Study of the effects of aqueous solvation on the structure of glucosamine using the Car-Parrinello molecular dynamics

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Introduction

Glucosamine is a monosaccharide that is an essential component of many cellular glycoproteins, glycolipids, and glycosaminoglycans. This compound is synthesized by the human body and it is produced commercially by the hydrolysis of crustacean exoskeleton (1). Glucosamine is the monomeric form of the chitosan biopolymer, which is nontoxic, biodegradable and biocompatible. These characteristics of the chitosan make it interesting for the development of new materials that can reduce the human impact on nature and for technological applications, such as, tissue engineering, pharmaceutical products, and water treatment (2).

Although there is a significant amount of experimental research on chitosan and glucosamine, theoretical studies are still limited in the literature. In this sense, this work aimed to study, theoretically, the effects of the aqueous solvation on the geometric and electronic parameters of the glucosamine using the Car-Parrinello molecular dynamics.

Methodology

The glucosamine's Car-Parrinello molecular dynamics was carried out using the CPMD package of programs (version 4.1) (3). To quantify the effect of the aqueous solvation on the geometric parameter of the glucosamine, two cubic boxes of 16 Å were built: one box with a single glucosamine molecule (system I), which was simulated for 120 ps and another box containing one glucosamine molecule plus 80 water molecules (system II), which was simulated for 74 ps. The Vanderbilt ultrasoft pseudopotentials were used to describe the ionic core and the wavefunctions of the valence electrons were expanded using plane wave basis set with a cutoff energy of 25 Ry. The molecular dynamics timestep used throughout the simulation was fixed at 5 au for both systems, and the fictitious electronic mass was set at 400 au. The exchange and correlation functional used to solve the Kohn-Sham equations was Perdew, Burke e Ernzerhof (PBE). The ionic temperature and the electronic fictitious kinetic energy were controlled by a chain of three Nose-Hoover thermostats and the ionic temperature was set at 300 K. The geometric parameters, pair distribution function, residence time and Helmholtz free energy were obtained using the gqtea program, developed by the Anápolis' theoretical and structural chemistry group.

Results and Discussion

The absolute percentage differences between vacuum glucosamines and solvated glucosamines simulations were calculated. The results of the highest absolute differences for bond length were observed for O₃-H₂₁ (1.986 %), O₁-C₆ (1.315%), O₂-H₂₀ (1.198), and N₁₂-H₂₃ (0.484%) bonds. For the bond angles, a greater influence of the water molecules was observed, with an absolute difference of 6.30% for C₁₁-C₁₀-O₁, 4.10% for H₂₃-N₁₂-H₂₄ and 3.79% for H₁₄-C₉-O₅ angles, showing the strong interactions with oxygen and nitrogen atoms of glucosamine with water molecules.

Through the trajectory analyses, it was possible to identify the formation of both intramolecular and intermolecular hydrogen bonds. All oxygen and nitrogen sites were analyzed (see Figure 1a). The intramolecular hydrogen bonds O₂ – H₂₀ --- O₃ and O₄ –

H₂₂ --- O₂ were observed during the simulation time, and several hydrogen bonds with water molecules were also detected in the simulation. In particular, a hydrogen bond with infinite residence time was formed between the nitrogen N₁₂ and the hydrogen of a water molecule (see Figure 1b). This result strongly suggests a possibility for hydrogen transfer from a water molecule to the N₁₂, resulting in a protonated glucosamine, which is observed experimentally. The protonation mechanism is under investigation by metadynamics technique.

To characterize the hydrogen bonds, geometric parameters for the interactions were also calculated (Table 1). An interaction was classified as a hydrogen bond only when the bond lengths were less than 3.2 Å and the bond angles were greater than 110°. The Helmholtz free energy calculated for N₁₂---H₂O hydrogen bond shows that it is very stable with a bond length of 1.9 Å

Figure 1. (a) Glucosamine with atomic numbering adopted in the calculations; (b) Residence time for N₁₂---H_w hydrogen bond; (c) Helmholtz free energy as a function of the N₁₂---H_w distance.

Table 1. Geometric parameters for the intramolecular and intermolecular interactions.

Interactions	Hydrogen bond length (Å)	Hydrogen bond angle (°)
N ₁₂ --- H _w - O _w	1.908 ± 0.262	162.516 ± 12.438
O ₂ - H ₂₀ --- O ₃	1.791 ± 0.164	150.307 ± 10.114
O ₄ - H ₂₂ --- O ₂	1.766 ± 0.158	159.657 ± 7.946

Conclusion

The Car-Parrinello molecular dynamics calculations of the glucosamine show that the glucosamine interacts strongly with the water molecules forming several hydrogen bonds. These interactions affect significantly the geometric parameters of the glucosamine when it is solvated by water molecules. It is noted, in particular, the hydrogen bond N₁₂-H_w with an infinite residence time that strongly suggests the -NH₂ group protonation, which is observed experimentally.

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