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Octyl 6-*O*-hexanoyl-β-D-glucopyranosides: Synthesis, PASS, antibacterial, in silico ADMET, and DFT studies

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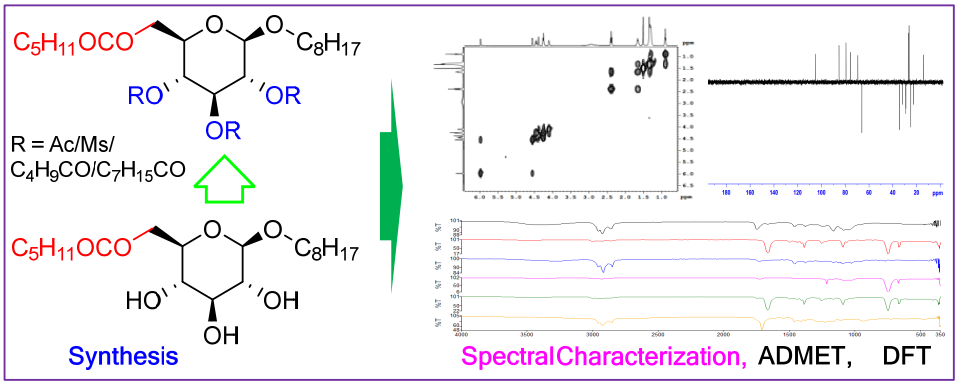
A B S T R A C T

Regioselective acylation of monosaccharides are highly significant for the preparation of both natural and non-natural carbohydrate compounds and their synthetic intermediates. In this respect, an efficient simple method for site selective 6-*O*-hexanoylation of octyl β-D-glucopyranoside (OG) at low temperature is described. The 6-*O*-hexanoylglucoside, thus formed, was then treated with five acyl halides and obtained novel corresponding *O*-acylglupyranosides at C-2, C-3 and C-4 positions with high yields. Activity spectra prediction for substances (PASS) indicated that these glucoside esters are potential against antimicrobials especially against fungi. *In vitro* antibacterial test indicated them as weak to moderate inhibitor of Gram-positive organisms. ADMET prediction indicated that these OGs are overall safe to use. Density functional theory (DFT) optimized electronic energy, enthalpy (ΔH), Gibbs free energy, entropy, dipole-moment (μ), and molecular electrostatic potential (MEP) are also discussed.

Graphical Abstract



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1. Introduction

Sugar derived esters (SEs), especially monosaccharide based mono- and oligo-fatty acid esters, have attracted considerable attention due to their non-ionic surfactant,[1] and broad-spectrum biological activities.[2-6] In most of the cases, SEs are constructed by joining hydrophilic sugar moieties and one or several hydrophobic acid(s) in a single molecular frame-work.[7] Thus, they possess higher stability, biodegradability under aerobic or anaerobic conditions, and low stimulatory effects.[8-9] Most of them are syrupy in nature with no colour and taste.[10] The significant structural feature of SEs is their HLB (hydrophilic-lipophilic balance) which can be easily manipulated, if necessary, *via* altering fatty acid(s) and monosaccharide moiety (glycon part).[11] Investigation of HLB and structural activities could led SEs based effective bio-surfactant, stable and biodegradable potential drugs.[12-14] Actually all the favorable properties of SEs led their suitable application in food (e.g. gelatinization of starch), cosmetics, pharmaceutical industries, and membrane protein research.[15-16] As of concern of environmental for renewable resources, SEs could be an excellent alternative to petrochemically derived similar type of products. In addition to surfactant and drug related uses, SEs are found ubiquitously and well documented for other health-protective effects such as antimicrobial, anti-inflammatory, antimutagenic, etc.[17-19] In plants, SEs can carry not only sugars but also long chain fatty acids into the plant cells. Hence, monosaccharide based SEs gained versatile interest to both the medicinal and biological chemists.[20-22]

Amongst the monosaccharides glucose are ubiquitous in nature.[10,23] It can exist in pyranose and furanose forms. Various natural and synthetic alkyl glycosides (AGs) and alkyl polyglycosides (APGs) are reported with their biological and pharmaceutical applications.[24-29] Glucoside based esters were found to show better antifungal activities than the antibacterial properties. For example, PASS spectra and microbial inhibitory studies showed that 2-*O*-(4-*t*-butylbenzoyl)-glucopyranoside **1a-d** (**Fig. 1**) possess higher fungal inhibitory activities than bacterial inhibitions.[30] Glucose–aspirin (GA, **2**), a highly water soluble glucose ester, was found to have significant anti-cancer activity.[31] Acyl group(s) of SEs with other modifications play significant role in producing metabolites especially in plants.[32] Of the glucosides, octyl β-D-glucoside **3** was introduced as a new non-ionic detergent for membrane research by Baron and Thompson.[33] Later on its different promising applications were thoroughly studied and found potent detergent for brush border membranes with selectivity.[34]

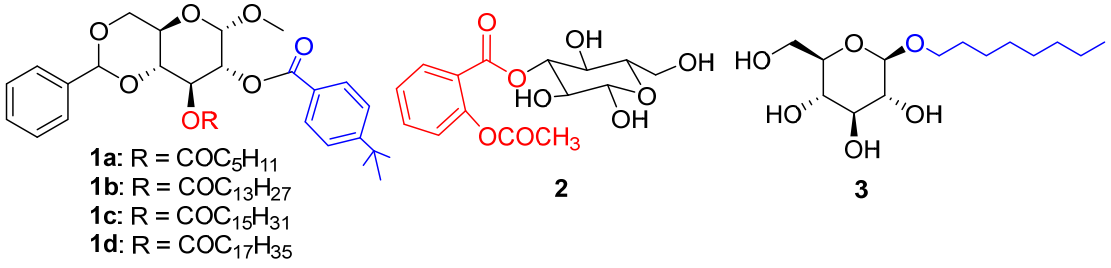


Fig. 1. Structures of compound **1-3**

The selective and regioselective acylation of the hydroxyl group(s) of sugars have long been a prominent challenge for the synthetic chemists. The basic reason is the existence of many 2° OH groups which have similar reactivities,[27,35] and hence, generally such reaction resulted a mixture of mono-*O*- to poly-*O*-acyl ester formation.[35-37] Several chemists utilized the small inherent differences of these 2° OH groups for the selective acylation/protection[35] which are, now-a-days, well known as different methods.[38-39] For example, (i) protection and deprotection method,[40-42] (ii) direct method,[43-44] (iii) catalyst mediated acylation,[45-46] (iv) enzymatic acylation,[47] and (v) microwave mediated acylation.[48] In our present study we utilized direct acylation technique maintaining several reaction conditions to improve selectivity. The higher reactivity and selectivity of 1° OH group as compared to the 2° OH groups in direct and some other catalyst method are well described.[49,50] The position, chain length and number of acyl group(s) definitely play significant role on SEs stability, conformation, and hence

activity.[51]

Despite plethora of biological and industrial applications different results are reported for SEs by different group of researchers. Hence, for better understanding with uniformity of SEs structure and activities further scientific and applied research are essential. Considering biotechnical and biochemical applications of OG **3**, this paper basically describes the regioselective hexanoylation of **3** followed by its tri-*O*-acylation. Also, PASS, *in vitro* antibacterial, ADMET, and DFT based thermodynamic properties of the synthesized OGs are also mentioned.

2. Results and Discussion

2.1 Selective hexanoylation of octyl β-D-glucopyranosides

One of our major aims was regioselective hexanoylation of octyl β-D-glucopyranoside (OG, **3**). In this respect, reaction of glucoside **3** with unimolar hexanoyl chloride at ice-cooled temperature for overnight followed by work-up gave a crystalline compound, mp 143-145 °C (**Scheme 1**).

Presence of a sharp carbonyl band at 1732 cm^{-1} in FT-IR (Fourier-transform infrared spectroscopy) informed the addition of hexanoyl group in this molecule. Its ^{1}H NMR spectrum showed a broad singlet at δ 4.19-4.25 corresponding to three protons of hydroxyl groups indicating the presence of three free OH groups in the solid. In other words, out of four OH groups only one OH group was protected with the hexanoyl group. Presence of additional eleven aliphatic protons as compared to its starting **3** confirmed the addition of only one hexanoyl group in the compound. In ^{13}C NMR spectrum, a carbonyl carbon (δ 174.3) and five aliphatic carbons were resonated in their anticipated positions. Also, both protons of C-6 (δ 4.39 and 4.32 ppm) resonated considerable down field than the precursor **3** indicating the joining of hexanoyl group at this position. It was finally confirmed by HMBC (heteronuclear multiple bond correlation) experiment where carbonyl carbon showed multiple bond correlation with H6a and H-6b (**Fig. 2**). Corroboration of its FT-IR, proton & carbon NMR, distortionless enhancement by polarization transfer (DEPT-135), 2D COSY (correlation spectroscopy), HMBC and HSQC (heteronuclear single quantum coherence) established this solid as octyl 6-*O*-hexanoyl-β-D-glucopyranoside (**4**).

