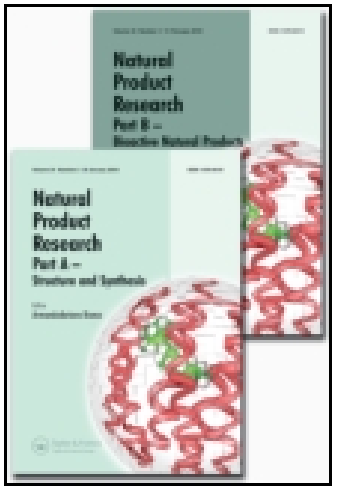

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Synthesis and antimicrobial studies of hydroxylated chalcone derivatives with variable chain length

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Synthesis and antimicrobial studies of hydroxylated chalcone derivatives with variable chain length

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A series of (E)-1-(4-alkyloxyphenyl)-3-(hydroxyphenyl)-prop-2-en-1-one have been successfully synthesised *via* Claisen–Schmidt condensation. The synthesised chalcone derivatives consisted of hydroxyl groups at either *ortho*, *meta* or *para* position and differed in the length of the alkyl groups, C_nH_{2n+1}, where $n = 6$, 10, 12 and 14. The structures of all compounds were defined by elemental analysis, IR, ^{1}H- and ^{13}C-NMR. The antimicrobial studies were carried out against wild-type *Escherichia coli* American Type Culture Collection 8739 to evaluate the effect of the hydroxyl and the alkyl groups of the synthesised chalcones. All the synthesised compounds have shown significant antimicrobial activities. The optimum inhibition was dependent on the position of the hydroxyl group as well as the length of the alkyl chains.

Keywords: chalcones; hydroxyl group; alkyl group; antimicrobial activities

1. Introduction

Chalcone is a natural pigment which is commonly found in plants. It is one of the important intermediates in the biosynthesis of flavonoid. A large number of chalcones have been studied in the recent decades mainly due to their numerous biological properties such as anticancer, antioxidant (Aichaoui et al., 2009; Echeverria, Santibañez, Donoso-Tauda, Escobar, & Ramirez-Tagle, 2009) as well as antimicrobial activities (Prasad, Rao, & Rambabu, 2008). Claisen–Schmidt condensation is a common method for the synthesis of chalcone, which involves cross aldol condensation of appropriate benzaldehyde and acetophenone in the presence of a base as a catalyst.

Chalcone with the presence of hydroxyl groups has been claimed to have antimicrobial activities (Devia, Pappano, & Debattista, 1998; Ngaini, Haris-Fadzillah, Hussain, & Kamaruddin, 2009; Oyedapo, Makanju, Adewunmi, Iwalewa, & Adenowo, 2004). Naturally occurring chalcones are mostly found in hydroxylated form and many reports have documented their biologically active

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properties such as cytotoxicity, antitumour, immunosuppresion and antioxidant (Go, Wu, & Liu, 2005). The presence of alkyl chains either in the naturally occurring chalcones (de Andrade Cunha et al., 2003; Stevens, Miranda, Frei, & Buhler, 2003) or in the synthetic chalcones (Hsieh, Tsao, Wang, & Lin, 2000) has also been reported for their significant biological activities.

The long alkyl chains have attracted significant attention as they could also give biologically active properties (Abel et al., 2002; Cohen et al., 2004). This is due to the lipophilic alkyl chains which have the ability to disrupt microorganism cell wall (Birnie, Malamud, & Schnaare, 2000; Park et al., 2004). For instance, water-soluble methacrylate polymers with alkyl chain of 12, 14 and 16 carbons for ammonium groups have shown an increase in antibacterial activities against *Staphylococcus aureus* (Dizman, Elasri, & Mathias, 2006). However, the presence of short chain also has a significant influence on the antimicrobial activities (Birnie et al., 2000).

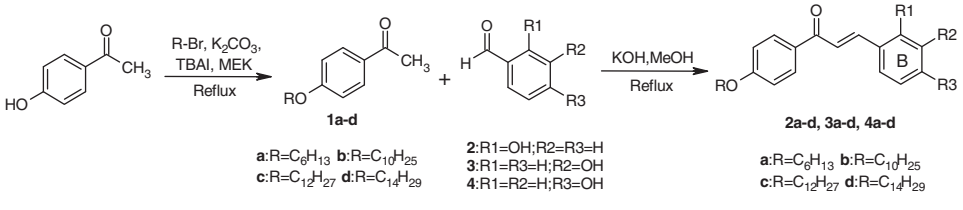
In view of the involvement of hydroxyl groups and long alkyl side chains, in this article, we report the synthesis of novel chalcone derivatives (E)-1-(4-alkyloxyphenyl)-3-(hydroxyphenyl)-prop-2-en-1-one (**2a–d**, **3a–d** and **4a–d**) possessing alkyl chain of varying length (C_6, C_{10}, C_{12} and C_{14}) except **4a–4b** (Nam, Kang, & Chang, 2007). The antibacterial activities of these novel chalcone derivatives were performed towards *Escherichia coli* ATCC 8739 to evaluate the effect of the hydroxyl group arrangement as well as the optimum length of alkyl chain.

