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ORIGINAL ARTICLE

Synthesis and Antimicrobial Studies of Novel (E)-3-(3-(4-FLUORO-3-Methylphenyl)-1-Phenyl-1H-Pyrazol-4-YL)-1-(Substituted Aryl) PROP-2-EN-1-ONE

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ABSTRACT
A new series of (E)-3-(3-(4-Fluoro-3-methylphenyl)-1-phenyl-1H-pyrazol-4-yl)-1-(substituted aryl)prop-2-en-1-one (6a-6j) were designed and synthesized by Clasaein-Schmidt condensation of 3-(4-fluoro-3-methylphenyl)-1-phenylpyrazol-4-carboxaldehyde (4a) and aromatic ketones (5a-5j). The synthesized compounds were characterized by FT-IR, ^{1}H-NMR, Mass spectroscopy and bases of elemental analysis. The agar-cup plate method was employed for antimicrobial screening. From the study, it was revealed that compounds 6f and 6j showed increased potency. From the results, it was revealed that the synthesized compounds with electron releasing groups showed the most potent activity compared to that of standard drug.
Keywords: *Chalcones, Antimicrobial activity, Pyrazole, Docking studies.*

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INTRODUCTION

The multidrug-resistant Gram-positive and Gram-negative species like *Aeromonas hydrophila*, *Yersinia enterocolitica, Listeria monocytogenes* and *Staphylococcus aureus* are responsible for bacterial infections such as food poisoning, salmonellosis and diarrhea [1]. Due to the advent of newer microbes with increased resistance towards the existing drugs, there is a growing need for antimicrobial agents with novel structural features and potency [2]. Resistance towards β-lactam antibiotics is due to the production of multiple inducible, chromosomally encoded β-lactames [3]. The development of nitrogen-containing five-member heterocycles, Pyrazole derivatives have been studied extensively because of their ready accessibility diverse chemical reactivity and variety of industrial applications. They are well known, representing a class of compounds of great importance of pyrazole derivatives that possess biological activities like antidepressant [4], anticonvulsant [5], antimicrobial [6], analgesic [7] activities and also serve as human acyl-CoA: cholesterol acyltransferase inhibitors.

Considering the findings above and in continuation of our efforts for the development of antimicrobial agents, we undertook the design and synthesis of some novel prototypes which possess advantage of the pharmacophores of pyrazole and chalcone in single molecular backbone

MATERIAL AND METHODS

The organic solvents such as methanol, ethanol, acetone, chloroform, n-hexane and ethyl acetate were of spectral grade and used as such without further purification. Some of the solvents were purchased from the local distributors of S.D. Fine Chem. Ltd, Mumbai, India.

All the chemicals used in the synthesis were obtained from standard commercial sources. 4-fluoro-3-methyl-acetophenone was purchased from Avra chemicals. Reactions were monitored by TLC using silica

gel-G (Merck grade) as the adsorbent and the solvent systems are indicated at appropriate places. Silica gel (100-200 mesh, Merck grade) has been used for column chromatography. Each fraction of 100 ml was collected. The separations of the compounds were checked on TLC under UV lamp and also by spraying the plates with 10 % sulphuric acid.

All the melting points were determined in open capillaries, using Boitus digital melting point apparatus, expressed in ºC and are uncorrected. The 1H NMR spectra of the compounds were recorded on Bruker Ultra Shield (400 MHz) NMR spectrometer in CDCl3 using tetramethylsilane [(CH3)4Si] as the internal standard. Chemical shift (δ) are expressed in ppm.

The Mass spectra were obtained on a JEOL-SX-102 instrument using electron impact ionization. All the IR spectra were recorded in KBr pellets on a Jasco FT-IR 410 spectrometer. Elemental analyses were performed on a Perkine Elmer model 240c analyzer and were within ±0.4% of the theoretical values.

