Molecular Dynamics Simulation Study of *N*-Alkyl Glycoside Micelles in Aqueous Systems: Influence of Carbohydrate Headgroup

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Keywords: *molecular dynamics, micelle, sugar-based surfactant, alkyl glycoside, hydrogen bond.*

Introduction

Nonionic sugar-based surfactants, like glycolipids, are attracting attention due to their biodegradation behavior and toxicological safety, and have been applied in extraction and crystallization of membrane proteins[1] and as drug carrier devices[2].

Molecular dynamics (MD) simulations have proved to be a useful tool to investigate micellar properties, providing insights into the shape, hydration behavior, and dynamic properties of micelles in aqueous systems[3]. In this work, we computationally evaluated the influence of open-chain (alditols) and ring-chain (aldoses) sugar headgroups to the structural properties of the micelles formed by *N*-dodecylamino-1-deoxylactitol (C_{12}N-lactitol) and *N*-dodecyl-D-lactosylamine (C_{12}N-lactosyl) in water (Figure 1).

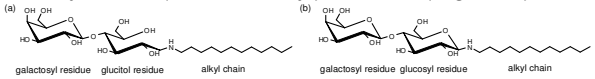

Figure 1. Structure of (a) C_{12}N-lactitol and (b) C_{12}N-lactosyl molecules with residue labeling scheme

Results and Discussion

C_{12}N-lactitol and C_{12}N-lactosyl molecules were modeled with GLYCAM_04 force field. A spherical micelle with 88 monomers from both compounds was constructed employing in-house software. Each micelle was solvated with 17,000 TIP3P water molecules in an octahedron periodic cell. All-atom MD simulations were performed using the AMBER 9.0 package. Non-bonded cutoff was fixed at 9.0 Å. After minimization and thermalization steps, a 10 ns NPT MD simulation was carried out for each system.

During our MD simulation both micelles remained stable and full escape events by monomer were not observed (Figure 2). The radius of gyration (R_g) displays a mean value of 22.06 and 21.43 Å for C_{12}N-lactitol and C_{12}N-lactosyl, respectively (Figure 3a). The higher R_g value for C_{12}N-lactitol could be related to the high flexibility of the acyclic residue (glucitol) present in the alditol compound. The total average solvent-accessible surface area (SASA) was similar in both systems (21,567 Å^2 for C_{12}N-lactitol, and 22,108 Å^2 for C_{12}N-lactosyl), although the contribution of each saccharide residue to the SASA was notably different (Figure 3b).

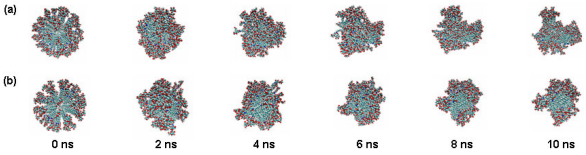

Figure 2. Time series MD snapshots of (a) C_{12}N-lactitol and (b) C_{12}N-lactosyl over 10 ns simulation

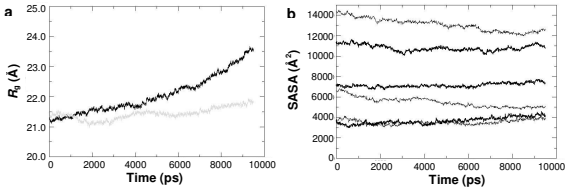

Figure 3. (a) R_g of C_{12}N-lactitol (black) and C_{12}N-lactosyl (light grey) micelles. **(b)** SASA of C_{12}N-lactitol (bold) and C_{12}N-lactosyl micelles. Alkyl chain (bottom), glucosyl/glucitol residue (middle), and galactosyl residue (top) SASA are displayed.

Despite molecular structural similarities, the hydrogen bond network in both systems showed large differences, mainly in terms of inter- and intra-monomer interactions (Table 1). Considering that the energetic contribution for each hydrogen bond is 5 kcal/mol, the net difference of 0.19 inter-monomer hydrogen bonds indicates that formation of C_{12}N-lactitol micelle is more enthalpically favorable than C_{12}N-lacosyl by about 0.95 kcal/mol per surfactant.

Table 1. Average total hydrogen bonds (HBond) of C_{12}N-lactitol and C_{12}N-lactosyl micellar systems*.

HBond type	C_{12}N-lactitol		C_{12}N-lactosyl	
	donor	*acceptor*	*donor*	*acceptor*
Inter-monomer	1.07	1.05	0.86	0.86
Intra-monomer	1.37	1.37	0.48	0.48
Monomer-solvent	3.07	4.22	2.93	4.23

* HBond defined based on geometric criteria: (i) oxygen-oxygen distance cutoff of 3.0 Å, and (ii) O–H···O angle greater than 120º

Conclusions

MD simulations presented herein characterize structural properties of sugar-based micelles. The differences found in hydrogen bond network suggest that an alditol headgroup is more favorable for micelle formation than an aldose headgroup.

Acknowledgements

We wish to thank the CNPq, CAPES and FAPERJ.

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