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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

Synthesis and biological evaluation of naphthalene, furan and pyrrole based chalcones as cytotoxic and antimicrobial agents

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Abstract Chalcone is an aromatic ketone that forms the central core for a variety of important biological compounds, which are collectively known as chalcones. These show antibacterial, antifungal, antitumour and anti-inflammatory properties, and also are intermediates in the biosynthesis of flavonoids, substances widespread in plants with an array of biological activities. These biaryl propenones show potent toxicity to several cancer cell lines and interact with tubulin at its colchicine-binding site. Tubulin binding molecules interfere with the dynamic instability of microtubules and thereby disrupt microtubule inducing cell cycle arrest in the M phase, forming abnormal spindles and finally leading to apoptotic cell death. Basically Chalcones consists of C_6–C_3–C_6 units but in the present study we report the reactions of 1-acetylnaphthalene, 2-acetylfuran and 2-acetylpyrrole with aldehydes, thus getting compounds akin to chalcones. 31 analogues have been synthesised and evaluated for cytotoxic potential against PC-3, OVCAR, IMR-32 and HEP-2. Compound **9** was found to be the most cytotoxic with inhibition ranging from 72 to 88% against the cell lines employed. The synthetics were also evaluated for antimicrobial activity and compound **25** was found to be the most potent.

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Keywords Chalcones · Cytotoxic · Cancer · Cell lines

Introduction

In the recent years, there has been a growing interest in chalcones and their presumed role in the prevention of various diseases such as cancer, chronic inflammation etc. The term chalcone refers to the structurally simple and largest class of plant secondary metabolites, which serve as defense mechanism in plants to counteract reactive oxygen species (ROS) to prevent damage by micro-organisms, insects or herbivores (Vaya *et al.*, 1997).

These flavonoid family compounds display an impressive array of biological activities, amongst which antibacterial (Vibhute and Basser, 2003), anti-fungal (Azad *et al.*, 2007), antioxidant (Dinkova *et al.*, 2001; Rezk *et al.*, 2002), antileishmanial (Boeck *et al.*, 2006), anti-malarial (Lawrence *et al.*, 2006), angiogenesis inhibitor (Nam *et al.*, 2003), anti-inflammatory (Won *et al.*, 2005; Laskin and Pendino, 1995), antiviral (Pandey *et al.*, 2004), anti-mitotic (Edwards *et al.*, 1990), anticancer (Bhat *et al.*, 2005), anti-invasive (Mukherjee *et al.*, 2001; Modzelewska *et al.*, 2005) and antiproliferative (Calliste *et al.*, 2001) activities have been citied in the literature. Chalcones strongly inhibit the polymerization of tubulin by binding to the colchicine-binding site (Lawrence *et al.*, 2006).

Chemically chalcones are open chain flavonoids in which the two aromatic rings are joined together by three carbons, α, β-unsaturated carbonyl system. Fundamentally they are considered as derivatives of phenyl styryl ketone. In view of the varied biological and pharmacological applications, we synthesized some chalcone like, compounds. Generally chalcones contain C_6–C_3–C_6 unit but the

compounds reported in the present study contain C_{10}–C_3–C_6 and C_5–C_3–C_6 unit.

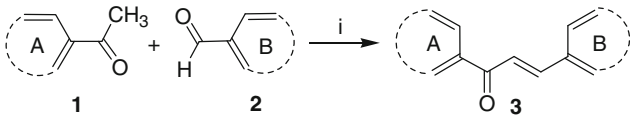
Results and discussion

Synthesis of 1,3-diarylpropenones

Claisen–Schmidt condensation of a series of aryl ketones (**1**) with aryl aldehydes (**2**) in ethanol yielded several 1,3-diarylpropenones (**3**; 65–94%) (Scheme 1). The products were recrystallized from methanol and characterized by using spectroscopic techniques such as IR and NMR (Fig. 1).

Biological evaluation of synthesized compounds for cytotoxic potential

All the synthetics were assayed for in vitro cytotoxicity against PC-3, OVCAR, IMR-32 and HEP-2 human cancer cell lines using sulforhodamine B19. The cells were allowed to proliferate in the presence of test material for 48 h. From the data, it is clear that the compounds **8**, **9** and **16** exhibited broad spectrum of cytotoxicity against all the four cell lines (Table 1). Compound **9** was found to be the most potent with inhibition ranging from 72 to 88% against the four different cell lines.

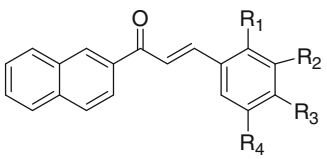


Scheme 1 Reagents and conditions: (i) 5% NaOH, ethanol, rt, 1 h, 65–94%.

