

Regular Article

Novel 3-(substitutedbenzylideneamino)-5-methyl-1H-pyrazol-1-yl)(phenyl)methanone Derivatives Against Gram-positive, Gram-negative and fungal pathogenic strains

Deepthi. D. Kini^{*a}, Jessy Elizabeth Mathew^b

^aDepartment Pharmaceutical Chemistry, Karnataka college of pharmacy, Bangalore, Karnataka, India

^bDepartment Pharmaceutical Chemistry, Manipal college of pharmaceutical sciences, Manipal, Karnataka, India

*Corresponding author email: deepthikini@gmail.com

A series of novel 3-(substitutedbenzylideneamino)-5-methyl-1H-pyrazol-1-yl)(phenyl)methanone **P1-12** derivatives were synthesized. The chemical structures of the compounds were proved by means of their IR, ¹H-NMR, mass spectroscopic data and elemental analyses. The results showed that most of the synthesized compounds exhibited significant anti-bacterial and anti-fungal activities. Among the synthesized compounds **P2**, **P5**, **P8**, and **P9** exhibited most potent *in vitro* antimicrobial activity. On the basis of the microbial results, further insight into the structural requirements for targeting pyrazol-1-yl)(phenyl)methanone to develop potential new agents to combat treatment of pathogenic strains.

Keywords: pyrazole, Gram-positive, Gram-negative, fungal pathogenic strains

The clinical potential of microbial creation as therapeutic agents was first investigated by Pasteur and Joubert, who recorded their observation and speculation in 1877. The golden age of antibiotics began with the production of penicillin in 1941. The treatment of communicable diseases still leftovers an important and demanding problem because of amalgamation of factors including rising infectious diseases and the increasing number of multi-drug resistant microbial pathogens with particular relevance for bacteria and fungi (Tenover and McDonald 2005), (Roberts 2004). In this connection, we have found that, the pyrazole structure has been known to possess a broad spectrum of biological activities. Several research articles reported that pyrazole compounds possess many chemical, biological, medicinal and agricultural applications because of their adaptable and well recognized biological activities such as antimicrobial (Tanitame et al. 2004), (Bekhit and Abdel-Aziem 2004), (Tanitame et al. 2004), (Bekhit et al. 2008), antitumor (Park et al. 2005), antihistaminic (Yamashita et al. 2005) and antidepressant (Bailey et al. 1985). As documented in the literature, many pyrazole act as antimicrobial agents (Tanitame et al. 2004), (Liu et al. 2008), (Liu et al. 2008). Based on the above fact, we executed a series of compounds 3-(substitutedbenzylideneamino)-5-methyl-1H-pyrazol-1-yl)(phenyl)methanone **P1-12** containing pyrazole which could be effective for antimicrobial activity.

Materials and Methods

Materials

Synthetic starting material, reagents, and solvents were of analytical grade or of the highest quality commercially available. The chemicals were purchased from Aldrich Chemical Co., and Merck Chemical Co., Biotium, Inc., and were dried whenever necessary. The melting points were determined in open capillary tubes and are uncorrected. Infrared (IR) spectra were recorded with KBr pellets (ABB Bomem FT-IR spectrometer MB 104 ABB Limited, Bangalore, India). Proton nuclear magnetic resonance (^1H NMR) spectra (Bruker 400 NMR spectrometer, Mumbai, India) were recorded with tetramethylsilane as internal reference. Mass spectral data were recorded with a quadrupole mass spectrometer (Shimadzu GC MS QP 5000, Chennai, India), and microanalyses were performed using a *vario EL V300 elemental analyzer* (Analytensysteme GmbH, Chennai, India). The purity of the compounds was checked by TLC on pre-coated SiO_2 gel (HF₂₅₄, 200 mesh) aluminum plates (E. Merck). IR, ^1H -NMR, mass spectral data, and elemental analyses were consistent with the assigned structure.

Methods

Dissolve a 0.48g of the 5-methyl-1H-pyrazol-3-amine in a small quantity of absolute ethanol or methanol, and then excess quantity of benzaldehyde derivatives was added to the mixture. The ratio used was of 3:1 means the mole quantity of benzaldehyde to each 1 mole of the pyrazole compound. The reaction mixture refluxed at 80°C for 12h and the reaction completion monitored by TLC. After the 1st step product separation and purification the solubility of the product is checked by using different solvents. Followed by the product is dissolved in ether and the exactly equal mole quantity of acetyl chloride is added carefully dropwise with shaking then refluxed at 80-100°C for 2-3h to afford the final product 3-(substituted benzyldene amino)-5-methyl-1H-pyrazol-1-yl (phenyl) methanone **P1-12**

3-(2-fluorobenzyldeneamino)-5-methyl-1H-pyrazol-1-yl(phenyl)methanone (P1)

The compound was obtained as a solid; Yield: 67%; m.p. 174-176 °C IR cm^{-1} : 3112 (Aromatic-CH), 2942 (Alkane-CH), 1660 (Hetero-C=N), 1731 (C=O), 1012 (C-F). ^1H NMR (CDCl_3) δ (ppm): 7.82 (s, 1H; Alkene-CH), 7.12-7.41 (m, 9H; Ar-H), 6.92 (s, 1H; Pyrazole-CH), 2.69 (s, 3H; -CH₃). EI-MS m/z (M+2): 309 (calcd for $\text{C}_{18}\text{H}_{14}\text{FN}_3\text{O}$; 307.32). Anal. calcd for $\text{C}_{18}\text{H}_{14}\text{FN}_3\text{O}$; C, 70.35; H, 4.59; N, 13.67; Found C, 70.37; H, 4.53; N, 13.62.