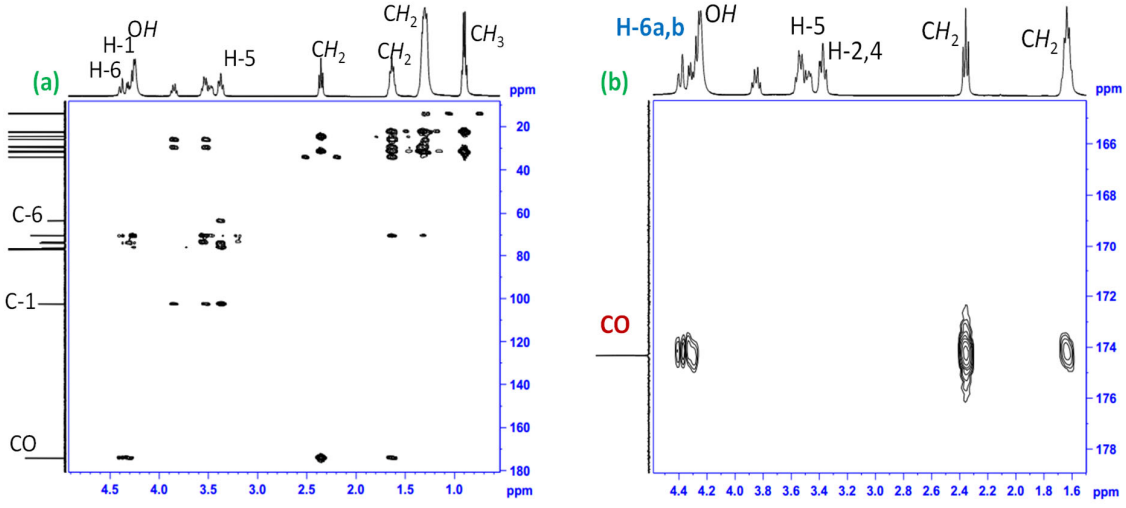
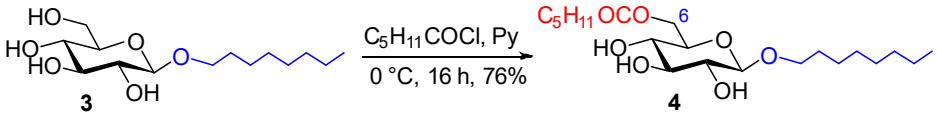


Fig. 2. HMBC correlation between (a) all carbon and protons, (b) H-6a,b and CO group in compound **4**

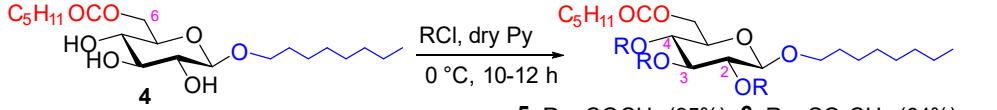


Scheme 1. Regioselctive 6-*O*-hexanoylation of octyl glucoside **3**.

Thus, the successful synthesis of 6-*O*-hexanoate **4** from OG (**3**) indicated the necessary condition of site selective acylation of OG might be- (i) slow addition of acylating agent(s) and preferably use of bulky acylating agent(s), (ii) reaction temperature must be lower, and (iii) use of no catalyst.

*2.2. Preparation of tri-O-acylates **5-9** of hexanoate **4***

To get novel glucoside derivatives hexanoate **4** was treated with five acylating agents separately. Initially, **4** was treated with acetic anhydride and obtained a clear solid, mp 142-144 °C in excellent yield (95%) (**Scheme 2**). FT-IR spectrum of this compound (Figure 3) clearly informed the full acetylation of the compound as OH stretching band was found to disappear. This information was supported by its ^{1}H NMR, where three singlets resonated at δ 2.11, 2.08 and 2.04 were due to three acetyloxy groups. Finally, attachment of three acetyl groups was confirmed by its ^{13}C NMR spectrum where additional three carbonyl carbons at δ 170.5, 170.3 and 169.4 and three methyl carbons at δ 20.5 and 20.3(2) were assigned for three acetyloxy groups. Again, H-2 (δ 5.01), H-3 (δ 5.21), and H-4 (δ 5.11) shifted considerable down fields as compared to its precursor compound **4**. So, the attachment position of three acetyl groups was assigned at C-2, C-3, and C-4 positions. Hence, the solid was named as octyl 2,3,4-tri-*O*-acetyl- 6-*O*-hexanoyl-β-D-glucopyranoside (**5**).



5: R = $COCH_3$ (95%); **6**: R = SO_2CH_3 (64%)
7: R = COC_4H_9 (90%); **8**: R = $COCH_2CH(CH_3)_2$ (83%); **9**: R = COC_7H_{15} (76%)

Scheme 2. Derivatization of the hexanoate compound **4**.

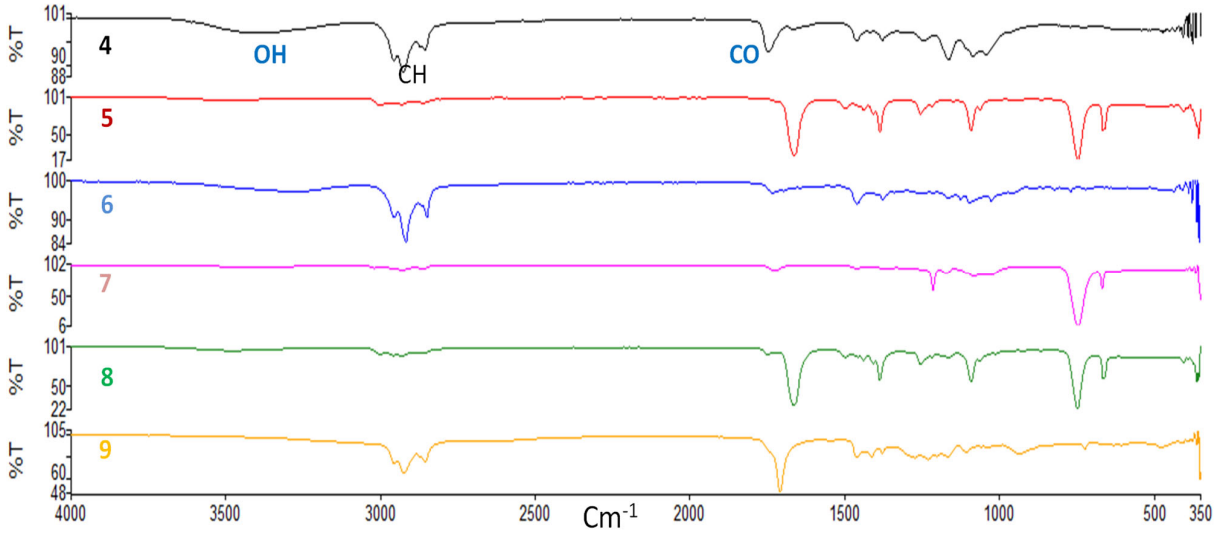


Fig. 3. Comparative FT-IR spectral stretchings of the octyl glucosides **4-9**

In the next step, trimolar mesylation of hexanoate **4** for 10 h and purification gave a solid, mp 161-163 °C (Scheme 2). In this solid's FT-IR spectrum, new bands at 1395, 1381 and 1378 cm^{-1} was indicative of mesylation of the molecule. In the proton NMR spectrum, signals at δ 3.20, 3.18 and 3.14, each integrated for three-protons, clearly indicated addition of three mesyl groups in it. High down field shifts of three protons at 2, 3 and 4 positions compared to its starting **4** supported the joining of mesyl groups at those positions. In ^{13}C NMR, mesyl groups' related carbons resonated at δ 38.7, 38.6 and 38.3 which supported the above observation. Combined analyses of all spectral data established structure of the solid as octyl 6-*O*-hexanoyl-2,3,4-tri-*O*- methanesuphonyl-β-D-glucopyranoside (**6**).