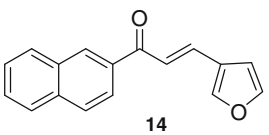
Biological evaluation of synthesized compounds for antimicrobial activity

The synthetics were also evaluated for antimicrobial activity against five reference bacterial strains; *Staphylococcus aureus* (MTCC 96), *Bacillus subtilis* (MTCC 2451), *Pseudomonas aeruginosa* (MTCC 2642), *Escherichia coli* (MTCC 82) and *Salmonella typhi* (MTCC 1251) and two fungal strains; *Aspergillus niger* (MTCC 1344), *Candida albicans* (MTCC 3018). The antimicrobial activity of synthesized compound was determined by observing the zone of inhibition in comparison to standard antibiotic (Amoxicillin, Gentamycin) and a standard antifungal (fluconazole) disc. On this basis, from the data shown in Table 2, compounds **8** and **9** were found to be the most potent amongst all test compounds with an MIC value ranging from 3.9 to 125 μg/ml against the various microbial strains employed.

Fig. 1 Chemical structures of synthesized compounds.

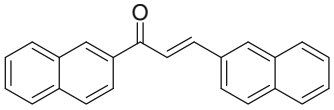


4, $R_1 = R_2 = R_3 = R_4 = H$
5, $R_2 = NO_2$; $R_1 = R_3 = R_4 = H$
6, $R_2 + R_3 = O\text{-}CH_2\text{-}O$; $R_3 = R_4 = H$
7, $R_1 = R_2 = Cl$; $R_3 = R_4 = H$
8, $R_1 = H$; $R_2 = R_3 = R_4 = OCH_3$
9, $R_1 = R_2 = R_3 = OCH_3$; $R_4 = H$
10, $R_1 = R_4 = OCH_3$; $R_1 = R_3 = H$
11, $R_1 = R_4 = H$; $R_2 = R_3 = OCH_3$
12, $R_1 = R_4 = H$, R_2 =OH, $R_3 = OCH_3$
13, $R_1 = R_3 = R_4 = H$, R_2 =Br

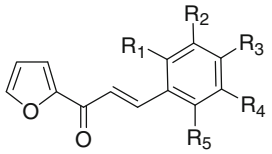


14

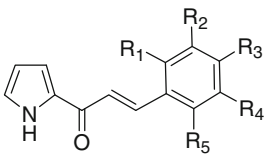
15, $R_1 = R_2 = R_4 = H$, $R_3 = OCH_3$



16



17 $R_1 = R_2 = R_3 = R_4 = R_5 = H$
18, $R_2 + R_3 = O\text{-}CH_2\text{-}O$; $R_1 = R_4 = R_5 = H$
19, $R_2 = NO_2$, $R_1 = R_3 = R_4 = R_5 = H$
20, $R_1 = R_4 = OCH_3$; $R_2 = R_3 = R_5 = H$
21, $R_2 = R_3 = R_4 = OCH_3$; $R_1 = R_5 = H$
22, $R_2 = R_3 = OCH_3$; $R_1 = R_4 = R_5 = H$
23, $R_2 = OH$, $R_3 = OCH_3$; $R_1 = R_4 = R_5 = H$
24, $R_1 = R_5 = Cl$; $R_3 = R_4 = R_5 = H$



25, $R_1 = R_2 = R_3 = R_4 = R_5 = H$
26, $R_3 = NO_2$; $R_1 = R_2 = R_4 = R_5 = H$
27, $R_2 = NO_2$, $R_1 = R_3 = R_4 = R_5 = H$
28, $R_1 = R_3 = Cl$; $R_2 = R_4 = R_5 = H$
29, $R_1 = R_2 = OCH_3$; $R_3 = R_4 = R_5 = H$
30, $R_1 = R_2 = Cl$; $R_3 = R_4 = R_5 = H$
31, $R_1 = R_5 = Cl$; $R_2 = R_3 = R_4 = R_5 = H$

Table 1 In vitro cytotoxicity of the compounds **4–31** against human cancer cell lines at concentration 1×10^{-5} mol

Entry	Prostate (PC-3) % Growth inhibition	Ovary (OVCAR)	Neuroblastoma (IMR-32)	Liver (HEP-2)
4	28	21	19	27
5	16	13	11	17
6	42	46	39	42
7	–	11	–	9
8	**84**	**87**	**81**	**79**
9	**81**	**88**	**75**	**72**
10	49	52	51	47
11	53	49	51	53
12	47	52	61	57
13	–	14	11	–
14	16	–	13	21
15	33	31	36	29
16	**79**	**76**	**77**	**73**
17	19	–	13	–
18	21	11	16	13
19	–	13	–	16
20	23	–	31	29
21	42	28	49	47
22	29	–	33	27
23	21	23	16	19
24	–	–	–	11
25	22	18	14	23
26	11	14	11	13
27	13	–	14	17
28	–	13	–	16
29	31	24	28	33
30	11	–	–	15
31	–	–	12	16

"–" indicates no activity

Bold value indicates the best activity of synthetics

Structure activity relationship for cytotoxicity

From the data shown in Table 1, naphthone proved to be the most potent synthone for cytotoxic activity. The replacement of naphthyl (ring A) with heterocycles led to dilution of the activity (compare the compounds **4**, **6** and **10** with **17**, **18** and **20**). The decrease in the cytotoxic potential was more pronounced with furan than pyrrole which can be attributed to less aromatic character of the furan ring (compare the compounds **17**, **24** with **25**, **31**). As Napthone was found to be the most potent synthone, emphasis has been laid on SAR studies of Naphthyl based chalcones and the following conclusions have been made: (i) The presence of electron donating substituents at Ring B led to enhanced cytotoxic potential of the synthetics (**6**, **8**, **9**, **10**, **11** and **12**). (ii) The prescience of electron withdrawing substituents at Ring B led to decreased cytotoxic potential (**5**, **7** and **13**). (iii) Replacement of ring B with a heterocyclic ring remarkably reduced the activity (**14**). (iv) Replacement of Ring B with another naphthyl ring drastically increased the cytotoxic potential (**16**).