EXPERIMENTAL

Preparation of 3-(4-fluoro-3-methylphenyl)-1-phenyl-1H-pyrazole-4-carbaldehyde (4a)

A mixture of the 4-fluoro-3-methylacetophenone (10 mmol) and phenyl hydrazine (10 mmol) was reflexed at 75º C temperature, in the presence of few drops of H_2SO_4, for 6hrs. The reaction mixture was poured into water and the solid product was collected by filtration followed by washing with ethanol. The crude product was then recrystallized from acetic acid to give the corresponding hydrazone derivative **3a.**

Phosphorus oxychloride (20 mL, 20 mmol) was added drop wise with stirring to dimethyformamide (150 mL) at 0–5°C. Then the synthesized hydrazone derivative **3a** (20 mmol) was added portion-wise with continuous stirring, refluxed for 6hrs, left overnight at room temperature, poured onto ice-cold water and neutralized with ammonium hydroxide solution (5%). The formed precipitate was filtered, dried and recrystallized from acetic acid to give the 3-(4-fluoro-3-methylphenyl)-1-phenyl pyrazol-4-carboxaldehyde (**4a**) (*Insuasty B, Tigreros A, Orozco F, Quiroga J, Abonía R, Nogueras M, Sanchez A, and Cobo J. (2010) 'Synthesis of novel pyrazolic analogues of chalcones and their 3-aryl-4-(3-aryl-4,5-dihydro-1H-pyrazol-5-yl)-1-phenyl-1H-pyrazole derivatives as potential antitumor agents.', Bioorganic & medicinal chemistry, 18(14), pp. 4965–4974*)

Preparation of (E)-3-(3-(4-fluoro-3-methylphenyl)-1-phenyl-1H-pyrazol-4-yl)-1-(substituted aryl) prop-2-en-1-one (6a-6j)

To a solution of 3-(4-fluoro-3-methylphenyl)-1-phenylpyrazol-4-carboxaldehyde (**4a**) (1.0 mmol), substituted acetophenone (**5a-5j**) (1.0 mmol), ethanol (30 mL) and a pellet of $LiOH_2$ was added. The reaction mixture was stirred at ambient temperature until formation of a precipitate. The solid obtained was isolated by filtration, washed and recrystallized from a (1:1) EtOH/DMF mixture.

(E)-3-(3-(4-fluoro-3-methylphenyl)-1-phenyl-1H-pyrazol-4-yl)-1-(4-fluorophenyl)prop-2-en-1-one (6a)

Yield = 78 %, m.p. 135-137°C. IR (KBr) cm^{-1}: 3070 (CH=CH), 2985 (Ar-CH), 2944 (CH_3-CH), 1727 (C=O), 1675 (C=N), 1586 (C=C), 1233 (C-F). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ ppm: 8.56-8.68 (d, 1H, CH=CH-CO), 8.09 (s, 1H, C_5-H of pyrazole), 7.86-7.98 (d, 1H, CH=CH-CO), 6.88-7.79 (m, 12H, Ar-CH), 2.18 (s, 3H, CH_3). EI-MS *m/z*: 400 (M^+). *Anal*. Calcd for $C_{25}H_{18}F_2N_2O$: C, 74.99; H, 4.53; N, 7.00; Found: C, 74.91; H, 4.50; N, 6.90.

(E)-3-(3-(4-fluoro-3-methylphenyl)-1-phenyl-1H-pyrazol-4-yl)-1-(4-methoxyphenyl)prop-2-en-1-one (6b)

Yield = 78 %, m.p. 150-152 °C. IR (KBr) cm^{-1}: 3068 (CH=CH), 3024 (Ar-CH), 2955 (CH_3-CH), 1694 (C=O), 1642 (C=N), 1607 (C=C), 1227 (C-F) & 1024 (C-O-C). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ ppm: 8.86-8.96 (d, 1H, CH=CH-CO), 8.71 (s, 1H, C_5-H of pyrazole), 8.40-8.52 (d, 1H, CH=CH-CO), 7.05-8.10 (m, 11H, Ar-CH), 3.63 (s, 3H, OCH_3), 2.48 (s, 3H, CH_3). EI-MS *m/z*: 412 (M^+). *Anal*. Calcd for $C_{26}H_{21}FN_2O_2$: C, 75.71; H, 5.13; N, 6.79; Found: C, 75.64; H, 5.07; N, 6.71.