3-(3-fluorobenzyldeneamino)-5-methyl-1H-pyrazol-1-yl(phenyl)methanone (P2)

The compound was obtained as a solid; Yield: 67%; m.p. 182-183 °C IR cm^{-1} : 3117 (Aromatic-CH), 2949 (Alkane-CH), 1653 (Hetero-C=N), 1729 (C=O), 1019 (C-F). ^1H NMR (CDCl_3) δ (ppm): 7.72 (s, 1H; Alkene-CH), 7.22-7.47 (m, 9H; Ar-H), 6.96 (s, 1H; Pyrazole-CH), 2.28 (s, 3H; -CH₃). EI-MS m/z (M+2): 309 (calcd for $\text{C}_{18}\text{H}_{14}\text{FN}_3\text{O}$; 307.32). Anal. calcd for $\text{C}_{18}\text{H}_{14}\text{FN}_3\text{O}$; C, 70.35; H, 4.59; N, 13.67; Found C, 70.34; H, 4.54; N, 13.66.

3-(4-fluorobenzyldeneamino)-5-methyl-1H-pyrazol-1-yl(phenyl)methanone (P3)

The compound was obtained as a solid; Yield: 67%; m.p. 162-164 °C IR cm^{-1} : 3118 (Aromatic-CH), 2918 (Alkane-CH), 1641 (Hetero-C=N), 1726 (C=O), 1072 (C-F). ^1H NMR (CDCl_3) δ (ppm): 7.75 (s, 1H; Alkene-CH), 7.31-7.42 (m, 9H; Ar-H), 6.71 (s, 1H; Pyrazole-CH), 2.52 (s, 3H; -CH₃). EI-MS m/z (M+2): 309 (calcd for $\text{C}_{18}\text{H}_{14}\text{FN}_3\text{O}$; 307.32). Anal. calcd for $\text{C}_{18}\text{H}_{14}\text{FN}_3\text{O}$; C, 70.35; H, 4.59; N, 13.67; Found C, 70.32; H, 4.52; N, 13.61.

3-(2-chlorobenzylideneamino)-5-methyl-1H-pyrazol-1-yl)(phenyl)methanone (P4)

The compound was obtained as a solid; Yield: 71%; m.p.165-167 °C IR cm⁻¹: 3117 (Aromatic-CH), 2949 (Alkane-CH), 1664 (Hetero-C=N), 1736 (C=O), 644 (C-Cl).

¹H NMR (CDCl₃) δ (ppm): 7.81 (s, 1H; Alkene-CH), 7.12-7.27 (m, 9H; Ar-H), 6.71 (s, 1H; Pyrazole-CH), 2.32 (s, 3H; -CH₃). EI-MS m/z (M+2): 325 (calcd for C₁₈H₁₄ClN₃O; 323.78).

Anal.calcd for C₁₈H₁₄ClN₃O; C, 66.77; H, 4.36; N, 12.98; Found C, 66.72; H, 4.35; N, 12.96.

3-(3-chlorobenzylideneamino)-5-methyl-1H-pyrazol-1-yl)(phenyl)methanone (P5)

The compound was obtained as a solid; Yield: 75%; m.p.175-176 °C IR cm⁻¹: 3122 (Aromatic-CH), 2942 (Alkane-CH), 1667 (Hetero-C=N), 1732 (C=O), 651 (C-Cl).

¹H NMR (CDCl₃) δ (ppm): 7.74 (s, 1H; Alkene-CH), 6.92-7.17 (m, 9H; Ar-H), 6.82 (s, 1H; Pyrazole-CH), 2.11 (s, 3H; -CH₃). EI-MS m/z (M+2): 325 (calcd for C₁₈H₁₄ClN₃O; 323.78).

Anal.calcd for C₁₈H₁₄ClN₃O; C, 66.77; H, 4.36; N, 12.98; Found C, 66.73; H, 4.33; N, 12.92.

3-(4-chlorobenzylideneamino)-5-methyl-1H-pyrazol-1-yl)(phenyl)methanone (P6)

The compound was obtained as a solid; Yield: 72%; m.p.185-187 °C IR cm⁻¹: 3128 (Aromatic-CH), 2927 (Alkane-CH), 1641 (Hetero-C=N), 1720 (C=O), 744 (C-Cl).

¹H NMR (CDCl₃) δ (ppm): 7.76(s, 1H; Alkene-CH), 6.96-7.19 (m, 9H; Ar-H), 6.85 (s, 1H; Pyrazole-CH), 4.44 (s, 1H; Alkene-CH), 2.17 (s, 3H; -CH₃). EI-MS m/z (M+2): 325 (calcd for C₁₈H₁₄ClN₃O; 323.78).

Anal.calcd for C₁₈H₁₄ClN₃O; C, 66.77; H, 4.36; N, 12.98; Found C, 66.72; H, 4.32; N, 12.94.

3-(2-bromobenzylideneamino)-5-methyl-1H-pyrazol-1-yl)(phenyl)methanone (P7)

The compound was obtained as a solid; Yield: 68%; m.p.163-165 °C IR cm⁻¹: 3129 (Aromatic-CH), 2931 (Alkane-CH), 1665 (Hetero-C=N), 1737 (C=O), 561 (C-Br).

¹H NMR (CDCl₃) δ (ppm): 7.81 (s, 1H; Alkene-CH), 7.12-7.67 (m, 9H; Ar-H), 6.91 (s, 1H; Pyrazole-CH), 2.37 (s, 3H; -CH₃). EI-MS m/z (M+2): 370 (calcd for C₁₈H₁₄BrN₃O; 368.23).

Anal.calcd for C₁₈H₁₄BrN₃O; C, 58.71; H, 3.83; N, 11.41; Found C, 58.73; H, 3.82; N, 11.44.