2. Results and discussion

2.1. *Synthesis of chalcone derivatives*

Preparation of **1a–d** prior to the chalcone synthesis is depicted in Scheme 1. Compounds **1a–d** were synthesised by refluxing 4-hydroxyacetophenone with a series of bromoalkanes (C_6, C_{10}, C_{12} and C_{14}) in the presence of K_2CO_3 and TBAI in MEK to give compounds in yields ranging from 78–94%. The infrared spectra of **1a–d** showed the presence of new bands attributed to aliphatic carbon chains at 2920–2850 cm^{-1}. The ^{1}H-NMR of **1a–d** indicated the presence of long alkyl chains in the structure, as revealed by the resonance at 0.84–0.85 ppm and 3.96–3.98 ppm. These assignments were complemented by the ^{13}C-NMR spectra which showed signals at 14.05–68.19 ppm indicating the presence of carbon chains.

All chalcone derivatives (**2a–d**, **3a–d** and **4a–d**) were synthesised *via* the base-catalysed Claisen–Schmidt condensation. Compounds **1a–d** were reacted with appropriate benzaldehydes in refluxing methanol to the target compounds with yields ranging from 22–61%. The relatively low yield was attributed to trace amount



Scheme 1. Synthesis of chalcone derivatives.

of side products of Cannizzaro reaction or ketone auto condensation (Calvino, Picallo, López-Peinado, Martín-Aranda, & Durán-Valle, 2006; Climent, Corma, Iborra, & Velty, 2004). The IR spectra showed the presence of ν_{OH} at 3100–3400 cm^{-1} and long carbon chain at 2924–2845 cm^{-1}. Strong bands attributable to $\nu_{C=O}$ appeared at 1636–1651 cm^{-1}. The chemical structures of all compounds were confirmed by ^{1}H- and ^{13}C-NMR spectroscopic methods and showed the peaks that corresponded to the structures. From the ^{1}H-NMR spectra, the coupling constant, $J_{ab} = 15$–16 Hz indicated that all chalcones obtained were in *trans* configuration.

2.2. *Antibacterial activities*

The results of the antibacterial study showed that **2a–d**, **3a–d** and **4a–d** exhibited bacteriostatic activities against *E. coli*. All synthesised chalcones demonstrated a similar trend of bacteriostatic activities upon introduction at different concentrations of 50, 80 and 100 ppm. The inhibition activities were greater with increasing concentration indicating that the bacteriostatic activities were concentration dependent as shown in Figure 1. Chalcone **2a** with C_6 alkyl chains showed almost complete inhibition at 100 ppm compared to **2b–d**. However, upon introduction of different alkyl chains, chalcones **2a–d** with C_6, C_{10}, C_{12} and C_{14} alkyl groups showed decreasing bacteriostatic activities.

The effect of the synthesised chalcones at various concentrations was further shown by their minimum inhibitory concentrations (MICs). The MIC of these compounds were determined by extrapolating the concentration at the zero growth rate of *E. coli* ($\mu = 0$) (Pappano et al., 1985).

