Asian Journal of Chemistry; Vol. 23, No. 5 (2011), 2121-2124

ASIAN JOURNAL OF CHEMISTRY

www.asianjournalofchemistry.co.in

Synthesis of Substituted Chromone Derivatives as Potent Antimicrobial Agents

P. VENKATESAN[1,*] and T. MARUTHAVANAN[2]

[1]Department of Chemistry, Mahendra Institute of Technology, Namakkal-637 503, India
[2]Department of Chemistry, Sona College of Technology, Salem-636 005, India

*Corresponding author: E-mail: venkatesanps@yahoo.co.in

(*Received*: 28 July 2010; *Accepted*: 19 January 2011) AJC-9505

Substituting heteroaryl group in C-2 position of chromone improves the biological activity of flavones. Thus, 2-(1*H*-indol-3-yl)-4*H*-chromen-4-one derivatives (**6a-e**) and 2-(2-chloroquinolin-3-yl)-4*H*-chromen-4-one derivatives (**7a-e**) were synthesized from corresponding chalcone. They were structurally confirmed by analytical and spectral data and evaluated for their antimicrobial activities. The results showed that this skeletal framework exhibited marked potency as antimicrobial agents. The most active antibacterial agent was 2-(1*H*-indol-3-yl)-5,7-dimethoxy-4*H*-chromen-4-one (**6e**) while 2-(2-chloroquinolin-3-yl)-6-methoxy-4*H*-chromen-4-one (**7b**) appeared to be the most active antifungal agent.

Key Words: Chalcone, Flavone, Chromone, Antibacterial activity, Antifungal activity.

INTRODUCTION

The flavones (2-phenylchromones) are naturally occurring heterocyclic compound belonging to the flavanoid group. It has found significant role in pharmaceutical effects[1] including leishmanicidal activity, oviposter stimulant phytoalexins, anti HIV, vasodilator, antiviral, antioxidants, bactericidal, DNA cleavage, antiinflamatory, antimutagenic and anticancer. Most of the flavones are synthesized by oxidative cyclization of 2'-hydroxy chalcones[2], by the cyclodehydration of 1-(2-hydroxyphenyl-3-phenyl-1,3-propanedione)[3], by auwers methods[4] and *via* intermolecular Witting reaction[5]. It has been observed that the substitution 5- and 6-membered heterocyclic group in C-2 position instead of phenyl group improves the biological activity of flavones[6-8]. In view of these report, we extended our earlier work to synthesize new substituted flavone derivative as possible antimicrobial agents, which could furnish better therapeutic results.

EXPERIMENTAL

All the common chemicals were obtained from Merck chemical company, SD fine chemicals and Sigma-Aldrich chemicals. TLC was carried out using and spotting was done using iodine or UV light. Melting points of synthesized compounds were determined in open glass capillaries and were uncorrected. UV spectra were recorded using Perkin-Elmer 402 UV-vis spectrophotometer. IR spectra were recorded on Perkin-Elmer 577 IR spectrophotometer using KBr pellets. ^{1}H and ^{13}C NMR spectra were recorded on Brucker 300 MHz NMR Spectrometer in $CDCl_3$ with tetramethyl silane as the internal standard and the chemical shifts were reported in ppm scale. Mass spectra were studied using Finnigan MAT 8230 mass spectrometer. Elemental analysis were done on Vario EL-III elemental analyzer and the analyzed reports were within ± 0.4 % of the theoretical values. The purity of the compounds was checked by thin layer chromatography on silica gel 60 F_{254} (Merck) and spots were developed using iodine vapour or ultraviolet light.

Synthesis of 1-(2'-hydroxy-aryl)-3-(1-indol-3-yl)-prop-2-en-1-one (3): The compounds were synthesized as per the procedure given in literature[9]. To a mixture of *o*-hydroxy-acetophenone (0.01 mol) and indole-3-carboxaldehyde/ 2-chloroquinoline-3-carboxaldehyde (0.01 mol) in ethanol (50 mL), piperidine (1 mL) was added and refluxed. After the completion of reaction, which was monitored by TLC, ethanol was distilled off and residue was poured on ice water (100 mL). It was kept overnight in the refrigerator. The resulting solid was collected by filtration, washed with distilled water and crystallized from methanol to give corresponding chalcone **3**.

