Bioinspired nanoparticles as trastuzumab and paclitaxel targeted carrier for HER2-positive breast cancer treatment

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Abstract

HER2-overexpression has long been associated with a worse prognosis for patients suffering from breast cancer. However, this overexpression has also allowed the development of targeted anti-HER2 agents that have remarkably improved patient outcomes, like trastuzumab, whose administration, along with taxanes, has notably increased the overall survival rate of this disease. Nevertheless, both trastuzumab and the taxanes, have significant side toxicity, and the apparition of resistances to them is frequent [1,2]. In this way, in other to overcome these drawbacks, a drug targeted nanovehicle made up of polydopamine nanoparticles (PDA NPs) (180 nm) was developed in the current work to transport both paclitaxel (PTX) and trastuzumab (Tmab). Since PDA has strong ability to load drugs [3,4], the mentioned taxane and antibody could be directly incorporated to the NPs synthesized. Besides, Tmab was also covalently bound to PDA NPs by means of the carbodiimide chemistry to compare the results obtained following both loading strategies. The effectiveness and selectivity of the NPs obtained were validated *in vitro* with different human HER2-overexpressing tumour and normal cells. They proved to have more noticeable antitumour activity than a nanosystem previously developed for the transport of PTX and Tmab and, in addition, to be more selective than the parent drug. Moreover, loaded PDA NPs, which were capable of highly increasing the number of apoptotic HER2-positive breast cancer cells upon administration, maintained their therapeutic activity when validated in HER2-overexpressing breast tumour spheroids. Thus, this novel Tmab and PTX nanocarrier may represent a great approach to reduce the severe side effects of the HER2-positive breast cancer therapies that already exist, while reducing the probability of the apparition of treatment resistances.

References

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