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Short Communication

Doxorubicin Efficiency is Improved by Sterically Stabilized Polymeric Mesoporous Silica Nanoparticles: Customized Cancer Therapy

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ABSTRACT

The realisation, commercialization, and clinical use of nanoengineering, nanomedicine, and material science for drug delivery are all becoming a reality. Nanomaterials must be developed carefully to assure physiological and biological compatibility before they can be successfully integrated into nanotherapeutics. MSNs are appealing nanocarriers because of their biodegradable, biocompatible, and somewhat pliable porous frameworks, which can be functionalized for better targeting and delivery in a range of disease scenarios. To develop sterically stabilised, hydrophilic MSNs capable of efficient loading and delivery of the hydrophobic anti-neoplastic medication, doxorubicin, an optimum formulation of an MSN with polyethylene glycol (2% and 5%) and chitosan was conducted (DOX). The anticancer, apoptotic, and cell-cycle effects of DOX-loaded MSNs in selected cancer cell lines were examined, as well as the pH-sensitive release kinetics of DOX. MSNs ranging in size from 36 to 60 nm, with a pore diameter of 9.8 nm and a total surface area of 710.36 m^2/g were created. The PCMSN formulation (2% pegylated MSN) showed the highest DOX loading capacity (0.98 mgdox/mgmsn) and a 72-hour sustained release profile. At concentrations of 20 g/mL-50 g/mL, pegylated drug nanoconjugates were successful in triggering death in cancer cells, demonstrating their potential as drug delivery vehicles.

Keywords: Cancer; Doxorubicin; Drug delivery; Mesoporous silica nanoparticles; Chitosan; Polyethylene glycol

INTRODUCTION

Nanotherapeutics is a theory that nanotechnology can be used to cure a wide range of ailments by broadening therapy options and decreasing adverse effects associated with traditional treatments. This has prompted the development of a number of nanocarriers with the goal of lowering pure drug concentrations and dose frequencies, which are typically linked to the development of toxicities and drug resistance, by offering a therapeutically efficient and biocompatible administration route [1].

Nanoparticles (NPs) are appealing because of their small size, relative biosafety, and multifunctionality, which can be tailored to disease-specific models. They're built to easily traverse physiological barriers, are generally immunologically compatible, and can access a wide range of tissues. They also enable the reformulation and stabilisation of hazardous medications, diagnostic elements, and correcting genes, making them therapeutically and commercially advantageous.

A variety of NPs have been developed in recent material engineering and nano-architectural design research, with MSNs emerging as a front-runner in biomedical research. MSNs combine a highly flexible and customizable framework with a narrowly dispersed 2D hexagonal porous network that is biodegradable and biocompatible in biological systems. MSNs feature a large active surface area that may be selectively polymerized or functionalized for stimuli-responsive purposes, tunable pore size and huge pore volumes for cargo loading and controlled release, and have demonstrated good tolerance levels in vitro and in vivo. MSNs are being studied intensively as theranostic devices for diseases, particularly cancer treatment. Conventional cancer treatment techniques, such as surgery, radiation, and chemotherapy, have proven ineffective, leading in rising recurrence rates and decreased quality of life. Anti-neoplastic medicines, which function by suppressing cellular pathways of DNA replication that are up-regulated in cancer cells, are frequently connected to unpleasant side effects. Because these cytostatic or cytotoxic drugs have a limited bioavailability, they are frequently given in high doses or for long periods of time, resulting in systemic side effects at non-specific locations. Doxorubicin (DOX) is a highly effective anthracycline medication that is used to treat a variety of malignancies, including breast, cervical, bone, stomach, and leukaemia. Despite its widespread use, the drug's low solubility, combined with increased dose frequencies, has resulted in a slew of side effects, including cardiotoxicity, myelosuppression, induced vomiting with nausea, and alopecia [2]. After a thorough

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examination of these harmful side effects, which become more prominent as dose durations grow, researchers discovered that both chronic and acute DOX-induced cytotoxicity can be significantly reduced by using better and more focused administration routes. An optimised MSN with a large active surface area and large pore volume was selectively functionalised with the organic polymer Chitosan (C) and the inorganic polymer polyethylene glycol (P) to create a hydrophilic, polyelectrolyte complexed superficial layer that allowed the transport of the hydrophobic drug DOX. MSNs functionalized with chitosan and PEG, as used in this study, has previously been shown to deliver the anticancer medication 5-fluorouracil to mammalian cells in culture. When compared to non-cancer, Cell lines, the scientists demonstrated improved drug loading, drug release, and higher anticancer activity (>50%) in Caco-2, MCF-7, cells *in vitro* [3].

RESULT AND DISCUSSION

The localised tumour microenvironment is characterised by severe metabolic processing and rapid, uncontrolled reproduction, and so has unique characteristics that can be used to target specific sites. A typical tumour goes through rapid and increasing angiogenesis to generate aberrant vasculature for increased nutrition and oxygen delivery. These blood arteries are made up of flattened endothelial cells with vast gaps between their basement membranes, allowing molecules larger than 40 kDa to collect primarily in tumour tissue without being detected by the immune system. Polymerisation of the nanoparticle has been discovered to modulate cellular absorption rates, prolong *in vivo* circulation durations, and prevent rapid renal clearance and MPS (mononuclear phagocyte system) escape in addition to passive targeting. Polyethylene Glycol (PEG) grafting onto the surface of NPs, such as silica nanomaterials, has been shown to aid in phagocytosis escape by binding specific serum proteins such as dyopsonins, resulting in higher hemocompatibility with red blood cells and increasing the circulating half-life of PEG-MSNs. Smaller PEG-MSNs were effective in evading immune responses in mice models and decomposed slowly, with no systemic or tissue-specific damage observed for up to a month following treatment. Cellular absorption, biocompatibility, prolonged circulation time, and pharmacokinetic fate are all influenced by factors such as size, morphology, and favourable surface modifications.

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