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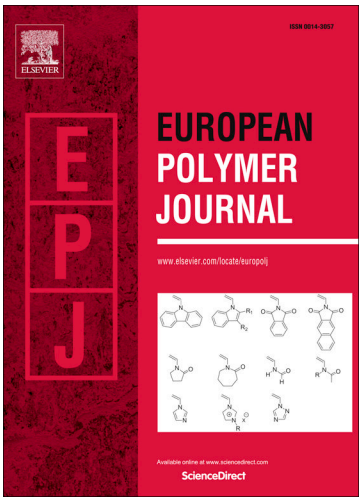

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Javier Perez Quinones, Johanna Jokinen, Salli Keinänen, Carlos Peniche Covas, Oliver Brüggemann, Dmitri Ossipov

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Self-assembled hyaluronic acid-testosterone nanocarriers for delivery of anticancer drugs

Javier Perez Quinones[a,*], Johanna Jokinen[b], Salli Keinänen[b], Carlos Peniche Covas[c], Oliver Brüggemann[a], Dmitri Ossipov[d]

[a] *Johannes Kepler University Linz, Institute of Polymer Chemistry, Altenberger Straße 69, 4040 Linz, Austria. javenator@gmail.com; oliver.brueggemann@jku.at*
[b] *University of Turku, Department of Biochemistry, Vatselankatu 2, 20500 Turku, Finland. johjok@utu.fi*; *sakakei@utu.fi*
[c] *University of Havana, Center of Biomaterials, Ave. Universidad s/n entre G y Ronda, Vedado, 10400 La Habana, Cuba. cpeniche2015@yahoo.com*
[d] *Uppsala University, Department of Chemistry-Angstrom Laboratory, Lägerhyddsvägen 1, Uppsala, SE 751 21, Sweden. dmitri.ossipov@kemi.uu.se*

Abstract

The present research aims at controlled delivery of anticancer drugs camptothecin and doxorubicin through encapsulation in self-assembled hyaluronic acid (HA)-testosterone conjugates. The conjugates were obtained by functionalization of either natural sodium hyaluronate or hydrazide-modified HA derivatives with testosterone hemisuccinate. From 2.0 to 7.7% of HA disaccharide units were linked to testosterone via two types of linkers of different length. Fourier transform infrared and proton nuclear magnetic resonance spectroscopies confirmed modification of HA. Conjugation of hydrophobic testosterone to hydrophilic backbone of HA resulted in the self-assembly of amphiphilic HA-testosterone conjugates in aqueous medium and the formation of stable and negatively charged nanoparticles with hydrodynamic diameter ranging from 172 to 380 nm and ζ-potential ranging from -37 to -26 mV, as evidenced from dynamic light scattering measurements. Examination of the dried conjugates by transmission electron microscopy revealed almost spherical particles of 50 to 100 nm size. Entrapment of camptothecin and doxorubicin in the hydrophobic core of HA-testosterone nanoparticles was performed with the drugs content of ca. 2.8 wt.% and 3.5 wt.% respectively. The sustained release of the anticancer drugs over 96 h was observed in phosphate buffered saline at pH 7.4. Cytotoxicity of camptothecin- and doxorubicin-loaded HA-testosterone nanoparticles against MCF-7 cancer cell line was found to be similar to the cytotoxicity of the free anticancer drugs. Based on the results of the *in vitro* studies, we can conclude that the developed HA-testosterone nanoparticles are promising candidates in chemotherapy treatments of cancers.

Keywords

Hyaluronic acid; testosterone; anticancer drugs; self-assembled nanoparticles; sustained release.

1. Introduction

Doxorubicin (DOX) is a traditional anticancer drug widely employed in combination with other chemotherapeutic agents for treatment of some leukemias, lymphomas, and cancers of bladder, stomach, breast, ovaries, lung, thyroid and multiple myeloma. However, high therapeutic doses of DOX administered over months of clinical tumor treatments raise the incidence of related life threatening side effects such as cardiomyopathy, with subsequent congestive heart failure, myelosuppression and acute bowel infection [1,2]. Another inhibitor of