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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF NOVEL CHALCONE DERIVATIVES OF IMIDAZOLONES

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ABSTRACT

A series of six 4-arylidene-2-phenyl-1-(4-(3-phenylacryloyl)phenyl)-1*H*-imidazol-5(4*H*)-ones (8a-f) have been synthesized by condensation of 1-(4-acetylphenyl)-4-arylidene-2-phenyl-1*H*-imidazol-5(4*H*)-ones (7a-e) with different aryl aldehydes (4a, 4c, 4f). The structures of the newly synthesized compounds were characterized by FT-IR, ^{1}H NMR, ^{13}C NMR and Mass spectral studies. All the final compounds synthesized were screened for their antimicrobial and antioxidant activities. 8a, 8d showed potent antibacterial activity whereas all the titled compounds showed highest antifungal activity and 8b showed excellent antioxidant activity.

KEYWORDS:Imidazolones, Chalcones, Antimicrobial activity, Antioxidant activity

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INTRODUCTION

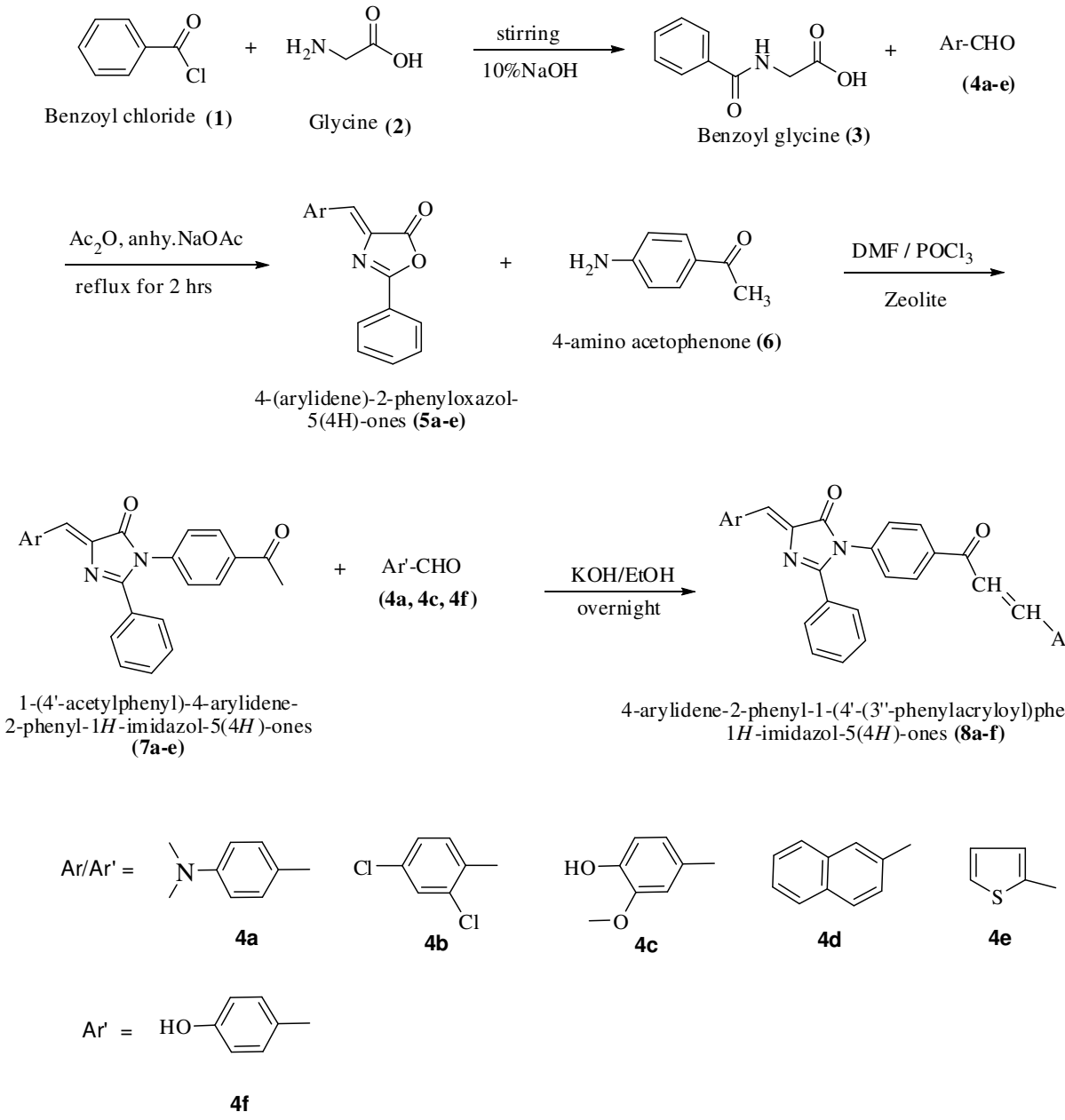
The synthesis of heterocyclic compounds has always drawn the attention of chemists over the years, mainly because of their important biological properties. As an important member of the five-membered ring heterocycles, imidazole moiety is present in a wide range of naturally occurring molecule. Compounds with imidazole moiety have many pharmaceutical activities. Diverse biological activities such as potent antibacterial activity, anti-inflammatory, anti-tubercular and antiviral activities have been found to be associated with 5-imidazolone derivatives. Recently, 1,2,4-trisubstituted-5-imidazolones have been reported to possess Mono Amino Oxidase [MAO] inhibitory and anticonvulsant activities[1-7]. Chalcones display interesting biological activities, including cytotoxic, anticancer and antimicrobial activities. The effect of chalcone analogues as cell cycle blockers, antimitotic, anti-infective, anti-inflammatory, antimalarial, antiviral, antifungal, insecticidal and cardiovascular agents[8-22]. From this point of view, the objective of the present work is to prepare new derivatives of chalcone linked imidazolones. Hence the present communication comprises the synthesis of 4-arylidene-2-phenyl-1-(4-(3-phenylacryloyl) phenyl-1*H*-imidazol-5(4*H*)-ones (8a-f). The synthetic approach is outlined in Scheme-1.