Conclusion

From the data shown in Table 1, it is evident that naphthyl based chalcones proved to be the most potent cytotoxic. Thus, it can be concluded that the enhancement of the electron density in the periphery as in the case of naphthyl based chalcones prevents the need of electron donating substituents on Ring A.

Experimental

All the chemicals used are commercially available and were used as received. Nuclear magnetic resonance spectroscopy was performed using Varian EM-360L and Bruker AC-300F, 200, 300 and 500 MHz spectrometer with TMS as an internal standard and the spectra were recorded in appropriate deuterated solvents, as indicated. IR spectra were recorded as KBr pellets on Perkin–Elmer 882 spectrophotometer model. Mass spectra were recorded on ESI-esquire 3000 Bruker Daltonics instrument. Melting points (mp) were determined on a Buchi–Tottoli apparatus and are uncorrected. All products reported showed ^{1}H NMR spectra in agreement with the assigned structures. Reaction courses and product mixtures were routinely monitored by TLC on silica gel (precoated F254 Merck plates).

General procedure for the synthesis of chalcones

Aryl ketone (0.003 mol) was taken in a flask (100 ml) and dissolved in methanol (10 ml). To the solution, substituted benzaldehyde (0.003 mol) followed by 5% aqueous NaOH solution (3 ml) was added. The reaction mixture was kept in stirred condition at room temperature for 15 h. Completion of reaction was monitored on TLC (20% Ethyl acetate in toluene). The reaction mixture was poured into water; precipitated solid was filtered and re-crystallized from ethanol. The physical data of the synthetics is shown below:

*(E)-1-(naphth-2-yl)-3-phenyl-prop-2-en-1-one (**4**)*

Yield 80%. Mp: 110–113°C. I.R. (KBr, cm^{-1}): 1662, 1604. ^{1}H NMR ($CDCl_3$, 300 MHz): 8.54 (1H, s), 8.10 (1H, dd, J = 1.8 and 8.7 Hz), 7.85–8.0 (4H, m), 7.66–7.71 (3H, m),

Table 2 MIC (μg/ml) of the compounds against standard microbial strains.

Diluted solution of compounds (μg/ml)	*B. subtilis*	*S. aureus*	*E. coli*	*S. typhi*	*P. aeruginosa*	*A. niger*	*C. albicans*
4	–	250	500	–	500	–	–
5	–	125	250	–	–	–	–
6	125	62.5	125	125	250	–	–
7	31.2	31.2	31.2	62.5	62.5	250	250
8	**3.9**	**1.9**	**3.9**	**15.6**	**15.6**	**125**	**125**
9	**3.9**	**3.9**	**15.6**	**15.6**	**7.8**	**62.5**	**125**
10	125	125	250	250	–	–	–
11	62.5	62.5	125	62.5	125	250	500
12	31.2	15.6	62.5	125	250	–	–
13	125	125	250	125	250	–	–
14	250	125	–	500	250	–	–
15	–	–	–	–	–	–	–
16	125	62.5	125	–	250	–	–
17	250	250	–	–	–	–	–
18	31.2	62.5	125	125	125	500	–
19	125	125	125	–	125	–	–
20	31.2	62.5	31.2	62.5	31.2	125	125
21	31.2	15.6	62.5	31.2	15.6	62.5	62.5
22	31.2	31.2	15.6	15.6	31.2	125	250
23	62.5	31.2	62.5	62.5	125	250	250
24	125	62.5	62.5	125	250	250	250
25	250	125	500	500	–	–	–
26	–	250	500	–	–	–	–
27	250	125	250	500	–	500	–
28	15.6	7.8	15.6	15.6	31.2	62.5	125
29	–	–	–	–	–	–	–
30	31.2	7.8	15.6	15.6	7.8	125	250
31	31.2	15.6	15.6	31.2	31.2	125	125
Amoxicillin	0.2	0.2	0.25	0.2	0.3	–	–
Gentamycin	0.3	0.4	0.25	0.2	0.25	–	–
Fluconazole	–	–	–	–	–	0.2	0.3

Bold value indicates the best activity of synthetics

7.53–7.61 (2H, m), 7.44 (3H, m). ^{13}C NMR ($CDCl_3$, 300 MHz): 186.76, 142.21, 135.56, 134. 31, 134.32, 132.45, 129.78, 128.43, 128.31, 128.11, 127.88, 127.76, 126.43, 126.11, 125.54, 124.54. M+ at *m/z*: −258. Anal. Calcd for $C_{19}H_{14}O$: C,88.34; H,5.46; O,6.19. Found: C,88.01;H,5.69.