3-(3-bromobenzylideneamino)-5-methyl-1H-pyrazol-1-yl)(phenyl)methanone (P8)

The compound was obtained as a solid; Yield: 75%; m.p.167-169 °C IR cm⁻¹: 3132 (Aromatic-CH), 2937 (Alkane-CH), 1662 (Hetero-C=N), 1732 (C=O), 582 (C-Br).

¹H NMR (CDCl₃) δ (ppm): 7.87 (s, 1H; Alkene-CH), 7.15-7.69 (m, 9H; Ar-H), 6.93 (s, 1H; Pyrazole-CH), 2.31 (s, 3H; -CH₃). EI-MS m/z (M+2): 370 (calcd for C₁₈H₁₄BrN₃O; 368.23).

Anal.calcd for C₁₈H₁₄BrN₃O; C, 58.71; H, 3.83; N, 11.41; Found C, 58.75; H, 3.83; N, 11.41.

3-(4-bromobenzylideneamino)-5-methyl-1H-pyrazol-1-yl)(phenyl)methanone (P9)

The compound was obtained as a solid; Yield: 72%; m.p.166-168 °C IR cm⁻¹: 3118 (Aromatic-CH), 2926 (Alkane-CH), 1641 (Hetero-C=N), 1697 (C=O), 592 (C-Br).

¹H NMR (CDCl₃) δ (ppm): 7.85 (s, 1H; Alkene-CH), 7.11-7.64 (m, 9H; Ar-H), 6.46 (s, 1H; Pyrazole-CH), 2.35 (s, 3H; -CH₃). EI-MS m/z (M+2): 370 (calcd for C₁₈H₁₄BrN₃O; 368.23).

Anal.calcd for C₁₈H₁₄BrN₃O; C, 58.71; H, 3.83; N, 11.41; Found C, 58.73; H, 3.85; N, 11.47.

3-(2-nitrobenzylideneamino)-5-methyl-1H-pyrazol-1-yl)(phenyl)methanone (P10)

The compound was obtained as a solid; Yield: 67%; m.p.157-159 °C IR cm⁻¹: 3131 (Aromatic-CH), 2937 (Alkane-CH), 2255 (Aliphatic-C=N), 1551 (N-O), 1652 (Hetero-C=N), 1712 (C=O).

^1H NMR (CDCl_3) δ (ppm): 7.82 (s, 1H; Alkene-CH), 7.19-7.76 (m, 9H; Ar-H), 6.94 (s, 1H; Pyrazole-CH), 2.17 (s, 3H; $-\text{CH}_3$). EI-MS m/z (M^+): 334 (calcd for $\text{C}_{18}\text{H}_{14}\text{N}_4\text{O}_3$; 334.33). Anal.calcd for $\text{C}_{18}\text{H}_{14}\text{ClN}_3\text{O}$; C, 64.66; H, 4.22; N, 16.76; Found C, 64.61; H, 4.24; N, 16.72.

3-(3-nitrobenzylideneamino)-5-methyl-1H-pyrazol-1-yl)(phenyl)methanone (P11)

The compound was obtained as a solid; Yield: 70%; m.p.141-143 °C IR cm^{-1} : 3136 (Aromatic-CH), 1554 (N-O), 1656 (Hetero-C=N), 1719 (C=O).

^1H NMR (CDCl_3) δ (ppm): 7.97 (s, 1H; Alkene-CH), 7.29-7.71 (m, 9H; Ar-H), 6.67 (s, 1H; Pyrazole-CH), 2.43 (s, 3H; $-\text{CH}_3$). EI-MS m/z (M^+): 334 (calcd for $\text{C}_{18}\text{H}_{14}\text{N}_4\text{O}_3$; 334.33). Anal.calcd for $\text{C}_{18}\text{H}_{14}\text{ClN}_3\text{O}$; C, 64.66; H, 4.22; N, 16.76; Found C, 64.65; H, 4.24; N, 16.74.

3-(4-nitrobenzylideneamino)-5-methyl-1H-pyrazol-1-yl)(phenyl)methanone (P12)

The compound was obtained as a solid; Yield: 76%; m.p.179-181 °C IR cm^{-1} : 3118 (Aromatic-CH), 1519 (N-O), 1641 (Hetero-C=N), 1714 (C=O).

^1H NMR (CDCl_3) δ (ppm): 7.92 (s, 1H; Alkene-CH), 7.15-7.74 (m, 9H; Ar-H), 6.69 (s, 1H; Pyrazole-CH), 2.47 (s, 3H; $-\text{CH}_3$). EI-MS m/z (M^+): 334 (calcd for $\text{C}_{18}\text{H}_{14}\text{N}_4\text{O}_3$; 334.33). Anal.calcd for $\text{C}_{18}\text{H}_{14}\text{ClN}_3\text{O}$; C, 64.66; H, 4.22; N, 16.76; Found C, 64.63; H, 4.22; N, 16.71.

Antimicrobial Screening

All the synthesized compounds were screened for antibacterial and antifungal activities by paper disc diffusion technique. The antibacterial activity of the compounds were evaluated against four gram positive bacteria (*Staphylococcus aureus* ATCC 9144, *Staphylococcus epidermidis* ATCC 155, *Micrococcus luteus* ATCC 4698 and *Bacillus cereus* ATCC 11778) and three gram negative bacteria (*Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 2853 and *Klebsiella pneumoniae* ATCC 11298). The antifungal activities of the synthesized compounds were evaluated against two fungi (*Aspergillus niger* ATCC 9029 and *Aspergillus fumigatus* ATCC 2091).

