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

Lilian T.F de M. Camargo1,2 (PG)*; Roberta Siginine1 (PQ); Allane Catharina1 (PQ)
Ademir João Camargo1 (PQ). lillianthaty@yahoo.com.br


Palavras-chave: Molecular Dynamics, Simulation, Glucosamine, Solvation

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 atu 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 Helmotz 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 –
H$_{22}$ --- O$_{2}$ 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 N$_{12}$ 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 N$_{12}$, 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 N$_{12}$---H$_{2}$O 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 N$_{6}$--H$_{w}$ hydrogen bond; (c) Helmholtz free energy as a function of the N$_{6}$--H$_{w}$ distance.

<table>
<thead>
<tr>
<th>Interactions</th>
<th>Hydrogen bond length (Å)</th>
<th>Hydrogen bond angle (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N$<em>{12}$ --- H$</em>{w}$ -- O$_{w}$</td>
<td>1.908 ± 0.262</td>
<td>162.516 ± 12.438</td>
</tr>
<tr>
<td>O$<em>{2}$ -- H$</em>{20}$ --- O$_{3}$</td>
<td>1.791 ± 0.164</td>
<td>150.307 ± 10.114</td>
</tr>
<tr>
<td>O$<em>{4}$ -- H$</em>{22}$ --- O$_{2}$</td>
<td>1.766 ± 0.158</td>
<td>159.657 ± 7.946</td>
</tr>
</tbody>
</table>

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 N$_{12}$--H$_{w}$ with an infinite residence time that strongly suggests the -NH2 group protonation, which is observed experimentally.

Acknowledgment
To the Fund for Research Support of the State of Goiás.
To the High-Performance Computing Center of the State University of Goiás.

References