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Assessing the solvation mechanism of $C_{60}(OH)_{24}$ in aqueous solution

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ABSTRACT

Using molecular dynamics simulations, combined with the thermodynamic integration algorithm, we examine the hydration mechanism of $C_{60}(OH)_{24}$ under ambient conditions. We analyze its structural features, dynamics, and hydration free energy. Our results have been compared with a pristine fullerene aqueous system. Despite the number of hydroxyl groups in the fullerenol, its hydration entropy is rather similar to that calculated for C_{60}. On the other hand, we have calculated a dramatically negative free energy of about −354 kJ/mol for the fullerenol, whereas pure fullerene presents a positive value of about 59 kJ/mol. On this basis, our study indicates that the hydration of $C_{60}(OH)_{24}$ is guided by an enthalpy-driven process.

1. Introduction

Understanding hydration and dispersion of C_{60} and other fullerene derivatives is of great value for both practical and fundamental studies [1–7]. Aqueous systems of these carbon cages have been proposed for use in molecular sensing devices, biomedical, and environmental applications [8–11]. Although several properties of these 'solutions' appear to be well understood, the intermolecular interactions between the medium and the solute are still unknown. Also, the room-temperature predicted solubility [12] of C_{60} in water is very low, but not as low as recent estimates [13]. In principle, the specific solute–solvent interactions in this case are dominated by van der Waals forces. On the other hand, Labille et al. [14] have recently demonstrated that pristine fullerene can acquire hydrophilic character because of the surface hydroxylation occurring in aqueous environment. They provided spectroscopic evidences for the fullerene hydroxylation under mild chemical conditions. However, the solubility mechanisms of fullerenes and their hydroxylated derivatives continue to be a controversial issue [15–17].

While the study of the biological properties of bare fullerene is greatly hampered by its poor solubility in water [18], highly hydroxylated cages, $[C_{60}(OH)_n]$ or fullerenols, should present good solubility in aqueous medium. Fullerenols are of great interest and they have been tested as biocompatible materials [19–21]. These molecules exhibit different degrees of solubility, depending on the number and distribution of hydroxyl groups on the fullerene surface [18,22]. Notwithstanding, the good solubility of some fullerenol structures can be hampered by certain ionic contamination resulting from the synthetic methods [17]. Indeed, studies on the solubility of fullerenols are scarce and the interaction free energy of the solute with the solvent has not yet been reported in the literature.

As mentioned above, aqueous solutions of fullerenols are especially important in biological applications. Thus, quantifying the solubility of fullerenols under ambient conditions is extremely useful to understand the impact of these species in several aqueous systems. Indeed, this can be investigated experimentally from the Gibbs energy of solution [12]. Although the knowledge of the thermodynamic properties are essential to understand the nature of the solute–solvent interactions, the structural and dynamic information is also indispensable. These latter aspects can be addressed by means of molecular dynamics (MD) simulations, and the hydration free energy with the thermodynamic integration (TI) technique [7,23].

We report in this work an atomistic MD/TI simulation study of a room-temperature aqueous solution of $C_{60}(OH)_{24}$, which has been by far one of the most exploited molecular species *in vitro* and *in vivo* [20,24,25]. Then, making use of proper atomistic parameters we analyze the thermodynamics of a $C_{60}(OH)_{24}$ aqueous solution under ambient conditions. Our study is systematically compared to the hydration properties of pristine C_{60}, for which we have successfully determined the free energy of transfer at different thermodynamic conditions via MD/TI simulations [7,23].

2. Simulation details

The aqueous solutions of $C_{60}(OH)_{24}$ and C_{60} have been studied using isothermal–isobaric (*NPT*) ensembles with MD simulations at $T = 298$ K and $P = 1$ atm. Each solution was prepared with 1000 water molecules and one solute (fullerenol or fullerene) molecule

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in cubic boxes with periodic boundary conditions. Technical details are given in our previous works [7,23,26] and in the Supporting material (Tables S1–S4, Figs. S1–S4). The extended simple point charge (SPC/E) [27] potential was used to describe the potential interaction of the water molecules. In the case of C_{60} we have adopted a 60-site model [5]. The potential for $C_{60}(OH)_{24}$ was generated on the basis of the OPLS force field (see parameters in Table S1). The atomic charges of this solute were obtained using the ChelpG scheme also discussed in Supporting material. As usual, the solute–solvent interactions were described by means of the Lennard–Jones and Coulomb potentials. These simulations were carried out by using the GROMACS code (version 4.0) [28].

From the *NPT* conditions, we have analyzed the structural and dynamic properties of the fullerene and fullerenol aqueous solutions after 10 ns simulations. To obtain information on the dynamic properties of these systems, we have calculated the time correlation functions. The translational mobility of the solutes (fullerenol or fullerene) in water was obtained from the velocity autocorrelation function (VACF) and mean square displacements (MSD). With VACF we can measure the effects of the local environment of the solutes. The MSD gives a good measure of the translational diffusivity of both solutes in aqueous environment, and from its long time behavior we can extract the Einstein diffusion constants (D).