Paper Disc Diffusion Technique

The sterilized (autoclaved at 120°C for 30 minutes) medium (40-50°C) was inoculated (1 mL/100 mL of medium) with the suspension (10^5cfu mL^{-1}) of the microorganism (matched to McFarland barium sulphate standard) and poured into a petri dish to give a depth of 3-4 mm. The paper impregnated with the test compounds ($\mu\text{g mL}^{-1}$ in dimethyl formamide) was placed on the solidified medium. The plates were pre-incubated for 1 h at room temperature and incubated at 37°C for 24 and 48 h for antibacterial and antifungal activities, respectively. Ciprofloxacin (Dr. Reddy's Laboratories, Batch No: IC666E04, India) and Ketoconazole (Wuhan Shengmao Corporation, Batch No: SBML/403, China) were used as standard for antibacterial and antifungal activities, respectively.

Minimum Inhibitory Concentration (MIC)

MIC of the compound was determined by agar streak dilution method. A stock solution of the synthesized compound ($100\ \mu\text{g mL}^{-1}$) in dimethylformamide was prepared and graded quantities of the test compounds were incorporated in specified quantity of molten sterile agar (nutrient agar for antibacterial activity and sabouraud dextrose agar medium for antifungal activity). A specified quantity of the medium (40-50°C) containing the compound was poured into a petri dish to give a depth of 3-4 mm and allowed to solidify. Suspension of the microorganism were prepared to contain approximately 10^5cfu mL^{-1} and applied to plates with

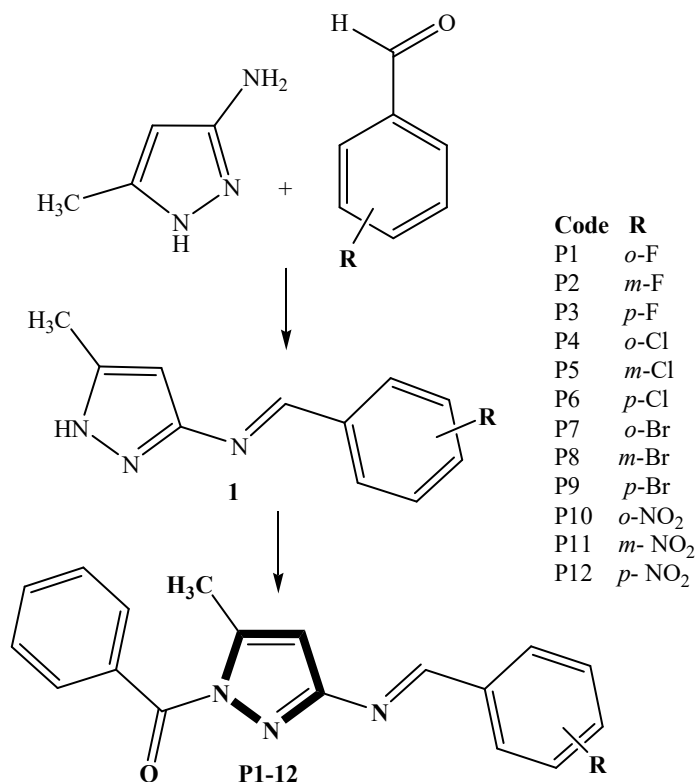
serially diluted compounds in dimethylformamide to be tested and incubated at 37°C for 24 h and 48 h for bacteria and fungi, respectively. The MIC was considered to be the lowest concentration of the test substance exhibiting no visible growth of bacteria or fungi on the plate.

Statistical Analysis

Student's *t*-test was used to determine a significant difference between the control.

Results and Discussion

Antimicrobial screening results of novel 3-(substituted benzylidene amino)-5-methyl-1H-pyrazol-1-yl) (phenyl) methanone **P1-12** derivatives exhibited moderate to significant activity. Among these, compound **P2**, **P5**, **P8**, and **P9** were found to possess significant antibacterial and antifungal activity when compared to standard drug Ciprofloxacin and Ketoconazole. Compounds **P3**, **P4**, **P6**, **P11** and **P12** displayed least antimicrobial activity whereas the remaining compounds **P1**, **P7** and **P10** showed moderate activity.



Scheme 1. The formation of 3-(substituted benzylideneamino)-5-methyl-1H-pyrazol-1-yl)(phenyl) methanone

The compounds 3-(3-fluorobenzylideneamino)-5-methyl-1H-pyrazol-1-yl)(phenyl)methanone **P2**, 3-(3-chlorobenzylideneamino)-5-methyl-1H-pyrazol-1-yl)(phenyl)methanone **P5**, 3-(3-bromobenzylideneamino)-5-methyl-1H-pyrazol-1-yl)(phenyl)methanone **P8** and 3-(4-bromobenzylideneamino)-5-methyl-1H-pyrazol-1-yl)(phenyl)methanone **P9**, were found to exhibit the highest antimicrobial activity against *S. aureus* (24, 24, 24 and 24 µg mL⁻¹), *S. epidermidis* (28, 24, 28 and 28 µg mL⁻¹), *M. luteus* (26, 23, 26 and 26 µg mL⁻¹), *B. cereus* (22, 21, 22

