Applied Surface Science 392 (2017) 189–195

Contents lists available at ScienceDirect

Applied Surface Science

journal homepage: www.elsevier.com/locate/apsusc

Folate-targeted single-wall metal-organic nanotubes used as multifunctional drug carriers

Linyan Yang[a,b,1], Min Liu[a,1], Kebin Huang[b], Xia Ai[a], Cun Li[a], Jifei Ma[a], Tianming Jin[a,*], Xin Liu[c,d]

[a] College of Animal Science and Veterinary Medicine, Tianjin Agricultural University, Tianjin, 300384, China
[b] State Key Laboratory for Chemistry and Molecular Engineering of Medicinal Resource, Guangxi Normal University, Guilin 541004, China
[c] College of Chemistry, Collaborative Innovation Center of Chemical Science and Engineering(Tianjin), Nankai University, Tianjin, 300071, China
[d] Key Laboratory of Advanced Energy Materials Chemistry(KLAEMC), Nankai University, Tianjin, 300071, China

ARTICLE INFO

Article history:
Received 8 August 2016
Received in revised form 9 September 2016
Accepted 9 September 2016
Available online 13 September 2016

Keywords:
SWMONTs
Drug delivery
Modification
Characterization

ABSTRACT

Doxorubicin (DOX) is a member of the anthracycline class of chemotherapeutic agents that are used for the treatment of many common human cancers. A self-assembled functionalized metal-organic nanotubes, SWMONTs could be loaded with the anticancer drug DOX. Via the modification of SWMONTs, DOX/SWMONTs-SiO_2, DOX/SWMONTs-SiO_2-NH_2, DOX/SWMONTs-SiO_2-NH_2-FA samples could be obtained. The SEM characterization of the samples indicated that the particle size of DOX/SWMONTs-SiO_2NH_2 samples were smaller than 200 nm. Drug-release experiments implied that DOX from the DOX/SWMONTs-SiO_2-NH_2-FA samples could be released faster at acidic tumor tissue than at normal body fluid (pH7.4). DOX has strong cytotoxicity, and at 20 μg/mL dosage of DOX large amount of apoptotic cells could be seen. Cellular uptaking experiments were used to study the apoptotic mechanism, while for DOX/SWMONTs-SiO_2-NH_2-FA samples, the strong drug fluorescence was found in the cytoplasm rather than in the nucleus.

© 2016 Elsevier B.V. All rights reserved.

1. Introduction

Cancer is one of the top three killers in the world, next to heart and cerebrovascular diseases [1]. In a number of situations, the malignancy of tumors is detected only at advanced stages when administration of chemotherapeutic drugs is toxic to healthy cells. Doxorubicin (DOX) is a member of the anthracycline class of chemotherapeutic agents that are used for the treatment of many common human cancers, including aggressive non-Hodgkin's lymphoma [2,3]. However, the drug is associated with severe, sometimes fatal cardiotoxicity due to a lack of target specificity. Over the past decades, various nanocarriers have been employed to deliver drugs based on either passive targeting and/or active targeting. Compared to passive targeting strategy, active targeting exhibits more effective accumulation of nanocarries in tumors by taking advantage of the selectively incorporation between the up-regulated receptors on the surface of tumor cells and the modified targeted moieties including monoclonal antibodies [4], peptides [5], aptamers [6,7], and small molecules [8]. The strategies used in advanced theranostics, such as solid lipid nanoparticles, magnetic nanoparticles, and quantum dots, may achieve fewer side effects [9]. Wang et al. has reported tamoxifen embedded in the lipid bilayer, which could improve the oncotarget of liposomal daunorubicin in vivo [10,11]. R.D.K. Misra et al. have described the synthesis of folate-decorated chitosan-CNT nanocarrier and chitosan-encapsulated ZnO quantum dots for targeted delivery of DOX [3,12], which belongs to active targeting. Magnetic targeting and thermal targeting have been widely reported, too [13,14]. Recently, metal-organic frameworks (MOFs) composed of metals (single-metal ions or metal clusters) connected by organic linkers have emerged as charming porous materials. Current researches suggest that MOFs are suitable candidates as drug delivery carriers in view of their large loadings of drugs [15]. Both single-walled carbon nanotubes (SWCNT) and multi-walled carbon nanotubes (MWCNT) are being considered as a drug delivery nanocarrier [16], because they were observed to cross cell membranes [17–19] and exhibit blood circulation half-lives of the order of hours [20]. There are a lot of advantages for tubular nano-materials. A limited number of single-wall metal-organic nanotubes (SWMONTs) have been synthesized, while a majority of reports have focused solely on structural details. SWMONTs have already shown promise in