Trimolar pentanoylation of **4** with pentanoyl chloride afforded a thick liquid in 90% (**Scheme 2**). The liquid showed characteristic carbonyl bands and no peak for hydroxyl stretching in FT-IR. More importantly, extra twenty-seven protons were observed at aliphatic region in its ^{1}H NMR spectrum along with anticipated octyl and hexanoyl protons. These twenty-seven protons corresponded to three pentanoyl groups which are found to attach its C-2, C-3 and C-4 positions as these position protons were shifted considerably to down fields than its starting compound **4**. ^{13}C NMR spectrum also indicated the presence of related carbons at their expected positions. Hence, the liquid was octyl 6-*O*-hexanoyl-2,3,4-tri-*O*-pentanoyl-β-D-glucopyranoside (**7**).

Trimolar isopentanoylation of **4** furnished a brownish liquid (**Scheme 2**) which showed no peak related to OH stretching in its FT-IR. It also showed additional twenty-seven aliphatic protons in its ^{1}H NMR and fifteen carbons in its ^{13}C NMR spectrum. Corroboration of all spectral analyses led it's structure as octyl 6-*O*-hexanoyl-2,3,4-tri-*O*-isopentanoyl-β-D-glucopyranoside (**8**).

Similarly, octanoylation of **4** and CC purification leave a syrup (**Scheme 2**). The compound exhibited characteristic four carbonyl peaks at 1740, 1718, 1715 and 1708 cm^{-1}, and absence of hydroxyl stretching in its FT-IR. Appearance of extra forty-five protons and twenty-four carbons in its ^{1}H and ^{13}C NMR spectra, respectively corresponded to three octanoyl groups, and indicated the existence of three octanoyloxy groups in the compound. Thus, its structure was confirmed as octyl 6-*O*-hexanoyl-2,3,4-tri-*O*-octanoyl-β-D-glucopyranoside (**9**).

2.3. Biological activities prediction

Having successful synthesis and characterization of OG esters **4-9**, their biological profile was predicted with the Prediction of Activity Spectrum for Substances (PASS; http://www.way2drug.com/). It should be noted that, PASS program enables prediction of multi-target profiles of drug-like compounds in a shorter time and less cost along with the unknown pharmacological properties of the predicted compounds.[40,44] In the present study, we considered antibacterial, antifungal, anti-carcinogenic and antioxidant properties of the OG **3-9**. The PASS predicted results are shown in **Table 1**. The results are mentioned as Pa and Pi. Here Pa stands for probability for active and Pi stands for probability for inactive drugs. In all the cases, Pa>Pi is considered in the scale 0.000 to 1.000 (Pa+Pi≠1).

In was evident from **Table 1** that the addition of hexanoyl group at C-6 position of OG **3**, as in **4**, increases its antifungal and anti-carcinogenic properties. Further incorporation of acetyl (**5**), pentanoyl (**7**), isopentanoyl (**8**), and octanoyl (**9**) groups at C-2, C-3 and C-4 positions of **4** increased its antifungal potentiality only. However, addition of mesyl groups at those positions decreased all the predicted biological properties (**Table 1**). In general, OG esters **4**, **5**, **7-9** (Pa = 0.705-0.723) possess better antifungal potentiality than standard antibiotic ciprofloxacin (Pa = 0.460) and tetracycline (Pa = 0.523), and also comparable to the azithromycin (Pa = 0.723). Interestingly, these OG esters had better antifungal potentiality than antibacterial activities like other SEs.[4,14,40]

Table 1. Biological spectra of OGs **3-9** obtained from PASS

Drug	Predicted activities							
	Antibacterial		Antifungal		Anti-carcinogenic		Antioxidant	
	Pa	Pi	Pa	Pi	Pa	Pi	Pa	Pi
3	0.529	0.014	0.685	0.010	0.751	0.007	0.600	0.005
4	0.520	0.015	0.700	0.010	0.786	0.006	0.575	0.005
5	0.551	0.012	0.707	0.009	0.699	0.009	0.504	0.006
6	0.400	0.030	0.492	0.032	0.458	0.023	0.321	0.020
7	0.544	0.013	0.705	0.009	0.646	0.011	0.508	0.006
8	0.559	0.011	0.723	0.009	0.580	0.014	0.445	0.009
9	0.544	0.013	0.705	0.009	0.646	0.011	0.508	0.006
AZM	0.964	0.000	0.723	0.009	-	-	-	-
CPC	0.507	0.016	0.460	0.038	-	-	-	-
TTC	0.694	0.005	0.523	0.023	-	-	-	-

AZM = azithromycin; CPC = chloramphenicol; TTC = tetracycline; Pa indicates probability to show activity; Pi indicates probability to show inactivity.

*2.4. Antibacterial activities of **3-9***

In vitro antibacterial activities of the octyl glucosides (OGs, **3-9**) were tested against three Gram-positive and three Gram-negative organisms using well-known agar disk-diffusion method.[52] The related antibacterial results are presented in **Table 2** (**Fig. 4**). For comparison two broad-spectrum standard antibacterial antibiotics namely azithromycin (AZM) and chloramphenicol (CPC) were used.

Table 2. Diameter of zone of inhibition against bacteria by the OGs **3-9**

Drugs	Diameter of zone of inhibition measured as mm					
	Gram-positive			Gram-negative		
	M. esteraromaticum	*M. yunnanenais*	*S. aureus*	*E. coli*	*S. typhi*	*S. flexneri*
3	7.20±0.24	--	11.10±0.76	--	11.30±0.65	--
4	17.20±0.46	13.95±0.66	12.10±0.45	--	11.35±0.88	--
5	7.95±0.33	--	--	--	--	--
6	--	--	--	--	10.45±0.58	--
7	12.50±0.50	10.50±0.50	--	--	--	--
8	--	11.95±0.63	9.75±0.39	--	--	--
9	14.20±0.76	--	10.50±0.50	8.10±0.49	--	--
AZM	15.85±1.2	13.85±1.3	12.75±0.63	*22.1±0.42	13.7±1.8	-
CPC	18.25±1.5	17.25±1.4	13.25±0.92	15.3±0.98	18.55±1.9	--

Measurement was conducted at 100 µg dw / disc; AZM = azithromycin; CPC = chloramphenicol; -- = No inhibition; control DMF showed no inhibition; Results are mentioned as (Mean±SD); SD = Standard deviation; * = Good inhibition values; dw = dry weight.

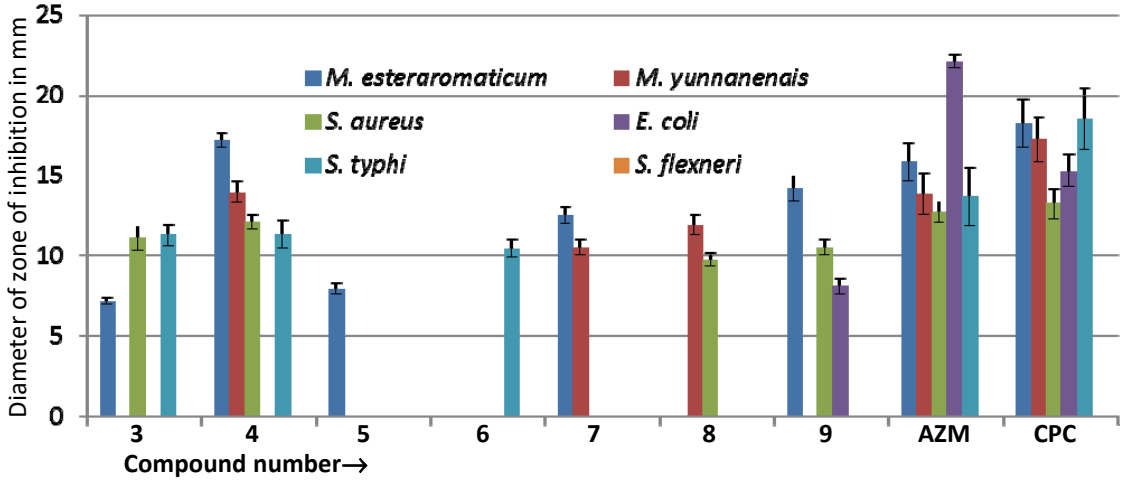


Fig. 4. Diameter of zone of inhibition against bacterial strains by the compounds

It is clearly evident from **Table 2** that the OGs showed weak to moderate diameter of zone of inhibition as compared to the azithromycin (AZM) and chloramphenicol (CPC). These results are in conformity of the PASS predicted results (**Table 1**). It should be noted that antifungal tests of the OGs will also be conducted upon availability of the fungal strains. The OGs esters showed more activity against Gram-positive bacteria than the Gram-negative organisms tested. Also, structurally it was observed that addition of hexanoyl, pentanoyl and octanoyl chain(s) increase OG's activity against *M. esteraromaticum*. All the compounds including standard antibiotics were found to be resistant against Gram-negative *S. flexneri* (**Table 2**).