and 22 $\mu\text{g mL}^{-1}$), *E. coli* (27, 24, 27 and 27), *P. aeruginosa* (24, 22, 24 and 23 $\mu\text{g mL}^{-1}$), *K. pneumoniae* (26, 24, 26 and 26 $\mu\text{g mL}^{-1}$), *A. niger* (MIC: 22, 20, 22 and 21 $\mu\text{g mL}^{-1}$) and *A. fumigatus* (MIC: 23, 21, 23 and 22 $\mu\text{g mL}^{-1}$) respectively. The MIC range of the synthesized compounds was 9.1-14.5 $\mu\text{g mL}^{-1}$ and compounds were active against all the tested microorganisms with a range of MIC values for *S. aureus* (9.1-11.7 $\mu\text{g mL}^{-1}$), *S. epidermidis* (9.1-13.1 $\mu\text{g mL}^{-1}$), *M. luteus* (9.2-11.6 $\mu\text{g mL}^{-1}$), *B. cereus* (9.1-12.1 $\mu\text{g mL}^{-1}$), *E. coli* (9.8-12.7 $\mu\text{g mL}^{-1}$), *P. aeruginosa* (9.3-14.5 $\mu\text{g mL}^{-1}$), *K. pneumoniae* (9.2-12.6 $\mu\text{g mL}^{-1}$), *A. niger* (MIC: 9.3-11.7 $\mu\text{g mL}^{-1}$) and *A. fumigatus* (MIC: 10.2-12.4 $\mu\text{g mL}^{-1}$). On the basis of biological data, improvement in biological activity was observed with electronic effects and positions (*ortho*, *meta*, *para*) of the substituents. Considering the influence of electronic effects on the biological activities, electron withdrawing groups were introduced at 3rd position on the 5-methyl-1H-pyrazol-1-yl(phenyl)methanone ring. Different analogues with electron withdrawing groups were synthesized e.g. electron withdrawing fluorine, chlorine, bromine and nitro, *ortho*, *meta* and *para* positions on the benzylidene ring. The potent antimicrobial activity exhibited by the compounds may be due to the incorporation of electron withdrawing groups. It was observed that the electrons withdrawing *ortho*, *meta* and *para* substituted compounds showed increase in antimicrobial activity. The observed inhibition figures on the antimicrobial activity of the synthesized compounds were shown in **Figure. 1** The values for the antimicrobial studies of the compounds (**P1-12**) and the standard are represented in **Table 1, 2 and 3**.

Table 1. *In vitro* antimicrobial activities of the synthesized compounds **P1-12**

Zone of Inhibition in mm (MIC 100 $\mu\text{g/ml}$)				
Gram Positive Bacteria				
Compound	<i>S.a</i>	<i>S.e</i>	<i>M.l</i>	<i>B.c</i>
P1	20(11.7)	21(13.1)	22(11.3)	20(10.2)
P2	24(9.6)	28(9.2)	26(9.8)	22(9.6)
P3	22(13.2)	22(11.6)	21(11.2)	21(12.1)
P4	21(11.1)	22(10.4)	21(11.6)	20(11.7)
P5	24(9.9)	24(10.1)	23(10.7)	20(10.5)
P6	21(10.4)	21(14.4)	21(11.5)	21(11.4)
P7	20(10.1)	20(10.1)	20(10.7)	21(10.6)
P8	20(9.9)	21(11.2)	21(10.9)	20(11.1)
P9	24(9.1)	28(9.7)	26(9.2)	22(9.4)
P10	21(10.2)	20(10.3)	20(10.4)	21(10.2)
P11	21(10.1)	21(14.3)	21(11.2)	21(11.1)
P12	20(10.3)	20(10.2)	20(10.3)	21(10.7)
Ciprofloxacin	25	29	27	23
DMF	-	-	-	-

S.a- *Staphylococcus aureus*, **S.e-** *Staphylococcus epidermidis*, **M.l-** *Micrococcus luteus*
B.c- *Bacillus cereus*

Table 2. *In vitro* antimicrobial activities of the synthesized compounds **P1-12**

<i>Zone of Inhibition in mm (MIC 100µg/ml)</i>			
<i>Gram Negative Bacteria</i>			
<i>Compound</i>	<i>E.c</i>	<i>P.a</i>	<i>K.p</i>
P1	21(11.7)	21(10.6)	21(12.6)
P2	27(10.2)	24(9.3)	26(9.7)
P3	21(10.4)	21(14.5)	22(11.7)
P4	22(11.2)	21(10.4)	20(12.2)
P5	24(12.1)	22(10.7)	24(10.7)
P6	23(12.1)	21(11.5)	21(10.2)
P7	20(12.7)	21(12.5)	21(11.8)
P8	23(10.1)	21(10.4)	21(11.1)
P9	27(10.1)	24(9.5)	26(9.3)
P10	20(12.2)	21(12.3)	21(11.2)
P11	21(10.1)	21(13.2)	22(11.2)
P12	21(11.4)	21(10.1)	20(12.5)
Ciprofloxacin	28	25	27
DMF	-	-	-

E.c- *Escherichia coli*; *P.a*- *Pseudomonas aeruginosa*; *K.p*- *Klebsiellapneumoniae*

Table 3. *In vitro* antimicrobial activities of the synthesized compounds **P1-12**

<i>Zone of Inhibition in mm (MIC 100µg/ml)</i>		
<i>Fungi</i>		
<i>Code</i>	<i>A.n</i>	<i>A.f</i>
P1	20(11.7)	19(11.3)
P2	22(10.1)	23(10.2)
P3	18(11.7)	20(11.1)
P4	18(11.1)	19(10.6)
P5	20(11.2)	21(12.1)
P6	19(11.4)	20(12.4)
P7	18(11.5)	19(12.3)
P8	20(11.6)	20(10.4)
P9	22(9.3)	23(10.7)
P10	18(11.2)	19(12.4)
P11	18(11.4)	19(11.5)
P12	18(11.2)	19(10.2)
Ketoconazole	27	25
DMF	-	-

