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The Effects of Different Sugar Head Groups on the Formation of Glycolipids N-Octyl-β-D-Glycosides Micelles: A Molecular Dynamics Simulation

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ABSTRACT Three glycolipids n-octyl-β-D-maltopyranoside (OM), n-octyl-β-D-galactopyranoside (OGal) and n-octyl-β-D-glucopyranoside (OG) were investigated for their micellar properties using molecular dynamics (MD) simulations. The effects of sugar head groups due to C4-linked hydroxyl group were investigated. Micelles of OM gave totally different geometry and radius of gyration compared to those of OG and OGal. From the simulations with Amber force field for Saccharides (*Ambers*), we found that OM formed bigger spherical micelles with gyration radii ranging from 8.93 to 12.27Å while those of OGal formed micelles with gyration radii ranging from 7.47 to 11.00Å. Meanwhile OG formed a cylindrical micelle with a radius of 12.24Å. Some of these results are qualitatively comparable to those obtained by the scattering experiments (SANS and SAXS) for the structural analysis of octyl-glycopyranoside micelles. Our results do show that different sugar head groups can affect the physical properties of the micelles formed.

ABSTRAK Ciri-ciri misel bagi tiga jenis glaikolipid iaitu n-octyl-β-D-maltopyranoside (OM), n-octyl-β-D-galactopyranoside (OGal) dan n-octyl-β-D-glucopyranoside (OG) telah diselidik dengan menggunakan dynamic molekular (MD). Kesan-kesan kumpulan kepala gula yang disebabkan oleh kumpulan OH pada karbon ke-4 telah dikaji dengan membandingkan OG dan OGal. Daripada simulasi dengan menggunakan medan daya Amber untuk sakarida (*Ambers*), didapati bahawa OM membentuk misel berbentuk sfera yang lebih besar dengan jejari girasi yang berukuran daripada 8.93 hingga 12.27Å manakala OGal membentuk misel yang lebih kecil berukuran 7.47 hingga 11.00Å. OG pula membentuk satu misel berbentuk silinder berjejari 12.24Å. Sebahagian keputusan simulasi yang diperolehi adalah secara kualitatif bersamaan dengan keputusan eksperimen pembelauan neutron dan sinar-X (SANS dan SAXS) dalam penentuan struktur misel OG. Keputusan kami berjaya menunjukkan bahawa perbezaan kumpulan kepala gula memang boleh mempengaruhi ciri-ciri fizikal misel yang terbentuk.

(Glycolipid micelles, molecular dynamics, *Ambers*, gyration radius, reversed micelle)

INTRODUCTION

Glycolipid is a class of useful biochemical in biology and chemistry. For example, commercially available alkyl glucosides [1] form a class of new and useful surfactant. One of these namely octyl glucoside is a nonionic detergent. It consists of a hydrophobic paraffin tail attached to a glucose head group (Figure 1). Solutions of alkyl glucosides are insensitive towards the addition of salt because they are neutral surfactants [2, 3, and 4]. Physico-chemical properties of alkyl glucosides are greatly influenced by the complex isomerism of the carbohydrate head group [5, 6, 7, and 8]. In biochemisty, alkyl glucosides have been used to stabilize, reconstitute, purify and crystallize membrane proteins and membrane associated-protein complexes without denaturation. Aqueous solutions of the glucosides from octyl through dodecyl foam on shaking but dodecylglucoside is only slightly soluble in cold water [9]. Thus, octyl glucoside was used for the purification of intact serine receptor to study the ligand site of a bacterial chemotaxis membrane receptor [10] and it has been of interest as an emulsifier, a cleaning

agent and a drug carrier due in part to its nontoxic and biodegradable nature [11]. The enzymes glucosidases contribute to this biodegradable nature of alkyl glucosides and enzymatically controlled the formation and breakdown of alkyl glucosides [12, 13]. So, all these show the commercial importance of glycolipids that requires the support of fundamental studies.

Generally, the term alkyl glycoside applies when other sugar head group such as maltose or galactose is attached to the hydrophobic paraffin tail. The diverse ranges of compounds, which can be generated by changing the head group makes glycolipids even more important as potentially useful material such as liquid crystal and hence promise many technological applications. Many glycolipids compounds can also form amphotropic liquid crystals [14] which means they form both thermotropic and lyotropic liquid crystals.

Although their roles in many biological systems are well studied and documented in the literature, their liquid crystalline natures have only recently been studied [15]. It was found for example, a small modification on the sugar head group in alkyl glycosides led to a large change in the liquid crystal phase behavior [16]. In particular, on the melting point, the clearing point, the solubility in water, and the extent of the lamellar and curved phases [17]. For example, in x-ray diffraction and calorimetric investigations, n-alkyl-β-D-glycopyranosides (AGs) showed thermotropic liquid crystal phases [18, 19, and 20]. Moreover, powder diffraction x-ray studies confirm that this phase is smectic A [21, 22].

To illustrate further how structure can affect liquid crystal properties, two very similar alkyl glycosides are used namely, n-octyl-β-D-glucopyranoside (OG) and n-octyl-β-D-galactopyranoside (OGal). In addition, n-octyl-β-D-maltopyranoside (OM), the maltose analog is also used in this comparison although it is not similar to OG or OGal structurally (hence property-wise). The chemical structures of OG, OGal and OM are shown in Figure 2(a), (b) and (c), respectively.