Synthesis of indolyl flavone (6a-e) and quinolyl flavone (7a-e) using DDQ: The chalcone (0.01 mol) in dry dioxane (50 mL) was added with DDQ (0.01 mol, 2.27 g) and the solution refluxed for 3-4 h until the completion of reaction. Then the reaction mixture was poured in crushed ice and the solid separated was filtered and dried. Then, it was crystallized

from chloroform-petroleum ether (5:1) to give pale yellow needles of expected compounds **6a-e** and **7a-e**.

Synthesis of indolyl flavone (6a-e) and quinolyl flavone (7a-e) using DMSO/I_2: The chalcone (0.01 mol) was suspended in dimethyl sulfoxide (6 mL) and iodine (0.01 mol, 1.27 g) was added to it. The mixture was refluxed for 20-50 min in an oil bath until the completion of reaction. Then the reaction mixture was poured in crushed ice and the solid separated was filtered and washed with 20 % aq. sodium thiosulfate until product becomes colourless. It was further purified by column chromatography using hexane-ethyl acetate (80:20 v/v) as eluting solvent.

Synthesis of indolyl flavone (6a-e) and quinolyl flavone (7a-e) using Ph-S-S-Ph: The chalcone (0.01 mol) pasted with diphenyl disulphide (0.01 mol, 2.18 g) in a mortar and the mixture was transferred to a 100 mL three necked round bottom flask equipped with nitrogen inlet and outlet tubes. The central neck was closed by a glass stopper. The flask was then dipped into a silicon oil bath and heated at 265 ºC under nitrogen atmosphere until the distillation of the thiols formed through the other outlet tube ceased (3-4 h). The reaction mixture was then cooled at room temperature and 20 mL chloroform was added. The organic layer was washed with water several times. It was dried over anhydrous sodium sulfate and the solvent was removed by distillation. The product crystallized from chloroform-petroleum ether (5:1) to give pale yellow needles.

Spectral data: The spectral data for the expected flavone derivatives **6a-e** and **7a-e** were identical to that are prepared by DDQ or DMSO/I_2 or Ph-S-S-Ph method.

2-(1*H*-Indol-3-yl)-7-methoxy-4*H*-chromen-4-one (6a): Pale yellow solid; m.p. 90-92 ºC; λ_{max} ($CHCl_3$, nm): 268, 382; IR (KBr, ν_{max}, cm^{-1}): 3168 (ArCH), 3066 (NH), 1668 (C=O), 1173 (C-N str), 1232 and 1028 (C-O str); ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.83 (s, 3H, 7-OCH_3), 6.61-6.92 (m, 3H, 5-, 6- and 8-H), 6.44 (s, 1H, 3-H), 7.04-7.96 (m, 5H, indolyl-H); ^{13}C NMR (300 MHz, $CDCl_3$): δ 193.86, 163.48, 139.61, 137.29, 135.79, 131.03, 129.42, 125.29, 123.2, 122.06, 121.3, 120.7, 118.74, 118.53, 115.52, 114.64, 112.7; m/z: 292 (M^+ + 1); Anal. calcd. (%) for $C_{18}H_{13}NO_3$: C, 74.22; H, 4.50; N, 4.81. Found (%) C, 74.21; H, 4.51; N, 4.81.