A.n- *Aspergillusniger*; *A.f*- *Aspergillusfumigatus*

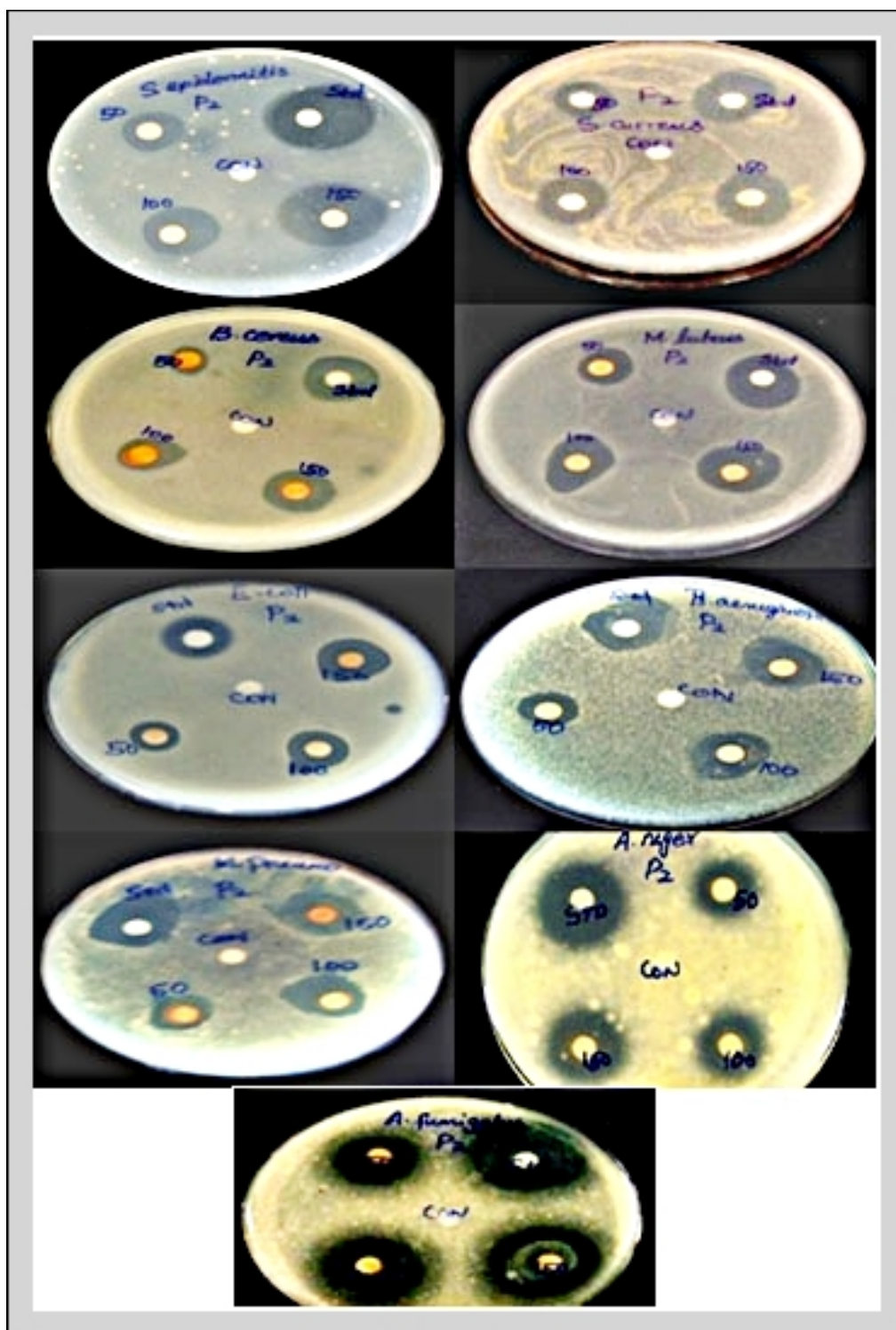


Figure 1. Antimicrobial activity slides of synthesized compounds P1-12

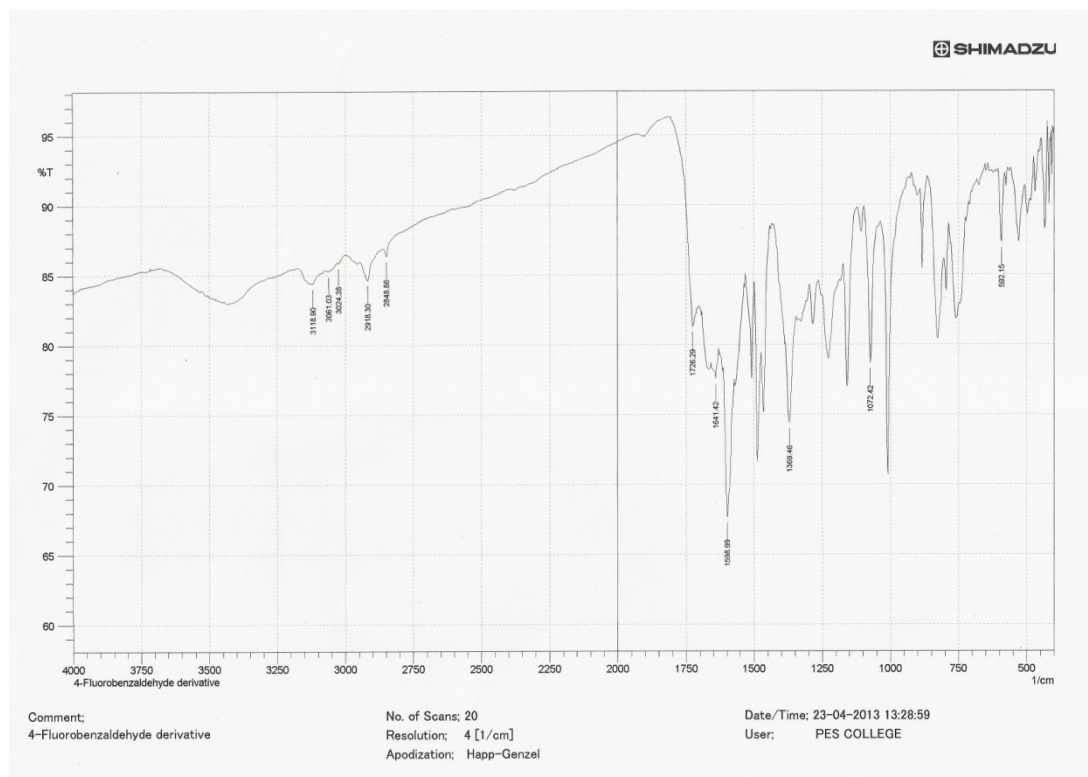


Figure 2. IR spectra of compound P3

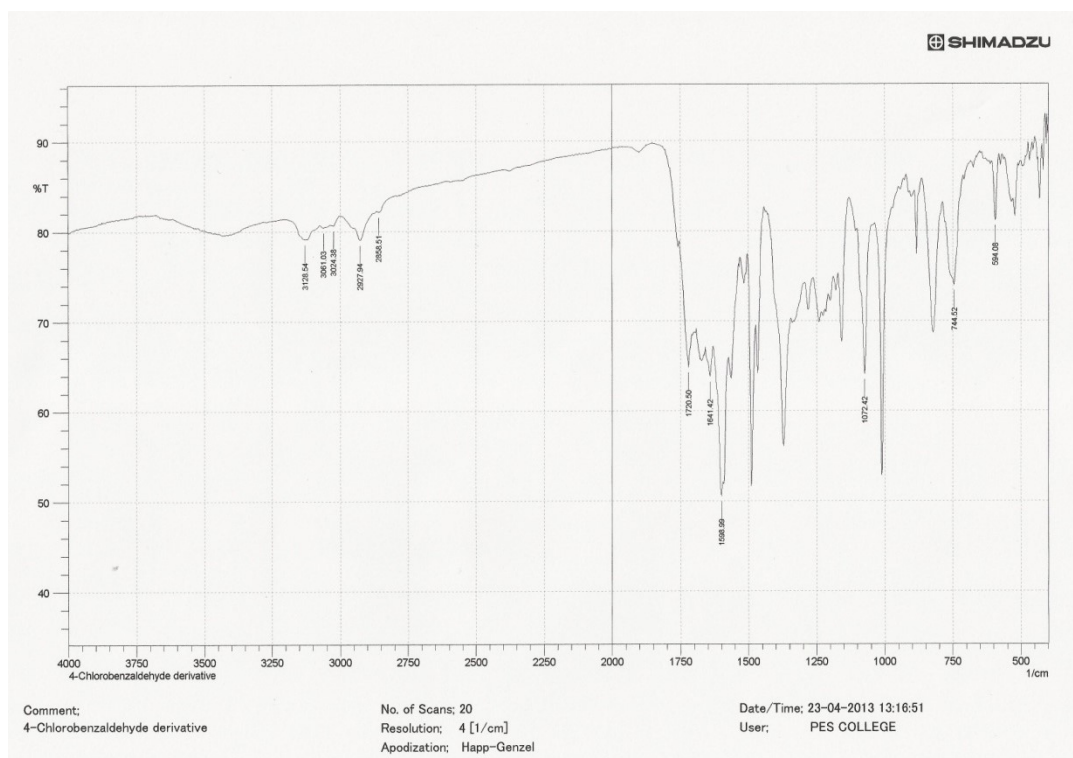


Figure 3. IR spectra of compound P6

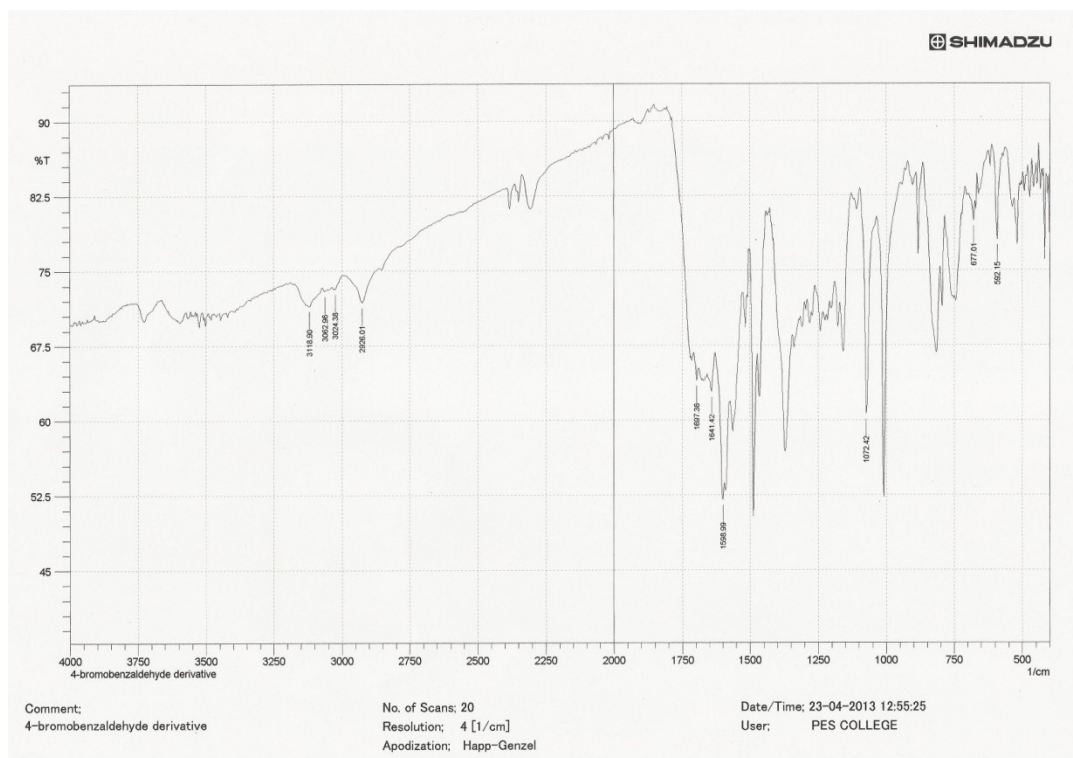


Figure 4. IR spectra of compound P9

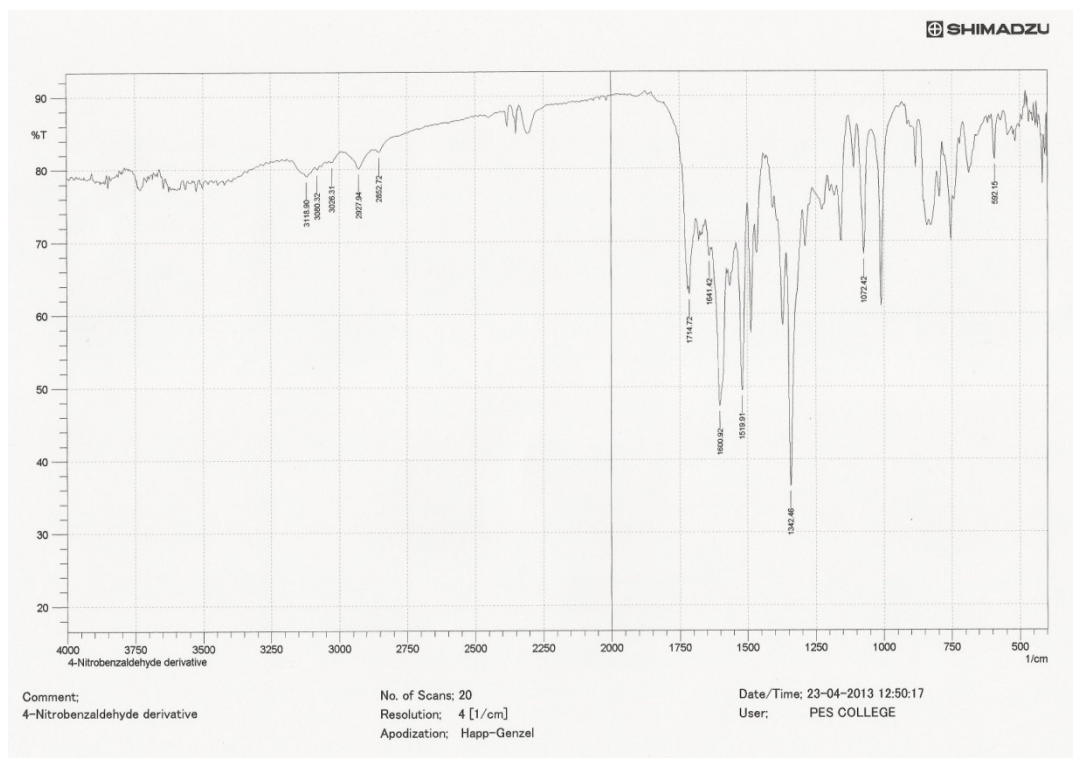


Figure 5. IR spectra of compound P12

Reference

- Bailey, DM. (1985). 3, 4-Diphenyl-1H-pyrazole-1-propanamine antidepressants. *J med chem* **28**(2): 256-260.
- Bekhit, AA, Abdel-Aziem, T. (2004). Design, synthesis and biological evaluation of some pyrazole derivatives as anti-inflammatory-antimicrobial agents. *Bioorg & med chem* **12**(8): 1935-1945.