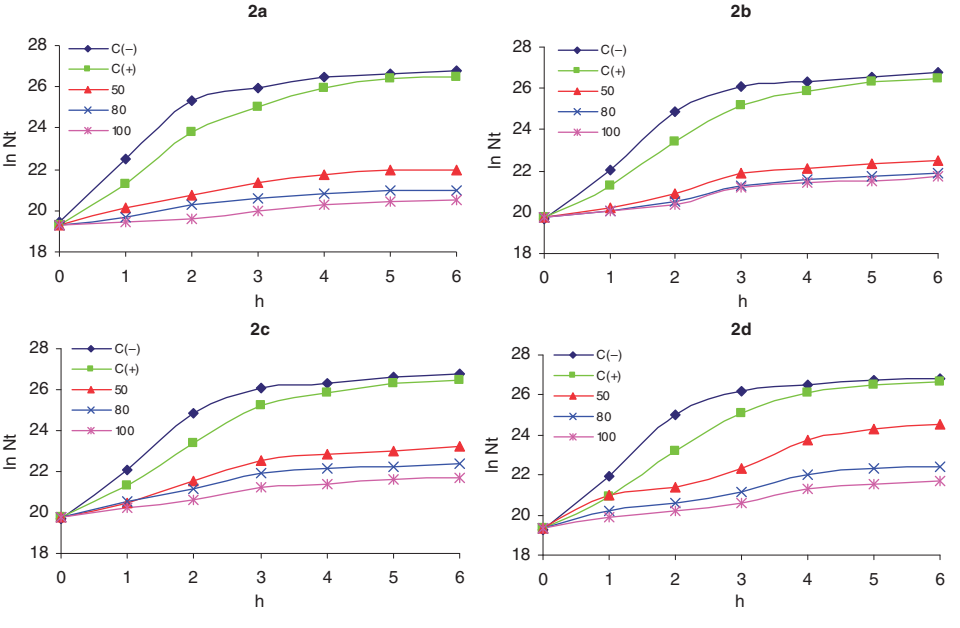


Figure 1. Inhibition activities of chalcones **2a–d** towards *E. coli* shown as $\ln N_t$ for *E. coli* growth *vs.* time.

Table 1. MIC of compounds **2a–d**, **3a–d** and **4a–d**.

Compound	MIC (ppm)	Compound	MIC (ppm)	Compound	MIC (ppm)
2a	109.8	**3a**	104.0	**4a**	111.9
2b	126.0	**3b**	129.8	**4b**	138.9
2c	132.1	**3c**	131.5	**4c**	143.3
2d	152.3	**3d**	156.5	**4d**	163.8

All compounds produced the MIC values ranging from 104–164 ppm (Table 1). These results indicated that the presence of hydroxyl groups in all the synthesised compounds influenced the antimicrobial activities (Anto et al., 1995; Tsuchiya et al., 1994; Won et al., 2005). The presence of hydroxyl group at *ortho* position further attenuated the inhibition activities. However, the activities decreased when the hydroxyl groups were at *meta* and *para* position. The importance of the hydroxyl group at the *ortho* position in chalcone derivatives was frequently reported for antimicrobial studies (Alvarez, Zarelli, Pappano, & Debattista, 2004; Mascaretti, 2003; Olivella, Zarelli, Pappano, & Debattista, 2001). In addition, the lipophilicity of alkyl chains appears to be another important factor for bacteriostatic activities where the inhibition activities decrease as the alkyl chain becomes longer. This trend could be observed for all chalcones with C_{14} alkyl chains with the MIC values greater than 150 ppm.

However, the antibacterial activities increased upon the introduction of C_6 aliphatic chain onto chalcone derivatives. *Meta*-hydroxyl group on the ring B chalcone displayed the best activity as shown by **3a** (104 ppm) followed by **2a** (109.8 ppm) and **4a** (111.9 ppm) respectively. This implied that the length of alkyl chain in the different compounds had a significant influence in giving the optimum antimicrobial activities (Birnie et al., 2000).

We believed that the bacteriostatic actions of the synthesised chalcones could be explained through the ability of compounds to cause perturbation of bacterial cell wall. This integration caused disruption thus rupturing the normal barrier property of the outer membrane (Kanazawa, Ikeda, & Endo, 1994; Scholar & Pratt, 2000). Several studies also reported on the membrane perturbation caused by the long chain molecules in promoting the antimicrobial activities (Birnie et al., 2000; Kanazawa et al., 1994; Sheu & Freese, 1973).

3. Experimental

3.1. *General*

4-Hydroxybenzaldehyde, 4-hydroxyacetophenone and 1-bromoalkanes were obtained from Merck and used without further purification. All other reagents and solvents were used as received. Melting points were determined by the open tube capillary method and are uncorrected. Infrared spectra were recorded on a Perkin Elmer 1605 FTIR Spectrophotometer (FTIR, Fourier transform infrared spectroscopy) using neat liquid film and potassium bromide (KBr) pellet. ^{1}H- and ^{13}C-NMR spectra were recorded on JEOL ECA 500 at 500 MHz with the chemical shifts

(δ, ppm) reported relative to deuterated chloroform ($CDCl_3$) and dimethyl sulphoxide (DMSO-d_6) as the standards. Flash column chromatography was performed at atmospheric pressure using Malinckrodt Silica Gel 60, (230–400 mesh) as a stationary phase.

3.2. *Synthesis of alkyloxyphenyl-ethanone (1a–d)*

3.2.1. *General procedure*

Bromoalkane (72 mmol), 4-hydroxyacetophenone (72 mmol), K_2CO_3 (72 mmol), tetrabutylammonium iodide (TBAI; 6 mmol) in methyl ethyl ketone (MEK; 200 mL) were heated at reflux for 10 h. The mixture was filtered and cooled at room temperature. Water (30 mL) was added to the filtrate and the layers separated. The aqueous layer was extracted with dichloromethane (2×30 mL). The combined layers were washed with water (2×20 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude was recrystallised from ethanol to give **1a–d**.