(E)-1-(2-chloro-6-hydroxyphenyl)-3-(3-(4-fluoro-3-methylphenyl)-1-phenyl-1H-pyrazol-4-yl)prop-2-en-1-one (6c)

Yield = 75 %, m.p. 133-135 °C. IR (KBr) cm^{-1}: 3358 (OH), 3074 (CH=CH), 3014 (Ar-CH), 2950 (CH_3-CH), 1734 (C=O), 1670 (C=N), 1614 (C=C), 1206 (C-F) & 930 (C-Cl). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ ppm: 8.83-8.92 (d, 1H, CH=CH-CO), 8.55 (s, 1H, C_5-H of pyrazole), 8.34-8.40 (d, 1H, CH=CH-CO), 7.22-8.06 (m, 12H, Ar-CH), 5.04 (s, 1H, OH), 2.24 (s, 3H, CH_3). EI-MS *m/z*: 432 (M^+). *Anal*. Calcd for $C_{25}H_{18}ClFN_2O$: C, 69.37; H, 4.19; N, 6.47; Found C, 69.29; H, 4.12; N, 6.40.

(E)-3-(3-(4-fluoro-3-methylphenyl)-1-phenyl-1H-pyrazol-4-yl)-1-(4-hydroxyphenyl)prop-2-en-1-one (6d)

Yield = 70 %, m.p. 145-147 °C. IR (KBr) cm^{-1}: 3374 (OH), 3045 (CH=CH), 3021 (Ar-CH), 2967 (CH_3-CH), 1714 (C=O), 1671 (C=N), 1629 (C=C) & 1210 (C-F). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ ppm: 9.03-9.12 (d, 1H, CH=CH-CO), 8.75 (s, 1H, C_5-H of pyrazole), 8.47-8.60 (d, 1H, CH=CH-CO), 7.15-8.12 (m, 12H, Ar-CH), 5.14

(s, 1H, OH), 2.62 (s, 3H, CH_3). EI-MS *m/z*: 398 (M^+). *Anal*. Calcd for $C_{25}H_{19}FN_2O_2$: C, 75.36; H, 4.81; N, 7.03; Found: C, 75.30; H, 4.75; N, 7.00.

(E)-3-(3-(4-fluoro-3-methylphenyl)-1-phenyl-1H-pyrazol-4-yl)-1-(4-nitrophenyl)prop-2-en-1-one(6e)

Yield = 72 %, m.p. 162-164 °C. IR (KBr) cm^{-1}: 3068 (CH=CH), 3044 (Ar-CH), 2983 (CH_3-CH), 1702 (C=O), 1643 (C=N), 1631 (C=C), 1534 & 1320 (NO_2) & 1246 (C-F). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ ppm: 9.13-9.30 (d, 1H, CH=CH-CO), 8.91 (s, 1H, C_5-H of pyrazole), 8.59-8.70 (d, 1H, CH=CH-CO), 6.83-7.88 (m, 12H, Ar-CH), 2.29 (s, 3H, CH_3). EI-MS *m/z*: 427 (M^+). *Anal*. Calcd for $C_{25}H_{18}FN_3O_3$: C, 70.25; H, 4.24; N, 9.83; Found: 70.20; H, 4.21; N, 9.75.

(E)-1-(3,4-dimethoxyphenyl)-3-(3-(4-fluoro-3-methylphenyl)-1-phenyl-1H-pyrazol-4-yl) prop-2-en-1-one (6f)

Yield = 68 %, m.p. 148-150 °C. IR (KBr) cm^{-1}: 3075 (CH=CH), 3026 (Ar-CH), 2955 (CH_3-CH), 1728 (C=O), 1654 (C=N), 1605 (C=C), 1220 (C-F) & 1028 (C-O-C). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ ppm: 9.18-9.28 (d, 1H, CH=CH-CO), 8.92 (s, 1H, C_5-H of pyrazole), 8.45-8.56 (d, 1H, CH=CH-CO), 7.12-8.09 (m, 11H, Ar-CH), 3.89 (s, 3H, OCH_3), 3.38 (s, 3H, OCH_3) 2.62 (s, 3H, CH_3). EI-MS *m/z*: 442 (M^+). *Anal*. Calcd for $C_{27}H_{23}FN_2O_3$: C, 73.29; H, 5.24; N, 6.33; Found: C, 73.26; H, 5.20; N, 6.25.