*2.5. ADMET properties of **3-9***

ADMET stands for the absorption, distribution, metabolism, excretion, and toxicity (ADMET) and predicted using many software packages. Here pkCSM protocol (http://biosig.unimelb.edu.au)[53] was used to predict ADMET of OGs **4-9**. The pharmacokinetic (PK) descriptors (ADMET) are presented in **Table 3.** Absorption of OGs are predicted as Caco-2 permeability (C2P), human intestinal absorption (HIA), and P-glycoprotein substrate or inhibitor (P-gpI). The HIA of all the OG esters were found better than the standard drug azithromycin (AZM). Like AZM all the OG esters are found to be P-glycoprotein inhibitor (P-gpI). Distribution of these compounds in the form of blood brain barrier (BBB), and central nervous system (CNS) permeability were found to be comparable with AZM (**Table 3**). Unlike AZM they are metabolic substrate of CYP3A4. The OGs have good renal excretion. More importantly, all the compounds are found to be non-inhibitor of human ether-a-go-go-gene (hERG) and hence OGs should have fewer side effects (less or non-toxic). These predicted results along with oral rat acute toxicity (LD_{50}) indicated these OG esters could be safer drug to use.

Table 3. ADMET properties of octyl glucosides **3-9**

Drug	Absorption			Distribution		Metabolism	Excretion	Toxicity	
	C2P	HIA (%)	P-gpI	BBB (permeability)	CNS (permeability)	CYP3A4	TC	hERG I	LD_{50} (rat)
3	-0.255	47.996	No	-1.137	-3.503	No	1.663	No	2.075
4	0.949	55.855	Yes	-1.459	-3.144	Yes	1.799	No	3.151
5	-0.92	76.115	Yes	-1.769	-3.238	Yes	1.557	No	2.149
6	0.327	58.013	Yes	-2.979	-3.850	Yes	1.384	No	2.308
7	0.824	93.555	Yes	-1.961	-2.791	Yes	1.769	No	1.278
8	0.968	100.00	Yes	-1.847	-2.548	Yes	1.249	No	1.584
9	0.761	91.514	Yes	-2.148	-2.374	Yes	1.936	No	1.943
AZM	-0.211	45.808	Yes	-1.857	-3.777	No	-0.424	No	2.769

TC = total clearance and measured in log mL/min/kg; I = inhibitor; AZM = azithromycin.

*2.6. DFT optimized structure and related properties of **3-9***

Having OGs **3-9** in hand it was thought to calculate their thermochemical properties using density function theory (DFT). Hence, initially OGs were optimized with DFT program in Gaussian 09 using B3LYP method and 6-31G* basis set.[54] Optimized structures (298.15 K, 1.0 atm), as shown in **Fig. 5**, indicated that these compounds possess $^1C_4$ conformation with the same C1 symmetry. Optimized structures of **3-9** (298.15 K and 1 atm) were used to calculate their several thermodynamic properties such as electronic energy, enthalpy (ΔH), Gibbs free energy (G), entropy, dipole moment (μ) etc. and are mentioned in **Table 4**. The increase of chain length and number of acyl group(s) affected RB3LYP energy, ΔH and G values which were found to decrease gradually, indicating that the electrons are tightly bound to the nucleus affecting more stability of **4-9** as compared to non-acyl glucoside **3**.

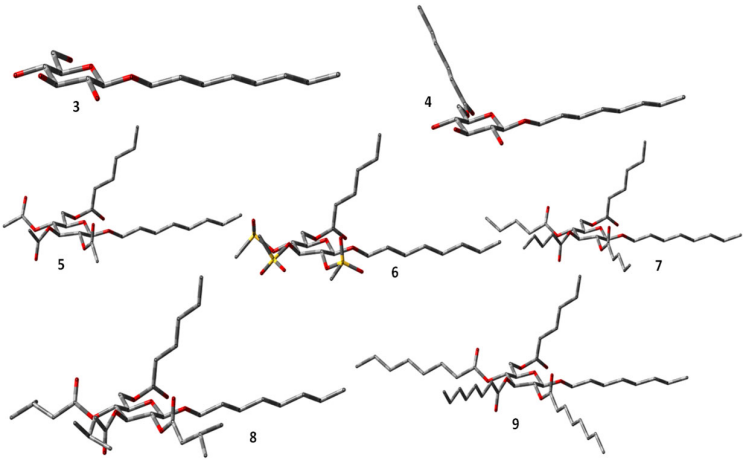


Fig. 5. DFT optimized structures of the octyl glucosides **3-9** (H atoms are not shown)

Also, these thermodynamic parameters are in consistent with their exothermic esterification reaction. The lowest EE, ΔH and G values were observed for trimesylate **6**. However, μ of acyl esters **4**, **5** and **7-9** (3.0-3.7 Debye) were found to decrease than the non-ester **3** (4.299 Debye), although mesyl ester **6** showed higher dipole moment (5.5447 Debye).

Table 4. Selected thermodynamic properties of octyl glucosides **3-9**

OGs	MF	EE (Hartree)	Enthalpy (Hartree)	GFE (Hartree)	Entropy (cal/mol-K)	DM (Debye)
3	$C_{14}H_{28}O_6$	-1001.3688	-1000.9187	-1000.9983	167.542	4.2990
4	$C_{20}H_{38}O_7$	-1311.1882	-1310.5766	-1310.6805	218.719	3.5415
5	$C_{26}H_{44}O_{10}$	-1769.0232	-1768.2875	-1768.4193	277.394	3.0128
6	$C_{23}H_{44}O_{13}S_3$	-3075.2544	-3074.5139	-3074.6503	287.138	5.5447
7	$C_{35}H_{62}O_{10}$	-2122.7634	-2121.7567	-2121.9194	342.372	3.6107
8	$C_{35}H_{62}O_{10}$	-2122.7651	-2121.7598	-2121.9205	338.343	3.6794
9	$C_{44}H_{80}O_{10}$	-2476.5001	-2475.2223	-2475.4142	403.987	3.7559

