Determination of Molecular Interactions of Galactosides Solution with Water Using Computer Modelling

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***Abstract*— Galactosides as carbohydrate receptors play an important roles in biological recognition events. A galactoside is a glycoside that yields galactose on hydrolysis. Examination of the extent and pattern of hydrogen bonding between water and sugar molecule hydroxyl group resulting that galactose and glucose derivatives were substantially better hydrogen bond donors. The hydrophilic region is mainly dominate by the non-bonded van der Waals force, whilst in the hydrophilic region, the long range of electrostatic interaction from hydroxyl group plays a critical role. Molecular dynamics (MD) simulation of interaction between lauryl galactoside and water were assessed by using Accelrys Material Studio 7.0. Hence, the aim of this work is to identify the most stable hydrogen bond between lauryl galactoside and water by using computational technique. The viscoelastic properties by expansion in the amorphous region was shown in the molecular dynamic. By varying the number of water molecules with lauryl galactoside, the interaction between water molecules was observed. The simulations results show that for water with 4 molecules, the interaction between water molecules and lauryl galactoside is stronger at higher water molecules.**

Keywords—Galactoside, hydrogen bonding, molecular dynamics simulation, molecular interactions.

I. INTRODUCTION

Carbohydrates are very significant in functional constituents of the living systems. The term carbohydrate verbally means the hydrate of carbon with a compound of an empirical formula (CH2O)n. and this formula applies to many carbohydrates such as glucose which is $C_6H_{12}O_6$. Carbohydrates can be classified as monosaccharides, oligosaccharides and polysaccharides and the term saccharide is derived from a Greek word for sugar [1]. Galactosides as carbohydrate receptors play an important roles in biological recognition events [2]. A galactoside is a glycoside that yields galactose on hydrolysis. Glycosides are formed when the anomeric hydroxyl group of a monosaccharide undergoes condensation of a second molecule with the elimination of water. Acetal formation is an example of glycosides formation which is a reaction between a hemiacetal group and another hydroxyl group. The outcome linkage from the reaction is known as glycosidic bond.

Glycosides are named for the sugar that provides the hemiacetal group. Hence, the resultant molecule is a glucoside if the glucose provides the hemiacetal group whilst if galactose provides the hemiacetal group, the result is a galactoside [1]. The nature of these molecules captivate many industries such as food and pharmaceuticals and have been used widely as emulsifiers to stabilize suspended food mixtures [3].

It is crucial to consider the high hydroxyl (OH) content of carbohydrates when describing the interactions of the molecules which make with solvent and protein. Cooperativity is a phenomenon where intramolecular H-bond networks by arrangement of hydroxyl group is happened. Under cooperativity, in order to increase the strength of H-bond donor or acceptor components, H-bond can be arranged directionally [3]. As seen in the ability of these molecules to act as cryprotectants in cold-tolerant organism, carbohydrates can also interact with the solvent itself [3]. Thus, the necessity to understand how water structure and solute-solvent interactions with H-bond collaboratively affects it. Solute structure has been proved to affect the dynamic, structural and thermodynamic properties of nearby water molecules in aqueous solution [3]. Nevertheless, in deciding the exact details of solute-induced water structuring during experimental approaches has been only moderately successful. This is because of difficulties in detangled contributions of solute and solvent in the OH stretching region and the power of this region which is frequently pressures the intensity of the modes of scale. Despite that, computer simulation can be used productively as model solvent which structuring around a solute.

Hydrogen bonds plays an important role in terminating the crystallographic structures of biopolymers and it is assumed that intermolecular H-bonding also exerts a significant influence on the conformational properties of these molecules in aqueous solution. Understanding the interactions among the constituent molecules is of special interest and molecular interactions contribute much in determining the formation of mesophases. The hydrophilic region is mainly dominate by the non-bonded van der Waals force, whilst in the hydrophilic region, the long range of electrostatic interaction from hydroxyl group plays a critical role [4]. Attached in covalent bond by principle to a higher electronegativity atom, a hydrogen bond takes place between a proton donors (H). For instance, a proton acceptor (O) and -OH group which has two lone pairs of electrons. Since it falls between weak van der Waals interactions, it has been classified as a middle range interaction. [4].