MATERIALS AND METHODS

All the chemicals were of AR grade and were obtained from Sigma–Aldrich and Merck. Melting points (m. p.) were determined in open capillaries on Opti-Melt automated melting point system and are uncorrected. The purity of the compounds was routinely checked by thin layer chromatography (TLC) with silica gel F_{254} (Merck) with visualization by UV-light. The compounds are purified by using column chromatography on silica gel (60-120 mesh). The instruments used for obtaining the spectroscopic data were: OPTIZEN3220 UV-Visible spectrophotometer, FT-IR spectrophotometer SHIMADZU-435, ^{1}HNMR ($CDCl_3$, Avance300 MHz), ^{13}CNMR ($CDCl_3$, Inova 75 MHz). Mass spectral analysis using electrospray ionization (ESI) experiments were performed using a quadrupole time-of-flight mass spectrometer (QSTAR XL, Applied Biosystems/MDS Sciex, Foster City, CA, USA), equipped with an ESI source.

Chemistry

In the present study we have linked the chalcone pharmacophore with biologically active imidazolone moiety that were expected to have antimicrobial and antioxidant activities. 4-(arylidene)-2-phenyloxazol-5(4*H*)-ones (5a-e) on reaction with *p*-amino acetophenone (6) in DMF/$POCl_3$ yielded 1-(4-acetylphenyl)-4-arylidene-2-phenyl-1*H*-imidazol-5(4*H*)-ones (7a-e). This on further reaction with aryl aldehydes (4a, 4c, 4f) produced 4-arylidene-2-phenyl-1-(4-(3-phenylacryloyl) phenyl)-1*H*-imidazol-5(4*H*)-ones (8a-f). The synthetic pathway for the preparation of chalcone linked imidazolones is shown in Scheme-1.



Scheme-1
Synthesis of Compounds (8a-f)

General procedure for the synthesis of Benzoyl glycine (3) and 4-(arylidene)-2-phenyloxazol-5(4H)-ones (5a-e)

Benzoyl glycine (3) was synthesized by treating glycine (2) with benzoyl chloride (1) in presence of Sodium hydroxide. This on condensation with aryl aldehydes (4a-e) results in the formation of 4-(arylidene)-2-phenyloxazol-5(4*H*)-ones (5a-e) [23].

