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The effect of using the correct water model on the calculated octanol-water partition coefficient of 1,2-dipalmitoyl-sn-glycero-3-phosphatidylcholine using atomistic molecular dynamics: An open question

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Abstract: 1,2-dipalmitoyl-sn-glycero-3-phosphatidylcholine (DPPC) is one of the most important zwitterionic lipid components found in all living organisms [1]. Its structure consists of a hydrophilic head with a phosphate group, a choline group and two hydrophobic fatty acid tails, joined by a glycerol molecule [2]. Due to its structure, it has amphiphilic and surfactant characteristics. The octanol-water partition coefficient (log Kow) is one of the key parameters to estimate the environmental fate and bioavailability [3], however, we are not aware that there is an experimental methodology developed specifically to estimate the log Kow of amphiphilic molecules up to the moment. The objective of this study is to develop a methodology to calculate the octanol-water partition coefficient of DPPC using atomistic molecular dynamics and alchemical methods. In this study, the AMBER03 and CHARMM36 force fields, the water models SPC216, TIP3P, TIP4P, TIP5P, OPC3 and OPC4 will be used. All calculations are compared with the reference experimental result using the slow stirring method obtained in our laboratory and recently published in the literature [2]. The results of molecular dynamics simulations show that they depend on the surface tension of the water model used and most of the models tested are far from the experimental value. Studies are still being carried out with OPC3 and OPC4 waters in the CHARMM36 force field. The models mentioned above were developed for Tempra *et al* [4] and correct the surface tension.

Key-words: Octanol-water partition coefficient, water models and pulmonary surfactants
Support: CAPES, FAPERJ, CNPq and INCT-FCx

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