* EE indicates RB3LYP energy

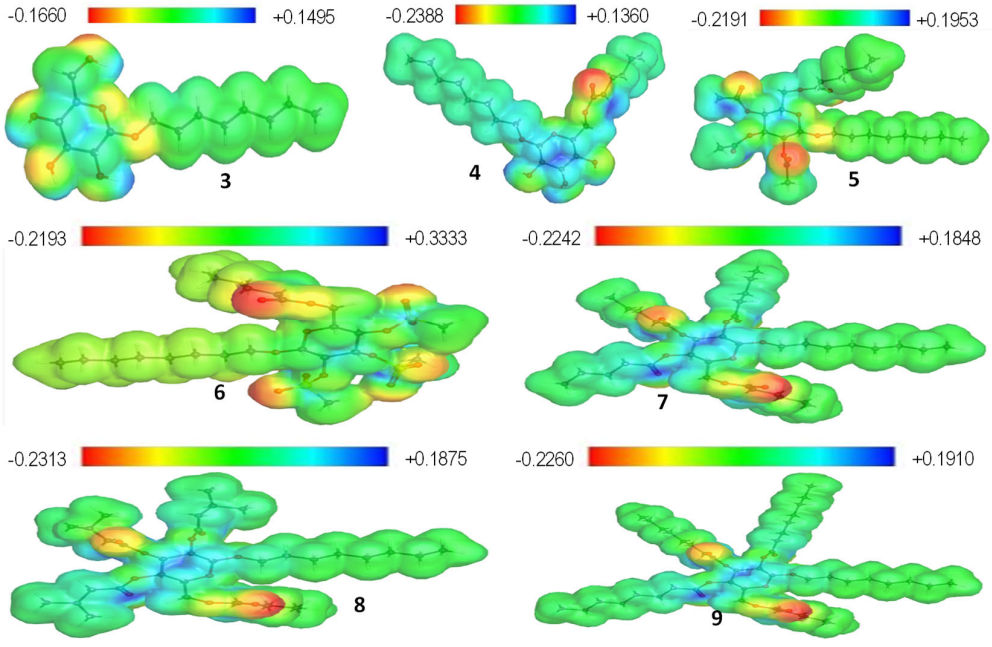


Fig. 6. MEP map (eV) of the octyl glucosides (OGs) **3-9**

Finally, molecular electrostatic potential (MEP) of all the OGs were predicted. MEP surface of a molecule generally indicates reactive (electrophilic and nucleophilic attack) sites. As shown in **Fig. 6**, maximum negative area (red color) indicated possible electrophilic attack site and maximum positive area (blue color) represented probable nucleophilic attack site. Also, green color indicated zero potential area. It is seen from **Fig. 6** that most of the OG esters with alkyl chain(s) (**4**, **5**, **7**-**9**) have ESP close to red (-0.2191 to -0.2388 Hartree) and higher than the non-ester glucoside **1** (-0.166 Hartree). Thus, these OG esters have more tendency of donating electrons as compared to their starting non-ester **1**. However, addition of mesyl groups in OG skeleton, as in **6**, highly increased blue colour intensity (+0.3333 Hartree) than the red colour (-0.2193 Hartree). Hence, only mesylate **6** has the tendency to accept electrons i.e. it will undergo nucleophilic attack.

3. Conclusions

A simple and convenient method for the selective hexanoylation of octyl β-D-glucopyranoside (OG) is described. For the structural diversification and getting newer 6-*O*-hexanoylglucosides, **4** was further transformed into several tri-*O*-acyl derivatives **5**-**9** with other acylating agents reasonably in good yields. PASS predication indicated that incorporation of different alkyl chain containing acyl groups' contributed to increase fungal inhibitory properties of OG (**3**). This fact was supported by their weak to moderate *in vitro* antibacterial activities. In addition, ADMET and DFT based different properties of these OG esters **4**-**9** are also predicted and duly discussed.

Acknowledgement

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4. Experimental

4.1 General methods

Chemicals for the synthesis such as octyl β-D-glucopyranoside, isovaleroyl chloride, valeroyl chloride, hexanoyl chloride, octanoyl chloride, 4-chlorobenzoyl chloride etc. and necessary solvents were purchased from supplier (Aldrich), and were used as received. Ethyl acetate (EA) and *n*-hexane were distilled and then used. TLC (thin layer chromatography) was conducted on Kieselgel GF_{254} silica gel plates, and displayed by spraying with 1% sulphuric acid with methanol followed by heating at ~200 °C until blackish colour appear. For the purification, column chromatography (CC) with silica gel G_{60} was used and *n*-hexane (or petroleum ether)-ethyl acetate (EA) was used as eluent in different proportions. Infrared spectra of the compounds were taken on a FT-IR spectrophotometer (PerkinElmer, Spectrum Two). Both the ^{1}H NMR and ^{13}C NMR spectra were scanned in $CDCl_3$ solution using δ scale (ppm). For appropriate chemical shift measurement reference tetramethylsilane was used. As usual coupling constant values are mentioned in Hertz.

4.2. Syntheses

4.2.1. Synthesis of octyl 6-O-hexanoyl-β-D-glucopyranoside (4)

Octyl β-D-glucopyranoside (**3**, 0.6 g, 2.05 mmol) in anhydrous pyridine (2 mL) was cooled to 0 °C whereupon hexanoyl chloride (0.303 g, 2.25 mmol) was added. It was stirred at the same temperature for 10 h and then continued 6 h at 22-25 °C. The progress of this reaction was monitored by TLC (petroleum ether/EA, 1/2, v/v), which showed the formation of one faster-moving product with little amount of unreacted starting. The reaction was quenched with a few drops of cold water to the flask and then extracted the product mixture with chloroform. The combined organic layer was washed with dilute hydrochloric acid (10%), saturated aqueous sodium hydrogen carbonate solution and water. The organic layer was dried over $MgSO_4$ and filtered. The filtrate was concentrated to leave a thick mass.

The thick mass was passed through silica gel column and eluted with petroleum ether/EA. It provided the 6-*O*-hexanoate **4** (0.609 g, 76%) as crystals, mp 143-145 °C.

*4.3. General procedure: preparation of tri-O-acyl derivatives of **4***

Selected three acyl halides such as acetyl, mesyl, valeroyl, isovaleroyl, and octanoyl chloride (2.2 eq.) was added separately to a cooled solution of triol **4** (0.2 g, 0.578 mmol) in anhydrous pyridine. Addition was conducted very slowly and small quantity of DMAP was put to the solution. Stirring was continued with the elevation of reaction temperature to 22-25 °C and continued stirring for 10-12 h. Quenching of excess acyl halide(s) was accomplished by adding 1-2 drop of freeze water. It was then extracted with organic solvent like dichloromethane (DCM) for three times using a separating funnel. The combined DCM layer was washed with dilute aqueous HCl solution, then with aqueous $NaHCO_3$ solution and finally with brine. This DCM layer was dried ($MgSO_4$) and concentrated in a rotavapor. This gave a thick syrup. The syrupy product was finally purified with silica gel column chromatography (CC). In CC elution was performed with different proportions of *n*-hexane and ethyl acetate (10:0 to 6:1). After CC the desired 2,3,5-tri-*O*-acylates **5-9** were obtained reasonably in good yields.

*4.3.1. Octyl 2,3,4-tri-O-acetyl- 6-O-hexanoyl-β-D-glucopyranoside (**5**)*

Colourless crystals, mp 142-144 °C; Yield 95%; R_f = 0.61 (pet. ether/EA = 4/1); FT-IR (neat): 1729, 1679, 1672, 1663, (CO), 1092 cm^{-1} (pyranose ring); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.21 (t, *J* = 9.6 Hz, 1H, H-3), 5.11 (t, *J* = 9.5 Hz, 1H, H-4), 5.01 (dd, *J* = 9.6 and 8.0 Hz, 1H, H-2), 4.51 (d, *J* = 8.0 Hz, 1H, H-1), 4.27 (dd, *J* = 12.2 and 4.8 Hz, 1H, H-6a), 4.14 (dd, *J* = 12.2 and 2.1 Hz, 1H, H-6b), 3.86 [dt, *J* = 9.5 and 6.5 Hz, 1H, $CH_3(CH_2)_6CH_AH_BO$], 3.67-3.71 (m, 1H, H-5), 3.48 [dt, *J* = 9.5 and 6.7 Hz, 1H, $CH_3(CH_2)_6CH_AH_BO$], 2.34 [t, *J* = 7.6 Hz, 2H, $CH_3(CH_2)_3CH_2CO$], 2.21-2.29 (m, 6H, 3×$CH_3(CH_2)_2CH_2CO$], 2.11 (s, 3H, CH_3CO), 2.08 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO), 1.50-1.67 [m, 4H, $CH_3(CH_2)_5CH_2CH_2O$ and $CH_3(CH_2)_2CH_2CH_2CO$], 1.25-1.35 [br m, 14H, $CH_3(CH_2)_5C_2H_4O$ and $CH_3(CH_2)_2(CH_2)_2CO$], 0.88-0.94 [m, 6H, $CH_3(CH_2)_7O$ and $CH_3C_7H_{14}CO$]; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.3, 170.5, 170.3, 169.4 (*C*O), 101.6 (C-1), 75.2 (C-3), 73.9 (C-5), 73.3 (C-2), 70.3 [$CH_3(CH_2)_6CH_2O$), 70.0 (C-4), 62.5 (C-6), 34.0 [$CH_3(CH_2)_3CH_2CO$], 31.4, 31.3, 29.6, 29.3(2), 26.0, 24.6, 22.7, 22.2 [$CH_3(CH_2)_6CH_2O$ and $CH_3(CH_2)_3CH_2CO$], 20.5, 20.3(2) (CH_3CO), 14.1 [$CH_3(CH_2)_7O$], 13.9 [$CH_3(CH_2)_4CO$].