* Corresponding author.
E-mail address: JTMSCl@163.com (T. Jin).
[1] These authors contributed equally to this work.

http://dx.doi.org/10.1016/j.apsusc.2016.09.030
0169-4332/© 2016 Elsevier B.V. All rights reserved.

highly selective adsorptions [21]. Herein, doxorubicin (DOX) could be loaded into the reported functionalized SWMONTs (named as DOX/SWMONTs), and the DOX/SWMONTs samples could be modified to obtain DOX/SWMONTs-SiO_2, DOX/SWMONTs-SiO_2-NH_2 and DOX/SWMONTs-SiO_2-NH_2-FA samples. SWMONTs was an one-dimensional tubular complex based on Zn(II) ions, the molecular formula of which could be expressed as $[Zn(C_{17}H_{11}N_3O_4)(H_2O)]_n \cdot nH_2O$ [22].

2. Experimental section

2.1. Materials and physical measurements

All commercially available chemicals and solvents were of reagent grade and used without further purification. SWMONTs was synthesized according to the method reported previously [22]. Thermogravimetric analysis (TGA) was performed on a NETZSCH TG 209 instrument with a heating rate of 10 °C/min in the flowing N_2 atmosphere. Flourescence spectroscopy data were recorded on HORIBA Jobin Yvon HJY-FL3-221-TCSPC spectrophotometer. Changes in morphology and size could be characterized by scanning electron microscope (SEM).

2.2. DOX loading

To evaluate the capacity as drug delivery carriers of SWMONTs, adsorption of DOX [23] was carried out by impregnating SWMONTs (20 mg) in ethanol solutions (20 mL) containing DOX (10 mg, 15 mg, 20 mg), and then oscillating at 37 °C and 160r/min for 72 h. The precipitation was isolated by centrifuging and washed with ethanol for twice. The sample was named as DOX/SWMONTs. The DOX content was calculated using TGA method.

2.3. Surface modification of DOX/SWMONTs

DOX/SWMONTs-SiO_2 preparation: $NH_3 \cdot H_2O$ (200 μL) was added to the samples of DOX/SWMONTs, and the mixture was reacted for 20 min under the 100W of ultrasound. Tetraethyl orthosilicate (TEOS) (50 μL) was dropwise added into the samples. And then the samples were oscillated at 37 °C and 160r/min overnight, followed by centrifugation at 12000g for 15 min. The supernatant was discarded, and the residue was washed with ethanol for twice to yield DOX/SWMONTs-SiO_2 [24].

DOX/SWMONTs-SiO_2-NH_2 preparation: The samples of DOX/SWMONTs-SiO_2 (20 mg) were then dipped in an ethanol solution (10 mL) with (3-Aminopropyl) trimethoxysilane (APTMS) (100 μL) for 24 h. After rinsing with ethanol for twice, the samples named as DOX/SWMONTs-SiO_2-NH_2 were vacuum-dried at room temperature overnight [25].

DOX/SWMONTs-SiO_2-NH_2-FA preparation: Folate (FA, 16 mg) was activated by EDC (8 mg) and NHS (4.8 mg) in DMSO (5 mL) for 24 h. The samples of DOX/SWMONTs-SiO_2NH_2 (20 mg) were suspended again in 60% aqueous solution (5 mL) of ethanol, and then were added into activated FA solution. The amidation reaction processed at room temperature for 24 h, followed by centrifugation at 12000g for 15 min. After washing by ethanol, the samples of DOX/SWMONTs-SiO_2-NH_2-FA could be obtained by vacuum-dried process (Fig. 1) [26].

