by a drug-containing liquid core (aqueous or lipophilic) surrounded by a single polymeric membrane. Nanocapsules may thus be considered as a "reservoir" system.

Nanotubes deliver high-potency punch to cancer tumors

The problem with using a shotgun to kill a housefly is that even if you get the pest, you'll likely do a lot of damage to your home in the process. Cancer researchers have long faced a similar situation in chemotherapy: how to get the most medication into the cells of a tumor without "spillover" of the medication adversely affecting the healthy cells in a patient's body. All blood vessel walls are slightly porous, but in healthy vessels the pores are relatively small. By tinkering with the length of the nanotubes, the researchers were able to tailor the nanotubes so that they were too large to get through the holes in the walls of normal blood vessels, but still small enough to easily slip through the larger holes in the relatively leaky blood vessels in the tumor tissue.

Targeted Delivery with Peptidomimetic Conjugated Self-Assembled Nanoparticles

Peptides produce specific nanostructures, making them useful for targeting in biological systems. Peptidomimetic self-assembled NPs can possess biological recognition motifs as well as providing desired engineering properties. Ligand conjugated NPs are attractive for cell-selective tumor drug delivery, since this process has high transport capacity as well as ligand dependent cell specificity. Peptidomimetic NPs can provide stronger interaction with surface receptors on tumor cells, resulting in higher uptake and reduced drug resistance. Self-assembled NPs conjugated with peptidomimetic antigens are ideal for sustained presentation of vaccine antigens to dendritic cells and subsequent activation of T cell mediated adaptive immune response.

Recycling Nanoparticles

Nanoparticles are opsonized by proteins, dock onto receptors on the cell surface. This initiates phagocytosis or internalization of the particle. Membrane material is recycled back to cell surface via the recycling compartment, as enzyme vesicles from the Trans-Golgi network fuse with the phagosomes(Fig.1). Nanoparticles of Heparin Conjugate as Recycling Anticoagulants

Polyvinyl alcohol-shell magnetic nanoparticles (PVA-shell MNPs, PMNPs) were successfully prepared by in-situ co-precipitation process. Heparin (HEP) was then covalently conjugated on the PMNPs by using aminotrimethoxysilane (ATMS) and 4,4-diphenyl methane diisocyanate (HMDI) as molecular coupling agent (spacer). The morphology of the core-shell PMNPs was examined using several spectroscpic methods to provide direct evidence that the heparin molecules were immobilized on the surface of the core-shell PMNPs. Anticoagulant activity was evaluated with several parameters including activated partial thrombin time (APTT), prothrombin time (PT), fibrinogen time (FT), and thrombin time (TT).

CONCLUSION

As the cancer has become one of most devastating disease, nanoparticles can be used as NDDS for diagnostic as well therapeutic purpose. The formulations using suitable self-assembled Nanoparticles which may also decrease the cost of formulation that should be milestone in the cancer therapy.

The rationale of using nanoparticles for tumor targeting is based on 1) nanoparticles will be able to deliver a concentrate dose of drug in the (1) vicinity of the tumor targets via the enhanced permeability and retention effect or active targeting by ligands on the surface of nanoparticles; 2) nanoparticles will reduce the drug exposure of health tissues by limiting drug distribution to target organ.

Provides an opportunity to effectively deliver therapeutic agents to these cells. This biodistribution can be of benefit for the chemotherapeutic treatment of MPS- rich organs/tissues localized tumors like hepatocarcinoma, hepatic metastasis arising from digestive tract or gynaecological cancers, brochopulmonary tumors, primitive tumors and metastasis, small cell tumors, myeloma and leukemia.

FIGURE NO: 1

LEGANDS

Fig. 1: Recycling of NPs and drug release in targeted cell.

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