3.2.1.1. *4-Hexyloxyacetophenone (**1a**)*. Compound **1a** was obtained as a viscous brown oil. Yield (82.6%); the FTIR and NMR were consistent with those reported in literature (Nam et al., 2007).

3.2.1.2. *4-Decyloxyacetophenone (**1b**)*. Compound **1b** was obtained as colourless solid. Yield (89%); m.p. 36–37°C. The FTIR and NMR were consistent with those reported in literature (Nam et al., 2007).

3.2.1.3. *4-Dodecyloxyacetophenone (**1c**)*. Compound **1c** was obtained as a colourless solid. Yield (78%); m.p. 52–53°C. (Found: C, 78.73 and H, 10.45%. $C_{20}H_{32}O_2$ requires the following: C, 78.90 and H, 10.59%); υ_{max} (KBr cm^{-1}) 2918, 2849, 1676, 1602 and 1255. δ_H: (500 MHz, $CDCl_3$) 0.85 (3H, t, $J = 5.45$, $J = 7.50$, $1CH_3$), 1.24–1.77 (20H, m, 10 CH_2), 2.52 (3H, t, $J = 6.85$, $J = 6.30$, $1 \times CH_3$), 3.98 (2H, t, $J = 6.30$, $J = 6.80$), 6.87 (2H, d, $J = 9.20$, Ar–H) and 7.88 (2H, d, $J = 9.20$, Ar–H). δ_C: (125.77 MHz, $CDCl_3$) 14.06, 22.63, 25.91, 26.24, 29.03, 29.29, 29.50, 29.53, 29.58, 29.60, 31.86, 68.19, 114.06, 130.01, 130.50, 163.06 and 196.71.

3.2.1.4. *4-Tetradecyloxyacetophenone (**1d**)*. Compound **1d** was obtained as a colourless solid. Yield (94%); m.p. 58–59°C; (Found: C, 79.23; H, 10.51%. $C_{22}H_{36}O_2$ requires the following: C, 79.46; H, 10.91%); υ_{max} (KBr cm^{-1}) 2917, 2849, 1676, 1605 and 1255. δ_H: (500 MHz, $CDCl_3$) 0.84 (3H, t, $J = 6.30$, $J = 7.45$, $1 \times CH_3$), 1.23–1.76 (24H, m, $12 \times CH_2$), 2.50 (3H, s, $1 \times CH_3$), 3.96 (2H, t, $J = 6.85$, $J = 6.30$, $1 \times CH_2$), 6.86 (2H, d, $J = 8.00$, Ar–H) and 7.87 (2H, d, $J = 8.00$, ArH). δ_C: (125.77 MHz, $CDCl_3$) 14.02, 22.60, 25.88, 26.16, 29.01, 29.28, 29.47, 29.51, 29.57, 29.59, 31.83, 68.13, 113.72, 129.97, 130.44, 163.02 and 196.55.

3.3. *Synthesis of (alkyloxy)phenyl-hydroxyphenyl]prop-2-en-1-one (2a–d, 3a–d and 4a–d)*

3.3.1. *General procedure*

A mixture of hydroxybenzaldehydes (12.5 mmol), **1a–d** (12.5 mmol) in 35 mL of methanol was added under stirring to a solution of KOH 2.52 g in methanol (10 mL). The mixture was heated at reflux for 10 h. The reaction was cooled to room temperature and acidified with cold diluted HCl (2 N). The resulting precipitate was filtered, washed and dried. The crude product was recrystallised from hexane : ethanol (7 : 1) to give (**2a–d**, **3a–d** and **4a–d**).

3.3.1.1. *(E)-1-(4-hexyloxyphenyl)-3-(2-hydroxyphenyl)-prop-2-en-1-one (**2a**).* 2-Hydroxybenzaldehyde (12.5 mmol) was reacted with **1a** (12.5 mmol). Compound **2a** was obtained as orange crystals. Yield (42.1%); m.p. 131.8–132.6°C; (Found: C, 78.34: H, 8.75. $C_{21}H_{24}O_3$ requires the following: C, 78.91: H, 8.48%; υ_{max} (nujol mull cm^{-1}) 3156, 2924, 2855, 1639, 1601, 1266, 996 and 754. δ_H: (500 MHz, DMSO-d_6) 0.84 (3H, t, $J = 6.85$, $J = 7.45$, $1 \times CH_3$), 1.25–1.69 (8H, m, $4 \times CH_2$), 4.02 (2H, t, $J = 6.30$, $J = 6.85$, $1 \times CH_2$), 6.83 (1H, t, $J = 7.45$, $J = 7.40$, Ar–H), 6.91 (1H, d, $J = 8.55$, Ar–H), 7.03 (2H, d, $J = 9.20$, Ar–H), 7.22 (1H, t, $J = 6.90$, $J = 6.85$, Ar–H), 7.80 (1H, dd, $J = 8.00$, Ar–H), 7.83 (1H, d, $J = 16.00$, $1 \times$ olefinic H), 7.95 (1H, d, $J = 16.00$, $1 \times$ olefinic H), and 8.04 (2H, d, $J = 9.20$, Ar–H). δ_C: (125.77 MHz, $CDCl_3$) 14.07, 25.75, 29.27, 31.57, 68.24, 115.11, 117.51, 118.59, 118.82, 120.03, 130.54, 130.65, 136.03, 145.52, 161.68, 163.54 and 193.85.

