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DEVELOPMENT OF B-CARYOPHYLLENE-FUNCTIONALIZED LIPID NANOPARTICLES CONTAINING PACLITAXEL FOR THE TREATMENT OF BREAST CANCER

Gabriela Geronimo*, Gustavo Henrique Rodrigues da Silva, Ludmilla David de Moura, Fabíola Vieira de Carvalho, Rayza Catheryne Pereira da Costa, Talita Cesarim Mendonça, Eneida de Paula.
Department of Biochemistry and Tissue Biology, Institute of Biology, UNICAMP, Campinas, SP, Brazil
*e-mail: gabrielageronimo95@gmail.com

The major challenges in the chemotherapy of breast cancer (BC) are related to drug resistance, especially in triple negative BC [1]. Nanotechnology strategies may improve the effectiveness of chemotherapy by promoting sustained release and reducing systemic toxicity, through drug delivery systems (DDS) [2]. This PhD project intends the development and characterization of nanostructured lipid carriers (NLC) containing β-caryophyllene (BCP) as a functional excipient (with anticancer and analgesic effects [3]) and the taxane paclitaxel (PTX) as a co-delivery experimental strategy to increase the bioavailability and decrease the toxicity of PTX. To achieve that, NLC will be developed using Design of experiments, to rationally select an optimized formulation. Then, the best formulations will be: i) characterized by different techniques (DLS, NTA, DSC, XRD, TEM) and also regarding PTX encapsulation efficiency, *in vitro* release, plus shelf stability; ii) tested *in vitro* to evaluate its effect over tumor (4T1-luciferase and MCF-7) and normal (3T3 fibroblast) cells in culture; iii) tested *in vivo* regarding the therapeutic efficacy in the treatment of BC-induced (murine orthotopic) model (by measuring tumor volume, *in vivo* tumor imaging, metastasis detection, biochemical and histological analyses) and for the prevention of peripheral neuropathy induced by PTX. We hope to develop a new, nanotechnology-based pharmaceutical formulation to be more effective and less toxic than the commercially available PTX formulations, aiming at improving the prognosis and quality of life of BM patients. Preliminary results with NLC-BCP-PTX shows a high encapsulation efficiency (99 %) both for PTX and BCP. The optimized formulation, determined by factorial design, exhibited homogeneous particle distribution (PDI < 0.2), average diameters of 200 nm, negative Zeta potential (-11 mV), ca. 10^{13} particles/mL and shelf-stability of 90 days (ongoing).

[1] MIGLIETTA, F. et al. Major advancements in metastatic breast cancer treatment: when expanding options means prolonging survival. *ESMO open*, 7:2(2022):100409-26.

[2] CHO, K. et al. Therapeutic nanoparticles for drug delivery in cancer. *Clin. Cancer Res.*, 14:5 (2008): 1310-16.

[3] FIDYT, K. et al. β-caryophyllene and β-caryophyllene oxide—natural compounds of anticancer and analgesic properties. *Cancer Medicine*, 5:10 (2016): 3007-17

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