Examination of the extent and pattern of hydrogen bonding between water and sugar molecule hydroxyl group resulting that galactose and glucose derivatives were substantially better hydrogen bond donors [5]. The choice of the appropriate thermodynamic property used to study the interaction between carbohydrate and water is important. In this study, the results from the molecular dynamic simulation helps to explain the large apparent hydrophobicities of the talosides relative the glucosides and galactosides. Molecular dynamics studies of carbohydrates with specific inclusion of water molecules have been responsible for a number of major insights into carbohydrates properties which includes solvation [6]. Hence, the molecular dynamics studies by Ha et. al [6] satisfactorily proliferate energy difference in water between ∝- and β-D-glucopyranose. It has been pointed out from previous journals that partial atomic charges, force fields, atom types, water models and hydrogen bonding parameters need careful consideration for accurate modelling [5].

Radial distribution function or also being referred as pair correlation function. It is used to measure of the probability of atoms present in a spherical shell with a distance, *r* from central atom. By integrating radial distribution function, the number of particle surrounding a central atom or coordination number can be determined [6].

In this study, the interactions between lauryl galactoside and water molecules was observed with varying the number of water molecules by using a molecular modelling technique. This study was carried out with the intention to determine their specific interactions.

II. METHODOLOGY

A. *Materials*

In this study, the interaction of lauryl galactosides and water molecules are being assessed. Fig.1 shows the structure of lauryl galactosides and a water molecule. All of the molecules were labelled with carbon, hydrogen and oxygen depends on the structure. For lauryl galactoside, every parts of the molecules were labelled with carbon, C1-C18 and oxygen O1-O6 respectively. In this simulation, water is included to simulate conditions during well simulation. Oxygen and hydrogen in water was labelled with O and H respectively.

(a) (b)

Fig. 1: Schematic diagram of (a) lauryl galactoside and (b) water. Hydrogen molecules are white in colour, oxygen is red and grey for carbon.

B. *Computational Technique*

The interaction between lauryl galactoside and water was simulated through molecular dynamic (MD) simulation using Accelrys Material Studio 7.0 (Accryls, Inc., San Diego, USA). The calculations of interaction energy, geometric optimizations and dynamic simulation were performed using condensed-phase optimized molecular potentials for atomic simulation studies Drieding force field. Based on previous studies, Drieding force filed has been widely used in a molecular dynamics simulation [10-11]. The output from the molecular modelling simulation was determined by radial distribution function (RDF) analysis.

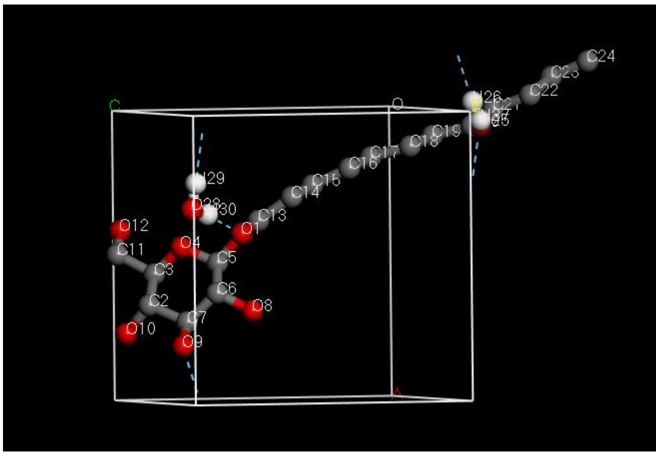
C. *Creation of 3D periodic structure of lauryl galactoside and water molecule*

The lauryl galactoside and water molecules were first drawn using embedded tools available in Materials Studio (MS). By using a built up molecule in MS, the molecules were subjected to energy minimization and geometry optimization procedures. A periodic amorphous cell model containing lauryl galactoside and water molecules was built with specific lattice dimensions which depends on the number of molecules (loading). Table 1 shows the lattice dimensions correspond to the number of loading for water molecules in the system. In this study, the number of lauryl galactoside molecule was kept to be at one, whilst the number of water molecules in the system were varied. The density of the cell was set at 0.5 g/cm3. The output of the simulation was set at 50 frames. The temperature is remain constant at 298 K representing the possible water temperature and was set in the construction of amorphous cell of lauryl galactoside with water and dynamic simulation of the system.

Table 1: Parameters adopted in the study, the cubic cell composition of one lauryl galctoside and varying number of water molecules with its respective cell lattice parameters and cell volume.