*4.3.2. Octyl 6-O-hexanoyl-2,3,4-tri-O-methanesuphonyl-β-D-glucopyranoside (**6**)*

Solid-mass, mp 161-163 °C; Yield 64%; R_f = 0.63 (pet. ether/EA = 4/1); FT-IR (neat): 1740 (CO), 1395, 1381, 1378 (SO_2), 1098 cm^{-1} (pyranose ring); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.31 (t, *J* = 9.6 Hz, 1H, H-3), 5.16 (t, *J* = 9.5 Hz, 1H, H-4), 5.05 (dd, *J* = 9.4 and 8.0 Hz, 1H, H-2), 4.54 (d, *J* = 8.0 Hz, 1H, H-1), 4.29 (dd, *J* = 12.0 and 4.8 Hz, 1H, H-6a), 4.14 (dd, *J* = 12.0 and 2.1 Hz, 1H, H-6b), 3.82 [dt, *J* = 9.5 and 6.4 Hz, 1H, $CH_3(CH_2)_6CH_AH_BO$], 3.68-3.73 (m, 1H, H-5), 3.45 [dt, *J* = 9.5 and 6.8 Hz, 1H, $CH_3(CH_2)_6CH_AH_BO$], 3.20 (s, 3H, CH_3SO_2), 3.18 (s, 3H, CH_3SO_2), 3.14 (s, 3H, CH_3SO_2), 2.36 [t, *J* = 7.5 Hz, 2H, $CH_3(CH_2)_3CH_2CO$], 2.21-2.29 (m, 6H, 3×$CH_3(CH_2)_2CH_2CO$], 1.51-1.66 [m, 4H, $CH_3(CH_2)_5CH_2CH_2O$ and $CH_3(CH_2)_2CH_2CH_2CO$], 1.26-1.36 [br m, 14H, $CH_3(CH_2)_5CH_2CH_2O$ and $CH_3(CH_2)_2C_2H_4CO$], 0.89-0.94 [m, 6H, $CH_3C_7H_{14}O$ and $CH_3C_4H_8CO$]; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.5, (*C*O), 101.1 (C-1), 75.4 (C-3), 73.4 (C-5), 73.2 (C-2), 70.5 [$CH_3(CH_2)_6CH_2O$), 70.0 (C-4), 63.2 (C-6), 38.7, 38.6 (SO_2CH_3), 34.3 [$CH_3(CH_2)_3CH_2CO$], 31.4, 31.1, 29.8, 29.3(2), 26.2, 24.6, 22.7, 22.3 [$CH_3(CH_2)_6CH_2O$ and $CH_3(CH_2)_3CH_2CO$], 14.0 [$CH_3(CH_2)_7O$], 13.9 [$CH_3(CH_2)_4CO$].

4.3.3. Octyl 6-O-hexanoyl-2,3,4-tri-O-pentanoyl-β-D-glucopyranoside (7)

Thick syrup; Yield 90%; R_f = 0.61 (pet. ether/EA = 4/1); FT-IR (neat): 1757, 1750, 1747, 1736 (CO), 1090 cm^{-1} (pyranose ring); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.25 (t, *J* = 9.2 Hz, 1H, H-3), 5.11 (t, *J* = 9.6 Hz, 1H, H-4), 5.02 (app t, *J* = 9.2 Hz, 1H, H-2), 4.50 (d, *J* = 8.0 Hz, 1H, H-1), 4.15-4.24 (m, 2H, H-6), 3.86 (dt, *J* = 9.6 and 6.4 Hz, 1H, $CH_3C_6H_{12}CH_AH_BO$), 3.68-3.72 (m, 1H, H-5), 3.42-3.50 (m, 1H, $CH_3C_6H_{12}CH_AH_BO$), 2.37 (t, *J* = 7.5 Hz, 2H, $CH_3C_3H_6CH_2CO$), 2.22-2.30 (m, 6H, $3\times CH_3(CH_2)_2CH_2CO$], 1.50-1.67 [m, 10H, $CH_3(CH_2)_5CH_2CH_2O$, $3\times CH_3CH_2CH_2CH_2CO$ and $CH_3(CH_2)_2CH_2CH_2CO$], 1.24-1.38 [br m, 20H, $CH_3(CH_2)_5CH_2CH_2O$, $3\times CH_3CH_2(CH_2)_2CO$ and $CH_3(CH_2)_2C_2H_4CO$], 0.84-0.94 (m, 15H, $CH_3C_7H_{14}O$, $3\times CH_3C_3H_6CO$ and $CH_3C_4H_8CO$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5, 173.0, 172.1, 172.0 (*C*O), 101.0 (C-1), 72.4 (C-3), 72.1 (C-5), 71.1 (C-2), 70.1 [$CH_3(CH_2)_6CH_2O$], 68.3 (C-4), 61.9 (C-6), 34.0, 33.8(2), 33.7 [$3\times CH_3(CH_2)_2CH_2CO$ and $CH_3(CH_2)_3CH_2CO$], 31.8, 31.3, 29.5, 29.3(2), 26.9, 26.8(2), 25.9, 24.5, 22.7, 22.3, 22.2(3) [$CH_3(CH_2)_6CH_2O$, $3\times CH_3(CH_2)_2CH_2CO$ and $CH_3(CH_2)_3CH_2CO$], 14.1 [$CH_3(CH_2)_7O$], 13.9, 13.7, 13.6(2) [$CH_3(CH_2)_4CO$ and $3\times CH_3(CH_2)_3CO$].

*4.3.4. Octyl 6-O-hexanoyl-2,3,4-tri-O-isopentanoyl-β-D-glucopyranoside (**8**)*

Brownish liquid; Yield 83%; R_f = 0.60 (pet. ether/EA = 4/1); FT-IR (neat): 1747, 1679, 1676, 1662 (CO), 1091 cm^{-1} (pyranose ring); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.27 (t, *J* = 9.6 Hz, 1H, H-3), 5.12 (t, *J* = 9.6 Hz, 1H, H-4), 5.02 (app t, *J* = 9.2 Hz, 1H, H-2), 4.50 (d, *J* = 7.8 Hz, 1H, H-1), 4.19 (br d, 2H, H-6), 3.82-3.88 (m, 1H, $CH_3C_6H_{12}CH_AH_BO$), 3.68-3.71 (m, 1H, H-5), 3.43-3.50 (m, 1H, $CH_3C_6H_{12}CH_AH_BO$), 2.35 [t, *J* = 7.7 Hz, 2H, $CH_3(CH_2)_3CH_2CO$], 2.01-2.20 (br m, 9H, $3\times(CH_3)_2CHCH_2CO$], 1.55-1.65 [m, 4H, $CH_3(CH_2)_5CH_2CH_2O$ and $CH_3(CH_2)_2CH_2CH_2CO$], 1.24-1.34 [br m, 14H, $CH_3(CH_2)_5C_2H_4O$ and $CH_3(CH_2)_2C_2H_4CO$], 0.84-0.97 [m, 24H, $CH_3(CH_2)_7O$, $3\times(CH_3)_2CHCH_2CO$ and $CH_3C_4H_8CO$]; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 173.3, 173.0, 172.1 (*C*O), 100.8 (C-1), 72.4 (C-3), 72.3 (C-5), 71.0 (C-2), 70.0 [$CH_3(CH_2)_6CH_2O$], 68.0 (C-4), 62.1 (C-6), 43.3, 43.2(2) [$3\times(CH_3)_2CHCH_2CO$], 34.0 [$CH_3(CH_2)_3CH_2CO$], 31.6, 31.1, 29.6, 29.4, 29.3, 26.0, 24.6, 22.7, 22.6 [$CH_3(CH_2)_6CH_2O$ and $CH_3(CH_2)_3CH_2CO$], 25.6, 25.5, 25.4 [$3\times(CH_3)_2CHCH_2CO$], 22.3, 22.2(2), 22.1(3) [$3\times(CH_3)_2CHCH_2CO$], 14.0 [$CH_3(CH_2)_7O$], 13.9 [$CH_3(CH_2)_4CO$].

