CHINESE JOURNAL OF ANALYTICAL CHEMISTRY
Volume 42, Issue 4, April 2014
Online English edition of the Chinese language journal

Available online at www.sciencedirect.com
ScienceDirect

Cite this article as: Chin J Anal Chem, 2014, 42(4), 475–481.

RESEARCH PAPER

Preparation and Application in Tumor Cells' Drug Delivery of Gold Nanocapsule

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Abstract: Nanocapsules is widely used in the biomedical field because of its unique features. A new nanocapsule was prepared by using gold cage as the core, anticancer drug doxorubicin hydrochloride (DOX) as the internal filler, and functionalized DNA nanomaterials as the shell. The mouth of the cage was blocked by the functionalized DNA nanomaterials. The nanocapsule can be used for the cell detection and drug delivery. The target cells (Ramos cells) can be detected by fluorescence microscope when the drug that can act on target cells and lead to cell death was released. The nanocapsule provides a new approach for the diagnosis and treatment of tumor cells.

Key Words: Au nanocuge; Ramos cells; DNA aptamer; Drug release; Fluorescence microscope

1 Introduction

Nanocapsules is an important branch of nanomaterials[1,2], and has a broad application in the biomedical field. Nanocapsules can penetrate biological barriers because of its tiny structures, load drugs because of its internal space, and can have a capacity of drug controlled release[3] by the functional design. One of a most important applications is the development of targeted control release[4]. Targeting drug delivery technology of nanocapsules is superior to the conventional drug administration since the nanocapsules can improve the biocompatibility of drugs, the absorption of organisms by loading of specific drugs which are insoluble in water. Currently, about 40 percent of drug is not soluble in water, which greatly limits the application of the drug. Drugs in nanocapsules can be directly delivered to the target lesions and in this way, the drugs release continuously and maintain the effective concentration of the drug in the target lesions[5–7]. Therefore this method enhanced the therapeutic effect and reduced the side effects[8,9] on other body tissues or organs, which could be used to solve the problem that common drugs can be easily decomposed in the course of absorption and blood transport. Therefore, the study of nanocapsules in recent years becomes a hot topic. The current research in this area focused on targeting of nanocapsules, optimizing the capsule carrier, and controlling drug release and so on.

Gold cage can be easily synthesized even in general laboratory as a novel nano-materials, and has a broad application potential in the biomedical field because of its biocompatible[10,11]. A new nanocapsule was designed with gold cage as the core and functionalized DNA nanomaterials as the shell. The hollow core gold cage is used to load drugs. The shell has the following features. First, DNA aptamer immobilized on the shell can recognize target tumor cells specially and release drugs to the target. Second, high SNR fluorescence imaging detection can be achieved by DNA fluorescence molecular switch. In summary, the novel nanocapsules can transport drugs, trace the release of drugs. The principle of Au nanocapsules is shown in Fig.1.

The formation process of AU nanocapsules follows several steps. First, the anticancer drug doxorubicin hydrochloride (DOX) are loaded in the hollow structure of Au nanocages, and then DOX is sealed in the Au nanocages by seal layer. The seal layer is formed by sulfur gold-bonded covalent bonding and base pairing hybridization of the improved DNA self-assembly nanostructures. Thus the drug-loaded

Received 12 September 2013; accepted 18 January 2014
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This work was supported by the National Natural Science Foundation of China (No. 21305073)

DOI: 10.1016/S1872-2040(13)60721-5

nanocapsules are obtained. Second, tumor cell specific recognition aptamers DNA S8 is introduced in the nanostructured functional design, which can be used to identify targeted tumor cells. To monitor and track the recognition of nanocapsules to specific cells, fluorescence switching mechanism (DNA aptamer-FAM/DNA-BHQ) is introduced. The DNA S_8 is modified by green fluorescein FAM and DNA S_9 is modified by fluorescence quencher BHQ. The sequences of both DNA are shown in Table 1.

DNA S_8 reacts with target cells only when the Au nanocapsules encounter the specific target cells, and then (BHQ) in DNA S_9 is falling down from the main structure, green fluorescence of FAM in DNA S_8 is recovered, thereby the fluorescence instructions of target cell are opened. The interference of background fluorescence signal is reduced because of fluorescent switch mechanism, thus the imaging signal-to-noise ratio is improved. Au nanocapsules couple with the surface of target cell by specific identification of DNA aptamer, and then enter into the interior of the target cells by means of endocytosis. The sealing layer begin to disintegrate under the action of endocytic vesicles lysosomal Dnase and the structure become loosen, resulting in DOX is released slowly. Owing to the fluorescence properties of DOX, the process of release can be detected by fluorescence confocal microscopy, thus the degree of release can be monitored. The proposed Au nanocapsules can be used to recognize cell specifically, make a signal of fluorescent, deliver targeted drug and trace the process of drug release. The study provides a reference value for the basic research of targeted drug delivery.