(E)-3-(3-(4-fluoro-3-methylphenyl)-1-phenyl-1H-pyrazol-4-yl)-1-(p-tolyl)prop-2-en-1-one (6g)

Yield = 65 %, m.p. 128-130 °C. IR (KBr) cm^{-1}: 3075 (CH=CH), 3024 (Ar-CH), 2916 (CH_3-CH), 1735 (C=O), 1644 (C=N), 1608 (C=C), 1221 (C-F). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ ppm: 8.59-8.68 (d, 1H, CH=CH-CO), 8.26 (s, 1H, C_5-H of pyrazole), 7.74-7.87 (d, 1H, CH=CH-CO), 6.92-7.86 (m, 12H, Ar-CH), 2.54 (s, 3H, CH_3), 2.10 (s, 3H, CH_3). EI-MS *m/z*: 396 (M). *Anal*. Calcd for $C_{26}H_{21}FN_2O$: C, 78.77; H, 5.34; N, 7.07; Found: C, 78.71; H, 5.30; N, 7.02;

(E)-1-(4-chlorophenyl)-3-(3-(4-fluoro-3-methylphenyl)-1-phenyl-1H-pyrazol-4-yl)prop-2-en-1-one (6h)

Yield = 80 %, m.p. 125-127 °C. IR (KBr) cm^{-1}: 3085 (CH=CH), 3022 (Ar-CH), 2959 (CH_3-CH), 1708 (C=O), 1659 (C=N), 1613 (C=C), 1213 (C-F) & 819 (C-Cl). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ ppm: 8.48-8.59 (d, 1H, CH=CH-CO), 8.19 (s, 1H, C_5-H of pyrazole), 7.76-7.89 (d, 1H, CH=CH-CO), 6.68-7.71 (m, 12H, Ar-CH), 2.10 (s, 3H, CH_3). EI-MS *m/z*: 418 (M^{+2}), 416 (M^+). *Anal*. Calcd for $C_{25}H_{18}ClFN_2O$: C, 72.03; H, 4.35; N, 6.72; Found: C, 71.97; H, 4.30; N, 6.62.

(E)-1-(benzo[d][1,3]dioxol-5-yl)-3-(3-(4-fluoro-3-methylphenyl)-1-phenyl-1H–pyrazol-4-yl)prop-2-en-1-one (6i)

Yield = 70 %, m.p. 170-172 °C. IR (KBr) cm^{-1}: 3080 (CH=CH), 3024 (Ar-CH), 2952 (CH_3-CH), 1717 (C=O), 1655 (C=N), 1620 (C=C), 1206 (C-F) & 1013 (C-O-C). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ ppm: 9.07-9.22 (d, 1H, CH=CH-CO), 8.84 (s, 1H, C_5-H of pyrazole), 8.50-8.62 (d, 1H, CH=CH-CO), 6.91-8.12 (m, 11H, Ar-CH), 5.69 (s, 2H, CH_2 of benzodioxol), 2.46 (s, 3H, CH_3). EI-MS *m/z*: 426 (M^+). *Anal*. Calcd for $C_{26}H_{19}FN2O_3$: C, 73.23; H, 4.49; N, 6.57: Found: C, 73.19; H, 4.42; N, 6.53

(E)-1-(4-bromophenyl)-3-(3-(4-fluoro-3-methylphenyl)-1-phenyl-1H-pyrazol-4-yl)prop-2-en-1-one (6j)

Yield = 78 %, m.p. 141-143 °C. IR (KBr) cm^{-1}: 3081 (CH=CH), 3017 (Ar-CH), 2956 (CH_3-CH), 1735 (C=O), 1640 (C=N), 1622 (C=C), 1225 (C-F) & 788 (C-Br). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ ppm: 8.66-8.78 (d, 1H, CH=CH-CO), 8.07 (s, 1H, C_5-H of pyrazole), 7.81-7.94 (d, 1H, CH=CH-CO), 6.84-7.91 (m, 12H, Ar-CH), 2.31 (s, 3H, CH_3). EI-MS *m/z*: 462 (M^{+2}), 460 (M^+). *Anal*. Calcd for $C_{25}H_{18}BrFN_2O$: C, 65.09; H, 3.93; N, 6.07; Found: C, 65.04; H, 3.90; N, 6.01;

Antibacterial activity

The antibacterial activity of the test compounds (**6a-6j**) was investigated by agar-cup plate method (Rose and Miller, 1939). DMSO (dimethylsulfoxide) was used as a solvent and control. The solutions of the standard drug and test compounds were prepared so as to get a concentration of 1000 µg/mL. The antimicrobial activity of pyrazole substituted chalcones were tested and compared with standard (ampicillin) solution at three different concentrations i.e. 50 µg/mL, 100 µg/ mL and 150 µg/ mL. Bacterial strains were cultured over night at 37 °C in Mueller-Hintonsbroth. The following organisms were used