*(E)-1-(naphth-2-yl)-3-(3-nitrophenyl)-prop-2-en-1-one (**5**)*

Yield 79%. Mp: 152–157°C. I.R. (KBr, cm^{-1}): 1660, 1606, 1525, 1347. ^{1}H NMR ($CDCl_3$, 500 MHz): 8.58 (2H, d, J = 2.09), 8.29 (1H, m), 8.13 (1H, dd, J = 1.7 and 8.6 Hz), 8.04 (1H, d, J = 8.00 Hz), 7.80–7.98 (5H, m), 7.59 (3H, m). M+ at *m/z*: −303. Anal. Calcd for $C_{19}H_{13}NO_3$: C,75.24; H,4.32; N,4.62; O,15.82. Found: C, 75.56; H,4.11; N,4.23.

*(E)-3-[benzo(d)1,3-dioxol-5-yl]-1-[naphth-2-yl]prop-2-en-1-one (**6**)*

Yield 78%. Mp 139–141°C. I.R. (KBr, cm^{-1}): 1655, 1583, 1208. ^{1}H NMR ($CDCl_3$, 300 MHz): 8.53 (1H, s), 8.10 (1H, dd, J = 1.5 and 18.5 Hz), 7.87–8.01 (3H, m), 7.81 (1H, d, J = 15.52 Hz), 7.53–7.63 (2H, m), 7.26 (1H, s), 7.24 (1H, d, J = 1.3 Hz), 7.17 (1H, dd, J = 1.4 and 7.9 Hz), 6.87 (1H, d, J = 8.00 Hz), 6.05 (2H, s). M+ at *m/z*: −302. Anal. Calcd for $C_{20}H_{14}O_3$: C,79.46; H,4.67; O, 15.88. Found: C,79.08; H,4.88.

*(E)-3-(2,3-dichlorophenyl)-1-(naphth-2-yl)-prop-2-en-1-one (**7**)*

Yield 65%. Mp 123–127°C. I.R. (KBr, cm^{-1}): 1655, 1592, 747. ^1H NMR ($CDCl_3$, 300 MHz): 8.49 (1H, s), 7.98 (1H, d, J = 15.8 Hz), 7.79–7.83 (2H, m), 7.67–7.75 (2H, m), 7.40 (1H, d, J = 15.8 Hz), 7.37 (2H, m), 7.21 (3H, m). M+ at *m/z*: −326. Anal. Calcd for $C_{19}H_{12}Cl_2O$: C,69.74; H,3.70; O, 4.89. Found: C,69.38;H,3.41.

*(E)-3-(3,4,5-trimethoxyphenyl)-1-(naphth-2-yl)-prop-2-en-1-one (**8**)*

Yield 81%. Mp 120–122°C. I.R. (KBr, cm^{-1}): 1650, 1579, 1121; ^1H NMR ($CDCl_3$, 200 MHz): 8.52 (1H, s), 7.93 (1H, d, J = 15.7 Hz), 7.80–7.84 (3H, m), 7.69 (2H, d, J = 8.1 Hz), 7.54 (1H, d, J = 15.7 Hz), 7.35 (1H, d, J = 7.8 Hz), 6.50 (2H, s), 3.89 (6H, s), 3.78 (3H, s). M+ at *m/z*: −348. Anal. Calcd for $C_{22}H_{20}O_4$: C,75.84; H,5.79; O, 18.37. Found: C,75.48;H,6.05.

*(E)-3-(2,3,4-trimethoxyphenyl)-1-(naphth-2-yl)-prop-2-en-1-one (**9**)*

Yield 82%. Mp 121–124°C. I.R. (KBr, cm^{-1}): 1653, 1556, 1230; ^1H NMR ($CDCl_3$, 300 MHz): 8.52 (1H, s), 7.93 (1H, d, J = 15.7 Hz), 7.80–7.84 (3H, m), 7.69 (2H, d, J = 8.1 Hz), 7.54 (1H, d, J = 15.7 Hz), 7.35 (1H, d, J = 7.8 Hz), 6.87 (1H, d, J = 8.7 Hz), 6.60 (1H, d, J = 8.7 Hz), 3.89 (6H, s), 3.78 (3H, s). M+ at *m/z*: −348. Anal. Calcd for $C_{22}H_{20}O_4$: C,75.84; H,5.79; O, 18.37. Found: C,75.58;H, 5.41.

*(E)-3-(2,5-dimethoxyphenyl)-1-(naphth-2-yl)-prop-2-en-1-one (**10**)*

Yield 73%. Mp 100–103°C. I.R. (KBr, cm^{-1}): 1655, 1583, 1259. ^1H NMR ($CDCl_3$, 200 MHz): 8.54 (1H, s), 7.85–8.09 (5H, m), 7.54–7.62 (3H, m), 7.21–7.26 (2H, m), 6.92 (1H, d, J = 8.6 Hz), 3.98 (3H, s), 3.95 (3H, s). M+ at *m/z*: −318. Anal. Calcd for $C_{21}H_{18}O_3$: C,79.22; H,5.70; O, 15.08. Found: C,78.84;H, 6.10.

