Derivation and testing of molecular mechanics model of $C_y(EO)_x$ based on *ab initio* estimates of the structural and electronic characteristics

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The amphiphilic nature of surfactant molecules leads to their aggregation and selfassembly in a variety of micellar aggregates when exposed to solvent. These structures provide physical, chemical, and biological functions that make them well suited for various applications. In particular, their use for biomedical applications, such as drug delivery, has grown rapidly in recent years. Promising candidates for this aim are compounds with general formula ($C_y(EO)_x$) obtained by coupling of oligo(ethylene glycol) to fatty alcohols. Variation of the number of the ethylene glycol units and the methylene groups of the alcohol leads to different hydrophilic-hydrophobic balance of the molecule resulting in different aggregation propensity. On the other hand, there exist evidences that at very low concentrations the surfactant molecules preserve the selfassembly aptitude, especially in the subsurfacial layer [1]. These properties, together with the lipid compatibility of oligo(ethylene glycol) ethers, suggest that $C_y(EO)_x$ systems could be used as reversible micellar nanotransporters across biomembranes.

The present study includes the results of quantum-chemical calculations for the derivation and testing of molecular mechanical parameters for adequate simulation of amphiphilic alkanoid ethers to design materials of similar type. As short-chain prototypes of the soluble surfactant $C_{12}(EO)_5$ are used a monomer and a dimer of ethylene oxide (EO) with two different types of end-groups: CH_3- and OH-termini. The electrostatic potential of molecules is generated with SCF/HF/6-31G* on the optimized structures obtained from DFT calculation with PBEPBE/aug-cc-pVTZ in vacuum and in implicit solvent. The parameterization is tested by means of molecular dynamic simulations in the NPT ensemble of diethyl ether with Amber99 force field, implementing our parameters for the ether groups. Basic features of the system as molecular volume, density and characteristic thermodynamic quantities such as enthalpy of solvation and heat of vaporisation are calculated. The results are compared with experimental data for the model system, which enables the assessment of the relevance of the theoretical approach for reliable description of the behaviour of the target molecules in solution.

References

1. E. Mileva, P. Tchoukov, D. Exerowa, *Adv. Colloid & Interface Sci.* 47 (2005) 114.