General procedure for the synthesis of 1-(4-acetylphenyl)-4-arylidene-2-phenyl-1H-imidazol-5(4H)-ones (7a-e)

DMF-$POCl_3$ reagent was prepared by slow addition of anhydrous DMF (5mL) to $POCl_3$ (1.96 mmol) with stirring at 0°C for 45 minutes. To this complex oxazolones (5a-e) (0.01M), *p*-amino acetophenone (6), (0.01M), catalytic amounts of (Y-H) Zeolite were added and refluxed for 2 h. Completion of the reaction was monitored by TLC. The contents of the beaker were poured in ice-

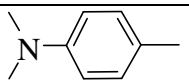
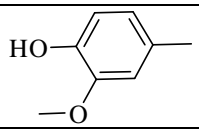
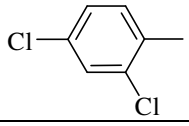
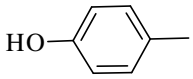
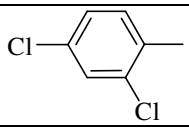
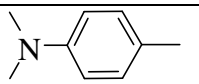
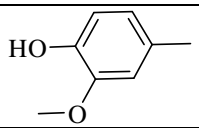
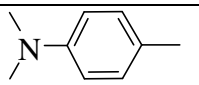
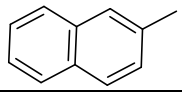
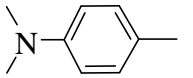
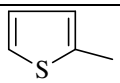
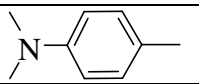
cold water and kept without shaking for a few minutes to settle down the formed product. The separated solid was filtered, washed with cold water followed by methanol. Purification of the compounds was done by column chromatography.

General procedure for the synthesis of 4-arylidene-2-phenyl-1-(4-(3-phenylacryloyl) phenyl)-1H-imidazol-5(4H)-ones (8a-f).

A mixture of 1-(4-acetylphenyl)-4-arylidene-2-phenyl-1H-imidazol-5(4H)-ones (7a-e) (0.01M) and aryl aldehydes (4a, 4c, 4f) (0.01M) were dissolved in ethanolic NaOH. The reaction mixture was kept overnight. Completion of the reaction was monitored by TLC. The separated solid was filtered, washed with cold water followed by methanol. Purification of the compounds was done by column chromatography.

Table-1

Physical-Chemical data of 4-arylidene-2-phenyl-1-(4-(3-phenylacryloyl) phenyl)-1H-imidazol-5(4H)-ones (8a-f).

Compound	Ar	Ar[1]	M.F	Colour	Yield(%)	M. P (°C)
8a			$C_{34}H_{29}N_3O_4$	Brick red	68	271-272
8b			$C_{31}H_{20}Cl_2N_2O_3$	Yellow	65	252-254
8c			$C_{33}H_{25}Cl_2N_3O_2$	Brick red	72	262-264
8d			$C_{34}H_{29}N_3O_4$	Brick red	68	276-277
8e			$C_{37}H_{29}N_3O_2$	Brick red	75	272-273
8f			$C_{31}H_{25}N_3O_2S$	Brick red	73	243-244

Spectroscopic analysis

1-(4-acetylphenyl)-4-(4-(dimethylamino)benzylidene)-2-phenyl-1H-imidazol-5(4H)-one (7a)

IR (KBr, cm^{-1}): 3134 (Ar-H str), 2896 (aliphatic-CH str), 1753 (C=O), 1065 (C-N str); ^{1}H NMR (300 MHz, $CDCl_3$, δ/ppm) : 2.20 (s, 3H, -C<u>H</u>$_3$), 3.20 (s, 6H, -N(C<u>H</u>$_3$)$_2$), 6.62 (m, 7H, Ar-<u>H</u>), 7.20 (s, 1H, Ar-<u>H</u>), 7.65 (m, 6H, Ar-<u>H</u> & Ar-C<u>H</u>=); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm): 27.51, 41.36, 106.40, 109.52, 116.76, 120.52, 125.79, 127.38, 128.58, 132.21, 142.00, 153.93, 166.08, 169.67, 198.51; ESI-MS (m/z): 410 $(M+1)^+$; Elemental analysis: calcd. C, 76.26; H, 5.66; N, 10.26; found: C, 76.22; H, 5.63; N, 10.23; HRMS calcd. For $C_{26}H_{24}N_3O_2$ $(M+1)^+$: 410.1790, found 410.1788.

1-(4-acetylphenyl)-4-(2,4-dichlorobenzylidene)-2-phenyl-1H-imidazol-5(4H)-one (7b)

IR (KBr, cm^{-1}): 3187 (Ar-H str), 2776 (aliphatic-CH str), 1675 (C=O), 1099 (C-N str); ^{1}H NMR (300 MHz, $CDCl_3$, δ/ppm) : 2.5 (s, 3H, -C<u>H</u>$_3$), 7.02 (m, 7H, Ar-<u>H</u>), 7.20 (s, 1H, Ar-<u>H</u> & Ar-C<u>H</u>=), 7.48 (m, 8H, Ar-<u>H</u>), 7.48 (d, 2H, Ar-<u>H</u>); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm): 26.44, 109.00, 116.92, 120.73, 125.82, 127.53, 128.29, 128.35, 129.40, 130.22, 131.82, 135.88, 144.46, 153.83, 166.49, 169.88, 198.54; ESI-MS (m/z): 435 $(M+1)^+$.