*(E)-3-(3,4-dimethoxyphenyl)-1-(naphth-2-yl)-prop-2-en-1-one (**11**)*

Yield 67%. Mp 101–105°C. I.R. (KBr, cm^{-1}): 1655, 1583, 1259; ^1H NMR ($CDCl_3$, 300 MHz): 8.51 (1H, s), 7.94 (1H, d, J = 15.3 Hz), 7.84–7.87 (2H, m), 7.65–7.71 (2H, m), 7.52 (1H, d, J = 15.3 Hz), 7.31–7.37 (2H, m), 6.70–6.73 (3H, m),3.74 (6H, s). M+ at *m/z*: −318. Anal. Calcd for $C_{22}H_{20}O_4$: C,79.22; H,5.70; O, 15.08. Found: C,79.46;H, 5.99.

*(E)-3-(3-hydroxy-4-methoxyphenyl) -1-(naphth-2-yl)-prop-2-en-1-one (**12**)*

Yield 65%. Mp 159–161°C. I.R. (KBr, cm^{-1}): 3426, 1662, 1603, 1247; ^1H NMR($CDCl_3$, 300 MHz): 8.49 (1H, s), 7.80 (1H, d, J = 15.3 Hz), 7.52–7.61 (5H, m), 7.18 (1H, d, J = 15.3 Hz), 6.93–7.10 (4H, m), 3.79 (3H, s). M+ at *m/z*: −304. Anal. Calcd for $C_{20}H_{16}O_3$: C,78.93; H,5.30; O, 15.77. Found: C,78.61;H, 5.51.

*(E)-3-(3-Bromo-phenyl)-1-naphthalen-2-yl-propenone (**13**)*

Yield 78%. Mp 126–130°C. I.R. (KBr, cm^{-1}): 1662, 1605, 1050. ^1H NMR ($CDCl_3$, 200 MHz): 8.58 (2H, s), 8.28 (1H, d, J = 7.79 Hz), 7.78–8.15 (7H, m), 7.56–7.68 (3H, m). M+ at *m/z*: −336. Anal. Calcd for $C_{19}H_{13}BrO$: C,67.67; H,3.89; O, 4.74. Found: C,67.34; H, 4.29.

*(E)-3-(furan-2-yl)-1-(naphth-2-yl)-prop-2-en-1-one (**14**)*

Yield 85%. Mp 45–48°C. I.R. (KBr, cm^{-1}): 1676, 1589, 1283. ^1H NMR ($CDCl_3$, 300 MHz): 8.51 (1H, s), 7.92 (1H, d, J = 15.6 Hz), 7.88 (2H, m), 7.81 (1H, d, J = 8.1), 7.64–7.67 (2H, m), 7.54 (1H, d, J = 15.6 Hz), 7.29–7.31 (2H, m), 6.25 (1H, d, J = 3.0 Hz), 6.22 (1H, dd, J = 1.8 and 3.0 Hz). M+ at *m/z*: −248. Anal. Calcd for $C_{17}H_{12}O_2$: C,82.24; H,4.87; O, 12.89. Found: C,82.55; H,4.54.

*(E)-3-(4-methoxyphenyl)-1-(naphth-2-yl)-prop-2-en-1-one (**15**)*

Yield 79%. Mp 92–95°C. I.R. (KBr, cm^{-1}): 1656, 1596, 1250; ^1H NMR ($CDCl_3$, 300 MHz): 8.53 (1H, s), 8.10 (1H, dd, J = 1.5 and 8.7 Hz), 7.83–8.01 (4H, m), 7.54–7.67 (5H, m), 6.95 (2H, d, J = 8.7 Hz), 3.87 (3H, s). M+ at *m/z*: −288. Anal. Calcd for $C_{20}H_{16}O_2$: C,83.31; H,5.59; O,11.10. Found: C,83.01; H,5.24.

*(E)-3-(naphth-3-yl)-1-(naphth-2-yl)-prop-2-en-1-one (**16**)*

Yield 77%. Mp 206–210°C. I.R. (KBr, cm^{-1}): 1646, 1592; ^1H NMR ($CDCl_3$, 300 MHz): 8.59 (1H, s), 8.14 (2H, dd, J = 1.8 and 8.7 Hz), 7.84–8.08 (8H, m), 7.48–7.65 (5H, m). M+ at *m/z*: −308. Anal. Calcd for $C_{23}H_{16}O$: C,89.58; H,5.23; O, 5.19. Found: C,89.27; H,5.49.

*1-(2-Furyl)-3-phenylprop-2-en-1-one (**17**)*

Yield 68%. Mp 87–89°C. I.R. (KBr, cm^{-1}): 1604, 1657. ^1H NMR (CD_3OD, 200 MHz): 7.87 (1H, bs), 7.84 (1H, d, J = 14.6 Hz), 7.73 (3H, m), 7.61 (d, 1H, J = 14.6 Hz), 7.59 (1H, m), 7.44 (2H, m), 6.71 (1H, dd, J = 1.6 and

3.3 Hz). M+ at *m/z*: −198. Anal. Calcd for $C_{13}H_{10}O_2$: C,78.77; H,5.09; O, 16.14. Found: C,78.40; H,4.74.

*1-(2-Furyl)-3-(3, 4-methylenedioxy phenyl) prop-2-en-1-one (**18**)*

Yield 69%. Mp 180–182°C. I.R. (KBr, cm^{-1}): 1597, 1663. ^1H NMR (CD_3OD, 200 MHz): 7.85 (1H, d, *J* = 1.6 Hz), 7.76 (1H, d, *J* = 15.6 Hz), 7.56 (1H, d, *J* = 3.5 Hz), 7.45 (1H, d, *J* = 15.6 Hz), 7.34 (1H, bs), 7.19 (1H, d, *J* = 2.4 Hz), 6.88 (1H, d, *J* = 8.1 Hz), 6.70 (1H, dd, *J* = 1.6 and 3.5 Hz), 6.03 (2H, s). M+ at *m/z*: −242. Anal. Calcd for $C_{14}H_{10}O_4$: C,69.42; H,4.16; O, 26.42. Found: C,69.03; H,3.87.

*1-(2-Furyl)-3-(3-nitrophenyl) prop-2-en-1-one (**19**)*

Yield 73%. Mp 181–183°C. I.R. (KBr, cm^{-1}): 1604, 1656. ^1H NMR (DMSO-d_6, 500 MHz): 8.72(*s*, 1H); 8.28 (2H, m), 7.92 (1H, d, *J* = 16 Hz), 7.87 (1H, bs), 7.74 (1H, d, *J* = 16 Hz), 7.72 (1H, bs), 7.63 (1H, d, *J* = 3.6 Hz), 6.71 (1H, dd, *J* = 1.6 and 3.6 Hz). M+ at *m/z*: −243. Anal. Calcd for $C_{13}H_9NO_4$: C,64.20; H,3.73; N,5.76; O, 26.31. Found: C,63.88; H,3.41; N,6.11.

*1-(2-Furyl)-3-(2, 5-dimethoxyphenyl) prop-2-en-1-one (**20**)*

Yield 86%. Mp 54–56°C. I.R. (KBr, cm^{-1}): 1583, 1646. ^1H NMR (CD_3OD, 200 MHz) 8.16 (1H, d, *J* = 15.9 Hz, H-3), 7.88 (1H, bs), 7.62 (1H, d, *J* = 15.9 Hz), 7.56 (1H, bs), 7.43 (1H, m), 7.13 (2H, m), 6.72 (1H, dd, *J* = 1.6 and 3.6 Hz), 3.88 (6H, s). M+ at *m/z*: −258. Anal. Calcd for $C_{15}H_{14}O_4$: C,69.76; H,5.46; O, 24.78. Found: C,69.55; H,5.08.

*1-(2-Furyl)-3-(3, 4, 5-tri methoxy phenyl)-prop-2-en-1-one (**21**)*

Yield 69%. Mp 149–151°C. I.R. (KBr, cm^{-1}): 1600, 1655. ^1H NMR (CD_3OD, 200 MHz): 7.87 (1H, s), 7.78 (1H, d, *J* = 15.7 Hz), 7.63 (1H, d, *J* = 3.6 Hz), 7.55 (1H, d, *J* = 15.7 Hz), 7.08 (2H, s), 6.71 (1H, dd, *J* = 1.6 and 3.6 Hz), 3.91 (6H, s), 3.81 (3H, s). M+ at *m/z*: −288. Anal. Calcd for $C_{16}H_{16}O_5$: C,66.66; H,5.59; O, 27.75. Found: C,65.28; H,5.80.

*1-(2-Furyl)-3-(3,4-dimethoxyphenyl)-prop-2-en-1-one (**22**)*

Yield 72%. Mp 109–112°C. I.R. (KBr, cm^{-1}): 1597, 1657. ^1H NMR (CD_3OD, 200 MHz): 7.85 (1H, bs), 7.81 (1H, d, *J* = 14.6 Hz), 7.46 (4H, m), 7.02 (1H, d, *J* = 8.2 Hz), 6.71 (1H, dd *J* = 1.6 and 3.5 Hz), 3.92 (3H, s), 3.89 (3H, s). M+ at *m/z*: −258. Anal. Calcd for $C_{15}H_{14}O_4$: C,69.76; H,5.46; O, 24.78. Found: C,69.97; H,5.67.

*1-(2-Furyl)-3-(3-hydroxy-4-methoxyphenyl) prop-2-en-1-one (**23**)*

Yield 66%. Mp 144–145°C. I.R. (KBr, cm^{-1}): 1604, 1666, 3386. ^1H NMR ($CDCl_3$, 200 MHz): 7.80 (*d*, 1H, *J* = 15.7 Hz), 7.65(*bs*, 1H), 7.29(*m*, 3H), 7.15(*dd*, 1H), 6.88(*d*, 1H), 6.59(*dd*, 1H), 3.95(*s*, 3H). M+ at *m/z*: −244. Anal. Calcd for $C_{14}H_{12}O_4$: C,68.85; H,4.95; O, 26.20. Found: C,68.97; H,4.64.

*1-(2-Furyl)-3-(2,6-dichlorophenyl) prop-2-en-1-one (**24**)*

Yield 86%. Mp 94–96°C. I.R. (KBr, cm^{-1}): 1604, 1657. ^1H NMR ($CDCl_3$, 200 MHz) 7.87 (1H, bs), 7.81 (1H, d, *J* = 15.9 Hz), 7.63 (1H, d, *J* = 3.6 Hz), 7.55 (3H, m), 7.31 (1H, d, *J* = 15.9 Hz), 6.71 (1H, dd, *J* = 1.6 and 3.5 Hz). M+ at *m/z*: −265. Anal. Calcd for $C_{13}H_8Cl_2O_2$: C,58.46; H,3.02; O, 11.98. Found: C,58.10; H,3.36.

*3-phenyl-1-(1H-pyrrol-2-yl)-propenone (**25**)*

Yield: 71%. Mp 195–197°C. I.R. (KBr, cm^{-1}): 1599, 1643, 3444. ^1H NMR (CD_3OD, 200 MHz) 7.76 (2H, bs), 7.45 (1H, d, *J* = 15.4 Hz), 7.24–7.40 (5H, m), 7.19 (1H, d, *J* = 15.4 Hz), 6.32 (1H, dd, *J* = 2.4 and 3.8 Hz). M+ at *m/z*: −197. Anal. Calcd for $C_{13}H_{11}NO$: C,79.16; H,5.62; N,7.10; O, 8.11. Found:C,79.40; H,5.26; N,6.79.

*3-(4-nitro-phenyl)-1-(1H-pyrrol-2-yl)-propenone (**26**)*

Yield: 75%. Mp 205–207°C. I.R. (KBr, cm^{-1}): 1340, 1543, 1599, 1643, 3335. ^1H NMR (CD_3OD, 200 MHz) 8.29 (2H, d, *J* = 8.8 Hz), 7.79 (2H, d, *J* = 8.8 Hz), 7.76 (2H, bs), 7.34 (1H, d, *J* = 15.2 Hz), 7.19 (1H, d, *J* = 15.2 Hz), 6.34 (1H, dd, *J* = 2.4 and 3.8 Hz). M+ at *m/z*: −242. Anal. Calcd for $C_{13}H_{10}N_2O_3$: C,64.46; H,4.16; N,11.56; O, 19.82. Found: C,64.06; H,4.52; N,11.20.

*3-(3-nitrophenyl)-1-(1H-pyrrol-2-yl)-propenone (**27**)*

Yield: 77%. Mp 204–206°C. I.R. (KBr, cm^{-1}): 1340, 1543, 1601, 1653, 3340. ^1H NMR (DMSO-d_6, 200 MHz): 8.72 (1H, s), 8.34 (2H, t), 7.92 (1H, dd, *J* = 16 Hz), 7.74 (1H, dd, *J* = 16 Hz), 7.72 (1H, t, *J* = 8.5 Hz), 7.48 (1H, bs), 7.21 (1H, bs), 6.31 (1H, bs), M+ at *m/z*: −242. Anal. Calcd for $C_{13}H_{10}N_2O_3$: C,64.46; H,4.16; N,11.56; O, 19.82. Found: C,64.76; H,3.85; N,11.95.

*3-(2, 4-dichloro-phenyl)-1-(1H-pyrrol-2-yl)-propenone (**28**)*

Yield: 83%. Mp 172–174°C. I.R. (KBr, cm^{-1}): 1596, 1654, 3334. ^1H NMR ($CDCl_3$, 200 MHz) 8.13 (*d*,1H,

J = 15.6 Hz), 7.69 (1H, d, J = 8.6 Hz), 7.47 (1H, d, J = 1.9 Hz), 7.30 (3H, m), 7.10 (1H, d, J = 15.6 Hz), 6.37 (1H, bs). M+ at *m/z*: −265. Anal. Calcd for $C_{13}H_9Cl_2NO$: C,58.67; H,3.41; N,5.26; O, 6.01. Found: C,58.31; H,3.01; N,4.86.

3-(2, 3-dimethoxy-phenyl)-1-(1H-pyrrol-2-yl)-propenone ***(29)***

Yield: 71%. Mp 107–109°C. I.R. (KBr, cm^{-1}): 1230, 1581, 1647, 3342. ^1H NMR ($CDCl_3$, 200 MHz): 8.11 (1H, d, J = 15.9 Hz), 7.42 (1H, d, J = 15.9 Hz), 7.28 (2H, m), 7.10 (2H, dd, J = 8.2 Hz), 6.96 (1H, d, J = 8.2 Hz), 6.35 (1H, bs), 3.89 (6H, s). M+ at *m/z*: −257. Anal.Calcd for $C_{15}H_{15}NO_3$: C,70.02; H,5.88; N,5.88; O, 18.66. Found: C,70.34; H,5.65; N,5.48.