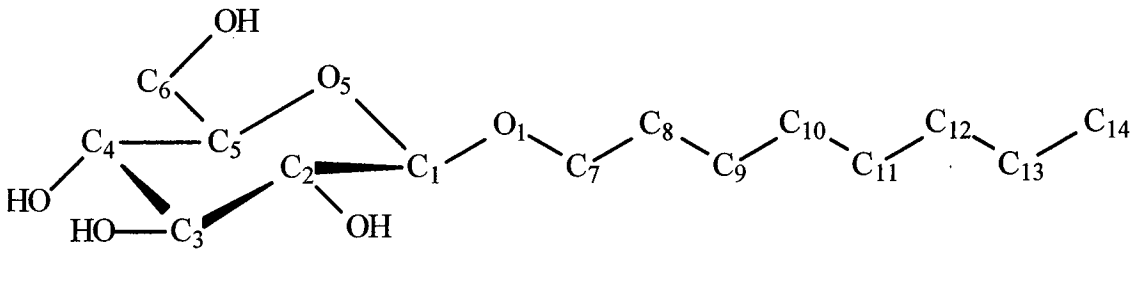
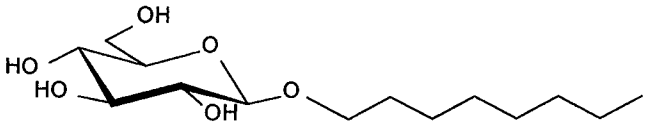
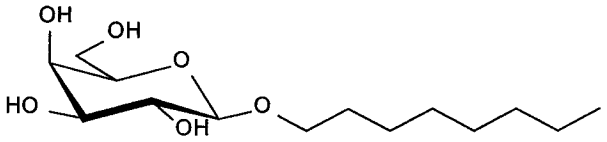


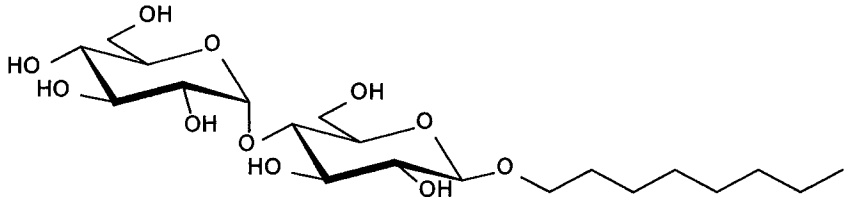
Figure 1. β-octyl glucoside with heavy atom numbering scheme



(a) β-octyl glucoside (OG)



(b) β-octyl galactoside (OGal)



(c) β-octyl maltoside (OM)

Figure 2. The chemical structures of β-octyl glucoside, β-octyl galactoside and β-octyl maltoside, respectively.

Structurally OGal and OG are very similar. The only difference between OGal and OG is that the C4-linked hydroxyl group in OGal is axial while that in OG is equatorial. However, the liquid crystalline property of OGal and OG is very different in terms of their temperature stability in the lyotropic system. Even at high hydrations, OGal always formed a lamellar L_β gel phase at room temperature, and is stable up to 42°C whereas OG formed micellar solution at 20°C and above [17]. Similar data for OM is not available experimentally.

In lyotropic system, the lamellar phase of n-octyl-β-D-galactopyranoside (OGal) has a bilayer spacing of 25.1Å. This is smaller than the value of 29.3 Å for n-octyl-β-D-glucopyranoside (OG). However in thermotropic system, the d-spacing of the OGal smectic A phase, 25.8 Å, is similar to the corresponding value for OG (25.6 Å). In thermotropic system, OGal solid melted at 96°C and the smectic phase was stable up to 127°C. On the other hand, OG solid melted at 69°C and the smectic phase was stable up to 107°C, respectively [17].

Although many computer simulations based on Monte Carlo (MC) lattice models [23] and sophisticated molecular dynamics (MD) have been performed to study biological membranes [24], those of glycolipids are relatively rare despite their importance in biological systems such as lipid bilayers, micelles, liposomes and in other areas of technology especially surfactants. The main reason is that suitable force fields for carbohydrate were not so widely available especially on commercial software. Only recently such force fields for carbohydrates were incorporated into software like CHARMM [25, 26, and 27]. Some of the early molecular dynamics simulations on glycolipids were carried

out to investigate the structural and dynamic properties for octyl glucosides [11, 25].

Exeprimentally alkyl glucosides with β-linkage were found to be more soluble in water, have higher cmc values (17 mM for OG and a lower 5.8 mM for OGal) [28], lower Krafft points, and forms smaller aggregates at dilute concentration than the alkyl glucosides with α-linkage [29]. Sakya et al. [30] and Nilsson et al. [29] independently determined the binary phase diagram for OG by using a penetration experiment for a whole range of concentration of OG. From these measurements they showed that a micellar solution was found below 20°C, followed by a hexagonal liquid crystalline phase, an isotropic region (a cubic phase) and finally a lamellar phase liquid crystalline phase. No two-phase regions between the phases were observed. Above 22°C, the hexagonal phase has melted and the micellar solution is in equilibrium with the cubic phase. At still higher temperatures, there is only a micellar solution in equilibrium with the lamellar phase (75 wt % OG) [29, 30].

From the region examined (0 – 94.8 wt % OG) in binary phase diagram for OG/water and below the temperature of 20°C, there are five different phases present. A hexagonal texture was found from 60 to 70 wt % OG. Above 22°C the hexagonal phase melts into an isotropic solution. Within the region from 70 to 80 wt %OG, there is a very stiff non fluid isotropic region identified as the cubic liquid crystalline phase. The cubic phase melts at temperature slightly above 50°C and forms a less viscous (fluid) isotropic solution. A lamellar phase is formed when the concentration is increased to more than 80 wt % OG. At high concentrations (above 93 wt %), the lamellar phase is in equilibrium with hydrated crystals. These are useful information to assist the generation of the starting configuration of glycolipids computer simulation studies. (See section Materials and Methods).