1-(4-acetylphenyl)-4-(4-hydroxy-3-methoxybenzylidene)-2-phenyl-1H-imidazol-5(4H)-one (7c)
IR (KBr, cm^{-1}): 3176 (Ar-H str), 2826 (aliphatic-CH str), 1756 (C=O), 1028 (C-N str); ^{1}H NMR (300 MHz, $CDCl_3$, δ/ppm) : 2.50 (s, 3H, -C<u>H</u>$_3$), 3.92 (s, 3H, -OC<u>H</u>$_3$), 6.62 (m, 7H, Ar-<u>H</u>), 7.28 (m, 3H, Ar-<u>H</u>), 7.51 (s, 1H, Ar-C<u>H</u>=), 7.76 (s, 6H, Ar-<u>H</u>), 7.98 (s, 3H, Ar-<u>H</u>), 9.20 (s, 1H, -O<u>H</u>); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm): 26.11, 56.23, 110.08, 116.93, 117.38, 121.11, 123.20, 125.53, 126.08, 126.16, 127.56, 129.91, 131.07, 133.67, 143.85, 153.03, 153.68, 161.46, 166.93, 169.93, 198.24; ESI-MS (m/z): 412 $(M)^+$.
1-(4-acetylphenyl)-4-(naphthalen-2-ylmethylene)-2-phenyl-1H-imidazol-5(4H)-one (7d)
IR (KBr, cm^{-1}): 3164 (Ar-H str), 2906 (aliphatic-CH str), 1718 (C=O), 1095 (C-N str); ^{1}H NMR (300 MHz, $CDCl_3$, δ/ppm): 2.50 (s, 3H, -C<u>H</u>$_3$), 6.82 (d, 2H, Ar-<u>H</u>), 7.20 (d, 2H, Ar-<u>H</u>), 7.50 (m, 9H, Ar-<u>H</u> & Ar-C<u>H</u>=), 7.90 (m, 4H, Ar-<u>H</u>); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm): 26.29, 109.00, 109.17, 116.92, 120.64, 120.73, 125.82, 127.53, 128.29, 128.35, 131.23, 139.05, 144.46, 153.83, 164.54, 169.69, 198.42; ESI-MS (m/z): 417 $(M+1)^+$.
1-(4-acetylphenyl)-2-phenyl-4-(thiophen-2-ylmethylene)-1H-imidazol-5(4H)-one (7e)
IR (KBr, cm^{-1}): 3316 (Ar-H str), 2784 (aliphatic-CH str), 1790 (C=O), 1082 (C-N str); ^{1}H NMR (300 MHz, $CDCl_3$, δ/ppm) : 2.50 (s, 3H, -C<u>H</u>$_3$), 6.75 (s, 1H, Ar-<u>H</u>), 6.92 (s, 1H, Ar-<u>H</u>), 7.24 (s, 2H, Ar-<u>H</u> & Ar-C<u>H</u>=), 7.45 (s, 2H, Ar-<u>H</u>), 7.60 (s, 5H, Ar-<u>H</u>), 7.92 (t, 3H, Ar-<u>H</u>); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm): 27.51, 106.40, 109.52, 116.76, 120.52, 125.79, 127.38, 128.58, 131.76, 136.83, 142.00, 166.08, 167.19, 198.51; ESI-MS (m/z): 373 $(M+1)^+$.
4-(4-(dimethylamino)benzylidene)-1-(4-(3-(4-hydroxy-3-methoxyphenyl)acryloyl)phenyl)-2-phenyl-1H-imidazol-5(4H)-one (8a)
IR (KBr, cm^{-1}): 3395.00 (Ar-OH str), 2998.50 (Ar-H str), 2920.10 (aliphatic-CH str), 1697.28 (C=O str), 1651.92 (CH=CH str), 1073.12 (C=N str); ^{1}H NMR (300 MHz, $CDCl_3$, δ/ppm) : 3.12 (s, 6H, -N(C<u>H</u>$_3$)$_2$), 3.80 (s, 3H, -OC<u>H</u>$_3$), 6.98 (m, 4H, Ar-<u>H</u>), 7.29 (m, 10H, Ar-<u>H</u> & Ar-C<u>H</u>=), 7.82 (m, 5H, Ar-<u>H</u>), 9.83 (s, 1H, Ar-O<u>H</u>); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm): 40.31, 56.78, 110.34, 116.92, 120.76, 125.76, 128.38, 19.48, 132.21, 144.41, 153.89, 163.24, 166.49, 189.23; ESI-MS (m/z): 544 $(M+1)^+$.