Also, to assess the hydration free energy, and consequently the water solubility, of $C_{60}(OH)_{24}$ or C_{60} stochastic dynamics simulations associated with the TI method were employed within the *NPT* ensembles [23]. We have performed a series of 26 simulations for C_{60} and 36 for $C_{60}(OH)_{24}$, varying the value of the coupling parameter according to Tables S3 and S4. The detailed calculations of the free energy are discussed in Supporting material. All stochastic and molecular dynamics simulations have been performed with the GROMACS 4.0.

3. Results and discussion

3.1. Structural features

We present the results for the structural properties of the aqueous solutions of $C_{60}(OH)_{24}$ in comparison with the aqueous solution of C_{60}. Because of the large molecular surface area and volume of these solutes, the hydrogen bonding network of water is disrupted, creating a large cavity in the liquid. For pure fullerene, new hydrogen bonds are not expected to be formed with the solvent under ordinary conditions [29]. On the other hand, in the case of $C_{60}(OH)_{24}$, the solubility will be determined not only by the geometric features but also by the hydrogen bonding interactions between the solute and solvent (Fig. S2 and S3). A hydration shell around these solutes is well defined as a spherical layer of water (Figure 1), determined by the center-of-mass radial distribution functions (RDFs).

In Figure 2a we show a comparison of the RDFs for $C_{60}(OH)_{24}$ and C_{60}. The heights of the peaks indicate a stronger densification of the solvent around C_{60} than around $C_{60}(OH)_{24}$. This is because the water molecules near the fullerene surface tend to form hydrogen bonds between themselves avoiding the solute. Therefore, in the case of fullerene the number of water molecules in the hydration shells increase, giving 63, 183, and 418 molecules on average. In the case of the fullerenol, because of the amount of hydroxyl groups in $C_{60}(OH)_{24}$, the water molecules tend to rebuild some hydrogen bonds that were broken in the solvation process. Also, we notice three hydration shells forming structures with 48, 121, and 229 molecules on average (see additional details in Table S1 and Fig. S1).

For a polyhydroxylated fullerene, it is more interesting to examine the RDFs of (i) the water oxygen atom with the solute hydrogen atoms ($O_W \ldots H_F$); and (ii) the fullerenol oxygen atoms with the water hydrogen atoms ($O_F \ldots H_W$). These calculated RDFs are shown in Figure 2b, where the height difference between the peaks shows a steric hindrance effect on the solute–solvent interaction. This means that $C_{60}(OH)_{24}$ works as a better proton-donor than a proton-acceptor species in aqueous solution. This result is consistent with the proton conductivity of low hydroxylated fullerenes, which is a function of the amount of hydroxyl groups [30,31].

Because of the hydrophilic groups in $C_{60}(OH)_{24}$, one could expect that this fullerenol should be much more water-soluble than C_{60}. Indeed, low hydroxylated fullerenes are less water-soluble species, whereas the highly hydroxylated cages present a good solubility in aqueous environment [17]. However, as a consequence of the steric hindrance, few water molecules can approach their hydrogen atoms to the fullerenol surface, avoiding a formation of an extended hydrogen bonding network around the solute. A detailed analysis of the hydrogen bonds is given in Supporting material (see Figs. S2–S4).

3.2. Dynamic properties

Figure 3 shows the time correlation function for the average hydrogen bonds life time of $C_{60}(OH)_{24}$ aqueous solution and in bulk water. As discussed in Supporting material, the correlation function describes the probability that a particular hydrogen bond keeps intact at a small time interval. From Figure 3, we note that the correlation function decays faster for the hydrogen bonds in bulk water than at the fullerenol surface. This indicates that the

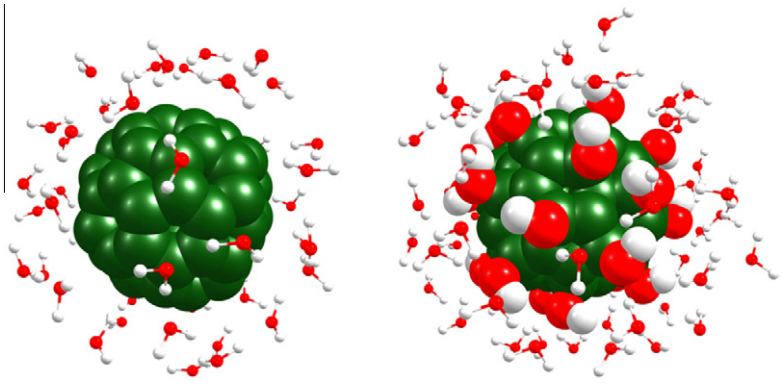

Figure 1. The first hydration shells of C_{60} (left) and $C_{60}(OH)_{24}$ (right) in ordinary aqueous solutions. The big atom model is only used to represent the carbon cages and the covalently bound hydroxyl groups in the fullerenol structure. Green, red, and white spheres represent carbon, oxygen, and hydrogen atoms, respectively. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)