International Journal of Pharmaceutics 604 (2021) 120776

Contents lists available at ScienceDirect

International Journal of Pharmaceutics

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

Mitochondria-targeted mesoporous silica nanoparticles noncovalently modified with triphenylphosphonium cation: Physicochemical characteristics, cytotoxicity and intracellular uptake

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ARTICLE INFO

Keywords:
Mesoporous silica
Hexadecyltriphenylphosphonium bromide
Rhodamine B
Encapsulation
Mitochondrion targeting

ABSTRACT

Novel nanocomposite system based on mesoporous silica nanoparticles (MSNs) noncovalently modified with hexadecyltriphenylphosphonium bromide (HTPPB) has been prepared, thoroughly characterized and used for encapsulation of model cargo Rhodamine B (RhB). The high encapsulation efficacy of this dye by HTPPB-modified mesoporous particles was demonstrated by spectrophotometry and thermography techniques. The bioavailability of MSN@HTPPB was testified. Cytotoxicity assay revealed that a marked suppression of M−HeLa cancer cells (epithelioid carcinoma of the cervix) occurs at concentration of 0.06 μg/mL, while the higher viability of Chang liver normal cell line was preserved in the concentration range of 0.98–0.06 μg/mL. Hemolysis assay demonstrated that only 2% of red blood cells are destructed at ~ 30 μg/mL concentration. This allows us to select the most harmless compositions based on MSN@HTPPB with minimal side effects toward normal cells and recommend them for the development of antitumor formulations. Fluorescence microscopy technique testified satisfactory penetration of HTPPB-modified carriers into M−HeLa cells. Importantly, modification of the MSN with HTPPB is shown to promote efficient delivery to mitochondria. To the best of our knowledge, it is one of the first successful examples of noncovalent surface modification of the MSNs with lipophilic phosphonium cation that improves targeted delivery of loads to mitochondria.

1. Introduction

In recent years various smart nanostructured colloids (micelles, microemulsions, liposomes), polymeric and inorganic nanoparticles have been of fundamental and practical interest as drug delivery systems (Jin et al., 2019; Buck et al., 2019; Agrawal et al., 2019; Liao et al., 2019; Nurunnabi et al., 2019; Gao et al., 2019; Huang et al., 2019; Mirgorodskaya et al., 2019; Gu et al., 2018; Kuznetsova et al., 2019a; Kashapov et al., 2018; Kuznetsova et al., 2019b). Among them mesoporous silica nanoparticles (MSNs) reported in 1992 by scientists of Mobil Oil Corporation (Yanagisawa et al., 1990; Kresge et al., 1992), attract increasing attention as perspective carriers. MSNs demonstrate a number of unique and practically useful properties, such as large surface area ($\geq$700 m^2/g) and volume of pores (>1 cm^3/g); uniform and tunable size; shape of pores allowing of entrapment of various molecules, with high efficiency of encapsulation and loading achieved; excellent protective properties against decontamination of cargo by endogenous enzymes (Singh et al., 2017; Maleki et al., 2017; Li et al., 2019). In addition, mesoporous materials based on silica are perfect platform for engineering the polyfunctional composites with suitable bioavailability.

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https://doi.org/10.1016/j.ijpharm.2021.120776
Received 14 January 2021; Received in revised form 1 June 2021; Accepted 2 June 2021
Available online 4 June 2021