- Bekhit, AA. (2008). Synthesis and biological evaluation of some thiazolyl and thiadiazolyl derivatives of 1H-pyrazole as anti-inflammatory antimicrobial agents. *Eur j med chem* **43**(3): 456-463.
- Liu, XH. (2008). Synthesis, structure and antibacterial activity of novel 1-(5-substituted-3-substituted-4, 5-dihydropyrazol-1-yl) ethanone oxime ester derivatives. *Bioorg & med chem* **16**(7): 4075-4082.
- Liu, XH. (2008). Synthesis, structure, and antibacterial activity of novel 5-arylpyrazole derivatives. *Australian journal of chemistry* **61**(3): 223-230.
- Park, HJ. (2005). Identification of antitumor activity of pyrazole oxime ethers. *Bioorg & med chem lett* **15**(13): 3307-3312.
- Roberts, MC. (2004). Distribution of macrolide, lincosamide, streptogramin, ketolide and oxazolidinone (MLSKO) resistance genes in Gram-negative bacteria. *Curr Drug Tar Infec Dis* **4**(3): 207-215.
- Tanitime, A. (2004). Synthesis and antibacterial activity of a novel series of potent DNA gyrase inhibitors. Pyrazole derivatives. *J med chem* **47**(14): 3693-3696.
- Tanitime, A. (2004). Synthesis and antibacterial activity of novel and potent DNA gyrase inhibitors with azole ring. *J med chem* **12**(21): 5515-5524.
- Tanitime, A. (2004). Design, synthesis and structure-activity relationship studies of novel indazole analogues as DNA gyrase inhibitors with Gram-positive antibacterial activity. *Bioorg & med chem lett* **14**(11): 2857-2862.
- Tenover, FC, McDonald, LC. (2005). Vancomycin-resistant staphylococci and enterococci: epidemiology and control. *Curr opi infec dis* **18**(4): 300-305.
- Yamashita, A. (2005). Crystal structure of a bacterial homologue of Na⁺/Cl⁻-dependent neurotransmitter transporters. *Nature* **437**(7056): 215-223.