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Review Article

Nano cocoons – A novel stimuli-responsive drug delivery system

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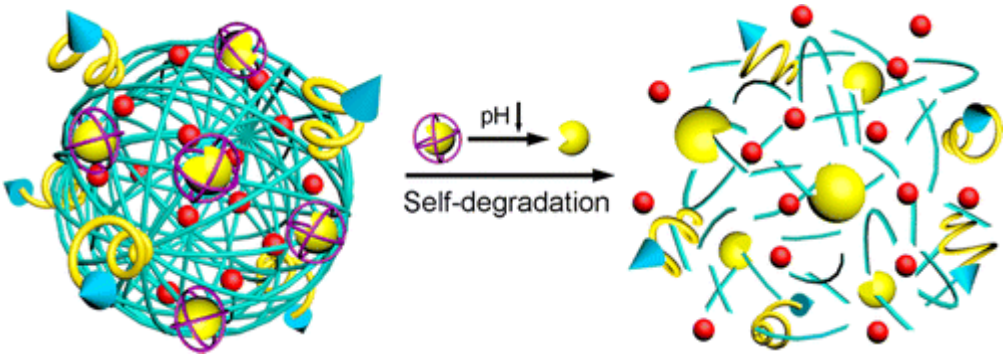
ABSTRACT

A bio-inspired cocoon-like anticancer drug delivery system consisting of a deoxyribonuclease -degradable DNA nanoclew embedded with acid-responsive DNAse I. Nanocapsule was developed for targeted cancer treatment. The NCl was assembled from a long chain single stranded DNA synthesized by the rolling circle amplification. Multiple GC-pair sequences were integrated in the NCl for enhanced loading capacity of anticancer drug. Meanwhile, negatively charged DNAse I was encapsulated in a positively charged acid-degradable polymeric nanogel to facilitate decoration of DNAse I into NCl by electrostatic interaction. At an acidic environment, the activity of DNAse I was activated due to the acid-triggered shedding of the polymeric shell of NCa, resulting in the cocoon-like self-degradation of NCl and promoting the release of drug for enhanced therapeutic efficacy.

KEYWORDS: Nano cocoons, DNA, DNAse, cancer

INTRODUCTION

Novel stimuli drug delivery system is a immediate release system consisting of nanoscale "cocoons" made of DNA that targets cancer cells and trick the cells into absorbing the cocoon before unleashing anticancer drugs. This drug delivery system is DNA-based, which is biocompatible and less toxic to patients than systems that use synthetic materials.



METHOD OF PREPARATION

A new method in bio-nanotech has recently been developed to deliver anti-cancer drugs. Bio-inspired "nano-cocoon" is solely made of DNA. This specially designed system is not only effective in delivering drugs but also is completely bio-compatible. This DNA nano-cocoon is completely self-assembled. Each capsule is only made of one strand of DNA which then rolls up and folds into a ball-like shape through various DNA folding techniques like rolling-circle amplification. The ball that is formed measures around 150 nanometers across. Within the capsule, the scientists have placed the anticancer drug doxorubicin as well as a protein called DNase. The DNase is protected by a thin polymer so that the enzyme may not cut up the DNA which makes up the capsule. Furthermore, the nano-cocoon has multiple folic acid ligands spread throughout its

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surface. The ligands are used to bind to receptors on the surface of a cancer cell so that the cell will automatically suck in the DNA nano-cocoon. Ultimately, the acidic environment within the cancer cell causes the polymer to break down and release the DNase. This causes the nano-cocoon to break apart leading to a massive dose of the drug.

TEMPLATING METHOD

Templating against colloidal particles is probably the most effective and general method for preparation of hollow particles, especially for studies in which a narrow size distribution is required. For example, self assembly and photonic crystals. Monodisperse latex and silica spheres are commonly used as colloidal templates because they are readily available in a wide range of sizes.

