Proceedings of the 9th World Congress on Recent Advances in Nanotechnology (RAN 2024)
London, United Kingdom –April 8 – 10, 2024
Paper No. NDDTE 118
DOI: 10.11159/nddte24.118

DOX-Couped Polymeric Micelles as a State-of-the-Art Strategy Against Triple Negative Breast Cancer

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Extended Abstract

Triple-negative breast cancer (TNBC), a unique type of breast cancer, is defined by the absence of ER, PR, and HER-2 receptors in the tumor. This particularly aggressive form of breast cancer, TNBC, shows early signs of resistance to chemotherapy [1]. One significant challenge with this subtype is its less favorable outlook compared to other types of breast cancer, resulting in lower overall survival rates, frequent relapses, and increased mortality. Current treatments for Triple-Negative Breast Cancer (TNBC) typically include chemotherapy, surgery, and radiation therapy. However, the use of these treatments remains limited due to high systemic toxicity, the development of chemotherapy resistance, tumor heterogeneity, and a high risk of metastasis [2]. Therefore, new, and effective treatment approaches should be developed for TNBC. Doxorubicin (DOX) remains the primary chemotherapy agent employed in the traditional treatment of triple-negative breast cancer (TNBC). Nevertheless, its clinical use is suboptimal due to issues such as drug resistance, non-discriminatory distribution, cardiac toxicity, limited solubility and restricted penetration [3]. Hence, the development of a drug delivery system that decreases the harmful effects of drug and enhances penetration is essential for the successful treatment of TNBC. With the aim of introducing treatment for TNBC, we have engineered polymeric nanoparticles that are coupled with doxorubicin. In our research, we effectively produced a new negatively charged SPMA/PMMA polymer using RAFT polymerization. Nanoparticles were generated via the nanoprecipitation technique. To create a complex between nanoparticles and DOX, we utilized electrostatic binding. Based on Dynamic Light Scattering (DLS) and ζ-potential assessment, our nanoparticles size increased slightly from 134.3 ± 1 nm to 189.7 ± 10 nm, whereas the charge of the particles were increased from -46.9 mV to -15 mV. Complexes were formed at different weight ratios (1:1, 1:2, 1:5), and the complex with the highest binding efficiency and the smallest size is 1:1 complexation ratio. Upon the formation of a complex between doxorubicin and the nanoparticles (DOX NPs), there was a slight increase in the size of the nanoparticles, growing from 134.3 ± 1 nm to 189.7 ± 10 nm. Simultaneously, the charge of the nanoparticles shifted from -46.9 ±3 mV to -15 ±4 mV. The critical micelle concentration (CMC) was established at 17 µg/mL, and the binding efficiency was assessed at 64.5 ±2 % based on the measurement of free doxorubicin absorbance in the supernatants. While bare NPs did not exhibit significant cytotoxicity, the presence of DOX within the nanocarriers reduced the viability of breast cancer cells, and this effect was observed similarly to free DOX treatment. In line with these results, our biocompatible carrier system, which we designed, successfully delivered DOX to breast cancer cells, and demonstrated its potential as an anti-cancer agent by reducing cell viability.

Keywords: PMMA/SPMA polymer, polymeric micelles, TNBC, DOX.

Acknowledgements

Berrin Chatzi Memet is supported by the TUBITAK (121C221).

References

[1] Cansu Umran Tunc and Omer Aydin, *Co-delivery of Bcl-2 siRNA and doxorubicin through gold nanoparticle-based delivery system for a combined cancer therapy approach.* Journal of Drug Delivery Science and Technology, 2022. **74**: p. 103603.

[2] Rebecca Dent , Maureen Trudeau, Kathleen I Pritchard, Wedad M Hanna, Harriet K Kahn, Carol A Sawka, Lavina A Lickley, Ellen Rawlinson, Ping Sun, Steven A Narod, *Triple-Negative Breast Cancer: Clinical Features and Patterns of Recurrence.* Clinical Cancer Research, 2007. **13**(15): p. 4429-4434.

[3] Jingyi Zhou, Kangkang Li, Xinlong Zang, Yi Xie, Jinxiao Song, Xuehong Chen, *ROS-responsive Galactosylated-nanoparticles with Doxorubicin Entrapment for Triple Negative Breast Cancer Therapy.* Int J Nanomedicine, 2023. **18**: p. 1381-1397.