2-(1*H*-Indol-3-yl)-6-methoxy-4*H*-chromen-4-one (6b): Yellow solid; m.p. 106-108 ºC; λ_{max} ($CHCl_3$, nm): 275, 384; IR (KBr, ν_{max}, cm^{-1}): 3172 (ArCH), 3084 (NH), 1668 (C=O), 1173 (C-N str), 1233 and 1024 (C-O str); ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.79 (s, 3H, 6-OCH_3), 6.78-6.99 (m, 3H, 5-, 7- and 8-H), 6.42 (s, 1H, 3-H), 7.06-7.88 (m, 5H, indolyl-H); ^{13}C NMR (300 MHz, $CDCl_3$): δ 193.78, 162.42, 136.96, 136.34, 135.82, 131.13, 128.92, 126.01, 123.02, 122.16, 122.03, 121.07, 118.68, 118.43, 115.52, 114.62, 111.98; m/z: 292 (M^+ + 1); Anal. calcd. (%) for $C_{18}H_{13}NO_3$ (%): C, 74.22; H, 4.50; N, 4.81. Found (%) C, 74.23; H, 4.50; N, 4.82.

2-(1*H*-Indol-3-yl)-7,8-dimethoxy-4*H*-chromen-4-one (6c): Yellow solid; m.p. 96-98 ºC; λ_{max} ($CHCl_3$, nm): 268, 378; IR (KBr, ν_{max}, cm^{-1}): 3158 (ArCH), 3088(NH), 1666 (C=O), 1177 (C-N str), 1232 and 1028 (C-O str); ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.78 (s, 3H, 8-OCH_3), 3.89 (s, 3H, 7-OCH_3), 6.64-6.72 (m, 2H, 5- and 6-H), 6.42 (s, 1H, 3-H), 7.04-7.92 (m, 5H, indolyl-H); ^{13}C NMR (300 MHz, $CDCl_3$): δ 194.64, 162.53, 137.44, 136.28, 135.68, 131.28, 128.62, 126.06, 122.84, 122.09, 121.93, 121.16, 118.56, 118.12, 115.04, 114.44, 111.48; m/z: 322 (M^+ + 1); Anal. calcd. (%) for $C_{19}H_{15}NO_4$: C, 71.02; H, 4.71; N, 4.36. Found (%) C, 71.04; H, 4.70; N, 4.35.

2-(1*H*-Indol-3-yl)-5,7,8-trimethoxy-4*H*-chromen-4-one (6d): Yellow solid; m.p. 98-100 ºC; λ_{max} ($CHCl_3$, nm): 269, 384; IR (KBr, ν_{max}, cm^{-1}): 3164 (ArCH), 3074 (NH), 1664 (C=O), 1174 (C-N str), 1236 and 1026 (C-O str); ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.76 (s, 3H, 8-OCH_3), 3.88 (s, 3H, 5-OCH_3), 3.92 (s, 3H, 7-OCH_3), 6.84 (s, 1H, 6-H), 6.44 (s, 1H, 3-H), 7.08-7.98 (m, 5H, indolyl-H); ^{13}C NMR (300 MHz, $CDCl_3$): δ 190.64, 164.41, 136.42, 136.02, 135.11, 131.75, 129.11, 127.01, 124.04, 122.14, 122.01, 121.11, 118.74, 118.55, 115.54, 114.54, 112.21; m/z: 352 (M^+ + 1); Anal. calcd. (%) for $C_{20}H_{17}NO_5$: C, 68.37; H, 4.88; N, 3.99. Found (%) C, 68.37; H, 4.87; N, 3.96.

2-(1*H*-Indol-3-yl)-5,7-dimethoxy-4*H*-chromen-4-one (6e): Yellow solid; m.p. 96-98 ºC; λ_{max} ($CHCl_3$, nm): 265, 386; IR (KBr, ν_{max}, cm^{-1}): 3162 (ArCH), 3072 (NH), 1668 (C=O), 1178 (C-N str), 1234 and 1022 (C-O str); ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.78 (s, 3H, 5-OCH_3), 3.91 (s, 3H, 7-OCH_3), 6.66-6.94 (m, 2H, 6- and 8-H), 6.42 (s, 1H, 3-H), 7.06-7.94 (m, 5H, indolyl-H); ^{13}C NMR (300 MHz, $CDCl_3$): δ 193.78, 163.22, 136.27, 136.44, 134.76, 131.13, 128.23, 126.45, 123.02, 122.75, 122.24, 122.07, 118.68, 119.43, 114.52, 112.62, 113.24; m/z: 322 (M^+ + 1); Anal. calcd. (%) for $C_{19}H_{15}NO_4$: C, 71.02; H, 4.71; N, 4.36. Found (%) C, 71.03; H, 4.71; N, 4.36.

2-(2-Chloroquinolin-3-yl)-7-methoxy-4*H*-chromen-4-one (7a): Yellow solid; m.p. 110-112 ºC; λ_{max} ($CHCl_3$, nm): 271, 382; IR (KBr, ν_{max}, cm^{-1}): 3166 (ArCH), 1672 (C=O), 1578 (C=N), 1238 and 1021 (C-O str), 731 (ArCl); ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.85 (s, 3H, 7-OCH_3), 6.66-6.84 (m, 3H, 5-, 6- and 8-H), 6.56 (s, 1H, 3-H), 8.16-8.48 (m, 4H, 5-, 6-, 7- and 8-H), 8.81 (s, 1H, 4'-H); m/z: 338 (M^+ + 1); Anal. calcd. (%) for $C_{19}H_{12}NO_3Cl$: C, 67.56; H, 3.58; N, 4.15. Found (%) C, 67.51; H, 3.57; N, 4.14.

2-(2-Chloroquinolin-3-yl)-6-methoxy-4*H*-chromen-4-one (7b): Pale yellow solid; m.p. 112-114 ºC; λ_{max} ($CHCl_3$, nm): 271, 376; IR (KBr, ν_{max}, cm^{-1}): 3162 (ArCH), 1672 (C=O), 1582 (C=N), 1242 and 1026 (C-O str), 732 (ArCl); ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.76 (s, 3H, 6-OCH_3), 6.74-6.96 (m, 3H, 5-, 7- and 8-H), 6.54 (s, 1H, 3-H), 8.22-8.44 (m, 4H, 5-, 6-, 7- and 8-H), 8.86 (s, 1H, 4'-H); m/z: 338 (M^+ + 1); Anal. calcd. (%) for $C_{19}H_{12}NO_3Cl$: C, 67.56; H, 3.58; N, 4.15. Found (%) C, 67.54; H, 3.59; N, 4.13.

2-(2-Chloroquinolin-3-yl)-7,8-dimethoxy-4*H*-chromen-4-one (7c): Yellow solid; m.p. 108-110 ºC; λ_{max} ($CHCl_3$, nm): 269, 358; IR (KBr, ν_{max}, cm^{-1}): 3184 (ArCH), 1674 (C=O), 1574 (C=N), 1241 and 1024 (C-O str), 732 (ArCl); ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.77 (s, 3H, 8-OCH_3), 3.86 (s, 3H, 7-OCH_3), 6.58-6.82 (m, 2H, 5- and 6-H), 6.58 (s, 1H, 3-H), 8.25-8.57 (m, 4H, 5-, 6-, 7- and 8-H), 8.84 (s, 1H, 4'-H); m/z: 368 (M^+ + 1); anal. calcd. (%) for $C_{20}H_{14}NO_4Cl$: C, 65.31; H, 3.84; N, 3.81. Found (%) C, 65.35; H, 3.83; N, 3.80.

2-(2-Chloroquinolin-3-yl)-5,7,8-trimethoxy-4*H*-chromen-4-one (7d): Yellow solid; m.p. 106-108 ºC; λ_{max} ($CHCl_3$, nm): 267, 374; IR (KBr, ν_{max}, cm^{-1}): 3178 (ArCH),

1676 (C=O), 1576 (C=N), 1239 and 1028 (C-O str), 730 (ArCl); ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.74 (s, 3H, 8-OCH_3), 3.86 (s, 3H, 5-OCH_3), 3.91 (s, 3H, 7-OCH_3), 6.89 (s, 1H, 6-H), 6.56 (s, 1H, 3-H), 8.18-8.52 (m, 4H, 5-, 6-, 7- and 8-H), 8.88 (s, 1H, 4'-H); m/z: 398 (M^+ + 1); Anal. calcd. (%) for $C_{21}H_{16}NO_5Cl$: C, 63.40; H, 4.05; N, 3.52. Found (%) C, 63.44; H, 4.05; N, 3.54.

2-(2-Chloroquinolin-3-yl)-5,7-dimethoxy-4*H*-chromen-4-one (7e): Pale yellow solid; m.p. 102-104 ºC; λ_{max} ($CHCl_3$, nm): 274, 386; IR (KBr, ν_{max}, cm^{-1}): 3182 (ArCH), 1672 (C=O), 1577 (C=N), 1241 and 1025 (C-O str), 732 (ArCl); ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.74 (s, 3H, 5-OCH_3), 3.92 (s, 3H, 7-OCH_3), 6.52-6.96 (m, 2H, 6- and 8-H), 6.54 (s, 1H, 3-H), 8.24-8.46 (m, 4H, 5-, 6-, 7- and 8-H), 8.84 (s, 1H, 4'-H); m/z: 368 (M^+ + 1); Anal. calcd. (%) for $C_{20}H_{14}NO_4Cl$: C, 65.31; H, 3.84; N, 3.81. Found (%) C, C, 65.33; H, 3.83; N, 3.81.

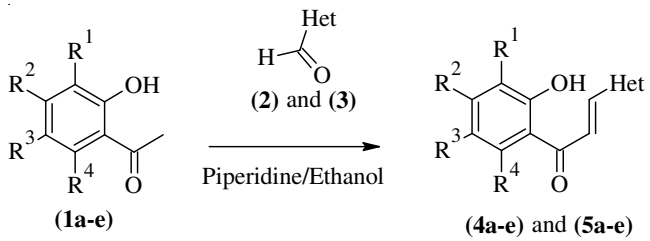
Antimicrobial activity

Disc diffusion method: The antimicrobial activity of newly synthesized compounds was evaluated using the agar diffusion method[10]. Briefly, a 24/48 h-old culture of selected bacteria/fungi was mixed with sterile physiological saline (0.85 %) and the turbidity was adjusted to the standard inoculum of Mac-Farland scale 0.5 [10^6 colony forming units (CFU)/mL]. Petri plates containing 20 mL of Mueller Hinton Agar (MHA, Hi-Media) were used for all the bacteria tested. Fungi were cultured in Sabouraud's dextrose agar (SDA)/ potato dextrose agar (PDA) (Hi-Media) and were purified by single spore isolation technique. The inoculums was spread on the surface of the solidified media and Whatman No. 1 filter paper discs (6 mm in diameter) impregnated with the test compound (20 µL/disc) were placed on the plates. Penicillin (5 µg/disc, Hi-Media) was used as positive control for bacteria. Nystatin (10 µg/disc, Hi-Media), was used as positive control for fungi. A paper disc impregnated with dimethyl sulfoxide (DMSO) was used as negative control. Plates inoculated with the bacteria were incubated for 24 h at 37 ºC and the fungal culture was incubated for 72 h at 25 ºC. The inhibition zone diameters were measured in millimeters. All the tests were performed in triplicate and the average was taken as final reading.

Determination of MIC: Solutions of the test compounds, ciprofloxacin and fluconazole were prepared in DMSO at a concentration of 100 mg/mL. From this stock solution, serial dilutions of the compounds (50, 25, …, 3.12 µg/mL) were prepared to determine the MIC. All determinations were done in triplicates and the average was taken as final reading. The standard antibiotic, ciprofloxacin (100 µg/mL) for bacteria and fluconazole (100 µg/mL) for fungi were used as positive controls and 100 mL of DMSO used as a negative control. At the end of the incubation period, the MIC values were determined.

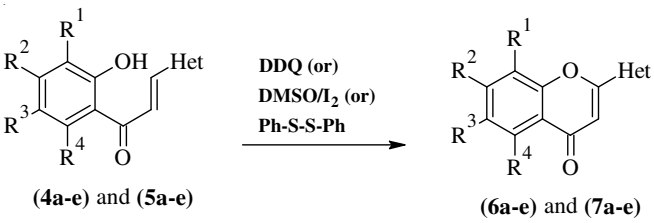
RESULTS AND DISCUSSION

Our earlier work[9] described the synthesis of the chalcone, 1-(2'-hydroxy-aryl)-3-(1-indol -3-yl)-prop-2-en-1-one (**4a-e**) and 1-(2'-hydroxyaryl)-3-(2-chloro-quinolin-3-yl)-prop-2-en-1-one (**5a-e**) by piperdine mediated Claisen-Schemidt condensation method as shown in **Scheme-I**. The IR spectra of compounds **4a-e** and **5a-e** gave absorption about 1654-1630 cm^{-1} for the unsaturated keto group and absorption about 3436-3431 cm^{-1} for the presence of hydroxyl group. In addition, The ^{1}H NMR spectra gave two doublet centred about δ 7.6 ppm and δ 8.2 ppm with coupling constant about J = 15 Hz were assigned to the trans olefinic proton at C_α and C_β position. The ^{1}H NMR signal about δ 14 ppm indicating the presence of hydroxyl group.



Scheme-I: Synthesis of chalcone

On oxidative cyclization of 2'-hydroxy chalcone using DDQ/DMSO-I_2/diphenyl disulphide, corresponding flavone derivatives **6a-e** and **7a-e** were obtained as shown in **Scheme-II**. The UV-vis absorption spectrum of the compounds **6a-e** and **7a-e** in $CHCl_3$ showed λ_{max} at 265-275 and 358-386 nm indicating the presence of flavone moiety. IR spectra of compounds **6a-e** and **7a-e** showed the absorption at 1664-1668 cm^{-1} for carbonyl groups and absence of hydroxyl absorption confirmed the oxidation of hydroxyl groups in chalcones **4a-e** and **5a-e**. It was further supported by not observing corresponding ^{1}H NMR signals. The C-3 proton gave singlet about δ 6.42-6.44 ppm and δ 6.54-6.58 ppm for the compounds **6a-e** and **7a-e**, respectively showed that the C_β-H of corresponding chalcone involved in cyclization of chalcone to form corresponding flavone. The entire ^{13}C NMR spectral data, mass spectral data and elemental analysis data were in accordance with the structure of expected compounds **6a-e** and **7a-e** and they were given in experimental part.



Scheme-II: Synthesis of flavone

The compounds **6a-e** and **7a-e** obtained using three methods were showed identical melting points for corresponding flavone and the yields were differed as given in Table-1. On comparison of physical data, synthesis of compounds **6a-e** and **7a-e** by DMSO/I_2 gives comparably high yield with short time among the other methods. In addition, on oxidative cyclization of chalcones with hydroxyl substitution instead of methoxy group, it was failed to form the corresponding flavone.

The *in vitro* antibacterial activity of the compounds **6a-e** and **7a-e** were evaluated against pathogenic bacteria including *Staphylococcus aureus* (G^+), *Bacillus subtilis* (G^+), *Escherichia coli* (G^-) and *Salmonella typhi* (G^-). Penicillin was used as standard for comparing the antibacterial activities and the diameter of observed inhibition zone of **6a-e** and **7a-e** were

TABLE-1
PHYSICAL DATA OF COMPOUND **6a-e** AND **7a-e**

Compounds		m.p. (ºC)	Yield (g)		
			DDQ	$DMSO/I_2$	Ph-S-S-Ph
a: $R^2 = OCH_3$; R^1, R^3, R^4 = H	**6a**	90-92	1.96 (58 %)	2.23 (66 %)	2.1 (62 %)
b: $R^3 = OCH_3$; R^1, R^2, R^4 = H	**6b**	106-108	1.89 (56 %)	2.26 (67 %)	2.06 (61 %)
c: R^1, $R^2 = OCH_3$; R^3, R^4 = H	**6c**	96-98	2.1 (57 %)	2.5 g 68 %)	2.32 (63 %)
d: R^1, R^2, $R^4 = OCH_3$; R^3 = H	**6d**	98-100	2.07 (52 %)	2.67 (67 %)	2.39 (60 %)
e: R^2, $R^4 = OCH_3$; R^1, R^3 = H	**6e**	96-98	2.06 (56 %)	2.43 (66 %)	2.24 (61 %)
Het =	**7a**	110-112	1.64 (56 %)	1.87 (64 %)	1.81 (62 %)
	7b	112-114	1.58 (54 %)	1.96 (67 %)	1.81 (62 %)
	7c	108-110	1.67 (52 %)	2.19 (68 %)	1.96 (61 %)
	7d	106-108	1.83 (52 %)	2.32 (66 %)	2.18 (62 %)
2, **4** and **6** **3**, **5** and **7**	**7e**	102-104	1.73 (54 %)	2.13 (66 %)	2.03 (63 %)

TABLE-2
ANTIBACTERIAL AND ANTIFUNGAL ACTIVITY OF COMPOUNDS **4a-e**, **5a-e** AND **6a-e**

Comp.	Diameter of zone inhibition in mm (MIC value μg mL^{-1})							
	Staphylococcus aureus	*Bacillus subtilis*	*Escherichia coli*	*Salmonella typhi*	*Aspergillus niger*	*Aspergillus flavus*	*Penicillium chrysogenum*	*Fusarium moneliforme*
6a	11 ± 1.2 (12.5)	16 ± 0.7 (25)	–	–	20 ± 1.2 (25)	10 ± 1.2 (25)	13 ± 1.1 (6.25)	20 ± 1.2 (12.5)
6b	–	–	17 ± 1.2 (25)	15 ± 1.4 (25)	14 ± 1.2 (50)	–	–	–
6c	–	16 ± 1.2 (50)	–	–	14 ± 1.2 (6.25)	–	–	–
6d	18 ± 1.5 (6.25)	15 ± 0.3 (25)	12 ± 1.3 (25)	20 ± 1.0 (6.25)	9 ± 1.1 (6.25)	13 ± 1.2 (25)	19 ± 1.1 (25)	18 ± 1.6 (25)
6e	16 ± 1.4 (25)	18 ± 1.2 (25)	20 ± 0.8 (6.5)	20 ± 1.2 (25)	–	11 ± 1.1 (6.25)	16 ± 1.3 (50)	16 ± 1.4 (50)
7a	14 ± 1.3 (12.5)	19 ± 1.1 (6.25)	14 ± 1.1 (50)	–	14 ± 1.2 (6.25)	13 ± 1.2 (50)	–	14 ± 1.2 (6.25)
7b	17 ± 1.4 (6.25)	11 ± 1.4 (25)	10 ± 0.9 (25)	14 ± 1.1 (12.5)	20 ± 1.1 (25)	18 ± 1.1 (6.25)	20 ± 1.2 (50)	17 ± 1.3 (6.25)
7c	–	14 ± 1.3 (25)	18 ± 1.2 (50)	18 ± 1.2 (6.25)	–	20 ± 1.1 (6.25)	7 ± 1.1 (50)	9 ± 1.3 (25)
7d	9 ± 1.3 (6.25)	–	12 ± 1.2 (25)	10 ± 1.1 (50)	8 ± 1.1 (50)	16 ± 0.9 (6.25)	8 ± 1.2 (50)	9 ± 1.2 (50)
7e	19 ± 1.4 (25)	19 ± 0.7 (12.5)	18 ± 1.2 (50)	19 ± 1.2 (25)	16 ± 1.3 (50)	16 ± 1.1 (25)	20 ± 1.1 (25)	19 ± 1.2 (25)
Penicillin	23 ± 1.2 (6.25)	22 ± 1.1 (25)	23 ± 1.2 (50)	22 ± 1.1 (25)	–	–	–	–
Nystatin	–	–	–	–	21 ± 1.2 (6.25)	22 ± 1.1 (25)	24 ± 1.1 (25)	23 ± 0.8 (25)

