Research and Development

Extended Abstract

Nanomedicine 2017: Anticancer theranostic approaches for in vitro and in vivo drug delivery- Subhra Mohapatra- University of South Florida

Abstract

The last decade has seen significant advances in anti-cancer drug delivery approaches, although many challenges including availability of limited nano- and bio-materials, uptake and release of drugs from the endosomes, targeting of drugs to the desired diseased cells or tissues, and the lack of translatable models to study drug delivery. To address these challenges, we have developed and tested a number of novel drug delivery approaches. To this end, we first developed a near infrared (NIR) triggered drug delivery platform based on the chitosan-modified chemically reduced graphene oxide (CRGO) incorporated into a thermosensitive nanogel (CGN). CGN exhibited an NIR-induced thermal effect similar to that of CRGO, reversible thermo-responsive characteristics at 37-42°C and high doxorubicin hydrochloride (DOX) loading capacity (48 wt%). The DOX loaded nanogel released DOX faster at 42 °C than at 37 °C. Second, since combining chemotherapy with gene therapy has been one of the most promising strategies for the treatment of cancer, we developed a chitosan functionalized magnetic graphene (CMG) nanoparticle platform for simultaneous gene/ drug and SPIO delivery to tumor. The results of these research indicated that CMGs grant a sturdy and safe theragnostic platform, which integrates targeted transport of both gene remedy and chemotherapeutic drug(s) and more advantageous MR imaging of tumors. Further, considering the fact that gadolinium (Gd) contrast agents that are predominantly used for T1 MR imaging, have excessive toxicity and plausible side outcomes together with nephrogenic systemic fibrosis, we developed an choice T1 contrast agents, such as Mn for lung imaging. Here we document on the graph and synthesis of multifunctional lipid-micellar nanoparticles (LMNs) containing Mn oxide (M-LMNs) for MRI that can also be used for DNA and drug delivery. Finally, we have developed an in vitro model of tumoroid culture platform for testing drug delivery to tumors that carefully mimics in vivo tumors. Taken collectively these developments are predicted to lead to better anticancer drug delivery in against cancers.

Current diagnostic strategies want to be expanded to supply beforehand detection capabilities, and normal chemotherapy methods to cancer remedy are restrained through lack of specificity and systemic toxicity. This evaluation highlights advances in nanotechnology that have allowed the development of multifunctional platforms for most cancers detection, therapy, and monitoring. Nanomaterials can be used as MRI, optical imaging, and photoacoustic imaging distinction agents. When used as drug carriers, nanoformulations can extend tumor publicity to therapeutic dealers and end result in elevated treatment consequences by using prolonging circulation times, defending entrapped capsules from degradation, and improving tumor uptake thru the EPR effect as well as receptor-mediated endocytosis. Multiple therapeutic marketers such as chemotherapy, antiangiogenic, or gene therapy retailers can be concurrently delivered by nanocarriers to tumor web sites to beautify the effectiveness of therapy. Additionally, imaging and therapy dealers can be co-delivered to furnish seamless integration of diagnostics, remedy

and follow-up, and exceptional therapeutic modalities such as chemotherapy and hyperthermia can be coadministered to take gain of synergistic effects. Liposomes, steel nanoparticles, polymeric nanoparticles, dendrimers, carbon nanotubes, and quantum dots are examples of nanoformulations that can be used as multifunctional systems for cancer theranostics. Nanomedicine approaches in cancer have tremendous possible for clinically translatable advances that can positively affect the average diagnostic and therapeutic process, and end result in stronger best of lifestyles for cancer patients. However, a concerted scientific effort is nonetheless integral to completely discover long-term risks, effects, and precautions for safe human use.

Liposomes are concentric, closed bilayer membranes of water insoluble polar lipids that can be used to encapsulate biomolecules and tablets for centered delivery while protecting their bioactivity. Liposomal DOX has been investigated clinically for breast cancer, ovarian cancer, AIDS-related Kaposi's sarcoma, head/neck cancer, and intelligence tumors. A approach to overcome these limitations by way of decorating the surface of the nanoparticles with focused on moieties such as small ligands, antibodies, or biomarkers that can direct the delivery car toward precise molecular aims which are overexpressed through tumor cells. Targeted particles can then be internalized with the aid of tumor cells by means of receptor-mediated endocytosis/phagocytosis, resulting in extended concentrations in tumor tissue.

Although antibodies can be at once conjugated to capsules except the use of a vehicle, scientific trials have highlighted the difficulties of applying this approach, on the whole due to possible loss of bioactivity upon conjugation, steric hindrance, and immunogenicity of the antibodies when used in their full form. In contrast, conjugating antibodies to the floor of a shipping vehicle does no longer interfere with the bioactivity or traits of the entrapped drug, and does no longer result in loss of affinity of the antibody for the target, which makes nanocarriers an fantastic platform for the improvement of nice targeted therapies. The purposes of antibodies in centered treatment options have evolved toward the preferential use of monoclonal antibodies (mAbs), especially making an attempt to avoid or reduce immunogenicity by using using engineered chimeric or humanized types to maximize the chances of successful medical translation.

Different nanocarriers have been investigated for topical/dermal transport of drugs. This part will talk about the most regularly used, topically applied carriers for the cure of pores and skin cancer. Topical nanocarriers ought to enhance skin targeting, enhancing the drug's capability to reach and penetrate into tumor cells. Moreover, nanocarriers can improve drug steadiness and limit skin irritation by way of heading off direct contact of the drug with the skin's surface. Different nanocarriers have been used for topical application. Present investigations emphasize theories and complete explorations about lipid-based nanocarriers, polymer-based nanocarriers, nano emulsions, and nanogels for skin most cancers treatment. They were characterized for in vitro checking out such as surface morphology, particle dimension distribution, zeta potential, pH value, viscosity, drug content, entrapment efficiency, pores and skin permeation studies, pores and skin retention/deposition studies, ex vivo vesicle-skin interplay studies, in vitro anticancer activity, , spread ability, and in vitro stability studies. Several research focus on in vivo anticancer research in 7,12-dimethylbenz[a]-anthracene (DMBA) mice model, xenografts model, and biodistribution and pharmacokinetic studies. In future, more attentiveness should be concentrated on pores and skin stimulation, skin irritation, sensitization studies, organ toxicity, and systemic toxicity of the topical nanocarriers containing anticancer drug. The universal purpose is to discover the tactics for administration of skin most cancers by way of novel methodology instead of growing novel lively moiety.

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