Principle: Template method is very versatile for producing hollow nanostructures with various shapes. However, in practice, one often encounters difficulty in coating a layer of designed material (or its precursors) on the template surface primarily due to arterials incompatibility, and in fact prior surface modification is usually required in template synthesis. In the process of coating, various methods have been exploited including sol-gel coating, preparation of oxide hollow particles surface adsorption, double-walled metal oxide structures were prepared by adsorption on both inner and outer surfaces of hollow latex spheres. Silica coating not only reduces the surface curvature but also modifies the surface properties, chemical vapor deposition, atomic layer deposition, and the powerful layer-by-layer adsorption technique utilizing Electrostatic interaction. Preparation of hollow particles with other shapes (e.g., ellipsoidal shape), are relatively few, partly because of the paucity of nonspherical templates and difficulty in forming a uniform coating around surfaces with large variation in curvature. These particles bear some resemblance to silkworm cocoons, and are hereafter termed "nano-cocoons". This method is based on hydrothermal shell-by-shell deposition of polycrystalline SnO on ellipsoidal a-Fe/SiO .This silica coating step by modified Stöber's process is highly reproducible. Indeed, free silica particles formed due to homogeneous nucleation are only occasionally observed during TEM. Which are beneficial to subsequent hydrothermal deposition of polycrystalline SnO forming uniform shells. Interestingly, this deposition step can be repeated to form double-walled structures supporting after annealing at 550 °C, the sandwiched silica layer is dissolved in sodium hydroxide solution to produce double-walled. The surface of the nano-cocoon is studded with folic acid ligands. When the nano-cocoon encounters a cancer cell, the ligands bind the nano-cocoon to receptors on the surface of the cell, causing the cell to suck in the nano-cocoon. Once inside the cancer cell, the cell's acidic environment destroys the polymer sheath containing the DNase. Freed from its sheath, the DNase rapidly slices through the DNA cocoon, spilling DOX into the cancer cell and killing it.

ADVANTAGES:

1. A "nano-cocoon" DNA drug delivery system may offer several advantages over other nanotechnology-based delivery systems, according to new research.
2. "This drug delivery system is DNA based, which means it is biocompatible and less toxic to patients than systems that use synthetic materials,"
3. "This technique also specifically targets cancer cells, can carry a large drug load and releases the drugs very quickly once inside the cancer cell."
4. The DNA cocoon tackles many of the challenges of drug delivery by nanotechnology.
5. The bioinspired nanoclew may prove to be stable in the circulatory system however, targets folate receptors for internalization to the cell, and the rapid acid-activated release of the anticancer drug enhances therapeutic efficacy. The structure is also relatively easy to manufacture. The process of rolling circle amplification produces a single DNA strand containing multiple copies of the circular DNA template. The template includes a palindromic sequence that helps the single DNA strand self-assemble into a nanoclew resembling a ball of yarn 150 microns in diameter.

Mechanism: By conjugating folic acid to complementary DNA and hybridizing it to the nanostructure, the resulting folate-spiked nanoclew binds folate receptors and targets the cancer cell surface. The cargo of the cocoon-like DNA structure includes an anticancer drug as well as (DNase) for self-degradation. The encapsulated DNase represents a novel stimuli-responsive drug delivery system that is activated by the cellular environment. To achieve proper timing of degradation, the negatively charged DNase is encapsulated by a thin positively charged polymeric shell held together by acid-degradable cross-linkers. At physiologic pH, the shell effectively blocks DNase activity. Once the DNA cocoon is inside the endolysosome of cancer cells, the acidic environment degrades the cross-linkers freeing DNase to cleave apart the DNA nanostructure and release doxorubicin. "Besides doxorubicin, other small drugs (eg, camptothecin), Peptides/proteins or nucleic acids can also be delivered using our formulation.

FUTURE OUTCOMES: To launch preclinical testing, with hopes of phase I and II trials to follow in a few years, they are currently evaluating their model in breast cancer cells. The relative simplicity of functionalizing DNA-based carriers may enable broader applications in the future. "We're very excited about this system and think it holds promise for delivering a variety of drugs targeting cancer and other diseases."

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