*4.3.5. Octyl 6-O-hexanoyl-2,3,4-tri-O-octanoyl-β-D-glucopyranoside (**9**)*

Thick oil; Yield 76%; R_f = 0.68 (PE/ethyl acetate = 4/1); FT-IR (neat): 1740, 1718, 1715, 1708 (CO), 1107 cm^{-1} (pyranose ring); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.24 (t, *J* = 9.6 Hz, 1H, H-3), 5.11 (t, *J* = 9.8 Hz, 1H, H-4), 5.01 (app t, *J* = 9.8 Hz, 1H, H-2), 4.50 (d, *J* = 8.0 Hz, 1H, H-1), 4.14-4.24 (m, 2H, H-6), 3.86 [dt, *J* = 9.6 and 6.4 Hz, 1H, $CH_3(CH_2)_6CH_AH_BO$], 3.68-3.72 (m, 1H, H-5), 3.43-3.50 [m, 1H, $CH_3(CH_2)_6CH_AH_BO$], 2.33-2.39, 2.22-2.30 (2×m, 8H, $3\times CH_3(CH_2)_5CH_2CO$ and $CH_3(CH_2)_3CH_2CO$], 1.52-1.67 [m, 10H, $CH_3(CH_2)_5CH_2CH_2O$, $3\times CH_3(CH_2)_4CH_2CH_2CO$ and $CH_3(CH_2)_2CH_2CH_2CO$], 1.24-1.38 [br m, 38H, $CH_3(CH_2)_5CH_2CH_2O$, $3\times CH_3(CH_2)_4(CH_2)_2CO$ and $CH_3(CH_2)_2C_2H_4CO$], 0.86-0.96 (m, 15H, $CH_3C_7H_{14}O$, $3\times CH_3C_6H_{12}CO$ and $CH_3C_4H_8CO$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5, 173.0, 172.1, 172.0 (*C*O), 100.8 (C-1), 72.5 (C-3), 72.0 (C-5), 71.2 (C-2), 70.1 [$CH_3(CH_2)_6CH_2O$], 68.4 (C-4), 62.0 (C-6), 34.2, 34.1, 34.0(2) [$3\times CH_3(CH_2)_5CH_2CO$ and $CH_3(CH_2)_3CH_2CO$], 31.8, 31.7, 31.6(2), 31.3, 29.7, 29.5, 29.3(2), 29.1(2), 29.0(2), 28.9, 25.9, 24.9(2), 24.8, 24.7, 24.5, 22.7, 22.6(2), 22.3, [$CH_3(CH_2)_6CH_2O$, $3\times CH_3(CH_2)_5CH_2CO$ and $CH_3(CH_2)_3CH_2CO$], 14.1, 14.0(3) [$CH_3(CH_2)_7O$ and $3\times CH_3(CH_2)_6CO$], 13.9 [$CH_3(CH_2)_4CO$].

4.4. Antibacterial activity evaluation

For *in vitro* antibacterial evaluation all the compounds **3**-**9** were dissolved in DMF and finally prepared 2% solution of OGs. Necessary media plates were subjected for incubation at 37 °C for 2 days. DMF without chemicals was used as control.

Three Gram-positive such as *Micobacterium esteraromaticum*, *Micrococcus yunnanenais*, and *Staphylococcus aureus* were used in this study. Also, three Gram-negative bacteria viz. *Escherichia coli*, *Salmonella typhi*, and *Shigella flexneri* were employed. For culture of these bacteria Mueller-Hinton medium was used throughout. The activity was assessed by agar disk-diffusion method[52] and expressed as diameter of zone of inhibition. The average of three experiments with standard deviation (SD) is calculated. For comparison two standard antibiotics namely azithromycin and chloramphenicol (chloromycetin) were used.

4.5. Prediction of ADMET

ADMET properties of the OGs **3-9** were calculated using the pkCSM ADMET algorithm protocol (http://biosig.unimelb.edu.au).[53] The pharmacokinetic (PK) properties prediction generally conducted before *in vivo* experiments which tremendously reduce time and cost for drug discovery process. For the ADMET prediction OGs and standard antibiotics, their structures were drawn with appropriate geometry and were converted into InChI Key and SMILES. These formats were then applied during the ADMET evaluation.

4.6. DFT optimization

Basic geometry of octyl glucoside **3** was taken from Chemspider. All other OGs **4-9** were then drawn in GaussView (5.0) program.[54] These structures were duly optimized using density function theory (DFT) in B3LYP method and 6-31G* basis set in Gaussian 09 program.[54] Thermodynamic properties of **3-9** were measured from their optimized structures. Also, molecular orbital potentials (MEP) were visualized using WebMo server (available online).

References

1. Plat T., and Linhardt R. J. (**2001**) Syntheses and applications of sucrose-based esters. *J. Surfactants Deterg.*, 4 415–421.
2. Lucarini S., Fagioli L., Campana R., Cole H., Duranti A., Baffone W., Vllasalium D., and Casettari L. (**2016**) Unsaturated fatty acids lactose esters: cytotoxicity, permeability enhancement and antimicrobial activity. *Eur. J. Pharm. Biopharm.*, 107 88–96.
3. Zhao L., Zhang H. Y., Hao T. Y., and Li S. R. (**2015**) In vitro antibacterial activities and mechanism of sugar fatty acid esters against five food-related bacteria. *Food Chem.*, 187 370–377.
4. Matin M. M., Bhattacharjee S. C., Chakraborty P., and Alam M. S. (**2019**) Synthesis, PASS predication, in vitro antimicrobial evaluation and pharmacokinetic study of novel n-octyl glucopyranoside esters. *Carbohydr. Res.*, 485 107812.
5. Shao S-. Y., Shi Y-. G., Wu Y., Bian L-. Q., Zhu Y-. J., Huang X-. Y., and et al. (**2018**) Lipase-catalyzed synthesis of sucrose monolaurate and its antibacterial property and mode of action against four pathogenic bacteria. *Molecules*, 23 e1118.
6. Dhavale D. D., Matin M. M., Sharma T., and Sabharwal S. G. (**2003**) N-Hydroxyethyl-piperidine and –pyrrolidine homoazasugars: preparation and evaluation of glycosidase inhibitory activity. *Bioorg. Med. Chem.*, 11 (15) 3295–3305.
7. Matin M. M., and Iqbal M. Z. (**2021**) Methyl 4-*O*-(2-chlorobenzoyl)-α-L-rhamnopyranosides: Synthesis, characterization, and thermodynamic studies. *Orbital: Electron. J. Chem.*, 13 (1) 19–27.
8. Tarahomjoo S., and Alemzadeh I. (**2003**) Surfactant production by an enzymatic method. *Enzyme Microb. Technol.*, 33 33–37.
9. Szüts A., Pallagi E., Regdon G., Aigner Z., and Révész P. S-. (**2007**) Study of thermal behaviour of sugar esters, *Int. J. Pharm.*, 336 199–207.
10. A. B. M., Dave Zaitlin D., and Wagner G. J. (**2016**) Natural variability in acyl moieties of sugar esters produced by certain tobacco and other Solanaceae species. *Phytochem.*, 130 218–227.
11. Kobayashi T., Takahashi T., and Adachi S. (**2012**) Synthesis of 6-*O*-Octanoyl-1,2-*O*-isopropylidene-α-D-glucofuranose by lipase-catalyzed esterification in an organic solvent. *J. Oleo Sci.*, 61 (2) 75–79.
12. Allen D. K., and Tao B. Y. (**1999**) Carbohydrate-alkyl ester derivatives as biosurfactants. *J. Surfactants Deterg.*, 2 383–390.
13. Matin M. M., Chakraborty P., Alam M. S., Islam M. M., and Hanee U. (**2020**) Novel mannopyranoside esters as sterol 14α-demethylase inhibitors: Synthesis, PASS predication, molecular docking, and pharmacokinetic studies. *Carbohydr. Res.*, 496 108130.

