PREPARATION OF FOLIC ACID MODIFIED PEG-PCL COPOLYMERS FOR CONTROLLED RELEASE OF METHOTREXATE.

J. V. Brandt[1,*,#], R. D. Piazza[2], M. Jafelicci Junior [3], R. F. C. Marques[4]

[1]Undergraduated Research. Laboratory of Magnetic Materials and Colloids, Department of Physical-Chemistry, São Paulo State University, Institute of Chemistry, Araraquara.
[2]Ph. D. Student. Laboratory of Magnetic Materials and Colloids, Department of Physical-Chemistry, São Paulo State University, Institute of Chemistry, Araraquara.
[3]Researcher Teacher. Laboratory of Magnetic Materials and Colloids, Department of Physical-Chemistry, São Paulo State University, Institute of Chemistry, Araraquara.
[4]Researcher Teacher. Laboratory of Magnetic Materials and Colloids, Department of Physical-Chemistry, São Paulo State University, Institute of Chemistry, Araraquara.

[#]Corresponding author: joao.brandt@gmail.com

Several drugs have low solubility within the human body, decreasing its bioavailability. Currently, several drug delivery systems (DDS) have been studied in order to overcome this limitation. Among the DDS employed, functionalized block copolymers can be developed to interact with hydrophilic and/or hydrophobic drugs. Thus, the study of these platforms is fundamental for the encapsulation of hydrophobic drugs, improving the bioavailability. The incorporation efficiency and controlled release are dependent on the size, morphology and interactions of the copolymer blocks. The challenge is focused on the physicochemical properties of these materials (colloidal stability and micelle size, polymer chain length and micelle-drug affinity) in order to better promote the drug delivery. The reduction of the side effects, due to the use of these carriers, will allow the patient a less aggressive and more efficient treatment, improving the quality of life. In this work, the formation of micelles of PEG-co-PCL diblock copolymers with and without folic acid functionalization with varying chain size was investigated and the efficiency of methotrexate incorporation was evaluated. The samples were obtained by adding the monomers in a round bottom flask with inert atmosphere in the presence of a catalyst. The samples were characterized by several techniques, such as infrared spectroscopy, proton nuclear magnetic resonance spectroscopy, gel permeation chromatography, thermogravimetry, differential scanning calorimetry and X-ray powder diffraction. It was obtained copolymers with a molecular weight from 2900 to 12000 g mol^{-1}. The pH and temperature dependence were evaluated by hydrodynamic diameter and zeta potential, which results in a micellar stability above pH 4 and temperature between 25 to 50 °C. The higher incorporation efficiency of methotrexate (94.03%) was obtained to sample with largest hydrophobic chain, with a hydrodynamic diameter of 246 nm.

[1] Y. Lu, K. Park, International Journal of Pharmaceutics – Review. **453**, (2013).

[2] X. Wei, C. Gong, M. Gou, S. Fu, Q. Guo, S. Shi, F. Luo, G. Guo, L. Qiu, Z. Qian, International Journal of Pharmaceutics – Historical Perspectives. **381**, (2009).

[3] M. A. Souza, H. T. Santos, T. S. Pretti, A. C. G. G. Nascimento, T. P. da Costa, F. J. Santos, A. F. Fraga, M. J. Jafelicci, R. F. C. Marques, Journal of Nanopharmaceutics and Drug Delivery. **3**, (2016) 1.

[4] B. N. Cronstein, Molecular Therapeutics – Review. **39**, (1996) 12.