The extensive isotropic region from neat water to ca. 60 wt % OG suggests the surfactant aggregates remain relatively small and do not grow into extended rods. Moreover the aggregate-aggregate interaction is relatively short-ranged hence no ordering of the aggregates takes place. One possible explanation for the aggregates to remain relatively small was due to the area requirement for the glucose molecules at the hydrophobic/hydrophilic interface is limited, and it is unfavorable to vary that area by increasing the aggregate size [29].

The short-ranged aggregate-aggregate interaction of alkyl glucosides has been established by direct surface force measurements [31]. This fact implies that two aggregates can come in close proximity to each other, and as a consequence the system may be disordered up to high volume fractions of aggregates.

Another interesting feature of the phase diagram is the fact that the hexagonal phase melts at a relatively low temperature (around 22 °C), while the cubic phase melts at a comparatively higher temperature. It has been suggested [32] that this implies the micellar structure (at least close to the phase boundary to the cubic phase) can be described as a melted cubic phase. Since the cubic phase is bicontinuous, this implies that the micellar microstructure is also bicontinuous, in that the micelles form a connected network.

As a function of micelle size, effective micellar radius, R and radius of gyration, R_G were calculated [25]. Assuming the micelles formed are solid spheres,

$$R = \sqrt[3]{\frac{3V}{4\pi}} \qquad \text{and} \qquad R_G = \sqrt{\frac{3}{5}}R$$

These equations define R_G^2 as the ratio of volume per circumference.

Bogusz et al. [25] used the latter equation in computing the radius of gyration for lyotropic system. From this, they also reported the linear relationship between the radius of gyration (R_G) and the number of lipids (N) for OG micelles. They found that R=16.8Å for 27mer from the interpolation of the linear fit of radius of gyration (R_G) versus the number of lipids (N) for OG micelles, which is slightly larger than the experimental result of 15.0 Å for purported 27mer reported by VanAken et al. and Lorber et al. [33, 34].

However, similar linear relationships for OGal and OM have not been established. Besides that, they reported the formation of micelles consist of 5, 10, 20, 27, 34, 50 and 75 glycolipids. In his simulation, 500 glycolipids were used and he rotated the lipid until the tail was pointing inward to build roughly a micelle structure as the starting configuration.

The purpose of generating micelles is to obtain the critical micelles concentrations (cmc) and the generation of micelles can be extended to the more complicated geometry such as the glycolipids bilayers, which construct the liposomes. If drugs or bioactive compounds are engulfed by the micelles or liposomes generated, then drug carrier mechanism through the plasma membrane could be studied. In addition, from the MD simulations of liposomes, further studies of the interactions among cells, drugs and antigens such as bacteria and viruses would be possible.

The aim of the present work is to investigate the micellar structures of n-octyl-β-D-maltopyranoside (OM) and n-octyl-β-D-glucopyranoside (OG) using molecular dynamics simulation with a dielectric constant of 78.5 to simulate the solvent effect of water. The results such as the gyration radii and structures of OM and OG micelles are compared with the experimental results obtained by Niemeyer et al. [35] and He et al. [36] who used small angle scattering (SANS) and small angle x-ray scattering (SAXS) experiments for the structural analysis of OG micelles. In order to investigate the effect of head group, the micellar structure of n-octyl-β-D-galactopyranoside (OGal) was also studied.

MATERIALS AND METHODS

The molecular dynamic simulations were perfomed on OG, OGal and OM using Amber force field for saccharides (*Ambers*) [37] on the commercially available HyperChem simulation package version 6.01, 2000 for Windows. The Lennard-Jonnes interactions were truncated between 10 and 14Å with a smooth switching of the potential. A default electrostatic interaction scale factor of 0.833 and 0.5 of van de Waals interactions scale factor were used. Parameters for linking the sugar head to the octane tail were also based on *Ambers* force field parameters (Table 1). Minimizations were carried out using the more accurate Polak-Ribiere conjugate gradient algorithm with RMS gradient of 0.1 kcal/(Åmol) *in vacuo*.

The starting configurations were generated using the method described by Bogusz et al. [25] but modified slightly so that for example 100 OG were arranged in lamellar form since at high concentrations, OG forms lamellar phase which is in equilibrium with micelles [29] and geometrically minimized with the Polak-Ribiere conjugate gradient algorithm. After minimization, molecular dynamics (MD) was applied to the system at 298K for 120ps. A dielectric constant of 78.5 was used to simulate the solvation effect of water. A step size of 0.001ps was used and data was recorded for every time step. A series of random micelles obtained were named according to the number of lipid monomers present in one micelle (for example, 10mer, 12mer, etc). Finally, the radius of gyration was calculated as those of Bogusz et al. [25].

Computer simulation using atomistic model such as the one attempted here is a challenging task in terms of computational power. Previously even for other non-glycolipids bilayer system (such as DPPC), computer simulations studies were confined to small sample sizes. For example a simulation of 72 lipid/water systems running for 170 ps in 1990's would take 6 months cpu time! (see Pastor et al. [38]). A system of 100 lipids/water at 10-100 ns simulations has become feasible only recently [39]. To reduce the computational time, sometimes it is necessary to use "cheaper" numerical algorithm. For example energy minimization could be performed *in vacuo* using a quasi-Newton-Raphson method while steepest descent algorithm was applied in solvated system [37]. Our current simulation work for glycolipids although is modest, aimed to prove initial concepts rather than to reproduce accurate results. In the literature, there are numerous examples of comparative studies especially for proteins using implicit and explicit solvent models [40, 41, 42, and 43]. Further discussions on some of these are in the results and discussions section below.