4-(2,4-dichlorobenzylidene)-1-(4-(3-(4-hydroxyphenyl)acryloyl)phenyl)-2-phenyl-1H-imidazol-5(4H)-one (8b)
IR (KBr, cm^{-1}): 3433.93 (Ar-OH str), 3057.15 (Ar-H str), 2926.86 (aliphatic-CH str), 1648.75 (C=O str), 1597.94 (CH=CH str), 1067.33 (C=N str); ^{1}H NMR (300 MHz, $CDCl_3$, δ/ppm) : 6.80 (m, 6H, Ar-<u>H</u>), 7.23 (s, 10H, Ar-<u>H</u> & Ar-C<u>H</u>=), 7.83 (t, 3H, Ar-<u>H</u>), 9.85 (s, 1H, Ar-O<u>H</u>); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm): 107.57, 116.77, 120.95, 125.88, 127.82, 127.91, 134.91, 135.88, 141.36, 150.69, 153.50, 153.67, 163.24, 169.67, 189.00; ESI-MS (m/z): 538 $(M)^+$.
4-(2,4-dichlorobenzylidene)-1-(4-(3-(4-(dimethylamino)phenyl)acryloyl)phenyl)-2-phenyl-1H-imidazol-5(4H)-one (8c)
IR (KBr, cm^{-1}): 3374.50 (Ar-H str), 2926.06 (aliphatic-CH str), 1734.02 (C=O str), 1599.25 (CH=CH str), 1044.82 (C=N str); ^{1}H NMR (300 MHz, $CDCl_3$, δ/ppm) : 3.02 (s, 6H, -N(C<u>H</u>$_3$)$_2$), 6.81 (m, 3H, Ar-<u>H</u>), 7.18 (m, 5H, Ar-<u>H</u> & Ar-C<u>H</u>=), 7.29 (s, 1H, Ar-<u>H</u>), 7.45 (m, 7H, Ar-<u>H</u>), 6.70 (s, 1H, Ar-<u>H</u>),8.18 (d, 2H, Ar-<u>H</u>); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm): 41.21, 110.34, 116.92, 120.76, 125.76, 127.62, 128.38, 129.48, 132.21, 144.41, 153.89, 163.24, 166.49, 189.38; ESI-MS (m/z): 566 $(M+1)^+$.
1-(4-(3-(4-(dimethylamino)phenyl)acryloyl)phenyl)-4-(4-hydroxy-3-methoxybenzylidene)-2-phenyl-1H-imidazol-5(4H)-one (8d)
IR (KBr, cm^{-1}): 3424.5 (Ar-OH str), 2924.81(aliphatic-CH str), 1648.38 (C=O str), 1591.64 (CH=CH str), 1098.24 (C=N str); ^{1}H NMR (300 MHz, $CDCl_3$, δ/ppm) : 3.04 (s, 6H, -N(C<u>H</u>$_3$)$_2$), 3.88 (s, 3H, -OC<u>H</u>$_3$), 6.93 (m, 5H, Ar-<u>H</u>), 7.53 (m, 6H, Ar-<u>H</u> & Ar-C<u>H</u>=), 7.82 (m, 7H, Ar-<u>H</u>), 8.08 (s, 1H, Ar-<u>H</u>), 9.83 (s, 1H, Ar-O<u>H</u>); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm): 40.31, 56.78, 110.34, 116.92, 120.76, 125.76, 127.62, 128.38, 129.48, 132.21, 144.41, 153.89, 163.24, 166.49, 189.23; ESI-MS (m/z): 544 $(M+1)^+$.
1-(4-(3-(4-(dimethylamino)phenyl)acryloyl)phenyl)-4-(naphthalen-2-ylmethylene)-2-phenyl-1H-imidazol-5(4H)-one (8e)

IR (KBr, cm^{-1}): 3020 (Ar-H str), 2929.55 (aliphatic-CH str), 1600.02 (C=O str), 1519.12 (CH=CH str), 1069.00 (C-N str); ^{1}H NMR (300 MHz, $CDCl_3$, δ/ppm) : 3.18 (s, 6H, -N($C\underline{H}_3$)$_2$), 6.80 (t, 3H, Ar-H), 7.08 (m, 6H, Ar-H & Ar-C<u>H</u>=), 7.31 (m, 3H, Ar-H), 7.48 (m, 5H, Ar-H), 7.70 (s, 3H, Ar-H), 8.18 (s, 3H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm): 41.78, 67.45, 97.24, 110.19, 114.78, 116.64, 120.97, 123.36, 125.15, 126.51, 126.90, 127.59, 128.32, 128.56, 129.69, 131.84, 132.31, 138.97, 143.45, 153.18, 153.71, 167.45, 168.78, 186.97; ESI-MS (m/z): 548 $(M+1)^+$.

1-(4-(3-(4-(dimethylamino)phenyl)acryloyl)phenyl)-2-phenyl-4-(thiophen-2-ylmethylene)-1H-imidazol-5(4H)-one (8f)

IR (KBr, cm^{-1}): 3378.46 (Ar-H str), 2985.74 (aliphatic-CH str), 1737.64 (C=O str), 1640.02 (CH=CH str), 1047.42 (C=N str); ^{1}H NMR (300 MHz, $CDCl_3$, δ/ppm) : 3.15 (s, 6H, -N($C\underline{H}_3$)$_2$), 7.18 (m, 3H, Ar-H & Ar-C<u>H</u>=), 7.30 (s, 3H, Ar-H), 7.41 (s, 1H, Ar-H), 7.52 (s, 7H, Ar-H), 8.15 (m, 5H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm): 41.65, 106.40, 109.52, 116.76, 120.52, 125.79, 127.38, 127.51, 128.58, 129.34, 131.76, 135.93, 143.00, 164.40, 170.19, 189.51; ESI-MS (m/z): 505 $(M+1)^+$.

Biological activity

Titled compounds were tested for their *invitro* antimicrobial activity against gram positive bacteria *B. subtilis* MTCC 441, *S. aureus* MTCC 96, gram negative bacteria *E. coli* MTCC 443, *P. vulgaris* MTCC1771and the yeast *C. albicans* MTCC183 strains by using filter paper disc method for the zone of inhibition and MIC was determined by the broth micro dilution method. All the novel compounds were screened for antioxidant activity by DPPH (2, 2-diphenyl-1-picrylhydrazyl) method.

Antimicrobial activity

i) Disc diffusion assay

The synthesized compounds were tested for their antimicrobial (antibacterial and antifungal) activities by disc-diffusion method[24] using Mueller– Hinton medium for bacteria and the same medium with 4% glucose for fungi. In the disc-diffusion method, sterile paper discs (Ø5 mm) impregnated with compound dissolved in dimethylsulfoxide (DMSO) at concentrations of 100 µg/mL were used. Discs containing DMSO were used as control. The microorganism cultures were spread over the following appropriate media: Mueller–Hinton agar for *B. subtilis, S. aureus, E. coli, P. vulgaris* andSabouraud's agar for the yeast-like fungi (*C. albicans*) in Petri dishes. Then the paper discs impregnated with the solutions of the compound tested were placed on the surface of the media inoculated with the microorganism. The plates were incubated at 35°C/ 24 h for the microorganism cultures. After incubation, the growth inhibition zones around the discs were observed, indicating that the examined compound inhibits the growth of microorganism[25-26]. Each assay in this experiment was repeated three times. Benzyl Pencillin and Fluconazole were used as standard drugs. Results were interpreted in terms of the diameter of the inhibition zone and MIC as µg/mL was shown in Table-2.

ii) Micro dilution assays

The minimal inhibitory concentration (MIC) values for all tested compounds, were determined by using the microdilution broth method. The inocula of microorganisms were prepared from 24 h broth cultures and suspensions were adjusted to 0.5 McFarland standard turbidity. The test compounds dissolved in DMSO were first diluted to the highest concentration (1mg/mL) to be tested[26]. Then serial twofold dilutions were made in concentration ranges from 31.25 µg/mL to 1 mg/mL in 10 mL sterile tubes. A prepared suspension of the standard microorganisms was added to each dilution in a 1:1 ratio. Growth (or its lack) of microorganisms was determined visually after incubation for 24 h at 37°C. The lowest concentration at which there was no visible growth (turbidity) was taken as the MIC[27]. Benzyl Pencillin and Fluconazole were used as standard drugs for comparison in the antimicrobial studies. Control experiments using DMSO were done. The presented results were obtained from three independent measurements[28].