Gram positive bacteria

- *Bacillus cereuss* ATCC 11778
- *Staphylococcus epidermidiss* ATCC 155
- *Staphylococcus aureus* ATCC 9144

Gram negative bacteria

- *Pseudomonas aeruginosa* ATCC 2853
- *Escherichia coli* ATCC 25922
- *Klebsiella pneumonia* ATCC 11298

Antifungal activity

The antifungal activity of pyrazole substituted chalcones (**6a-6j**) were tested and compared with standard drug fluconazole at 50 µg/ mL (0.05 mL), 100 µg/smL (0.1 mL) and 150 µg/imL (0.15 mL) dose levels. The following organisms were used

- *Aspergillus niger* ATCC 9029
- *Aspergillus fumigatus* ATCC 46645

Antibacterial activity

Experimental Procedure

Nutrient agar (Hi-media) was dissolved and dispersed in 25 mL amounts in 100 mL conical flasks and was sanitized in an autoclave at 121º C (15 lbs/sq.in) for 20 minutes. The medium was inoculated at 1 % level utilizing 18 hrs old cultures of the test microbe referenced above, aseptically into clean Petri dishes and permitted to set at room temperature for around 30 minutes.

In a size of 6 inch petridishes, three cups of 8mm diameter at equal distance were made in each plate. The stock solution was prepared by dissolving 10mg of test sample (**6a-6j**) to DMSO in a 10 mL volumetric flask. From which 0.5 mL, 1 mL, and 1.5 mL is taken into 3 different 10 mL volumetric flask and diluted up to the mark with DMSO to form desired concentrations (50 µg, 100 µg, 150 µg). Similarly standard drug ampicilin is also prepared for 50 µg, 100 µg, 150 µg solutions are prepared and the solution was placed in the cups by means of sterile pipettes. For each test organisms one cup was filled with DMSO as a control. The plates thus prepared were left standing for 90 minutes in a refrigerator to allow the test solutions for diffusion. After incubation for 24 hrs at 37^0 C, the plates were examined for inhibition zones. The experiments were performed in duplicates and the average diameter of the zones of inhibition was measured and recorded.

Antifungal Activity

Experimental Procedure

Potato-dextrose-agar (Hi-media) was dissolved and distributed in 25 mL amounts in 100 mL conical flasks and was disinfected in an autoclave at 121º C (15 lbs/sq.in) for 20 minutes. The medium was inoculated at 1% level utilizing 18 hrs old cultures of the test microbes referenced above, aseptically in to clean Petri dishes and permitted to set at room temperature for around 30 minutes.

In a size of 6 inch petridishes, three cups of 8mm diameter at equal distance were made in each plate. The stock solution was prepared by dissolving 10mg of test sample (**6a-6j**) in DMSO in a 10 mL volumetric flask. From which 0.5 mL, 1 mL, and 1.5 mL is taken into 3 different 10 mL volumetric flask and diluted up to the mark with DMSO to form desired concentrations (50 µg, 100 µg, 150 µg). Similarly, standard drug flucanazole is also prepared for 50 µg, 100 µg, 150 µg solutions are prepared and the solution was placed in the cups by means of sterile pipettes. For each test organisms one cup was filled with DMSO as a control. The plates thus prepared were left standing for 90 minutes in a refrigerator to allow the test solutions for diffusion. After incubation for 24 hrs at 25^0 C, the plates were examined for inhibition zones. The experiments were performed in duplicates and the average diameter of the zones of inhibition was measured and recorded.

RESULTS AND DISCUSSION

Chemistry

The protocol for the synthesis of target compounds 6a-6j is shown in Scheme 1. In this study, a series of novel pyrazole substituted chalcone derivatives 6a–6j were synthesized by substituting various aromatic rings. Initially, 4-fluoro-3-methyl acetophenone 1a was treated with phenylhydrazine **2a** to obtain (E)-1-(1-(4-fluoro-3-methylphenyl) ethylidene)-2-phenylhydrazine 3a. Later, the obtained (E)-1-(1-(4-fluoro-3-methylphenyl) ethylidene)-2-phenylhydrazine 3a was subjected to cyclo-oxidation in presence of phosphoryl oxychloride, dimethyformamide and $NaHCO_3$ to produced 3-(4-fluoro-3-methylphenyl)-1-phenyl-1H-pyrazole-4-carbaldehyde 4a. In the succeeding step, compound 4a was treated with aromatic ketones (5a-5j) to yield the final compound (E)-3-(3-(4-fluoro-3-methylphenyl)-1-phenyl-1H-pyrazol-4-yl)-1-(substitutedaryl)prop-2-en-1-one (6a-6j).