Molecules	Loading	Weight (%)	Cubic lattice cell parameters, a (Å) = b (Å) = c (Å)	Cell Volume (Å^3)
Lauryl Galactoside	1	94.5	10.3	1096.6
Water	1	5.5		
Lauryl Galactoside	1	89.7	10.5	1156.6
Water	2	10.3		
Lauryl Galactoside	1	81.2	10.8	1276.2
Water	4	18.8		

D. *Geometry Optimization of the Periodic System*



Geometry optimization of lauryl galactoside and water has been carried out in search for the stable geometry after the periodic cell was built. During this process, the charges of the atoms responded either by moving away from the same charges or closer to the opposing charges [12]. The coordinates of the atoms were adjusted at this point and thus the energy of the structures produced to a stationery point which resulting in zero for overall atomic forces. In order to calculate the total energy of the system, the force field used is Drieding with atom method as the energy summation method for the non-bonded interactions. The atomic charges were calculated using force field assigned for electrostatic and van der Waals interaction. The atomic charges were calculated using Gasteiger.

E. *Molecular Dynamics Run for the Periodic System*

The dynamic simulation was carried out after geometry optimization in order to find the potential functional groups attached to the water molecules during interaction. The cell pressure was fixed at 1 atm (1 x 10-4 GPa) at 298 K in dynamic system. The molecular dynamic system was run under isothermalisobaric ensemble (NPT) to stimulate the condition at 298 K for 25 ps with 1 fs timestep, Nose [13] thermostat, and Berendsen [14] barostat for constant temperature and pressure control respectively with frame output for every 500 steps. Ewald was used as the non-bonded energy summation method with Gasteiger method for atomic charges calculation.

The interaction between the selected functional group was analysed through trajectory output analysis using Radial Distribution Function (RDF). RDF value, g(r), indicates the probability of finding an atom or molecules a distance r from another atom or molecules compared to ideal gas distribution and it is dimensionless [15]. This can be explained as the shorter interatomic distance (r) and higher peak (g(r)) will indicates stronger interactions [16]. In this study, all plots demonstrate a typical liquid distribution with a small number as short distances which gradually converge to 1 at a large distance [17-18].

III. RESULTS AND DISCUSSION

A. Lauryl galactoside-water bond with one water molecule

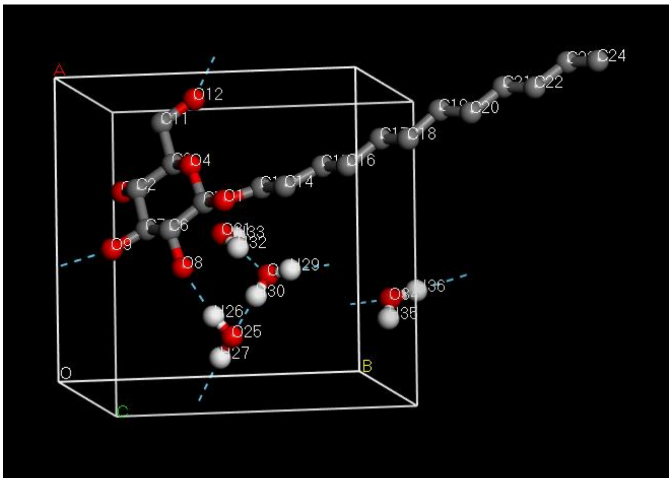
The simulation has been done and the results does not show any interactions between one molecule of water and one molecule of lauryl galactoside. However, for two water molecules and four water molecules shows intermolecular hydrogen bond with lauryl galactoside molecule.

Hydrogen bond formed when a hydrogen atom bound to an electronegative atom such as oxygen, fluorine or nitrogen and then transferred its charge to a nearby attracted electronegative atom [19]. Polarization shifts in different environments of hydrogen-bonded and when water molecules bound to solutes and ion will change angles and lengths of hydrogen bond. The strength of the hydrogen bond varies linearly with distance. Thus, the shorter the distance of hydrogen bond that formed, the stronger the hydrogen bonding [20].

B. Lauryl galactoside-water bond with two water molecules

As shown in Figure 2, hydrogen bond (dashed line) is formed between a water molecule and lauryl galactoside structure. Hydrogen bond occurs in between a proton donor (H) which is attached covalently to a higher electronegative atom. For this case, -OH group and a proton acceptor (O) which has two lone pair of electrons has been classified as a middle range interactions which falls between weak van der Waals interaction and strong covalent interactions. The intermolecular bond between the sugar groups and the solvent which is water play a crucial role in determining the behavior of the conformations.

Fig 2: Schematic diagram of H_2O molecule with the OH of lauryl galactosides, observed in the periodic cell containing 2 molecules of H_2O and 1 molecule of lauryl galctoside.