Antioxidant activity

DPPH Free radical Scavenging Activity

DPPH solution (0.004% w/v) was prepared in 95% methanol. All the test compounds (8a-f) were mixed with 95% methanol to prepare the stock solutions (10 mg/100 mL or 100 µg/mL). 2ml, 4ml, 6ml, 8ml & 10ml of this solution were taken in five test tubes & the final volume was made up to 10 mL whose concentration was then20 µg/mL, 40 µg/mL, 60 µg/mL, 80 µg/mL & 100 µg/mL respectively. Freshly prepared DPPH solution was added in each of these test tubes and after 10 min, the absorbance was taken at 517 nm using a spectrophotometer. Ascorbic acid was used as a reference standard[29-30].

% Scavenging of the DPPH free radical was measured using the following equation

$$\% \text{ DPPH radical-scavenging} = \frac{(\text{Absorbance of control} - \text{Absorbance of test Sample})}{(\text{Absorbance of control})} \times 100$$

Results of % DPPH scavenging activity of the titled compounds were given in Table-3.

RESULTS AND DISCUSSIONS

Chemistry

The key precursor 4-(arylidene)-2-phenyloxazol-5(4*H*)-ones (5a-e) required for the synthesis of target compounds was obtained by the reaction of Benzoyl glycine (3) with aryl aldehydes (4a-e). The key intermediates of 1-(4-acetylphenyl)-4-arylidene-2-phenyl-1*H*-imidazol-5(4*H*)-ones (7a-e) were obtained by the reaction of 4-(arylidene)-2-phenyloxazol-5(4*H*)-ones (5a-e) with *p*-amino acetophenone (6) in the presence of DMF/$POCl_3$. This complex was used for intramolecular cyclization and cyclo dehydration of imidazolones (7a-e). Earlier imidazolones have been prepared by heating a mixture of 5-oxazolone derivatives, aromatic amines in presence of pyridine for 10-15 h and yields of imidazolones were very poor[31]. In the present work, imidazolones formed at a faster rate in excellent yields. This method was found to be a better alternative for the synthesis of imidazolones. IR Spectrum of 1-(4-acetylphenyl)-4-arylidene-2-phenyl-1*H*-imidazol-5(4*H*)-ones (7a-e) showed absorption bands between 3134-3316 cm^{-1}, 2776-2906 cm^{-1}, 1675-1790 cm^{-1}, 1028-1099 cm^{-1} due to aromatic C-H, aliphatic C-H, C=O and C=N functional group stretching vibrations respectively. ^1H NMR spectra of compounds (7a-e) showed singlet between δ 2.20-2.50 due to -C<u>H</u>$_3$ protons, singlet between δ 3.20 due to –N(C<u>H</u>$_3$)$_2$ protons, multiplets between δ 6.62-8.00 integrates for aromatic protons. In the ^{13}C NMR spectra of the compounds (7a-e) the chemical shift values of carbon atoms appeared between: δ 26.11-27.51 (aliphatic, -<u>C</u>H$_3$), δ41.36 (aliphatic, –N(<u>C</u>H$_3$)$_2$, 7a), δ56.23 (-O<u>C</u>H$_3$, 7c), δ164.54-166.93 (cyclic imine, -<u>C</u>=N), δ167.19-169.93 (cyclic amide, -<u>C</u>ONH), δ198.24-198.54 (aliphatic, -<u>C</u>=O). The mass spectra of (7a-e) are in conformity with the proposed structures. The reaction of (7a-e) with arylal dehydes (4a, 4c, 4f) in the presence of ethanolic NaOH resulted in the formation of titled compounds i. e., 4-arylidene-2-phenyl-1-(4-(3-phenylacryloyl) phenyl)-1*H*-imidazol-5(4*H*)-ones (8a-f) in good yields (65-75%). Physical data of these compounds were reported in Table-1. IR Spectra of compounds (8a-f) showed absorption bands in the region of 2998-3378 cm^{-1} due to aromatic-CH stretching, 2920-2985 cm^{-1} due to aliphatic C-H stretching, 1600-1737 cm^{-1} due to -C=O functional group, 1519-1651 cm^{-1} due to –CH=CH- stretching and 1044-1098 cm^{-1} due to C=N stretching, indicating the evidence for the formation of the titled compounds (8a-f). ^1H NMR spectra of compounds (8a, 8c, 8d, 8e, 8f) showed singlet between δ 3.02- 3.18 due to –N(C<u>H</u>$_3$)$_2$ protons, (8a, 8d) showed singlet between δ 3.80-3.88 due to –OCH$_3$ group, for all the compounds (8a-f) multiplets between δ 6.80-8.18 due to aromatic and arylidene protons (Ar-<u>H</u> & Ar-C<u>H</u>=) and for compounds 8a**,** 8b, 8d singlet between δ 9.83-9.85 was observed due to Ar-O<u>H</u>. In the ^{13}C NMR