Error Estimation

χ^2 (chi-squared) tests were performed on the data obtained. This test allows us to compare our observed results with the expected simulation results by Bogusz et al. [25], and conclude whether or not there is a significant difference between them.

The formula $\chi^2 = \Sigma\left[\frac{(O-E)^2}{E}\right]$ was used for the calculation of the χ^2 values, where Σ denotes summation and O and E are the observed and the expected values, respectively.

RESULTS AND DISCUSSION

Some minimized structural information such as bond lengths and bond angles for OG, OM and OGal in the regions linking sugar head and octane tail were given in Table 1. The OG results for bond lengths and angles were compared with a previous calculation [25] given in Italic (Table 1) using CHARMM [39] forcefield [26, 27] and adopted basis Newton-Raphson (ABNR) algorithm for the minimization because ABNR is a generally useful second-derivative method which is particularly suited for large systems. As expected their results are more accurate than ours. However a statistical comparison χ^2 (chi-squared) demonstrated an error of less than 2% between the two set of results. The χ^2 value for OG bond length is 0.000011 (P= 0.997) and the χ^2 value for bond angle is 0.727 (P= 0.981) for a probability of 0.05 as the default probability for biological account for both cases. Therefore, we can conclude our calculation for the structural properties of these glycolipids is reliable qualitatively and comparable with those of Bogusz et al. [25].

From Table 1 the calculated bond lengths for various glycolipids for the region linking the octyl tail to sugar groups (C7-O1 and C1-O1), (comparing OG and OM, P = 0.979, OG and OGal, P = 0.978) are similar to within 2% difference. The calculated bond angles for the various glycolipids for all regions (O1-C7-C8 and O1-C7-H7; O1-C1-C2, O5-C1-O1, H1-C1-O1 and C1-O1-C7) (comparing OG and OM P = 0.999, OG and OGal, P= 0.993), were found to be similar to 1% difference. So, the difference is small when comparing all regions, i.e. the sugar head groups and the paraffin tails for all glycolipids.

On the other hand as expected, considering only OG and OGal, we found that the variations in bond angles around the glycosidic bonds region closer to the sugar head groups are quite significant (up to 8%). The glycosidic bonds nearer to octyl tail as comparison for OG and OGal (O1-C7-C8 and O1-C7-H7) are different within 5% (P = 0.951). But for the glycosidic bonds nearer to the sugar head groups when comparing OG and OGal (O1-C1-C2, O5-C1-O1, H1-C1-O1 and C1-O1-C7, P = 0.922) the variations between them are as high as 8% and this further proves that constituents and conformations of the head groups affects the overall behavior of these glycolipids. These differences can be observed in the lyotropic system, where the lamellar phase of OGal has a smaller bilayer spacing compared to OG. In addition, OGal is thermally more stable than OG in thermotropic and lyotropic system [17].

Consider OG and OM, we found that the glycosidic bond angles nearer to the octyl tail between OG and OM (O1-C7-C8 and O1-C7-H7) are different within 12% (P = 0.886), which is relatively big. But for the glycosidic bonds nearer to the sugar head groups (O1-C1-C2, O5-C1-O1, H1-C1-O1 and C1-O1-C7, P = 0.922) the variations between them are as low as 2% (P = 0.980). This is due to the fact that the constituents and conformations of the head groups in OG and OM are quite similar as maltose is derived from glucose but it seems that maltose can affect quite vastly the bond angles in octyl tail. Unfortunately, up to date experimental data for OM is not available to prove the above results and thus further studies are underway to investigate in some detail in the future either experimentally or *in silico*.

The dihedral angles of OG, OM and OGal were all found to be significantly different from each other. The stereochemistry of OGal at the fourth carbon (C4) position play a significant role in these variations of the dihedral angles and this is further reflected in the difference of bulk properties of OG and OGal as reported in reference [17].

The physical properties of micelles generated are shown in Table 2 for 100 lipids molecules in each of OG, OM and OGal using *Ambers* forcefield. OG formed a cylindrical micelle containing 65mer and a spherical micelle of 11mer; OGal formed seven micelles containing 17mer, 14mer, 8mer, 8mer, 7mer, 7mer and 5mer while OM formed five micelles of 33mer, 23mer, 11mer, 6mer and 6mer. These showed that the spherical micellar aggregation number of OM is bigger than that of OG. These results are qualitatively in agreement to those recently obtained by He et al. using SANS and SAXS [36] which shall be discussed further below.

Figure 3 below show the relationship between the radius of gyration (R_G) and the number of lipids $(N)^{1/3}$ for OM and OGal micelles. From the results, it was found that the radius of gyration, R_G versus the number of lipids, (N) to the 1/3

power for both OM (continuous line) and OGal (broken line) show a linear relationship as found by Bogusz *et al.* [25] who also reported a linear dependency of R_G for OG with $N^{1/3}$. Our graphs show a better fit for OGal (correlation coefficient, r = 0.99) compared to OM (r = 0.97) that again indicates a satisfactory qualitative agreement.

Bogusz et al. [25] found that the radius of gyration for OG is 13.0 Å for a 27mer. In our calculation the results show that the radius of gyration for 11mer is 4.3 Å. If we extrapolate the value for 27mer, the radius of gyration of OG in our simulation is estimated to be 5.8 Å. This means the forcefield used for our simulation results in a smaller micelle compared to that of Bogusz et al. whose results are qualitatively comparable to the experimental result obtained by VanAken et al. and Lorber et al. in which the radius of gyration is 11.6 Å for purported 27mers [33, 34].

