Novel mesoporous nanoparticles for the targeted delivery of anticancer agents to estrogen receptor overexpressing breast cancer

Key word: breast cancer, targeting, nanotechnology, doxorubicin, nanoparticles

Candace DAY[1], Sally PLUSH[1], May SONG[1], Na ZHANG[1], Sanjay GARG[1]

1. School of Pharmacy and Medical Sciences, University of South Australia, SA, Australia.

2. School of Pharmaceutical Science, Shandong University, Ji'nan, China.

Breast cancer is one of the leading causes of death from cancer in women [1]. Besides conventional treatments, targeted therapy has emerged as a promising treatment approach. Exploiting the advantageous properties of nanotechnology, various nanomaterials have been synthesized to deliver anticancer drugs specifically to tumours, with high accuracy, low toxicity and minimal side effects. One of the most cutting-edge nanotechnology-based drug delivery systems is mesoporous silica nanoparticles (MSNs). Owing to their large surface area and pore volumes, enhanced tumour absorption of incorporated drugs can be achieved via the surface functionalization of MSNs, for the targeted delivery of anticancer agents [2]. Doxorubicin (DOX) is a potent drug commonly used in chemotherapy, owing to its ability to interfere with DNA and RNA of solid tumors [3]. However, the therapeutic potentials of DOX are limited by its cardiotoxicity. Therefore, in order to minimize side effects, the targeted delivery of DOX to breast cancers could be achieved using MSNs as its nanocarriers.

To delivery DOX specifically to estrogen receptor (ER) - overexpressing breast tumours, and to release it at the tumour micro-environment, a novel nanocarrier was proposed based on MSNs, grafted with the guiding vector Tamoxifen (TAM) which is known to bind to ER, and initiate active cellular endocytosis. Poly(L-histidine) (PLH) will be introduced into the systems as a pH-sensitive component, and Poly(ethylene glycol) (PEG) will be employed as a hydrophilic coating. The mesoporous structure of resulting MSNs were confirmed through XRD and BET techniques. PEG molecules of different molecular weights were used to synthesize the intermediate compound *Tosylated PEG*, in order to introduce TAM molecules onto the surface of MSNs via PEG linkages. LC-MS, H-NMR and C-NMR were employed to confirm the structure of *Tosylated PEG*. The use of PEG 400 and PEG 1450 demonstrated the best preliminary results for the tosylation process.

References

[1] Australia C. Breast cancer. In: Government A, editor. 2017.
[2] Slowing II, Vivero-Escoto JL, Wu C-W, Lin VSY. Mesoporous silica nanoparticles as controlled release drug delivery and gene transfection carriers. Advanced Drug Delivery Reviews. 2008;60(11):1278-88
[3] Lao J, Madani J, Pu, et al. Liposomal Doxorubicin in the Treatment of Breast Cancer Patients: A Review. Journal of Drug Delivery. 2013;2013: