Synthesis and Biological Activity of 4-Hydroxy-3-(1,5-diaryl-3-oxo-pent-4-enyl)chromen-2-ones

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The substituted warfarin acid chalcones have been prepared by condensation of warfarin acid and aromatic/aliphatic aldehyde using aq. NaOH as catalyst. The method is simple, cost-effective and gives good yield in a short reaction time. All the compounds synthesized have been characterized by IR, NMR and Mass spectra. A new series of 4-hydroxy-3-(3-oxo-1,5-diaryl-3-oxo-pent-4-enyl)-chromen-2-ones were synthesized and submitted to biological activity. Result of the biological screening showed the compounds **3b**, **3h** being the most effective among the various treatments in antimicrobial screening. Compounds **3c**, **3d**, **3k** and **3l** showed moderate activity against the microorganisms tested. Compounds **3e**, **3h** have shown good antifungal activity.

Keywords chalcone, antibacterial, warfarin acid

Introduction

Heterocycles are abundant in nature and are of great significance to life because of their structural subunits existing in many natural products such as vitamins, harmones, antibiotics *etc*.[1] Hence they have attracted attention in the design of biologically active molecules.[2] A practical method for the synthesis of such compounds is of great interest in the synthetic organic chemistry. Among the heterocycles, 1,3-thiazines are a class of compounds with biological activity, such as antimicrobial,[3] antitumor,[4] antioxidant,[5] calcium channel modulator,[6] and antipyretic.[7]

On the other hand, the classes of pyrimidines possess abroad spectrum of biological effectiveness such as antitubercular,[8] antitumor,[9] anticancer,[10] and prostaglandin bindings[11] and antibacterial properties.[12-15]

In view of these properties and increasing importance in pharmaceutical and biological field, it was interesting and chalenging to synthesize some new chemical entities involving an active pharmacophore, combination with condensing compound in a single molecular frame work to evaluate their biological activities.

The Claisen-Schmidt condensation reaction is an important reaction for ketoethylenic group formation. Kostanecki and Tambo assigned the name chalcone,[16] the chalcones are intermediate compounds for the synthesis of various heterocyclic compounds such as pyrazolines, quinoxalines, pyrimidines, pyridines, isooxazalines, flavones, and flavanoles as well as certain compound like deoxibenzoins and hydantoins which are of some therapeutic value. The chalcones have been found to be useful in proving the structure of natural products like protein,[17] sackuranetin,[18,19] homoeriodictyl, eriodictyol,[20] cynomacturin,[21] *etc*. Chalcone derivatives are associated with some important biological activity such as antitubercular, anthelmentic,[22] funngicidal,[23] antioxidant,[23-26] antimalerial,[27] anti-inflammatory[28] and antitumor agent.[29]

Warfarin acid occupies an important place in organic chemistry. Warfarin acid was synthesized by condensation of 4-hydroxycoumarin with benzylacetone,[30-33] which possesses biological activity like anticonvulsant,[34] inflammation,[35] antagonists[36] and heart diseases.[37]

Present work

Here we have described synthesis, characterization and biological activity of new series of 4-hydroxy-3-(1,5-diaryl-3-oxo-pent-4-enyl)-chromen-2-ones as antibacterial, antifungal agents, along with their *in vitro* biological activity (MIC activity). The synthesis of all new compounds (**3a**—**3q**) is outlined in Scheme 1. They were obtained in high purity and good yield. The substituted chalcones were synthesized by Claisen-Schmidt condensation by reacting warfarin acid and aromatic/aliphatic aldehyde using aq. NaOH. The method is simple, cost-effective and good yield. Structures of all new chalcones (**3a**—**3q**) were established on the basis of IR, ^{1}H NMR and Mass (ES/MS). Among the new chalcones screened for biological activity, compounds **3b**, **3h**, **3e** and **3h**, were found to demonstrate good activity among the various treatments in antimicrobial and antifungal screening respectively. Compounds **3c**, **3k**, **3m**, **3o** and **3l** exhibited activity against the specific microorganism tested.

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Received February 7, 2009; revised September 24, 2009; accepted October 27, 2009.

Numerous methods have been reported in the literature to synthesize chalcone from aldehyde and ketone, using alcohol as solvent. Although the base-catalyzed reaction of aldehyde with ketenes of the type RCH_2COCH_3 can in principally, occur with two possible orientations. Condensation of aromatic/aliphatic aldehydes with such ketones usually occurs at the methyl group.[38] The present communication reports the condensation of warfarin acid and aromatic aldehyde in 30% aqueous NaOH. It was observed that condensation occurs at methyl (CH_3) group rather than (CH_2) group. The formation of chalcone was confirmed by chemical methods and characterized by modern analytical methods. In conclusion, we have demonstrated an efficient and simple alternative for the preparation of substituted new chalcone via the condensation using aqueous NaOH. All the new compounds (**3a**—**3q**) were subjected to biological screening for antibacterial and antifungal activity. The MIC was determined using tube dilution method. Antifungal activity was determined against *Candida albicans*, and for comparasion Fluconazole was used as standard. The results are presented in Tables 2 and 3. Prominent advantages of this method are operational simplicity, good yield, organic solvent-free and economic easy workup procedure.

Experimental section

Melting points were determined on a quality precise melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on Brucker 400 MHz spectrometer. Chemical shifts (δ) are reported relative to TMS as an internal standard. Electron spray ionization mass spectra (ES-MS) were recorded on a water micromass Quattro spectrometer. All the solvents and reagents used were of AR grade and were used without further purification. IR spectra of the compounds of this series have been scanned on JASCO spectrophotometer using KBr pellets.

General procedure for synthesizing chalcones (3a—3q)

To a well-stirred mixture of warfarin acid (0.01 mol) and adehyde (0.01 mol) in water, was added a solution of 30% aqueous NaOH. The reaction mixture was stirred overnight at room temperature. Reaction completion was checked on TLC [*V*(Methanol)∶*V*(chloroform)=8∶2]. After the reaction was complete, the reaction mixture was poured in cooled 10% HCl solution. The precipitate obtained was filtered to get targeted desired chalcone. The solid was washed with water until free from acid and crystallized from ethanol, to afford chalcone. All new chalcones of this series (**3a**—**3q**), were synthesized by using the same procedure (Scheme 1).

Scheme 1

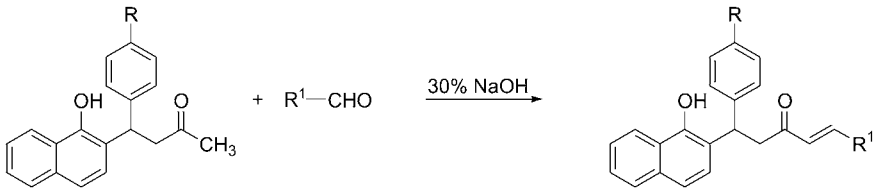

Table 1 Physical data of **3a**—**3q**

Entry	R	R^1	Yield/%	Molecular formula/M_r	m.p./℃
3a	H	C_6H_5	85	$C_{26}H_{20}O_4$/396	105—110
3b	H	4-$NO_2C_6H_4$	93	$C_{26}H_{19}NO_6$/441	132
3c	H	4-ClC_6H_4	93	$C_{26}H_{19}ClO_4$/430	128
3d	H	4-$OCH_3C_6H_4$	85	$C_{27}H_{22}O_5$/426	147
3e	H	3-$NO_2C_6H_4$	95	$C_{26}H_{19}NO_6$/441	127
3f	H	2-ClC_6H_4	93	$C_{26}H_{19}ClO_4$/430	138
3g	H	2-Furyl	85	$C_{24}H_{18}O_5$/386	103
3h	4-OCH_3	C_6H_5	85	$C_{27}H_{22}O_5$/426	141
3i	4-OCH_3	4-$NO_2C_6H_4$	88	$C_{27}H_{21}O_7$/471	152
3j	4-OCH_3	4-ClC_6H_4	92	$C_{27}H_{21}ClO_5$/460	148
3k	4-OCH_3	4-$OCH_3C_6H_4$	88	$C_{28}H_{24}O_6$/456	161
3l	4-OCH_3	2-Furyl	85	$C_{25}H_{20}O_6$/416	162
3m	4-Cl	C_6H_5	88	$C_{26}H_{19}ClO_4$/430	135
3n	4-Cl	4-ClC_6H_4	90	$C_{26}H_{18}Cl_2O_4$/464	149
3o	4-Cl	4-$OCH_3C_6H_4$	90	$C_{27}H_{21}ClO_5$/460	152
3p	4-Cl	3-$NO_2C_6H_4$	95	$C_{26}H_{18}NClO_6$/475	145
3q	4-Cl	2-Furyl	85	$C_{24}H_{17}ClO_5$/420	170

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Table 2 Antibacterial activity of **3a**—**3q**, as minimum inhibitory concentration

Compound	Antibacterial activity [MIC/(μg•mL^{-1})]		
	E. coli	*S. aureus*	*B. subtilis*
Warfarin acid	25	50	70
3a	100	—	—
3b	25	25	25
3c	25	75	50
3d	50	75	100
3e	25	25	50
3f	25	50	25
3g	75	100	—
3h	25	25	25
3i	50	25	25
3j	75	50	—
3k	25	25	50
3l	25	25	75
3m	25	25	50
3n	50	90	100
3o	25	30	25
3p	70	90	—
3q	52	35	50
Streptomycin	10	10	10
Neomycin	30	30	30

Table 3 Antifungal activity of **3a**—**3q** in spore germination inhibition (%) at different concentration against *Candida albicans*

Compound	Concentration/(μg•mL^{-1})			
	160	320	480	640
Warfarin acid	55	67	69	72
3a	23.4	26.2	28.0	29.0
3b	45.4	79.1	89.5	91.0
3c	42.0	49.4	83.1	90.0
3d	19.6	27.0	29.0	31.2
3e[a]	79.0	84.0	87.0	88.4
3f	77.1	79.3	81.0	86.5
3g	68.2	74.1	82.1	86.4
3h[a]	82.4	86.4	87.6	92.3
3i	71.3	78.2	79.4	87.6
3j	59.7	65.2	69.9	72.1
3k	77.3	78.0	81.0	84.0
3l	75.1	78.7	80.3	83.2
3m	50.4	48.9	51.2	42
3n	61.4	60.3	59.8	58.7
3o	45.3	72.6	80.1	79.5
3p	77.9	89.3	86.9	88
3q	75.3	66.7	78.9	90
Fluconazole	84.0	87.0	95.0	98.0

[a] Compound shows high activity; rest all shows moderate activity.

Spectral evaluation of all new synthesized compounds (3a—3q)

4-Hydroxy-3-(3-oxo-1,5-diaryl-3-oxo-pent-4-enyl)-chromen-2-one (3a) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.50 (d, J=12.7 Hz, 2H), 4.90 (t, J=14.1 Hz, 1H), 6.58 (d, J=14.3 Hz, 1H), 6.93 (d, J=15.2 Hz, 1H), 7.10—7.95 (m, 14H, Ar-H), 10.00 (s, 1H, OH); IR (KBr) v: 3500, 3027, 1684, 1610, 1568, 880 cm^{-1}; ES/MS m/z: 397 (M+H)$^+$. Anal. calcd for $C_{26}H_{20}O_4$: C 78.77, H 5.09; found C 78.72, H 5.07.

4-Hydroxy-3-[5-(4-nitro-phenyl)-3-oxo-1-phenyl-pent-4-enyl]-chromen-2-one (3b) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.50 (d, J=12.4 Hz, 2H), 3.72 (t, J=13.2 Hz, 1H), 6.40 (d, J=14.3 Hz, 1H), 6.70 (d, J=15.3 Hz, 1H), 7.25—7.80 (m, 13H, Ar-H), 9.20 (s, 1H, OH); IR (KBr) v: 3545, 3027, 1680, 1600, 1560, 1375, 880 cm^{-1}; ES/MS m/z: 442 (M+H)$^+$. Anal. calcd for $C_{26}H_{19}NO_6$: C 70.44, H 4.34, N 3.17; found C 70.04, H 4.30, N 3.12.

4-Hydroxy-3-[5-(4-chloro-phenyl)-3-oxo-1-phenyl-pent-4-enyl]-chromen-2-one (3c) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.55 (d, J=12.2 Hz, 2H), 3.72 (t, J=13.8 Hz, 1H), 6.40 (s, J=14.4 Hz, 1H), 6.70 (d, J=151 Hz, 1H), 7.20—7.80 (m, 13H, Ar-H), 9.50 (s, 1H, OH); IR (KBr) v: 3400, 3027, 1700, 1600, 1570, 880, 750 cm^{-1}; ES/MS m/z: 431 (M+H)$^+$. Anal. calcd for $C_{26}H_{19}ClO_4$: C 72.47, H 4.44; found C 72.40, H 4.41.

4-Hydroxy-3-[5-(4-methoxy-phenyl)-3-oxo-1-phenyl-pent-4-enyl]-chromen-2-one (3d) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.20 (s, 3H, OCH_3), 3.50 (d, J=12.5 Hz, 2H), 5.00 (s, br, 1H, OH), 4.10 (t, J=14 Hz, 1H), 6.50 (d, J=14.5 Hz, 1H), 6.82 (d, J=15.3 Hz, 1H), 7.10—7.79 (m, 9H, Ar-H), 7.40—7.60 (d, 4H, Ar-H); IR (KBr) v: 3400, 3027, 1700, 1600, 1570, 880, 750 cm^{-1}; ES/MS m/z: 427 (M+H)$^+$. Anal. calcd for $C_{27}H_{22}O_5$: C 76.04, H 5.20; found C 74.0, H 5.10.

4-Hydroxy-3-[5-(3-nitro-phenyl)-3-oxo-1-phenyl-pent-4-enyl]-chromen-2-one (3e) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.35 (d, J=12.1 Hz, 2H), 4.20 (t, J=13.7 Hz, 1H), 6.60 (d, J=14.7 Hz, 1H), 6.80 (d, J=15.4 Hz, 1H), 7.10—7.79 (m, 9H, Ar-H), 7.40—7.60 (d, J=14.2 Hz, 4H, Ar-H), 9.00 (s, 1H, OH); IR (KBr) v: 3450, 3100, 1670, 1620, 1570, 880, 1375 cm^{-1}; ES/MS m/z: 442 (M+H)$^+$. Anal. calcd for $C_{26}H_{19}NO_4$: C 70.74, H 4.34, N 3.17; found C 70.42, H 4.52, N 3.18.

4-Hydroxy-3-[5-(2-chloro-phenyl)-3-oxo-1-phenyl-pent-4-enyl]-chromen-2-one (3f) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.45 (d, J=12.3 Hz, 2H), 3.60 (t, J=13.8 Hz, 1H), 6.72 (d, J=14.2 Hz, 1H), 6.80 (d, J=15.3 Hz, 1H), 7.10—7.25 (m, 13H, Ar-H), 8.90 (s, 1H, OH); IR (KBr) v: 3450, 3100, 1750, 1620, 1570, 880, 750 cm^{-1}; ES/MS m/z: 431 (M+H)$^+$. Anal. calcd for $C_{26}H_{19}ClO_4$: C 72.47, H 4.44; found C 72.43, H 4.41.

4-Hydroxy-3-(5-furan-2-yl-3-oxo-1-phenyl-pent-4-enyl)-chromen-2-one (3g) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.45 (d, J=12.2 Hz, 2H), 3.52 (t, J=13.4 Hz, 1H), 6.75 (d, J=14.2 Hz, 1H), 6.83 (d, J=15.3 Hz, 1H), 6.60 (dd, J=14.3, 13.8 Hz, 1H, Ar-H), 6.95 (dd, J=14.3 Hz, 1H, Ar-H), 7.10—7.25 (m, 9H, Ar-H), 7.60 (d,

J=13.8 Hz, 1H, Ar-H), 11.50 (s, 1H, OH); IR (KBr) v: 3450, 3100, 1750, 1620, 1570, 880 cm^{-1}; ES/MS m/z: 387 $(M+H)^+$. Anal. calcd for $C_{24}H_{18}O_5$: C 74.60, H 4.7; found C 74.52, H 4.60.

4-Hydroxy-3-[1-(4-methoxy-phenyl)-3-oxo-5-phenyl-pent-4-enyl]-chromen-2-one (3h) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.30 (s, 3H, OCH_3), 3.50 (d, J=11.9 Hz, 2H), 3.60 (t, J=13.5 Hz, 1H), 6.72 (d, J=14,4 Hz, 1H), 6.80 (d, J=15.4 Hz, 1H), 7.10—7.25 (m, 13H, Ar-H), 8.70 (s, 1H, OH); IR (KBr) v: 3450, 3100, 1750, 1620, 1570, 880 cm^{-1}; ES/MS m/z: 427 $(M+H)^+$. Anal. calcd for $C_{27}H_{22}O_5$: C 76.04, H 5.20; found C 76.00, H 5.12.

4-Hydroxy-3-[1-(4-methoxy-phenyl)-5-(4-nitro-phenyl)-3-oxo-pent-4-enyl]-chromen-2-one (3i) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.30 (s, 3H, OCH_3), 3.50 (d, J=12.2 Hz, 2H), 3.70 (t, J=13.7 Hz, 1H), 6.20 (d, J=14.3 Hz, 1H), 6.50 (d, J=15.4 Hz, 1H), 7.10—7.25 (m, 12H, Ar-H), 9.70 (s, 1H, OH); IR (KBr) v: 3450, 3100, 1670, 1620, 1570, 880, 1375 cm^{-1}; ES/MS m/z: 472 $(M+H)^+$. Anal. calcd for $C_{27}H_{21}NO_7$: C 69.78, H 4.49, N 2.97; found C 68.72, H 4.45, N 2.95.

4-Hydroxy-3-[5-(4-chloro-phenyl)-1-(4-methoxy-phenyl)-3-oxo-pent-4-enyl]-chromen-2-one (3j) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.75 (s, 3H, OCH_3), 3.45 (d, J=12.1 Hz, 2H), 3.63 (t, J=14.1 Hz, 1H), 6.78 (d, J=14.5 Hz, 1H), 6.83 (d, J=15.4 Hz, 1H), 7.10—7.25 (m, 12H, Ar-H), 9.10 (s, 1H, OH); IR (KBr) v: 3400, 3200, 1700, 1620, 1570, 890, 750 cm^{-1}; ES/MS m/z: 461 $(M+H)^+$. Anal. calcd for $C_{27}H_{21}ClO_5$: C 70.36, H 4.59; found C 70.25, H 4.5.

4-Hydroxy-3-[1,5-bis-(4-methoxy-phenyl)-3-oxo-pent-4-enyl]-chromen-2-one (3k) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.80 (s, 3H, CH_3), 2.20 (s, 3H, CH_3), 3.20 (d, J=12.1 Hz, 2H), 3.50 (t, J=12.7 Hz, 1H), 6.20 (d, J=14.2 Hz, 1H), 6.85 (d, J=15.2 Hz, 1H), 7.20—7.4 (m, 12H, Ar-H), 8.70 (s, 1H, OH); IR (KBr) v: 3400, 3200, 1700, 1620, 1570, 890 cm^{-1}; ES/MS m/z: 457 $(M+H)^+$. Anal. calcd for $C_{28}H_{24}O_6$: C 73.67, H 5.30; found C 73.65, H 5.25.

4-Hydroxy-3-[5-furan-2-yl-1-(4-methoxy-phenyl)-3-oxo-pent-4-enyl]-chromen-2-one (3l) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.20 (s, 3H, OCH_3), 2.50 (t, J=11.4 Hz, 1H), 3.42 (d, J=13.1 Hz, 2H, CH_2), 6.40 (d, J=14.2 Hz, 1H), 6.83 (d, J=15.3 Hz, 1H), 6.55 (dd, J=13.7, 14.2 Hz, 1H, Ar-H), 6.90 (dd, J=13.8, 13.6 Hz, 1H, Ar-H), 7.10—7.25 (m, 8H, Ar-H), 7.60 (d, J=13.8 Hz, 1H, Ar-H), 10.25 (s, 1H, OH); IR (KBr) v: 3400, 3200, 1690, 1620, 1570, 890 cm^{-1}; ES/MS m/z: 417 $(M+H)^+$. Anal. calcd for $C_{25}H_{20}O_6$: C 72.11, H 4.84; found C 72.10, H 4.81.

4-Hydroxy-3-[1-(4-chloro-phenyl)-3-oxo-5-phenyl-pent-4-enyl]-chromen-2-one (3m) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.20 (d, J=12.1 Hz, 2H), 3.72 (t, J=13.1 Hz, 1H), 6.40 (d, J=14.1 Hz, 1H), 6.70 (d, J=15.3 Hz, 1H), 7.20—7.80 (m, 13H, Ar-H), 9.50 (s, 1H, OH); IR (KBr) v: 3400, 3027, 1700, 1600, 1570, 880, 750 cm^{-1}; ES/MS m/z: 431 $(M+H)^+$. Anal. calcd for $C_{26}H_{19}ClO_4$: C 72.47, H 4.44; found C 72.40, H 4.42.

4-Hydroxy-3-[1,5-bis-(4-chloro-phenyl)-3-oxo-pent-4-enyl]-chromen-2-one (3n) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.40 (d, J=12.2 Hz, 2H), 3.72 (t, J=13.2 Hz, 1H), 6.40 (d, J=14.2 Hz, 1H), 6.70 (d, J=15.2 Hz, 1H), 7.20—7.80 (m, 12H, Ar-H), 9.50 (s, 1H, OH); IR (KBr) v: 34750, 3027, 1700, 1600, 1570, 880, 750 cm^{-1}; ES/MS m/z: 465 $(M+H)^+$. Anal. calcd for $C_{26}H_{19}ClO_4$: C 72.47, H 4.44; found C 72.43, H 4.41.

4-Hydrpxy-3-[1-(4-chloro-phenyl)-5-(4-methoxy-phenyl)-3-oxo-pent-4-enyl]-chromen-2-one (3o) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.80 (s, 3H, CH_3), 3.25 (d, J=11.9 Hz, 2H), 3.60 (t, J=13.1 Hz, 1H), 6.40 (d, J=14.4 Hz, 1H), 6.70 (d, J=15.4 Hz, 1H), 7.20—7.4 (m, 12H, Ar-H), 8.70 (s, 1H, OH); IR (KBr) v: 3400, 3200, 1700, 1620, 1570, 880, 750 cm^{-1}; ES/MS m/z: 461 $(M+H)^+$. Anal. calcd for $C_{27}H_{21}ClO_5$: C 70.36, H 4.59; found C 70.34, H 4.55.

4-Hydroxy-3-[1-(4-chloro-phenyl)-5-(3-nitro-phenyl)-3-oxo-pent-4-enyl]-chromen-2-one (3p) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.25 (d, J=12.4 Hz, 2H), 3.60 (t, J=13.1 Hz, 1H), 6.72 (d, J=14.2 Hz, 1H), 6.80 (d, J=15.3 Hz, 1H), 7.10—7.25 (m, 12H, Ar-H), 8.70 (s, 1H, OH); IR (KBr) v: 3400, 3000, 1690, 1620, 1570, 1370, 890, 750 cm^{-1}; ES/MS m/z: 476 $(M+H)^+$. Anal. calcd for $C_{26}H_{18}NClO_6$: C 65.62, H 3.81, N 2.94; found C 65.60, H 3.79, N 3.01.

4-Hydroxy-[1-(4-chloro-phenyl)-5-furan-2-yl-3-oxo-pent-4-enyl]-chromen-2-one (3q) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.25 (d, J=12.4 Hz, 2H), 3.52 (t, J=13.2 Hz, 1H), 6.40 (d, J=14.2 Hz, 1H), 6.83 (d, J=15.4 Hz, 1H), 6.60 (dd, J=13.7, 14.2 Hz, 1H, Ar-H), 6.95 (dd, J=13.7, 14.2 Hz, 1H, Ar-H), 7.30 (s, 1H, Ar-H), 7.50—8.10 (m, 8H, Ar-H), 8.90 (s, 1H, OH); IR (KBr) v: 3350, 3000, 1690, 1620, 1570, 890, 750 cm^{-1}; ES/MS m/z: 421 $(M+H)^+$. Anal. calcd for $C_{24}H_{17}ClO_5$: C 68.50, H 4.07; found C 68.92, H 4.11.

Results and discussion

Antimicrobial activity

The compounds **3a**—**3q** were screened for their antibacterial human pathogenic bacteria *Escheriichia coli*, *Staphylococcus aurenus*, and *Bacillus subtilis*. The minimum inhibition concentration (MIC) was determined using the tube dilution method.[39] DMF was used as a blank and streptomycin/neomycin was used as antibacterial standard. The antibacterial activity was compared with the known antibiotic streptomycin/neomycin and the results are presented in Table 2. A close assessment of the data reveals that all the compounds exihibit antibacterial activity ranging from 25 to 100 μg•mL^{-1}. The compounds **3b** and **3h** were highly active against all the three organisms. Both compounds have oxygen containing electronegative group on benzene nucleus. Compounds **3e**, **3k** and **3l** were active against *E. coli* and *S. aureus*. Here too oxygen containing electronegative group is present on benzene nucleus (both from

warfarin moiety and aldehyde moiety). Compound **3f** is highly active against *E. coli* and *B. subtilis*. Here chlorine as an electronegative group is present on benzene nucleus (R^1). Compound **3i** is highly active against *S. aureus* and *B. subtilis*. Compound **3a** is almost inactive against all three organisms employed. Compound **3m** is active against *E. coli* and *S. aureus*. Compound **3o** is active against *E. coli* and *B. sublitis*. Compounds **3n**, **3p** and **3q** are inactive against all three organisms employed. From the screened results it can be concluded that the functional group like methoxy or nitro as a substituent on benzene nucleus has shown promising activity. Compounds **3m** and **3o** having chlorine as electronegative group have shown activity against *E. coli* and *S. aureus*. Compound **3m** has chlorine group and **3o** has electronegative chlorine and methoxy group on respective benzene nucleus. Compound **3n** has electronegative chloro group on both benzene nucleus, which may have contributed towards inactivity. **3p** and **3q** have electronegative group chloro and methoxy. Both compounds are found to be inactive for human pathogen bacteria. This can be contributed to neutralizing effect of one electronegative by other. As a general conclusion apart from the nature of the group it is the specific group having oxygen item and position on benzene nucleus that is effective for promising contribution to antimicrobial activity.

Antifungal activity

The chalcones (**3a**—**3q**) were also screened for their antifungal activity against *Candida albicans* at 160, 320, 480 and 640 $\mu g \cdot mL^{-1}$ concentration, using agar plate technique.[40] The results are presented in Table 3. The antifungal activity was compared with the known antifungal fluconazole. The examination of the data reveals that compounds **3e** and **3h** are highly active against *Candida albicans*. Compounds **3b**, **3c** and **3d** are inactive as all values are far away from the standard value for Fluconazole. From the structure of **3e** it will be evident that nitro group is at 3 position of R^1 which could have contributed to antifungal activity. Compounds **3k**, **3l**, **3p** and **3q** show moderate antifungal activity. Compound **3i** shows activity at high concentration. Compounds **3m**, **3n** and **3o** do not have promising antifungal activity.

From the date presented in Tables 2 and 3 it appears that the compounds **3e** and **3h** shows antibacterial and antifungal activity and hence can be considered for further screening as perspective molecules having dual activity. Both are having electron withdrawing group having oxygen item. **3b** and **3h** can be independently further tried for their application in view of their promissing antibacterial activity as future perspective molecule.

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(E0902075 Sun, H.; Zheng, G.)

