Journal of Drug Delivery Science and Technology 66 (2021) 102881

Contents lists available at ScienceDirect

Journal of Drug Delivery Science and Technology

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

Fabrication of novel poly(*N*-vinylcaprolactam)-coated UiO-66-NH_2 metal organic framework nanocarrier for the controlled release of doxorubicin against A549 lung cancer cells

Navid Rakhshani [a], Nahid Hassanzadeh Nemati [a,*], Ahmad Ramazani Saadatabadi [b], S. K. Sadrnezhaad [c]

[a] Department of Biomedical Engineering, Science and Research Branch, Islamic Azad University, Tehran, Iran
[b] Department of Chemical and Petroleum Engineering, Sharif University of Technology, Tehran, Iran
[c] Department of Materials Science and Engineering, Sharif University of Technology, Tehran, Iran

ARTICLE INFO

Keywords:
Metal-organic framework
UiO-66-NH_2
Poly(*N*-Vinylcaprolactam)
Doxorubicin
Lung cancer

ABSTRACT

The nano metal-organic frameworks (NMOFs) have been developed for drug delivery systems due to their high porosity and large specific surface area. In this work, UiO-66-NH_2 NMOFs were synthesized via the microwave heating method and doxorubicin (DOX) as an anticancer drug was incorporated into the UiO-66-NH_2 NMOFs. Then, poly(*N*-vinylcaprolactam) (PNVCL) synthesized by the free radical polymerization was coated on the UiO-66-NH_2 NMOFs surface to fabricate dual pH/temperature-responsive nanocomposite against A549 lung cancer cells death in vitro. The synthesized nanocarriers were characterized using FTIR, ^{1}H NMR, DLS, XRD, SEM, FESEM, TGA, and BET analysis. The average particle sizes of UiO-66-NH_2, PNVCL 1% and PNVCL 2%-coated UiO-66-NH_2/DOX NMOFs were found to be 190 ± 110 nm, 265 ± 140 nm, and 360 ± 150 nm, respectively. TGA analysis showed that the PNVCL percentages-coated UiO-66-NH_2 NMOFs were found to be about 17.5%, and 27.3% for NMOFs incubated in 1% and 2% PNVCL solutions, respectively. The BET surface area of UiO-66-NH_2 NMOFs, UiO-66-NH_2 NMOFs/DOX 100 μg mL^{-1}, and PNVCL 1%-coated NMOFs/DOX was found to be 1052, 121, and 87 m^2g^{-1}, respectively. The DOX release data of UiO-66-NH_2 and PNVCL-coated UiO-66-NH_2/DOX were evaluated under pH values of 5.5, 7.4, and temperatures of 25 °C, 37 °C. The maximum cytotoxicity of A549 cancer cells treated with PNVCL 1%-coated UiO-66-NH_2/DOX 100 μg mL^{-1} NMOFs was found to be 76%. The obtained results revealed the high capability of UiO-66-NH_2/DOX/PNVCL dual-responsive nanocomposite for delivery of anticancer drugs.

1. Introduction

Metal-organic frameworks (MOFs) as crystalline porous materials have been widely used for targeted delivery of anticancer drugs due to their high specific surface area, large porosity, good biocompatibility, and fine pore sizes [1–7]. The nanosized-MOFs (NMOFs) prepared by the microwave heating method exhibited the unique physico-chemical properties in comparison to the micrometer scale of MOFs [1,8]. The advantages of MOFs compared with other inorganic drug delivery systems (DDSs) are their high encapsulation efficiency and their easier functionalization for targeted delivery [9–14]. Among various MOFs used in DDSs, UiO-66 MOFs due to having high stability and high biocompatibility as well as good biodegradability and high specific surface area have been of particular interest for DDSs [15–17]. Furthermore, UiO-66 MOFs with Zr–O clusters, and metal sites, as well as octahedral and tetrahedral cavities, could be considered for the controlled release of doxorubicin (DOX) due to having a coordination interaction between the Zr (IV) clusters of UiO-66 and hydroxyl groups of DOX [4,18]. Moreover, the presence of open cavities and clusters in the UiO-66 MOFs matrix cause to load the high content of drug molecules, and following its release could occur in a controlled manner. UiO-66 MOF is also a good candidate for the controlled release of anticancer agents into the cancer tissues as a pH-sensitive carrier [18]. Thus, DOX could be released from UiO-66 MOFs into the acidic tumor sites due to the protonation of phosphate and weaknesses of the interaction between DOX and Zr–O clusters of UiO-66 MOFs under acidic

* Corresponding author.
E-mail addresses: navid.rakhshani@gmail.com (N. Rakhshani), hasanzadeh@srbiau.ac.ir (N. Hassanzadeh Nemati).

https://doi.org/10.1016/j.jddst.2021.102881
Received 24 June 2021; Received in revised form 7 September 2021; Accepted 26 September 2021
Available online 23 October 2021
1773-2247/© 2021 Elsevier B.V. All rights reserved.