2.4. X-ray photoelectron spectroscopy (XPS) analysis

XPS spectra were recorded using a Kratos Axis Ultra DLD spectrometer employing a monochromated Al-Kα X-ray source (hv = 1486.6 eV). The vacuum in the main chamber was kept above 3×10^{-6} Pa during XPS data acquisitions. General survey scans (binding energy range: 0–1200 eV; pass energy: 160 eV) and high-resolution spectra (pass energy: 40 eV) in the regions of N1 s were recorded. Binding energies were referenced to the C1 s binding energy at 284.60 eV [27].

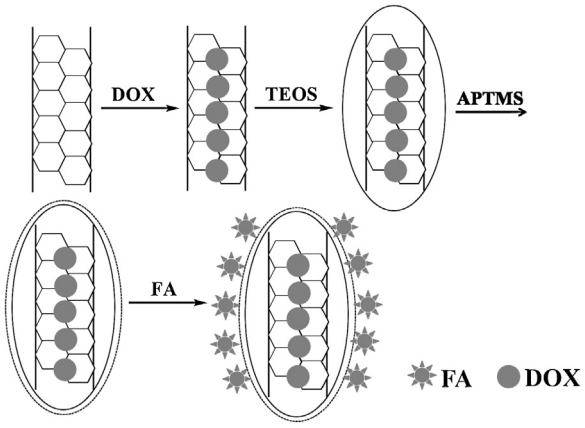

Fig. 1. Drug loading and modification procedures of SWMONTs.

2.5. Drug release

The in vitro release assay of DOX from DOX/SWMONTs-SiO_2-NH_2-FA samples was performed in a phosphate-buffered saline solution (PBS, 0.01 M, pH 5.7 and 7.4) at 37 °C [28]. Approximate 10 mg of DOX/SWMONTs-SiO_2-NH_2-FA samples was suspended into 10 mL of PBS buffer solution in a centrifuge tube, which was oscillated at 37 °Cand 160r/min. During each time interval (4 h, 6 h, 24 h, 72 h, 96 h, 144 h), about 3 mL of the solution was pulled out to test, and fresh PBS buffer was supplemented until the test was over. DOX was detected at 592 nm with the excitation wavelength (478 nm) by fluorescence spectrophotometer. Fluorescence intensity could be changed with the DOX concentration gradient.

2.6. Cell culture

Mice Breast Cancer 4T1 cells was all obtained from the Chinese Academy of Sciences (Shanghai, China). 4T1 cells were routinely cultured using RPMI-1640 supplemented with 10% fetal bovine serum (FBS), 100units/mL penicillin, and 100 μg/mL streptomycin in a humidified atmosphere of 5% CO_2 at 37 °C. To maintain cells in the exponential growth phase, they normally passed at a ratio of 1:3 every three days. Before use, the cells were harvested through trypsinization with 0.25% trypsin at 37 °C. Trypsinization was stopped by the addition of fresh supplemented RPMI-1640, and the cell suspension was centrifuged at a rotational speed of 800 rpm for 3 min. The cells were then resuspended in supplemented RPMI-1640 (2×10^4cells/mL) for use. Caution was used in handling all human biological material [29].

2.7. Cellular uptaking

4T1 cells were seeded in 24-well plates at a cell density of 2×10^4 cells/mL (100 μL/well). After 24 h of conventional cultivation, the cells were further incubated for 6 h, 15 h and 18 h in fresh culture media containing pure DOX, DOX/SWMONTs-SiO_2-NH_2, or DOX/SWMONTs-SiO_2-NH_2-FA with the concentration level of 20 μg/mL. After that, DAPI was added, and incubated for 15 min to stain the nucleus. After the incubation, the cells were softly washed for twice. An inverted microscope was used to acquire fluorescence images [30].

Download English Version:

https://daneshyari.com/en/article/5354630

Download Persian Version:

https://daneshyari.com/article/5354630

Daneshyari.com