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Computational and experimental study of cholesterol influence on the activity of liposomal zinc phthalocyanine

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Abstract: Treatment of diseases in modern civilization using new models of drugs delivery systems instead of classical interventions has been considered an important research line for infection and tumors treatment. In this context, a drug delivery system is capable to increase the delivery effectiveness of hydrophobic drugs into cells and tissues in several treatments [1]. Among these examples we can mention the liposomes, which are nanometric vesicles structured in bilayers of phospholipids organized surrounding aqueous compartments [2]. In this work, liposomes containing phospholipids and cholesterol were used to deliver a hydrophobic phototoxic drug, zinc phtalocyanine (ZnPC), to sheep red blood cells experimentally and the phospholipid bilayer sheet of proposed liposomal systems was simulated in a computational study. The computational 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. The molecules geometry and charges were parameterized using ORCA 3.0.3 and NWCHEM 5.1. It was performed computational simulations of lipid membranes containing zinc phthalocyanine and added or not with cholesterol, to obtain membrane density values, disposition of drug in systems and density maps of the lipid bilayers. In the experimental tests, the use of an appropriated delivery system was capable to promote the photoinactivation of red blood cells. Furthermore, liposomes containing cholesterol in mass to mass ratio of 5:1 was more effective in drug delivery than liposomes without cholesterol [3]. The molecular dynamics indicates that interaction between ZnPC and cholesterol may change the spatial disposition of these species in vesicle affecting directly the drug effectiveness. Computational simulations of systems, with or without cholesterol, containing DPPC/ZnPC showed to be effective in predicting the behavior of the drug in the phospholipid bilayer, indicating its greater mobility in cholesterol-containing systems, as well as the formation of rafts and the occurrence of a pronounced interaction between ZnPC and cholesterol molecules in its surroundings, which can potentiate the photodynamic activity of the drug.

Key-words: Liposome, photoinactivation, cholesterol

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