spectra of compounds (8a, 8c, 8d, 8e, 8f) the chemical shift values of carbon atoms appeared between: δ 40.31-41.78 due to aliphatic –N(CH_3)$_2$, for 8a, 8d compounds δ56.78 due to –OCH_3, δ 163.24-167.45 due to cyclic imine -C=N, δ 166.49-170.19 due to cyclic amide –CONH and δ 186.97-189.51 due to aliphatic -C=O functionality clearly confirms the final products formation (8a-f). Moreover, the mass spectrum of (8a-f) agrees with the molecular weight of the proposed structures.

Biological activity

The results of the antibacterial and antifungal effects of the newly synthesized compounds are reported as MIC and zone of inhibition (mm). Compounds 8a, 8d, 8f showed potent antibacterial activity whereas 8b, 8c, 8e markable activity**.** All the compounds (8a-f) were found to be highly effective against *candida albicans* strain. DPPH Scavenging activity results displayed that title compounds (8a-f) are able to show marked antioxidant activity. Compound 8b showed excellent antioxidant activity, whereas 8a, 8c, 8d exhibited good activity and 8e, 8f were moderately active. These have showed a comparable antioxidant potential with the standard ascorbic acid. Remaining compounds 8e, 8f have showed a moderate activity.

Table-2
Antimicrobial activity of synthesized compounds (8a-f)

Compound	Antimicrobial activity				
	Zone of Inhibition in mm (MIC in µg/mL)				
	B. s	S. a	E. c	P. v	C. a
8a	16 (62.5)	15 (125)	12 (250)	11 2(50)	16 (62.5)
8b	14 (125)	11 (250)	08 (500)	11 (250)	14 (125)
8c	13 (125)	12 (250)	10 (500)	11 (250)	13 (125)
8d	15 (125)	17 (62.5)	12 (250)	11 (250)	16 (62.5)
8e	08 (500)	09 (500)	07 (500)	07 (500)	15 (125)
8f	17 (62.5)	15 (125)	14 (62.5)	10(500)	15 (125)
Benzyl Pencillin	16 (2)	17 (2)	12 (2)	13 (2)	-
Fluconazole	-	-	-	-	21 (8)

B.s: B. subtilis MTCC 441, S.a: S. aureus MTCC 96, E.c: E. coli MTCC 443, P.v: P. vulgaris MTCC 1771, C.a: C. albicans MTCC183

Table-3
Antioxidant activity of the synthesized compounds (8a-f)

Compound	DPPH scavenging activity (%)					
	20 µg/mL	40 µg/mL	60 µg/mL	80 µg/mL	100 µg/mL	IC_{50}(µg/mL)
8a	36.13±0.2	46.10±0.6	51.92±0.1	69.46±0.5	73.46±0.6	0.046
8b	46.76±0.1	56.65±0.2	69.82±0.5	76.81±0.3	86.13±0.2	0.028
8c	38.00±0.6	45.11±0.4	52.92±0.4	66.31±0.7	70.48±0.3	0.056
8d	35.02±0.3	47.11±0.4	50.87±0.6	59.29±0.4	72.15±0.7	0.058
8e	32.15±0.7	37.63±0.6	42.34±0.4	56.91±0.6	66.25±0.4	0.067
8f	31.51±0.1	39.89±0.6	45.86±0.4	51.39±0.5	63.70±0.4	0.075
Ascorbic acid	55.12±0.2	65.08±0.2	75.26±0.2	85.82±0.4	93.74±0.2	0.010

Ascorbic acid (reference antioxidant compounds) was used as a standard. The scavenging capacities were represented as percentage inhibition and values were the means of three replicates (mean±SD, n=3).

CONCLUSION

In the present study, an easy and useful method to synthesize biologically active chalcone-linked imidazolone derivatives as an expected pharmacophore has been presented. Antibacterial, antifungal and antioxidant ability of these compounds were evaluated. The identified analogs in particular 8a, 8d showed potent antibacterial and all the titled compounds showed highest antifungal activity, can serve as novel templates for microbial infection chemotherapy. Compound 8b showed excellent antioxidant activity. Since analogs 8a, 8b, 8c are showing promising results, studies to establish their *in vivo* efficacy and safety are being planned for further development.

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