Infrared (IR), nuclear magnetic resonance (NMR), mass spectra, and elemental analysis of the synthesized compounds are in accordance with the assigned structures. The IR spectra of all synthesized compounds showed some characteristic peaks indicating the presence of particular groups. The formations of intermediate chalcones (6a-6j) were confirmed by the presence of IR peak in the region of 1735 to 1694 cm^{-1} range (CH=CH-C=O). The ^1H NMR peak at δ 8.19 can be assign to the C_5-H of pyrazole ring. The presence of fluoro group in the chalcones was characterized by the appearance of a strong band in its IR spectrum at 1233 cm^{-1}. The presence of methyl group was confirmed by ^1H NMR peak at δ 2.13 ppm and IR peak in the region of 2944 cm^{-1}.

Antimicrobial activity

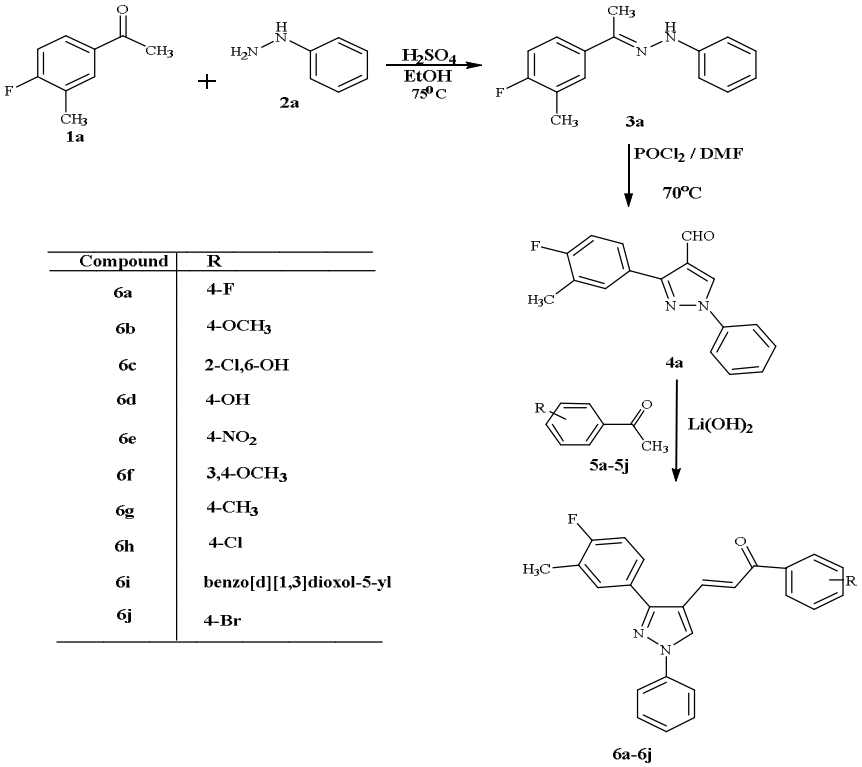
The *invitro* antimicrobial activity of title compounds **6a-6j** was analyzed by Cup plate method. A comparison of antimicrobial activity of the synthesized compounds with that of the standard drugs was effectively presented in Table 1. In order to control the sensitivity of the test organisms, activity of standard drugs (Ampicillin and Fluconazole) were determined in parallel experiments. From the screening information, it was uncovered that all the tested compounds indicated moderate to great microbial restraint.