3.3.1.2. *(E)-1-(4-decyloxyphenyl)-3-(2-hydroxyphenyl)-prop-2-en-1-one (**2b**).* 2-hydroxybenzaldehyde (12.5 mmol) was reacted with **1b** (12.5 mmol). Compound **2b** was obtained as yellow crystals. Yield (55.3%); m.p. 119.5–119.9°C; (Found: C, 78.83: H, 8.58. $C_{25}H_{32}O_3$ requires the following: C, 78.91: H, 8.48%); υ_{max} (nujol mull cm^{-1}) 3158, 2924, 2851, 1642, 1601, 1264, 995, and 761. δ_H: (500 MHz, DMSO-d_6) 0.84 (3H, t, $J = 6.30$, $J = 6.90$, $1 \times CH_3$), 1.24–1.73 (16H, m, $8 \times CH_2$), 4.05 (2H, t, $J = 6.90$, $J = 6.30$, $1 \times CH_2$), 6.87 (1H, t, $J = 7.45$, $J = 7.40$, Ar–H), 6.94 (1H, d, $J = 8.00$, Ar–H), 7.04 (2H, d, $J = 9.20$, Ar–H), 7.25 (1H, t, $J = 6.85$, $J = 6.85$, Ar–H), 7.83–7.86 (2H, m, Ar–H, $1 \times$ olefinic H), 8.00 (1H, d, $J = 16.00$, $1 \times$ olefinic H) and 8.08 (2H, d, $J = 9.20$, Ar–H). δ_C: (125.77 MHz, DMSO-d_6) 14.40, 22.56, 29.16, 29.21, 29.42, 29.47, 31.76, 68.32, 114.83, 116.66, 119.82, 121.28, 122.02, 129.04, 131.15, 132.20, 139.03, 157.57, 162.98 and 188.06.

3.3.1.3. *(E)-1-(4-dodecyloxyphenyl)-3-(2-hydroxyphenyl)-prop-2-en-1-one (**2c**).* 2-Hydroxybenzaldehyde (12.5 mmol) was reacted with **1c** (12.5 mmol). Compound **2c** was obtained as yellow crystals. Yield (30%); m.p. 111.1–111.5°C; (Found: C, 79.03: H, 8.70. $C_{27}H_{36}O_3$ requires the following: C, 79.37: H, 8.88%); υ_{max} (nujol mull cm^{-1}) 3359, 2919, 2851, 1651, 1607, 1267, 996 and 786. δ_H: (500 MHz, $CDCl_3$) 0.86 (3H, t, $J = 6.85$, $J = 6.90$, $1 \times CH_3$), 1.25–1.77 (20H, m, $10 \times CH_2$), 4.01 (2H, t, $J = 6.30$, $J = 6.90$, $1 \times CH_2$), 6.11 (1H, s, OH), 6.91 (1H, d, $J = 8.00$, Ar–H), 6.95 (2H, d, $J = 8.60$, Ar–H), 7.17–7.20 (2H, m, Ar–H), 7.24–7.26 (1H, m, Ar–H), 7.52 (1H, d, $J = 16.00$, $1 \times$ olefinic H), 7.77 (1H, d, $J = 16.00$, $1 \times$ olefinic H) and 8.01 (2H, d, $J = 9.20$, Ar–H). δ_C: (125.77 MHz, $CDCl_3$) 14.59, 23.16, 26.44, 29.56, 29.83,

30.10, 32.38, 68.81, 114.44, 115.27, 116.34, 117.83, 118.68, 122.23, 130.96, 131.37, 131.55, 136.87, 144.81, 157.00, 163.83 and 189.76.