However, our result for OG was found to be qualitatively comparable to those obtained by He et al. recently [36] from their SANS and SAXS experiments, where they also obtained a cylindrical micelle with the radius of cylinder of 12.7 Å for 90mers and ours is 12.2Å for 65mers. This obviously shows that the numbers of molecules are directly proportional to the gyration radius. Furthermore it must be noted that computer simulation studies by Bogusz et al. did not generate any cylindrical micelle hence no comparison could be made with our results.

In our calculation OM gave same micellar geometry namely spherical but different in radius of gyration compared to those found by He et al. [36]. They obtained a bigger gyration radius of 23.7 Å for 26mer while our calculation gave only 12.3 Å for 33mer. If our value is to be interpolated for 26mer, the resulting radius of gyration is only 12.0 Å. So, again the forcefield used in our simulation results in a smaller micelle, which may not be too surprising because our simulation assumed a dielectric constant of 78.5 for the solvent interaction of water and there was no explicit water molecules included.

Thus, we conclude that for both OG and OM, the *Ambers* forcefield used in our simulation resulted in a more constricted micelle with smaller gyration radius for the same number of molecules compared to those obtained by He et al. due to the absence of explicit water molecules. These results are tabulated in Table 3 for comparison. The interpolated values for 26mer for OM alone, 27mer for both OM and OGal were also calculated and shown in Table 3 for comparison with literature [25] and [36].

Here we make further comments on the use and relevance of implicit and explicit water models, which have been under much scrutiny in the literature. For example, the evaluation of explicit solvent models in the simulation of *E. coli* trp repressor, which was reported to be more accurate than the use of implicit dielectric constant [40]. On the other hand, force fields for proteins and nucleic acids developed using implicit dielectric constant and explicit water were found to be equally effective [41]. In the case of carbohydrate systems, significant contrast on the properties of α anomer and β anomer was found in terms of solubility, when implicit dielectric constant method was compared with the experiment [43]. Simulation using variable dielectric constant solvation values were applied to a model liquid crystalline (Lα phase) phosphotidylcholine (PC) bilayer interface where the 'interface energies' function was tested for its ability to reproduce experimental water-solvent partitioning energies and water-bilayer partitioning data. In both cases, the experimental data was reproduced fairly well with the use of implicit dielectric constant [42]. From this short list of literatures, there are advantages and disadvantages in using a dielectric constant compared to explicit waters for simulations. In some cases using dielectric constant sometimes produce similar results as explicit waters model system. Therefore the use of implicit dielectric constant is justified in cases where cpu resources are scarce.

It must be noted that, to our knowledge there has been no extensive simulation or experimental structural property studies reported in the literature for OGal except that Niemeyer et al. [35] who briefly reported its gyration radii to be 25.4 Å at 40 °C. This result is not comparable to ours since our simulation was performed at 25°C. Finally, our simulation results also show that, relatively OM is able to form bigger spherical micelle (12.3 Å, 33mer) compared to that of OG (4.3 Å, 11mer) and OGal (11.0Å, 17mer).

The results discussed above were obtained by applying Amber forcefield for saccharides

(*Ambers*). In our previous calculation where General Amber forcefield (*Amber*) was being used, OG formed a few smaller micelles and OM only formed a cylindrical micelle [44]. The expected difference is probably due to the fact that *Ambers* forcefield specially developed for saccharides is more suitable to be used to stabilize the micelle structures for OM (bigger micelles) and to also stabilize the cylindrical micelle for OG. *Ambers* forcefield was derived by the addition of new parameters to *Amber*. The parameters involved are the interactions of solvent-solvent and solvent-solute hydrogen bonds by taking the dielectric constant of water (78.5). This has the damping effect due to the stabilizing influence of a "cage" of solvent-solvent and solvent-solute hydrogen bonds [37]. Besides that, the gyration radii obtained from OG and OM generated by *Ambers* relatively speaking are in good agreement with the experimental results obtained by Niemeyer [35] and He et al. [36]. Compare to the previous paper [44], the present work has included some improvements in terms of the applied forcefield which is *Ambers* (instead of Amber) and the solvation factor by taking the dielectric constant of water to be 78.5. Finally, we conclude that *Ambers* is a more suitable forcefield to be used for the simulation of glycolipids compared to the general Amber forcefield.

Figure 4 (a), (b) and (c) show the structures of final configurations for OG, OGal and OM micelles, respectively. Figure 5 (a) to (d) show that the OGal micelles generated are reversed micelles as the tails are pointing outward and the glucose heads are pointing inward. Similarly OG and OM also gave similar micellar arrangements.

Table 1. Calculated bond lengths for OG, OM and OGal. The bond lengths for OG in Italics are those from Bogusz *et al.* [23].

	OG	OM	OGal
Bond		**Minimized bond length (Å)**	
C7-O1	1.4447 (*1.4450*)	1.4173	1.4189
C1-O1	1.4027 (*1.4066*)	1.4192	1.4187
Angle		**Minimized bond angle (°)**	
O1-C7-C8	108.2240 (*105.0000*)	109.6480	108.8640
O1-C7-H7	110.0450 (*107.2400*)	110.4720	110.0420
O1-C1-C2	106.6290 (*107.6019*)	109.4670	111.0660
O5-C1-O1	110.8800 (*115.7322*)	109.4560	111.9100
H1-C1-O1	112.5230 (*109.3850*)	109.3450	106.8370
C1-O1-C7	112.7050 (*107.5000*)	112.6770	113.3020
Dihedral		**Minimized bond angle (°)**	
O1-C1-O5-C5	-177.3560	-60.8771	-76.3746
C3-C2-C1-O1	-175.0320	60.5853	81.4639
O1-C1-C2-H2	66.2939	-61.7148	-39.6854
O1-C1-C2-O2	-53.6148	178.2350	-156.5170
C7-O1-C1-O5	-72.8390	-74.4289	-64.5000
C2-C1-O1-C7	169.3560	165.1480	167.9140
C8-C7-O1-C1	176.9060	170.6670	-179.8450

Table 2. The physical properties of aggregate structures for OG, OGal and OM.