2 Experimental

2.1 Instruments and reagents

Ethylene glycol, acetone and ethanol were purchased from Sanwa Chemical Reagent Co., Ltd. (China). Silver nitrate was purchased from Shanghai Chemical Reagent Co., Ltd. (China). Polyvinylpyrrolidone was from Aladdin. Sodium sulfide and sodium chloride were obtained from Tianjin Bodi Chemical Co., Ltd. (China). Chlorine acid was obtained from Guoyao chemical Company (China). Doxorubicin hydrochloride (DOX) was obtained from Shanghai chemical biological engineering Co., Ltd. (China). Tris (2-carboxyethyl) hydrochloric

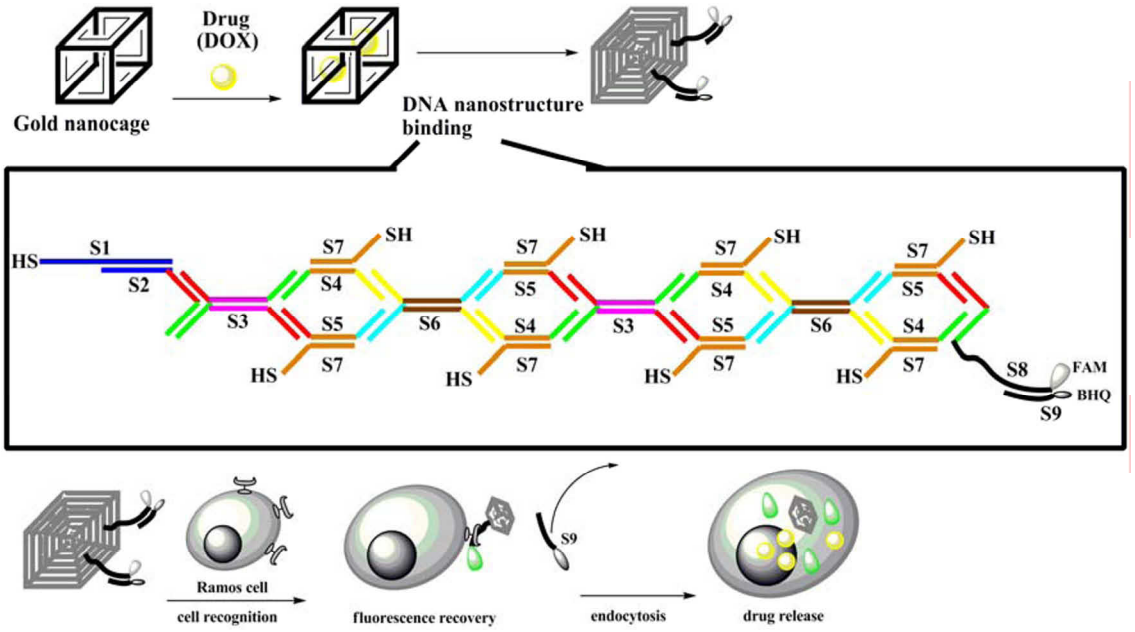

Fig.1 Formation process of Au nanocapsules

Table 1 DNA sequences used in experiment

Name	Sequences
S_1	5'-SH-(CH2)6 - TTT TTT TGA TGA AAC TGG GAG TAT GCA TGC TGG ATA G-3'
S_2	5'-AAA CGA GTC AGT T GTA TCG GAT AGT CTA TCC AGC ATG CAT ACT CCC AGT TTC ATC A-3'
S_3	5'-ACT ATC CGA TAC TGA ACT GGA TCC AGT TCT ACT GAC TCG TTT-3'
S_4	5'-CTA GCA AGA TCC TAC TTT AGA CGG TTG ACT AAA CGA GTC AGT-3'
S_5	5'-GTA TCG GAT AGT TAC TTT AGA CGG TTG ACT TAC AGG AGC TTA-3'
S_6	5'-GGA TCT TGC TAG TTC CTT GAC GTC AAG GAT TAA GCT CCT GTA-3'
S_7	5'- GTC AAC CGT CTA AAG TTT TTT T - (CH2)6 - SH - 3'
S_8	5'-ACT ATC CGA TAC ACT GAC TCG TTT T AAC ACC GGG AGG ATA GTT CGG TGG CTG TTC AGG GTC TCC TCC CGG TGT TT –FAM-3'
S_9	5'-BHQ-AAA CAC CGG GAG-3'