14. Matin M. M., Bhuiyan M. M. H., Kabir E., Sanaullah A. F. M., Rahman M. A., Hossain M. E., and Uzzaman M. (**2019**) Synthesis, characterization, ADMET, PASS predication, and antimicrobial study of 6-*O*-lauroyl mannopyranosides. *J. Mol. Struct.*, 1195 189–197.
15. Marshall D. L., and Bullermann L. B. (**1994**) Antimicrobial properties of sucrose fatty acid esters, in: Akoh C. C., and Swanson B. G. (Eds) *Carbohydrate Polymers as Fat Substitutes*. Marcel Dekker (New York), 149–167.
16. Kabara J. J., Conley A. J., Swieczkowski D. M., Ismail I. A., Jie M. L. K., and Gunstone F. D. (**1973**) Antimicrobial action of isomeric fatty acids on group *A Streptococcus*. *J. Med. Chem*., 16 1060–1063.
17. Kumar N., and Goel N. (**2019**) Phenolic acids: Natural versatile molecules with promising therapeutic applications. *Biotechnol. Rep.*, 24 00370.
18. Matin M. M., Islam N., Siddika A., and Bhattacharjee S. C. (**2021**) Regioselective synthesis of some rhamnopyranoside esters for PASS predication, and ADMET studies. *J. Turkish Chem. Soc. Sect. A: Chem.*, 8 (1) 363–374.
19. Matin M. M., Bhuiyan M. M. H., Azad A. K. M. S., and Akther N. (**2017**) Design and synthesis of benzyl 4-*O*-lauroyl-α-L-rhamnopyranoside derivatives as antimicrobial agents. *Curr. Chem. Lett.*, 6 (1) 31–40.
20. Yang L-. J., Yang X-. D., Yang S., Zhao J-. F., Zhang H-. B., and Li L. (**2006**) Two new benzoyl esters of glucose from *Lagotis yunnanensis*. *Chem. of Nat. Compd*., 42 (6) 649–651.
21. Matin M. M., Bhuiyan M. M. H., Azad A. K. M. S., and Rashid M. H. O. (**2015**) Synthesis of 6-*O*-stearoyl-1,2-*O*-isopropylidene-α-D-gluco-furanose derivatives for antimicrobial evaluation. *J. Phys. Sci.*, 26 (1) 1–12.
22. Lee K. P., and Kim H. K. (**2016**) Antibacterial effect of fructose laurate synthesized by Candidaantarctica B lipase-mediated transesterification. *J. Microbiol. Biotechnol.*, 26 (9) 1579–1585.
23. Pan H., and Lundgren L. N. (**1994**) Rhododendrol glycosides and phenyl glucoside esters from inner bark of *Betula pubescens*. *Phytochem*., 36 (1) 79–83.
24. Yakimchuk O. D., Kotomin A. A., Petel'skii M. B., and Naumov V. N. (**2004**) Cleaning action and surfactant properties of alkyl glucosides. *Russ. J. Appl. Chem.*, 77 2001–2005.
25. Matin M. M., Uzzaman M., Chowdhury S. A., and Bhuiyan M. M. H. (**2020**) In vitro antimicrobial, physicochemical, pharmacokinetics, and molecular docking studies of benzoyl uridine esters against SARS-CoV-2 main protease. *J. Biomol. Struct. Dyn.* DOI: 10.1080/07391102.2020.1850358.
26. https://www.mfc.co.jp/english/appli.htm
27. Matin M. M., Hasan M. S., Uzzaman M., Bhuiyan M. M. H., Kibria S. M., Hossain M. E., and Roshid M. H. O. (**2020**) Synthesis, spectroscopic characterization, molecular docking, and ADMET studies of mannopyranoside esters as antimicrobial agents. *J. Mol. Struct.*, 1222 128821.
28. Matin M. M., Bhuiyan M. M. H., Debnath D. C., and Manchur M. A. (**2013**) Synthesis and comparative antimicrobial studies of some acylated D-glucofuranose and D-glucopyranose derivatives. *Int. J. Biosci.*, 3 (8) 279–287.
29. Takada H., Takashima Y., Yokotsuka A., and Soyama Y. (**2000**) Eyelash Cosmetic Composition Containing Sucrose Fatty Acid Esters, U.S. Patent 6,024,950.
30. Chowdhury, S. A., Chakraborty, P., Kawsar, S. M.A., Bhuiyan, M. M. H., and Matin, M. M. (**2018**) Regioselective acylation, PASS prediction and antimicrobial properties of some protected glucopyranosides. *J. Bangladesh Chem. Soc.*, 30 (1), 1–9.
31. Jacob J. N., and Tazawa M. J. (**2012**) Glucose–aspirin: Synthesis and in vitro anti-cancer activity studies, *Bioorg. Med. Chem. Lett*., 22 3168–3171.
32. Wilson A. E., Matel H. D., and Tian L. (**2016**) Glucose ester enabled acylation in plant specialized metabolism, *Phytochem. Rev.*, 15 1057–1074.
33. Baron C., and Thompson T. E. (**1975**) Solubilization of bacterial membrane proteins using alkyl glucosides and dioctanoylphosphatidyl choline. *Biochim. Biophys. Acta*, 352 276–285.
34. Lin J. T., Riedel S., and Kinne R. (**1979**) The use of octyl β-D-glucoside as detergent for HOG kidney brush border membrane. *Biochim. Biophys. Acta*, 557 179–187.
35. Dimakos V., and Taylor M. S. (**2018**) Site-selective functionalization of hydroxyl groups in carbohydrate derivatives. *Chem. Rev*., 118 (23) 11457–11517.
36. Sugihara J. M. (**1953**) Relative reactivities of hydroxyl groups of carbohydrates. *Adv. Carbohydr. Chem.*, 8 1−44.

37. Haines A. H. (**1976**) Relative reactivities of hydroxyl groups in carbohydrates. *Adv. Carbohydr. Chem. Biochem*., 33 11−109.
38. Lawandi J., Rocheleau S., and Moitessier N. (**2016**) Regioselective acylation, alkylation, silylation and glycosylation of monosaccharides. *Tetrahedron*, 72 6283−6319.
39. Jäger M., and Minnaard A. J. (**2016**) Regioselective modification of unprotected glycosides. *Chem. Commun.*, 52 656−664.
40. Matin M. M., Nath A. R., Saad O., Bhuiyan M. M. H., Kadir F. A., Hamid S. B. A., Alhadi A. A., Ali M. E., and Yehye W. A. (**2016**) Synthesis, PASS-predication and in vitro antimicrobial activity of benzyl 4-*O*-benzoyl-α-L-rhamnopyranoside derivatives. *Int. J. Mol. Sci.*, 17 (9) 1412.
41. Dhavale D. D., and Matin M. M. (**2004**) Selective sulfonylation of 4-*C*-hyroxymethyl-β-L-threo-pento-1,4-furanose: Synthesis of bicyclic diazasugars. *Tetrahedron*, 60 (19) 4275–4281.
42. Matin M. M., and Ibrahim M. (**2010**) Synthesis of some methyl 4-*O*-octanoyl-α-L-rhamnopyranoside derivatives. *J. Appl. Sci. Res.*, 6 (10) 1527–1532.
43. Matin M. M., and Chakraborty P. (**2020**) Synthesis, spectral and DFT characterization, PASS predication, antimicrobial, and ADMET studies of some novel mannopyranoside esters. *J. Appl. Sci. Process Eng.*, 7 (2) 572–586.
44. Ali M., Karim M. H., and Matin M. M. (**2021**) Efficient synthetic technique, PASS predication, and ADMET studies of acylated n-octyl glucopyranosides. *J Appl. Sci. Process Eng*., 8 (1) 648–659.
45. Kabir A. K. M. S., and Matin M. M. (**1994**) Regioselective acylation of a derivative of L-rhamonse using the dibutyltin oxide method. *J. Bangladesh Chem. Soc*., 7 (1) 73–79.
46. Kabir A. K. M. S., and Matin M. M. (**1997**) Regioselective monoacylation of a derivative of L-rhamnose. *J. Bangladesh Acad. Sci.*, 21 (1) 83–88.
47. Staron J., Dabrowski J. M., Cichon E., and Guzik M. (**2018**) Lactose esters: synthesis and biotechnological applications. *Crit. Rev. Biotechnol*., 38 245–58.
48. Richel A., Laurent P., Wathelet B., Wathelet J. P., and Paquot M. (**2011**) Microwave-assisted conversion of carbohydrates. State of the art and outlook. *C. R. Chim.*, 14 (2-3) 224–234.
49. Jiang L., and Chan T-. H. (**1998**) Regioselective acylation of hexopyranosides with pivaloyl chloride. *J. Org. Chem*., 63 6035−6038.
50. Matin M. M. (**2006**) Synthesis of some silyl protected 1,4-galactonolactone derivatives. *J. Appl. Sci. Res*., 2 (10) 753–756.
51. Islam F., Rahman M. R., and Matin M. M. (**2021**) The effects of protecting and acyl groups on the conformation of benzyl α-L-rhamnopyranosides: An in silico study. *Turkish Comp. Theo. Chem*., 5 (1) 39–50.
52. Clinical and Laboratory Standards Institute (**2012**) Methods for antimicrobial susceptibility testing of anaerobic bacteria: approved standard, 8th Ed. CLSI document, Approved Standard M11-A8, Wayne.
53. Han Y., Zhang J., Hu C. Q., Zhang X., Ma B., and Zhang P. (**2019**) In silico ADME and toxicity prediction of Ceftazidime and its impurities. *Front. Pharmacol*., 10 434.
54. Frisch M. J., Trucks G. W., Schlegel H. B., Scuseria G. E., Robb M. A., et al. (**2013**) Gaussian 09W, Revision D.01. Gaussian, Inc., Wallingford CT.