

## Computational study of zinc phthalocyanine mobility in a phospholipid bilayer containing cholesterol

Brenda S. D. Frachoni<sup>1</sup>, Erick G. França<sup>2</sup>, Carlos A. de Oliveira<sup>1</sup>, Eduardo de F. Franca<sup>1</sup>

<sup>1</sup>*Universidade Federal de Uberlândia – Instituto de Química*

<sup>2</sup>*Instituto Federal de Goiás*

### Abstract:

Computational methods play an important role in the design of new drugs and the prediction of their behavior in biological environment. Many current studies seek to understand how these drugs are capable to interact with biological membranes and also the influence of these molecules into the stability of these biomembranes (1, 2). This work aims to understand the mobility and interaction forces between a hydrophobic drug, zinc phthalocyanine and membrane composed of phospholipids only, also the same drug interacting with a mixture of phospholipids and cholesterol in mass to mass ratio of 5:1. The methodology used was Molecular Dynamics simulations using the GROMACS 5.1.4 computational package with OPLS-AA force field, using NPT ensemble, at 310K and 1 bar with explicit spc water. In order to insert the zinc phthalocyanine into the oplosaa force-field, its RESP charges was obtained by the NWChem software (Valiev et al., 2010) after the geometry optimization and energy minimization have been made with 6-31G\* basis-sets in ORCA 3.0.3 software (Hočevar et al., 2016). The results showed that freedom of locomotion of drug through the lipid portion of phospholipid bilayer is higher in the presence of cholesterol, this fact is evidenced by higher values of MSD (mean square displacement) found in comparison with the same analysis made for the purely phospholipid bilayer. This interpretation is in agreement with experimental results obtained by our research group in previous studies (Oliveira et al., 2010), in which the drug in question has a higher pharmacological efficiency when encapsulated in phospholipid vesicles containing cholesterol. Recent studies have shown that biomembranes containing cholesterol are more organized and tend to pack the carbon chains of their phospholipids more easily (1). Additional structural analyzes such as the RMSF (root mean square fluctuation) were performed, which displayed that the fluctuation in the position of the atoms of biomolecules of the membrane was smaller in the system in which the cholesterol was present, evidencing a freedom of the carbonic chains when the cholesterol is not part of the vicinity of phospholipids. Faced with such results it is possible to conclude that the greater activity of the drug observed experimentally may be linked to a higher movement liberty that drug possesses through the proposed drug delivery system membrane.

**Key-words:** zinc phthalocyanine, phospholipid bilayer model, Molecular Dynamics.

**Support:** This work has been supported by FAPEMIG, CNPq and Rede Mineira de Química (RQ-MG-2014-2016 : RED-00010-14)



# XIX SBQT

## Simpósio Brasileiro de Química Teórica 2017

12 a 17/Nov, 2017, Águas de Lindóia/SP, Brasil

### References:

- 1 – RÓG, T.; PASENKIEWICZ-GIERULA, M.; VATTULAINEN, I.; KARTTUNEN, M. Ordering effects of cholesterol and its analogues. *Biochimica et Biophysica Acta (BBA)-Biomembranes*, v.1788, n. 1, p. 97-121, 2009.
- 2 – BUNKER, A.; MAGARKAR, A.; VIITALA, T. Rational design of liposomal drug delivery systems, a review: Combined experimental and computational studies of lipid membranes, liposomes and their PEGylation. *Biochimica et Biophysica Acta (BBA)-Biomembranes*, v.1858, n.10, p.2334–2352, 2016.
- 3 – VALIEV, M.; BYLASKA E. J.; GOVIND, N.; KOWALSKI, K.; STRAATSMA, T. P.; VAN DAM, H. J. J.; WANG, D.; NIEPLOCHA, J.; APRA, E.; WINDUS, T. L.; DE JONG, W. A. NWChem: a comprehensive and scalable open-source solution for large scale molecular simulations. *Comput. Phys. Commun.*, v. 181, p. 1477, 2010.
- 4 – HOČEVAR, T.; DEMŠAR, J. Computation of Graphlet Orbits for Nodes and Edges in Sparse Graphs. *Journal of Statistical Software*, v. 71, n. 10, p. 1-24, 2016.
- 5 – OLIVEIRA, C. A.; KOHN, L. K.; ANTÔNIO, M. A.; CARVALHO, J. E.; MOREIRA, M. R.; MACHADO, A. E. H.; PESSINE, F. B. T. Photoinactivation of different human tumor cell lines and sheep red blood cells in vitro by liposome-bound Zn(II) Phthalocyanine: Effects of cholesterol. *Journal of Photochemistry and Photobiology B: Biology*. v. 100, n. 2, p.92-99, 2010.