Octyl glycosides	Partial charges, (e)	Radius, R (Å)	Gyration radius, R_G (Å)	$N^{1/3}$	Volume, ($Å^3$)	Mass (amu)
OG[a]						
65mer (cylindrical)	0	12.24	-	4.02	16682.22	19004.23
11mer	0	5.55	4.30	2.22	7676.16	3216.10
OM[b]						
33mer	0	15.84	12.27	3.21	16651.21	14998.98
23mer	0	15.56	12.05	2.84	15779.57	10453.84
11mer	0	13.69	10.60	2.22	10753.07	4999.66
6mer	0	11.34	8.78	1.82	6107.45	2727.09
6mer	0	11.53	8.93	1.82	6416.33	2727.09
OGal[b]						
17mer	0	14.20	11.00	2.57	12002.33	4970.33
14mer	0	13.26	10.27	2.41	9755.53	4093.22
8mer	0	11.25	8.71	2.00	5961.18	2338.98
8mer	0	11.08	8.58	2.00	5705.12	2338.98
7mer	0	10.66	8.26	1.91	5070.65	2046.61
7mer	0	10.69	8.28	1.91	5119.36	2046.61
5mer	0	9.65	7.47	1.71	3767.59	1461.86

[a] For cylinder, radius, $R = \sqrt{\frac{V}{\pi t}}$; radius of gyration, $R_G = \frac{R}{\sqrt{2}}$ where t = the length of cylinder, t = 172.1723 Å

[b] For spheres, radius, $R = \sqrt[3]{\frac{3V}{4\pi}}$; radius of gyration, $R_G = \sqrt{\frac{3}{5}}R$

Table 3. Comparison of the geometry, radius and radius of gyration for OG, OM and OGal from different references

Reference	Glycolipids	Aggregation number	Geometry	Radius, (Å)	Gyration radius, R_G (Å)
		Experimental			
He et al. [36]	OM	26	sphere	23.7	18.4
	OG	90	cylinder	12.7	-
Niemeyer *et al.* [35]	OM	-	sphere	14.4	11.2
	OG	-	sphere	27.7	21.5
VanAken *et al.* [33] and Lorber *et al.* [34]	OG	27	sphere	15.0	11.6
		Molecular Dynamic Simulations			
Bogusz *et al.* [25]	OG	27	sphere	16.8	13.0
Current studies	OG	65	cylinder	12.2	-
	OM	27	sphere	15.6	12.1
	OGal	27	sphere	16.4	12.7
	OM	26	sphere	15.5	12.0

