An Enzyme-Responsive Controlled Release Drug Delivery System Based on Mesoporous Silica and DNA

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ABSTRACT

An efficient enzyme-responsive controlled release drug delivery system was fabricated using functional mesoporous silica nanoparticles (FMSN) encapsulated with the single-stranded DNA. Based on the electrostatic interactions between FMSN and single-stranded DNA, the DNA coating could act as gates for storage of drugs. When DNase I enzyme was added, the DNA could be hydrolyzed to plenty of tiny fragments through the hydrolysis effect of DNase I, and obviously, the gates started to open and drugs loaded in the mesopores of MSN could be released. The system showed an excellent drug release performance, and was expected to be helpful to increase the treatment efficiency of drugs.

Keywords: mesoporous silica, DNA, enzyme-responsive, controlled release

Controlled release carrier systems (CRCS) linked with targeted antibody can maintain valid drug concentration in the precise tissue sites, improve the therapeutic efficacy and reduce side effects [5-9]. Due to the nontoxicity, highly biocompatibility, chemically-stable porous nanostructure and outstanding drug delivery property, mesoporous silica nanoparticles (MSNs) have been used as the most promising based materials for CRCS [1-4].

It is well known that lysosomes can secrete a variety of enzymes to resist the intrusion of foreign organic matters into normal tissue through enzyme catalysis [5-7]. Based on this, a few CRCSs have been developed successfully through organic matter as the coating [8]. When organic matter coated nanomedicine are injected into living body, the nanoparticles can be delivered to lysosomes through endocytosis and then the organic matter will be degraded through the enzyme catalysis effect, thus the encapsulated drugs are released. Owing to the moderate and natural process of enzyme catalysis, CRCSs based on enzyme catalysis of organic matters show high biosafety and efficiency compared with other ones, and have attracted wide interests. However, CRCSs using biomolecules, which can own higher biosafety and biocompatibility, have been rarely developed.

Herein, we describe a enzyme-responsive CRCS using (3-Aminopropyl)triethoxysilane modified mesoporous silica nanoparticles (AMSN) coated by DNA as the carrier. The modification of (3-Aminopropyl)triethoxysilane makes mesoporous silica nanoparticles (MSN) amination and thus positively charged because of the amino protonation, which is beneficial for the coating of negatively charged DNA on AMSN through electrostatic interactions. Because this interaction just causes little influence on the bioactivity of DNA, the coating of DNA can improve the biocompatibility of MSN. As depicted in Figure 1, DNA molecules absorbed onto the surface of AMSN act as closed gates of the AMSN mesopores for storage of drugs. When DNase I enzyme is added into simulated body fluid (SBF), DNA are hydrolyzed to many tiny fragments, which can open the gates to release of drugs from the mesopores. In comparison with recently reported CRCSs, this system possesses high drug-loading capacity, excellent biocompatibility and suitable mesopores for the loading of drugs.

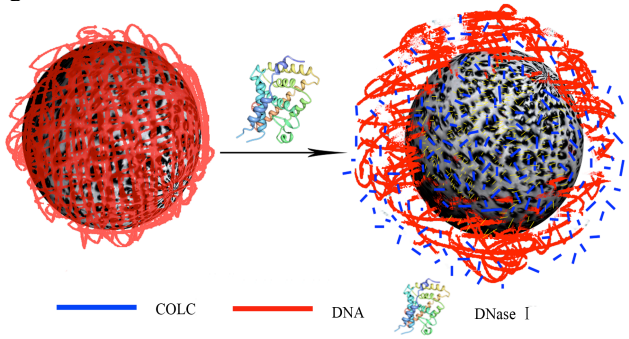

Figure 1. Schematic representation of the mechanism of CDAMSN.

Colchicine (COLC) was selected as a model drug to be loaded in AMSN. To investigate enzyme-responsive release performance of COLC, COLC-loaded DNA coated AMSN (CDAMSN) was immersed in DNase I SBF at 36.5 ^{o}C. Figure 2 showed that little COLC was released from CDAMSN when AMSN was encapsulated by DNA single strands, which indicated that the gates of the mesopores were almost closed. However, about 2 hours after the addition of DNase I, the COLC molecules began to be released in varying degrees, because the gate started to be opened resulting from the hydrolysis of DNA strands. These results suggested that CDAMSN was efficient for the storage of drugs and could control the release of them.

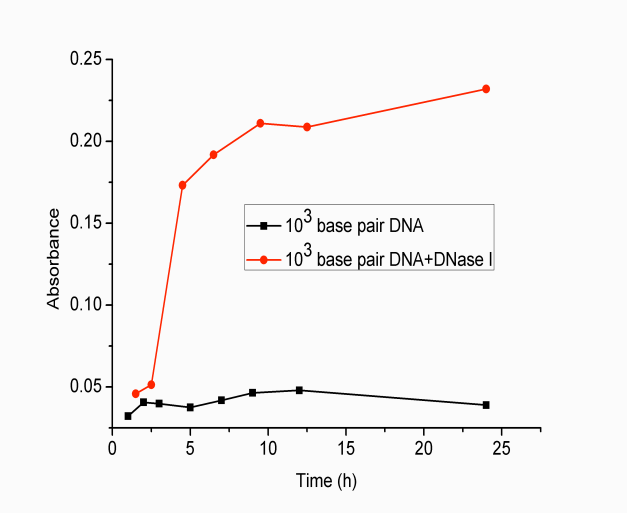

Figure 2. Release behavior of COLC.

In summary, an efficient enzyme-responsive carrier system was successfully fabricated using DNA-coated AMSN. Due to the electrostatic interaction between DNA and AMSN, the DNA coating could act as closed gates for storage of drugs. These gates could be opened through the enzyme hydrolysis effect of DNase I, so that the release performance of the drugs could be controlled by DNA.

References

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