3.3.1.4. *(E)-1-(4-tetradecyloxyphenyl)-3-(2-hydroxyphenyl)-prop-2-en-1-one (**2d**)*. 2-hydroxybenzaldehyde (12.5 mmol) was reacted with **1d** (12.5 mmol). Compound **2d** was obtained as an orange solid. Yield (61.1%); m.p. 107.9–109.6°C; (Found: C, 78.80: H, 9.10. $C_{29}H_{40}O_3$ requires the following: C, 79.77: H, 9.23%; υ_{max} (nujol mull cm^{-1}) 3182, 2918, 2845, 1636, 1605, 1273, 994 and 765. δ_H: (500 MHz, $CDCl_3$) 0.87 (3H, t, $J = 6.85$, J 6.90, $1 \times CH_3$), 1.25–1.82 (24H, m, $12 \times CH_2$), 4.03 (2H, t, $J = 6.90$, $J = 6.30$, $1 \times CH_2$), 6.77 (1H, s, OH), 6.91–6.97 (4H, m, Ar–H), 7.24–7.27 (1H, m, Ar–H), 7.58 (1H, d, $J = 8.00$, Ar–H), 7.70 (1H, d, $J = 16.00$, $1 \times$ olefinic H), 8.05 (2H, d $J = 9.20$, Ar–H) and 8.16 (1H, d, $J = 16.00$, $1 \times$ olefinic H). δ_C: (125.77 MHz, $CDCl_3$) 14.10, 22.68, 25.99, 29.13, 29.37, 29.59, 29.65, 31.92, 68.31, 114.30, 116.66, 120.79, 122.47, 122.54, 129.19, 130.99, 131.54, 139.96, 155.77, 163.14 and 190.08.

3.3.1.5. *(E)-1-(4-hexyloxyphenyl)-3-(3-hydroxyphenyl)-prop-2-en-1-one (**3a**)*. 3-Hydroxybenzaldehyde (12.5 mmol) was reacted with **1a** (12.5 mmol). Compound **3a** was obtained as tan crystals. Yield (22.2%); m.p. 118.6–118.9°C; (Found: C, 78.78: H, 8.45. $C_{21}H_{24}O_3$ requires the following: C, 78.91: H, 8.48%); υ_{max} (nujol mull cm^{-1}) 3306, 2930, 2845, 1650, 1580, 1268, 972 and 783. δ_H: (500 MHz, $CDCl_3$) 0.90 (3H, t, $J = 7.45$, $J = 6.85$, $1 \times CH_3$), 1.34–1.80 (8H, m, $4 \times CH_2$), 4.02 (2H, t, $J = 6.30$, $J = 6.85$, $1 \times CH_2$), 6.40 (1H, s, OH), 6.94 (1H, d, $J = 8.05$, Ar–H), 6.96 (2H, d, $J = 9.20$, Ar–H), 7.19–7.21 (1H, m, Ar–H), 7.20 (1H, d, $J = 7.50$, Ar–H), 7.27 (1H, t, $J = 8.00$, $J = 8.00$, Ar–H), 7.53 (1H, d, $J = 16.00$, $1 \times$ olefinic H), 7.75 (1H, d, $J = 16.00$, $1 \times$ olefinic H) and 8.00 (2H, d, $J = 9.00$, Ar–H). δ_C: (125.77 MHz, $CDCl_3$) 14.19, 22.76, 25.67, 29.07, 31.56, 68.37, 114.42, 115.31, 117.72, 120.62, 122.06, 130.14, 130.59, 130.99, 136.56, 144.18, 156.44, 163.35 and 189.21.

3.3.1.6. *(E)-1-(4-decyloxyphenyl)-3-(3-hydroxyphenyl)-prop-2-en-1-one (**3b**)*. 3-Hydroxybenzaldehyde (12.5 mmol) was reacted with **1b** (12.5 mmol). Compound **3b** was obtained as a tan solid. Yield (52%); m.p. 129.9–130.0°C; (Found: C, 78.48: H, 8.51. $C_{25}H_{32}O_3$ requires the following: C, 78.91: H, 8.48%); υ_{max} (nujol mull cm^{-1}) 3334, 2924, 2853, 1651, 1592, 1267, 977 and 787. δ_H: (500 MHz, $CDCl_3$) 0.86 (3H, t, $J = 6.85$, $J = 6.90$, $1 \times CH_3$), 1.26–1.79 (16H, m, $8 \times CH_2$), 4.02 (2H, t, $J = 6.30$, $J = 6.85$, $1 \times CH_2$), 5.70 (1H, s, OH), 6.90 (1H, d, $J = 8.00$, Ar–H), 6.96 (2H, d, $J = 9.20$, Ar–H), 7.15 (1H, s, Ar–H), 7.21 (1H, d, $J = 7.50$, Ar–H), 7.27 (1H, t, $J = 8.00$, $J = 8.00$, Ar–H), 7.52 (1H, d, $J = 15.00$, $1 \times$ olefinic H), 7.72 (1H, d, $J = 15.00$, $1 \times$ olefinic H) and 7.99 (2H, d, $J = 8.60$, Ar–H). δ_C: (125.77 MHz, $CDCl_3$) 14.56, 23.14, 26.45, 29.57, 29.82, 30.01, 32.35, 68.23, 114.85, 115.64, 118.10, 121.13, 122.57, 130.57, 131.11, 131.39, 137.02, 144.47, 156.87, 163.87 and 189.32.