Strong hydrogen bond interaction is relatively covalent while weak hydrogen bond includes electrostatic or dispersed interactions. Therefore, based on Figure 2, lauryl galactoside is shown to have intermolecular hydrogen bonding with water molecule in the dynamic system. The dynamic simulation was carried out using amorphous cell module which is an embedded module in Material Studio.

C. Lauryl galactoside-water bond with four water molecules

Fig 3: Schematic diagram of H_2O molecule with the OH of lauryl galactosides, observed in the periodic cell containing 4 molecules of H_2O and 1 molecule of lauryl galctosides.

As shown in Figure 3, intermolecular hydrogen bond (dashed line) is formed between a water molecule and lauryl galactoside structure. In Figure 3 also shows an intramolecular hydrogen bonds happens between water molecules as it occurs when two functional groups of molecules formed hydrogen bonds with each other. This is because both a hydrogen donor which is an acceptor present in one molecule and within close proximity of each other in water molecule. By comparison, hydrogen bonding in 4 water molecules is proved to be stronger. For carbohydrate monomer, multiple binding sites for primary and secondary hydroxyl group lead to many conformational preferences and observables and helps in balancing the structure prediction [20].

D. Radial Distribution Function (RDF) Analysis

The interactions of lauryl galactoside with varying loadings of water molecules ware determined at the same temperature which is 298 K and pressure of 1 atm. Figure 4 shows the RDF plot of the intermolecular interaction of selected functional group of lauryl galactoside and water molecule. In this system, the intermolecular interactions between 1 molecule of lauryl galactoside with 2 molecules of water and also 1 molecule of lauryl galactoside with 4 molecules of water is been observed. The purpose of this simulation is to determine the interaction of hydrogen bonding between lauryl galactoside and water.

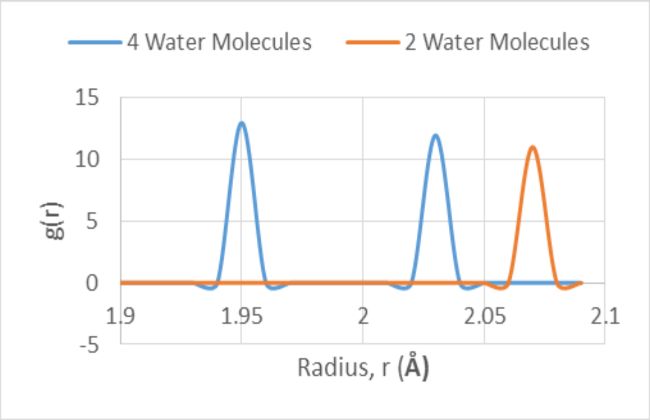


Fig. 4: RDF plot for the intermolecular interaction of selected functional group in lauryl galactoside with water.

The first peak in Figure 4 occurs at distance, *r*, 1.95 Å for with hydrogen in lauryl galactoside with four water molecule and the second peak occurs at a distance, *r*, 2.03 Å. The shorter radius shown by the results indicates that the hydrogen bonds forms are stronger than the first peak shown at higher radius distance [21].

However, for the system containing 1 lauryl galactoside and 2 water molecules, the first peak occurs at 2.07 Å. Hydrogen bond can exist at distance less than 3.25 Å between any two oxygen atoms and the OH vector angle from the same molecules was less than 35°[22]. The intermolecular hydrogen bonding in the carbohydrate moiety is in the range of 1.8-2.6 Å [23].

This can be explained as the shorter interatomic distance (r) and higher peak (g(r)) will indicates stronger interactions [16]. Thus, it can be shown for intermolecular hydrogen bond interactions of four water molecules with one molecule of lauryl galactoside, it indicates stronger interactions compared to intermolecular hydrogen bond with two water molecules.

IV. CONCLUSION

In summary, molecular dynamic simulation results showed that for water loading with 4 water molecules, the interaction between 4 water molecules and lauryl galactoside is stronger than with 2 water molecules based on the radial distribution function analysis. The water molecules have the tendency to bind hydroxyl group of glucose. The molecular dynamics simulation of lauryl galactoside and water has provided the molecular interaction between the molecules. The viscoelastic properties by expansion in the amorphous region was shown in the molecular dynamic. This simulation provides better understanding on the role of functional group in lauryl galactoside as well as for other application.

ACKNOWLEDGMENT

Gratefully appreciated and thank you to my supervisor, Dr Nurul Fadhilah for guidance in this project and Universiti Teknologi Mara.

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