3-(2, 3-dichloro-phenyl)-1-(1H-pyrrol-2-yl)-propenone ***(30)***

Yield: 92%. Mp 193–195°C. I.R. (KBr, cm^{-1}): 1579, 1645, 3330. ^1H NMR (CD_3OD, 200 MHz) 7.55 (*d*, 1H, J = 15.6 Hz,H-2), 8.06 (*d,* 1H, J = 15.9 Hz, H-3), 7.55 (*d*, 1H, J = 15.6 Hz), 7.23 (1H, m), 7.16 (4H, m), 6.32 (*dd*,1H, dd, J = 2.6 and 3.7 Hz). M+ at *m/z*: −265. Anal. Calcd for $C_{13}H_9Cl_2NO$: C,58.67; H,3.41; N,5.26; O, 6.01. Found: C,58.27; H,3.01; N,5.52.

3-(2, 6-dichloro-phenyl)-1-(1H-pyrrol-2-yl)-propenone ***(31)***

Yield: 94%. Mp 162–164°C. I.R. (KBr, cm^{-1}): 1579, 1655, 3340. ^1H NMR (CD_3OD, 200 MHz): 7.87 (1H, d, J = 15.9 Hz), 7.75 (1H, bs), 7.55 (3H, m), 7.31 (1H, d, J = 15.9 Hz), 7.17 (1H, m), 6.32 (1H, dd, J = 2.4 and 3.8 Hz). M+ at *m/z*: −265. Anal.Calcd for $C_{13}H_9Cl_2NO$: C,58.67;H,3.41; N,5.26; O, 6.01. Found: C,59.03; H,3.68; N,4.86.

Biology

Cytotoxic activity

The effect of compounds **4–31** on the growth of cancer cell lines was evaluated according to the procedure adopted by the National Cancer Institute for in vitro anticancer drug screening that uses the protein-binding dye sulforhodamine B to estimate cell growth. Briefly, cells in their log phase of growth were harvested, counted and seeded (104 cells/well in 100 ml medium) in 96-well microtitre plates. After 24 h of incubation at 37°C and 5% CO_2 to allow cell attachment, cultures were treated with varying concentrations (0.1–100 μM) of test samples made with 1:10 serial dilutions. Four replicate wells were set up for each experimental condition. Test samples were left in contact with the cells for 48 h under the same conditions. Thereafter, cells were fixed with 50% chilled TCA and kept at 4°C for 1 h, washed and air-dried. Cells were stained with sulforhodamine B dye. The adsorbed dye was dissolved in Tris-buffer and the plates were gently shaken for 10 min on a mechanical shaker. The optical density (OD) was recorded on ELISA reader at 540 nm. The cell growth was calculated by subtracting mean OD value of the respective blank from the mean OD value of experimental set. Percentage of growth in the presence of test material was calculated considering the growth in the absence of any test material as 100% and in turn percent growth inhibition in presence of test material was calculated (Monks *et al.,* 2005; Skehan *et al.*, 1990).

Antimicrobial activity

Compounds were tested against seven reference microbial strains. The standard microbial strains were procured from the Institute of Microbial Technology, Chandigarh, India. Antibacterial and antifungal activity of the compounds were carried out by the disc diffusion method, (1) against bacterial strains, *Staphylococcus aureus* (MTCC 96), *Bacillus subtilis* (MTCC 2451), *Pseudomonas aeruginosa* (MTCC 2642), *Escherichia coli* (MTCC 82), *Salmonella typhi* (MTCC 1251) and two fungal strains; *Aspergillus niger* (MTCC 1344), *Candida albicans* (MTCC 3018). The antimicrobial activity of synthesized compound was determined by observing the zone of inhibition in comparison to the standard antibiotic (Amoxicillin and Gentamycin) disc. Test compounds were dissolved in DMSO to make a stock solution of 1 mg/ml. The fresh sub culture of strains in normal saline was added to the sterile assay medium (Nutrient agar) at 40–45°C and mixed well. The medium was poured into each of the petridishes. Sterile discs of diameter 6 mm were placed on the medium. 20 μl of each test solution was added to the previously marked discs and the media was allowed to stand for 5 min. The petridishes were kept aside for 1 h and then incubated at 37°C for 24 h. Zone of inhibition was measured and the average of the three readings was calculated. DMSO was kept as negative control. The activity was compared with standard antibiotics discs. The antifungal activity was carried in the same way. The fresh sub culture were inoculated in Saboraud Dextrose agar at 28°C for 48 h and compared with Fluconazole as standard. The MIC of compounds was determined by serial tube dilution method. Different dilutions of test compounds were made from stock solution and were tested to get the MIC. 1 ml nutrient

broth was taken in each test tube and 20 µl of standard strains were added to previously marked test tubes.

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