3.3.1.7. *(E)-1-(4-dodecyloxyphenyl)-3-(3-hydroxyphenyl)-prop-2-en-1-one (**3c**)*. 3-Hydroxybenzaldehyde (12.5 mmol) was reacted with **1c** (12.5 mmol). Compound **3c** was obtained as a tan solid. Yield (39.9%); m.p. 110.1–111.0°C; (Found: C, 79.57: H, 8.93. $C_{27}H_{36}O_3$ requires the following: C, 79.37: H, 8.88%); υ_{max} (nujol mull cm^{-1}) 3338, 2923, 2853, 1651, 1606, 1267, 977 and 787. δ_H: (500 MHz, $CDCl_3$)

0.87 (3H, t, $J = 6.90$, $J = 6.85$, $1 \times CH_3$), 1.26–1.80 (20H, m, $10 \times CH_2$), 4.03 (2H, t, $J = 6.30$, $J = 6.90$, $1 \times CH_2$), 5.89 (1H, s, OH), 6.91 (1H, d, $J = 8.00$, Ar–H), 6.97 (2H, d, $J = 9.20$, Ar–H), 7.12 (1H, s, Ar–H), 7.22 (1H, d, $J = 8.10$, Ar–H), 7.28 (1H, t, $J = 8.05$, $J = 8.00$, Ar–H), 7.53 (1H, d, $J = 15.00$, $1 \times$ olefinic H), 7.74 (1H, d, $J = 15.00$, $1 \times$ olefinic H) and 8.00 (2H, d, $J = 8.60$, Ar–H). δ_C: (125.77 MHz, $CDCl_3$) 13.74, 21.37, 28.40, 29.29, 29.52, 29.83, 113.61, 114.05, 120.74, 122.75, 130.81, 131.04, 131.19, 142.53, 144.09, 156.12, 163.26 and 189.15.

3.3.1.8. *(E)-1-(4-tetradecyloxyphenyl)-3-(3-hydroxyphenyl)-prop-2-en-1-one (**3d**)*. 3-Hydroxybenzaldehyde (12.5 mmol) was reacted with **1d** (12.5 mmol). Compound **3d** was obtained as a tan solid. Yield (32%); m.p. 111.3–111.9°C; (Found: C, 78.61: H, 8.87. $C_{29}H_{40}O_3$ requires the following: C, 79.37: H, 8.88%); υ_{max} (nujol mull cm^{-1}) 3340, 2924, 2853, 1651, 1592, 1264, 976 and 786. δ_H: (500 MHz, $CDCl_3$) 0.86 (3H, t, $J = 6.25$, $J = 6.90$, $1 \times CH_3$), 1.24–1.79 (24H, m, $12 \times CH_2$), 4.01 (2H, t, $J = 6.85$, $J = 6.30$, $1 \times CH_2$), 6.91 (1H, d, $J = 8.00$, Ar–H), 6.95 (2H, d, $J = 8.60$, Ar–H), 7.16 (1H, s, Ar–H), 7.20 (1H, d, $J = 7.45$, Ar–H), 7.26 (1H, t, $J = 8.00$, $J = 8.05$, Ar–H), 7.52 (1H, d, $J = 16.00$, $1 \times$ olefinic H), 7.73 (1H, d, $J = 16.00$, $1 \times$ olefinic H) and 7.99 (2H, d, $J = 8.60$, Ar–H). δ_C: (125.77 MHz, $CDCl_3$) 14.22, 22.78, 26.07, 29.20, 29.45, 29.75, 32.01, 68.43, 114.03, 114.87, 117.41, 122.05, 130.67, 130.92, 131.10, 136.66, 144.04, 156.41, 163.37 and 189.11.

3.3.1.9. *(E)-1-(4-hexyloxyphenyl)-3-(4-hydroxyphenyl)-prop-2-en-1-one (**4a**)*. 4-Hydroxybenzaldehyde (12.5 mmol) was reacted with **1a** (12.5 mmol). Compound **4a** was obtained as yellow crystals. Yield (22.2%); the FTIR and NMR were consistent with those reported in literature (Nam et al., 2007).

3.3.1.10. *(E)-1-(4-decyloxyphenyl)-3-(4-hydroxyphenyl)-prop-2-en-1-one (**4b**)*. 4-Hydroxybenzaldehyde (12.5 mmol) was reacted with **1b** (12.5 mmol). Compound **4b** was obtained as yellow crystals. Yield (34%); the FTIR and NMR were consistent with those reported in literature (Nam et al., 2007).