From the obtained results, it was observed that the compound **6h** displayed similar activity like ampicillin against *S. aureus;* whereas rest of series displayed lesser activity. Compared to ampicillin, against *B. cereus* compounds **6h** and **6j** exhibited equal activity where as rest of the series exhibited slower activity. While others demonstrated lesser activity than standard against *S. epidermidis,* compounds **6h, 6d, 6e** and **6g** exhibited comparable activity as ampicillin. Compounds **6c** and **6e** showed the better activity whereas rest of the derivatives exhibited worse activity than standard drug against *E.coli*. Compounds **6e, 6c** and and **6j** showed the same activity as ampicillin, whereas rest of all compounds showed worse activity than standard against *P. aeruginosa*. All the derivatives had shown potent activity as that of standard drug ampicillin against *K. pneumonia* except **6h, 6g** and **6j.** Among the various tested derivatives, the compound **6h** displayed superior activity than rest of tested derivatives against all microorganisms except the gram negative bacteria.

The antifungal activities of the synthesized compounds (**6a-6j**) were challenged against *A. niger* and *A. fumigatus*. The title compounds exhibits varying degree of antifungal activity. None of the synthesized compounds displayed either equal/superior antifungal activity when compared to standard fluconazole against the tested fungi except **6h**. Compounds **6c and 6g** had displayed moderate antifungal activity; whereas rest of title compounds showed poor antifungal activity.

Structural activity relationship

In general, from the study it was found that compounds possessing electron withdrawing groups (6h, 6c and 6j) displayed better antimicrobial activity than compounds possessing electron donating groups (6b and 6f). Within electron donating/ withdrawing group compounds, the position of the group played important role while deciding the activity. Halogen substituted derivatives displayed potent activity when compared with that of standard drugs.



Compound	R
6a	4-F
6b	4-OCH_3
6c	2-Cl,6-OH
6d	4-OH
6e	4-NO_2
6f	3,4-OCH_3
6g	4-CH_3
6h	4-Cl
6i	benzo[d][1,3]dioxol-5-yl
6j	4-Br

Scheme 1. Synthesis of (E)-3-(3-(4-Fluoro-3-methylphenyl)-1-phenyl-1h-pyrazol-4-yl)-1-(substituted aryl)prop-2-en-1-one (6a-6j)

Table 1. Antimicrobial activity of chalcone derivatives (6a-6j)

Compound	Dose (µg/mL)	Antibacterial activity						Antifungal activity	
		Gram positive bacteria			Gram negative bacteria				
		S. aureus	*S. epidermidis*	*B. cereus*	*E. coli*	*P. aeruginosa*	*K. pneumoniae*	*A. niger*	*A. fumigatus*
6a	**50**	-	-	-	-	-	-	16	17
	100	-	14	-	12	14	12	18	20
	150	18	19	12	16	18	22	15	16
6b	**50**	-	-	-	-	-	10	-	-
	100	14	-	18	-	-	17	-	-
	150	18	10	20	-	11	22	9	-
6c	**50**	-	10	-	11	11	12	14	12
	100	10	14	9	15	16	15	20	18
	150	16	22	16	23	25	22	26	22
6d	**50**	-	15	-	-	-	10	-	-
	100	11	18	9	10	12	15	9	11
	150	16	23	14	16	19	21	16	18
6e	**50**	-	-	-	12	14	11	-	-
	100	11	10	12	14	16	15	10	11
	150	20	16	20	23	26	23	15	15
6f	**50**	-	-	-	-	-	-	-	-
	100	-	9	10	-	-	-	10	11
	150	13	14	16	14	12	12	16	19
6g	**50**	-	12	-	-	11	9	10	11
	100	12	16	11	9	14	14	16	15
	150	16	22	16	15	20	20	22	22
6h	**50**	12	14	13	-	12	13	15	16
	100	18	16	17	12	15	17	19	20
	150	26	25	24	18	20	21	26	24
6i	**50**	-	11	12	-	12	-	11	-
	100	10	14	16	15	18	12	17	10
	150	16	20	22	21	24	20	22	17
6j	**50**	10	-	11	12	-	11	12	12
	100	14	13	16	18	11	16	13	17
	150	22	20	21	22	18	19	19	22
Standard*	**50**	12	15	13	14	13	16	15	14
	100	18	19	18	19	18	20	22	20
	150	24	26	27	26	25	25	28	26
Control	-	-	-	-	-	-	-	-	-

CONCLUSION

Compounds showed mild to good antibacterial and antifungal activities. From the SAR studies it was found that, electron withdrawing group substituted derivative exhibited better antimicrobial activity than electron donating group substituted analogs. Compound **6h** emerged out as the lead molecule with a broad spectrum antimicrobial activity.

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