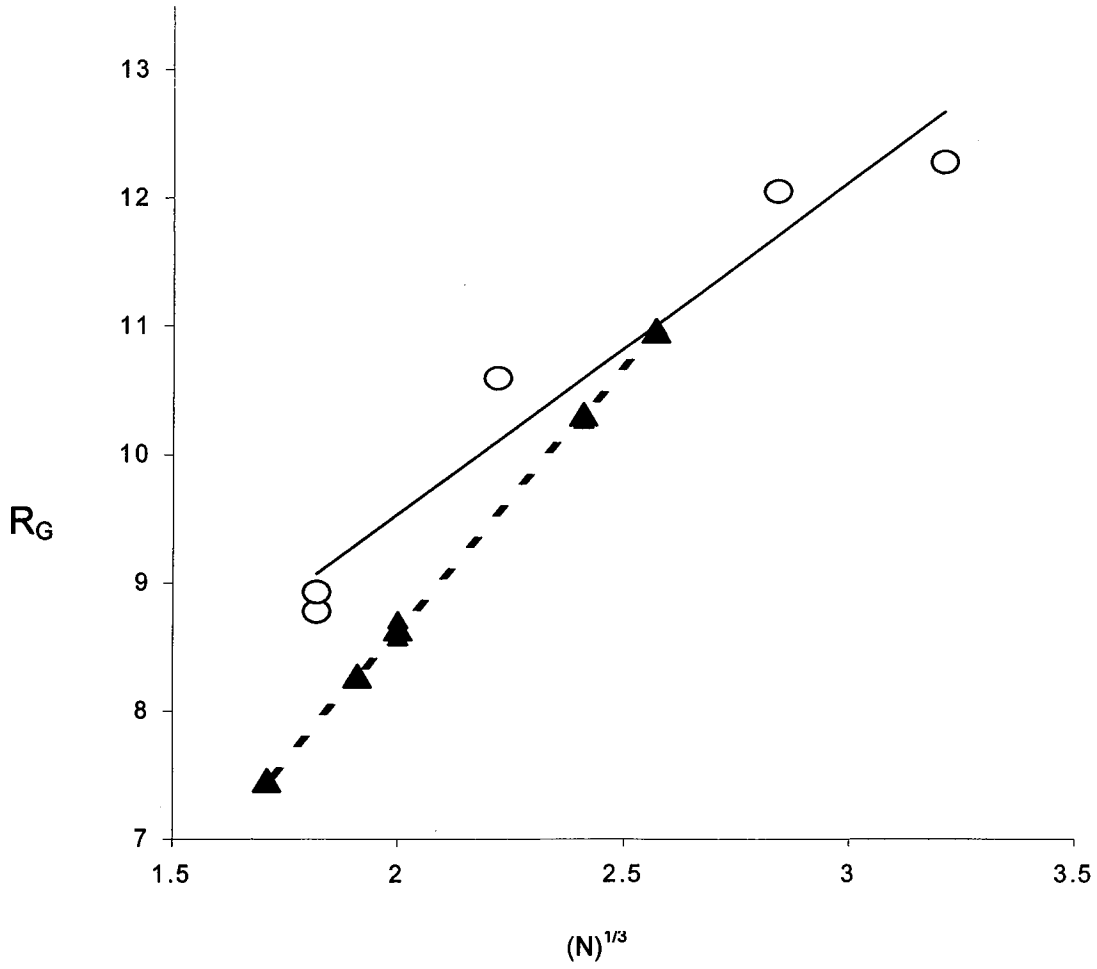
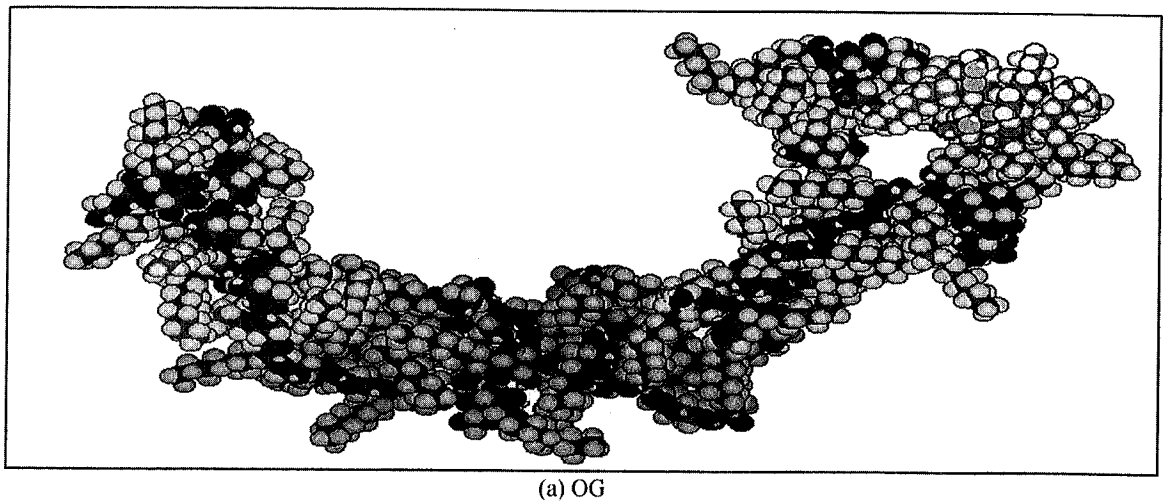
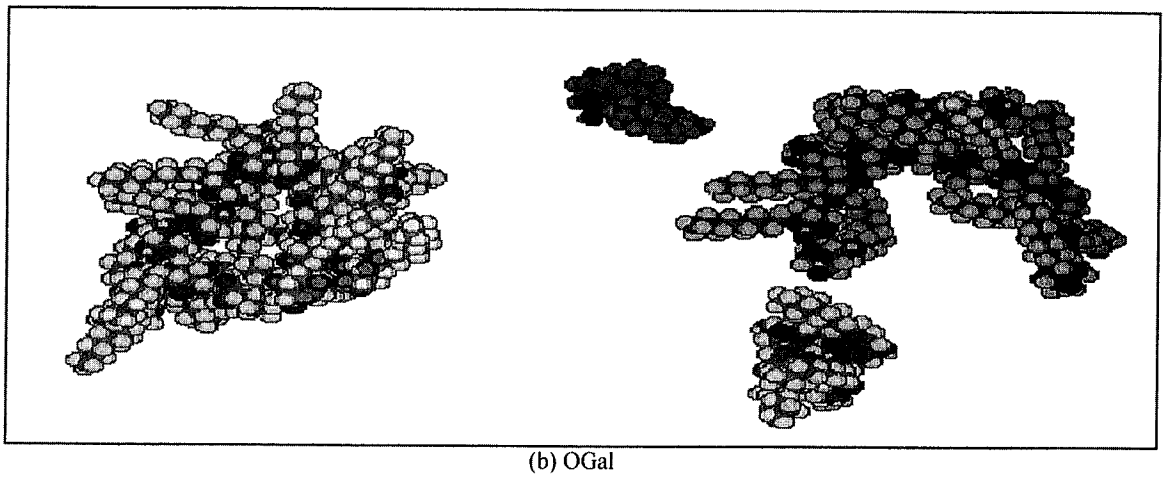


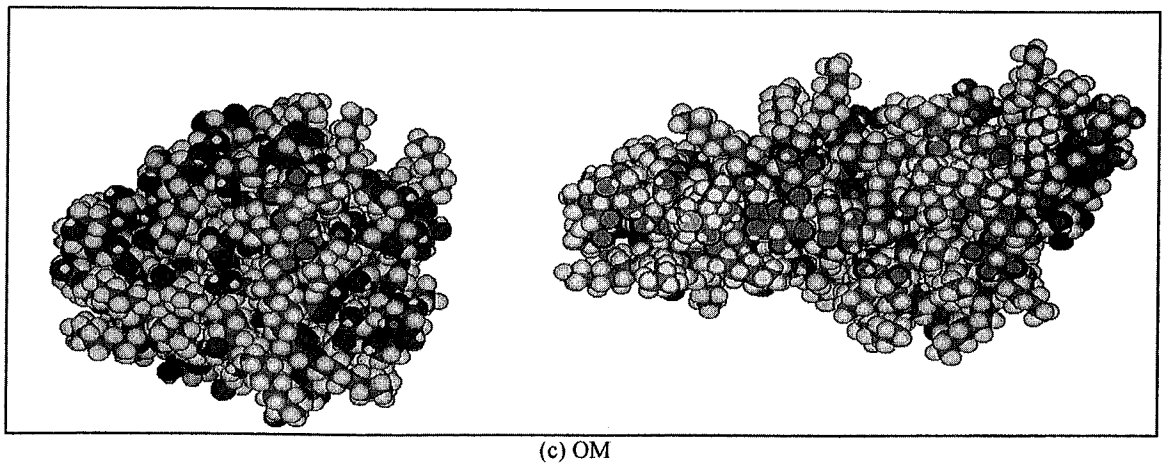
Figure 3. Radius of gyration, R_G vs. number of lipids, (N) to the 1/3 power for OM(open circle) and OGal (filled triangle). Given also the lines of regression for OM (continuous line) and OGal (broken line)