3.3.1.11. *(E)-1-(4-dodecyloxyphenyl)-3-(4-hydroxyphenyl)-prop-2-en-1-one (**4c**)*. 4-Hydroxybenzaldehyde (12.5 mmol) was reacted with **1c** (12.5 mmol). Compound **4c** was obtained as a yellow solid. Yield (44%); m.p. 110.6–111.2°C; (Found: C, 79.52; H, 8.90%. $C_{27}H_{36}O_3$ requires the following: C, 79.37: H, 8.88%); υ_{max} (nujol mull cm^{-1}) 3195, 2921, 2852, 1651, 1581, 1223, 990 and 825. δ_H: (500 MHz, $CDCl_3$) 0.87 (3H, t, $J = 6.85$, $J = 6.90$, $1 \times CH_3$), 1.25–1.79 (20H, m, $10 \times CH_2$), 4.02 (2H, t, $J = 6.30$, $J = 6.30$, $1 \times CH_2$), 6.91 (2H, d, $J = 8.60$, Ar–H), 6.96 (2H, d, $J = 9.20$, Ar–H), 7.42 (1H, d, $J = 16.00$, $1 \times$ olefinic H), 7.53 (2H, d, $J = 8.60$, Ar–H), 7.74 (1H, d, $J = 16.00$, $1 \times$ olefinic H) and 8.01 (2H, d, $J = 8.60$, Ar–H). δ_C: (125.77 MHz, $CDCl_3$) 14.10, 22.67, 25.96, 29.08, 29.33, 29.55, 29.58, 29.61, 30.96, 31.89, 68.29, 114.30, 116.09, 119.03, 127.24, 130.45, 130.84, 144.66, 158.75, 163.12 and 189.62.

3.3.1.12. *(E)-1-(4-tetradecyloxyphenyl)-3-(4-hydroxyphenyl)-prop-2-en-1-one (**4d**).* 4-Hydroxybenzaldehyde (12.5 mmol) was reacted with **1d** (12.5 mmol). Compound **4d** was obtained as a pale yellow solid. Yield (39%); m.p. 107.2–108.2°C. (Found: C, 78.83; H, 9.04%. $C_{29}H_{40}O_3$ requires the following: C, 79.77; H, 9.23%; υ_{max} (nujol mull cm^{-1}) 3208, 2918, 2850, 1646, 1585, 1223, 990 and 825. δ_H: (500 MHz, DMSO-d_6) 0.82 (3H, t, $J = 6.85$, $J = 6.90$, $1 \times CH_3$), 1.24–1.71 (24H, m, $12 \times CH_2$), 4.04 (2H, t, $J = 6.30$, $J = 6.90$, $1 \times CH_2$), 6.81 (2H, d, $J = 8.60$, Ar–H), 7.02 (2H, d, $J = 9.20$, Ar–H), 7.61 (1H, d, $J = 15.00$, $1 \times$ olefinic H), 7.69 (1H, d, $J = 15.00$, $1 \times$ olefinic H), 7.70 (2H, d, $J = 9.20$, Ar–H), 8.09 (2H, d, $J = 8.60$, Ar–H) and 10.04 (1H, s, OH); δ_C: (125.77 MHz, DMSO-d_6) 13.93, 22.09, 25.42, 28.54, 28.72, 28.97, 29.02, 29.05, 30.67, 31.29, 67.81, 114.28, 115.76, 118.36, 125.90, 130.60, 130.65, 130.81, 143.52, 159.92, 162.44 and 187.12.

3.3.2. *Antibacterial screening*

The antibacterial activities of the synthesised compounds were carried out towards *E. coli* ATCC 8739 using turbidimetric kinetic method. The inoculums were allowed to grow on media containing nutrient broth at 37°C with permanent stirring at 200 rpm for 18 h. The culture medium of volume 10 mL, with increasing concentration of the compounds dissolved in propanol was inoculated with 0.2 mL of inoculums and the mixture was shaken at 250 rpm at 37°C. Inoculums with the solvent were used as controls. Aliquots of each replicate were taken every 1 h interval for 6 h and the transmittances (T) were registered in a UV–vis spectrophotometer (Optima SP-300). The antibacterial activities were determined by a graph as $\ln N_t$ which was related to the number CFU mL^{-1} (CFU, colony forming units) for *E. coli versus* time (Pappano et al., 1985).

4. Conclusion

A series of hydroxylated chalcone derivatives with different chain lengths have been successfully synthesised. All the synthesised chalcones exhibited promising antibacterial activities against *E. coli*. The presence of hydroxyl groups at the *meta* position with C_6 alkyl chains showed the highest antimicrobial activities. Besides hydroxyl groups, the presence of alkyl chains also contributed to the antibacterial activities where the inhibition activity was observed to be concentration dependent. However, the inhibition activity decreased with increasing chain length.

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