measured (mM) and they are given in Table-2 with MIC. The antibacterial data could be observed that among the indolyl flavones **6a-e**, the compounds **6d** and **6e** showed appreciable antibacterial activity against all the test bacteria. They have also good activity against *S. aureus*, *B. subtilis* and *S. typhi*. Similarly, compound **6e** has good activity against *E. coli* with MIC of 6.5 μg mL^{-1}. Even though compounds **6a** and **6b** showed good activity against *S. aureus* and *B. subtilis*, they are inactive against *E. coli* and *S. typhi*. However, the antibacterial activity of compound **7a-e** showed moderate to good activity against all the test organism except **7c** and **7d**, which is inactive against *S. aureus* and *B. subtilis*. The compound, 2-(1*H*-indol-3-yl)-5,7-dimethoxy-4*H*-chromen-4-one (**6e**) showed excellent antibacterial activity against all the test bacteria. Interestingly, the antibacterial activity of the quinolyl flavones (**7a-e**) increased when compared to that of indolyl flavones (**6a-e**).

The *in vitro* antifungal activity of the compounds **6a-e** and **7a-e** with nystatin as a reference drug against fungi species including *Aspergillus niger*, *Aspergillus flavus*, *Penicillium chrysogenum* and *Fusarium moneliforme* is given in Table-2. The compounds **6a**, **6d**, **7a**, **7d** and **7e** showed moderate to good activity against all the test fungi. However, compounds **6b** and **6c** are showed inactive against *A. flavus*, *P. chrysogenum* and *F. moneliforme*. The compound, 2-(2-chloroquinolin-3-yl)-6-methoxy-4*H*-chromen-4-one (**7b**) showed excellent antifungal activity against all the test fungi. Like antibacterial activity, the quinolyl flavones (**7a-e**) showed more biological activity than that of indolyl flavones (**6a-e**).

ACKNOWLEDGEMENTS

The authors thank School of Chemistry, Madurai Kamaraj University, India for recording the spectral data.

REFERENCES

1. M.J. Menezes, S. Manjrekar, V. Pai, R.E. Patre and S.G. Tilve, *Indian J. Chem.*, **48B**, 1311 (2009).
2. D. Lokhande, S. Sakate, N. Taksande and B. Navghare, *Tetrahedron Lett.*, **46**, 1573 (2005).
3. W. Kabalka and R. Mereddy, *Tetrahedron Lett.*, **46**, 6315 (2005).
4. J. Li and E.J. Corey, Name Reactions in Heterocyclic Chemistry, John Wiley & Sons, p. 262 (2005).
5. M. Muthukrishnan, S. Patil, V. More and A. Joshi, *Mendeleev Commun.*, **15**, 100 (2005).
6. T. Kalai, G. Kulcsar, E. Osz, J. Jeko, B. Sumegi and K. Hidega, *Arkivoc*, 266 (2004).
7. C. Zhou, A.V. Dubrovsky and R.C. Larock, *J. Org. Chem.*, **71**, 1626 (2006).
8. V.P. Khilya and V.V. Ishchenko, *Chem. Heterocycl. Compd.*, **38**, 883 (2002).
9. P. Venkatesan and S. Sumathi, *J. Heterocycl. Chem.*, **47**, 81 (2010).
10. D. Shrinivasan, N. Sangeetha, T. Suresh and P. Lamanaperumalsamy, *J. Ethnopharmacol.*, **74**, 217 (2001).