(a) OG



(b) OGal



(c) OM

Figure 4. Final configurations of OG, OGal and OM, respectively.

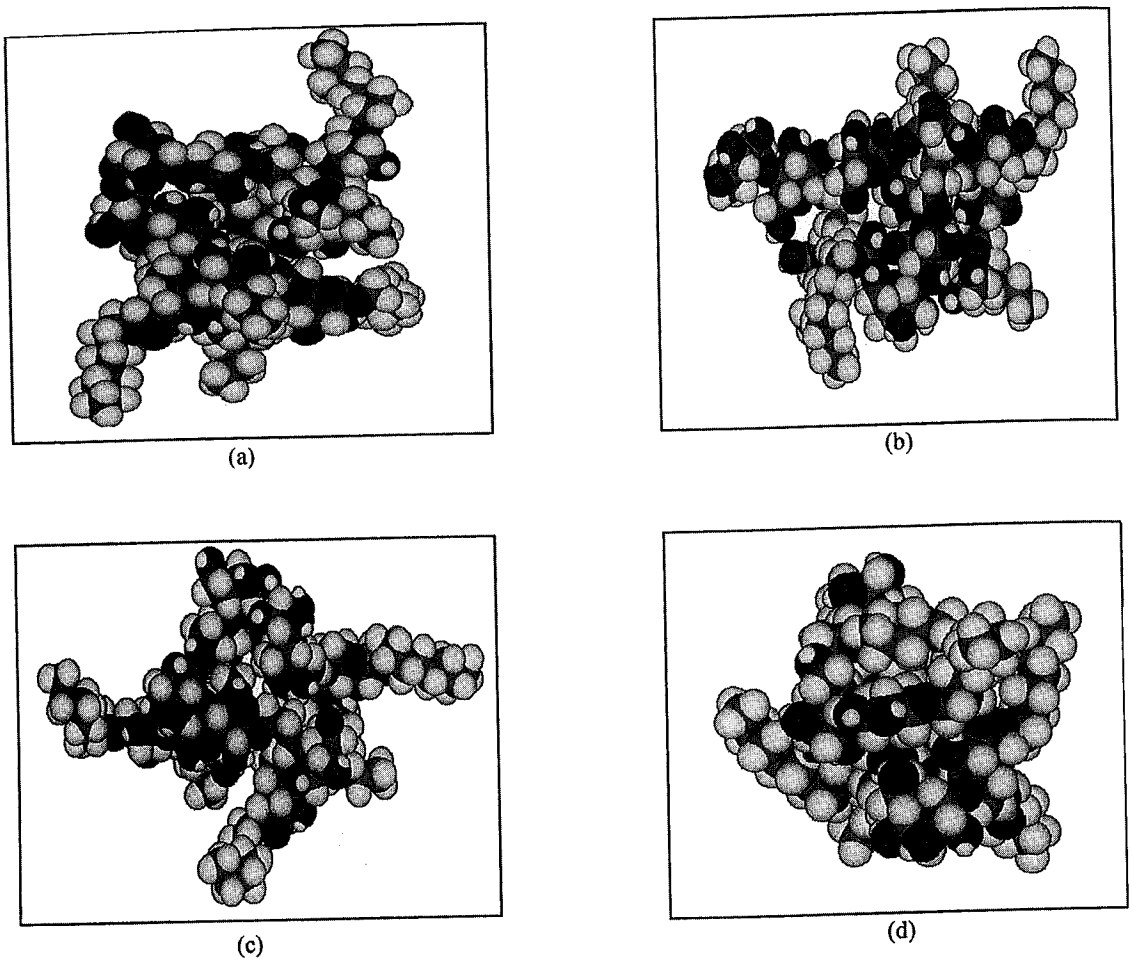


Figure 5. The evolution of a 6mer OM micelle during the course of simulation. The results shows that OGal micelles generated are reversed micelles as the tails are pointing outward and the glucose heads are pointing inward. As expected for simulation in vacuum, OG and OM gave similar micellar arrangements.

CONCLUSION

We have presented initial studies on three octyl glycosides (from glucose, galactose and maltose) using molecular dynamics calculations. Using *Ambers* force field our simple calculations for OG) agreed qualitatively with the more extensive calculation performed by Bogusz et al. [25]. To our knowledge there have been no previous computer simulation studies for galactose and maltose analogues for comparison. It was found that OM formed bigger micelles with gyration radii ranging from 8.78 to 12.27Å. OGal formed small micelles with gyration radius ranging from 7.47 to 11.00Å and OG formed a cylindrical micelle with a radius of 12.24Å and a spherical micelle with a radius of gyration of 4.30Å.

The structural properties for OG and OM were comparable to those obtained by SAXS and SANS experiments [36]. However the lack of explicit water molecules in the simulations resulted in micelles with smaller gyration radii for both OG and OM. Thus, our results do show that by varying the sugar head groups on glycolipids, the micelles of different physical properties will be obtained.

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