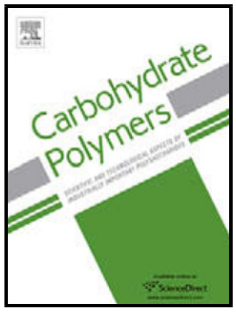

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Sequentially Self-Assembled Polysaccharide-based Nanocomplexes for Combined Chemotherapy and Photodynamic Therapy of Breast Cancer

Yaping Wang [a, Δ], Ming Yang [a, Δ], Junmin Qian [a, *], Weijun Xu [a], Jinlei Wang [a], Guanghui Hou [a], Lijie Ji [a], Aili Suo [b, *]

[a] State Key Laboratory for Mechanical Behavior of Materials, Xi'an Jiaotong University, Xi'an 710049, China

[b] Department of Oncology, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, China

[Δ] These authors contributed equally to this work.

*Corresponding Authors: E-mail address: jmqian@mail.xjtu.edu.cn (J.M. Qian); ailisuo@mail.xjtu.edu.cn (A.L. Suo); Tel: +86 29 82668614; Fax: +86 29 82663453

Highlights

1. Multifunctional hyaluronic acid/hydroxyethyl chitosan nanocomplexes were prepared.
2. DOX and ALA were loaded into polysaccharide nanocomplexes via Schiff base linkage.
3. Nanocomplexes displayed pH-responsive surface charge reversal and drug release.
4. Active targeting enhanced additive effect of chemotherapy and photodynamic therapy.

Abstract

Combination of chemotherapy and photodynamic therapy has emerged as a promising anticancer strategy. Polysaccharide-based nanoparticles are being intensively explored as drug carriers for different forms of combination therapy. In this study, novel multifunctional polysaccharide-based nanocomplexes were prepared from aldehyde-functionalized hyaluronic acid and hydroxyethyl chitosan via sequential self-assembly method. Stable nanocomplexes were obtained through both Schiff's base bond and electrostatic interactions. Chemotherapeutics doxorubicin and pro-photosensitizer 5-aminolevulinic acid were chemically conjugated onto the nanocomplexes via Schiff base linkage. Anti-HER2 antibody as targeting moiety was decorated onto the surface of nanocomplexes. The obtained near-spherical shaped nanocomplexes had an average size of 140 nm and a zeta potential of −24.6 mV, and displayed pH-responsive surface charge reversal and drug release. Active targeting strategy significantly enhanced the cellular uptake of nanocomplexes and combined anticancer efficiency of chemo-photodynamic dual therapy in breast cancer MCF-7 cells. These results suggested that the nanocomplexes had great potential for targeted combination therapy of breast cancer.

Keywords: hyaluronic acid; hydroxyethyl chitosan; nanocomplexes; pH-responsivity; chemo-photodynamic dual therapy; breast cancer

1. Introduction

Breast cancer is the most common type of cancer found in women and affects approximately one-eighth of women over their lifetime worldwide (Xu et al., 2017). Although some promising technologies for cancer therapies like immunotherapy (Flemming, 2016; Lebel, Chartrand, Tarrab, Savard, Leclerc & Lamarre, 2016; Wang, Xu, Liang, Xiang, Peng & Liu, 2014) have been developed, traditional chemotherapy still plays a dominant role (Chung et al., 2016; Im et al., 2016; Lin et al., 2013; Zhang et al., 2016a). Doxorubicin (DOX) is a well-known chemotherapeutic drug and can combat various tumors including breast cancer by intercalating and inhibiting the biosynthesis of DNA. However, DOX, like most chemotherapeutic drugs, may cause considerable toxic side effects and drug resistance in cancer cells after repeated sessions of chemotherapy (He, Liu & Lin, 2015;