

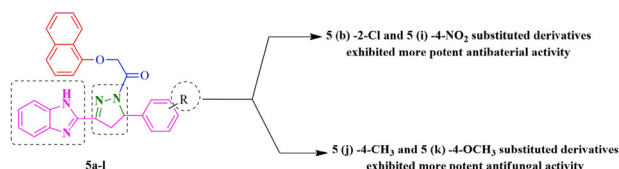
Synthesis and antimicrobial activity of some heterocyclic compounds bearing benzimidazole and pyrazoline motifs

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Abstract A series of 1-(3-(1*H*-benzimidazol-2-yl)-5-aryl-4,5-dihydro-1*H*-pyrazol-1-yl)-2-(naphthalene-1-yloxy)ethanones (**5a–l**) are synthesized and evaluated their antimicrobial activity against gram positive (*S. aureus* and *S. pyogenes*), gram negative bacteria (*E. coli* and *P. aeruginosa*), and strains of fungi (*C. albicans*, *A. niger*, and *A. clavatus*). Compounds were characterized by spectroscopic techniques such as ¹H NMR, ¹³C NMR, IR, and mass spectroscopy. The newly synthesized compounds **5b**, **5i** and **5j**, **5k** showed significant antimicrobial activity against tested microorganisms.

Graphical abstract



Keywords Pyrazoline · Benzimidazole · Antimicrobial activity · Antibacterial activity · Antifungal activity

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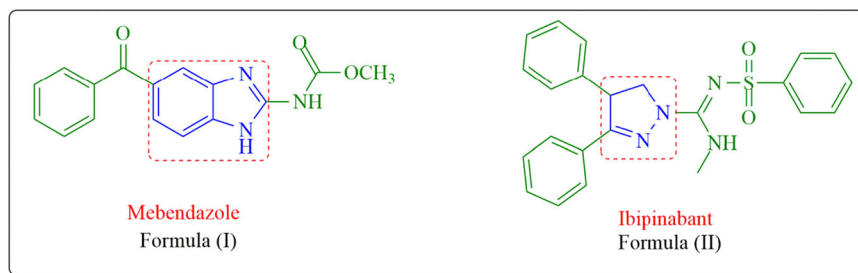
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Introduction

Bacteria and fungi have developed resistance strains against currently available antimicrobial agents and therefore it is essential for medicinal chemists to design and synthesize novel antimicrobial agents having less toxicity and more potent effects in much lesser time. In continuation to this, chemists have successfully synthesized effective agents based on heterocyclic compounds. The shining examples are furamizole, nasapadil, tazobactam, and cefatrizine. Benzimidazoles have various types of pharmacological effects, including antimicrobial (Sekar et al. 2016), anthelmatics (Mckellar and Scott 1990), and antiprolifretive (Garuti et al. 2000). Numerous examples show that benzimidazole and its derivatives play an important role in development of antimicrobial agents. Benzimidazole derivatives have been synthesized by the condensation of o-phenylenediamine with acids, their nitriles, imidates and orthoesters (Alaqeel 2017).

Our research group has previously synthesized benzimidazole derivatives and we have received some exiting antimicrobial results (Desai et al. 2014a, b). Therefore, we have focused on benzimidazole-based pyrazoline derivatives which possess diverse chemical structures. These hybrid structures may be useful for the development of antimicrobial agents. The development of efficient preparation of benzimidazole-based pyrazoline played a key role in modern organic synthesis. The pyrazoline scaffold displays important biological activities such as antioxidant (Padmaja et al. 2011), analgesic (Gawad et al. 2012), anti-inflammatory (Kumar et al. 2015), anti-infective (Desai et al. 2014a, b), anti-HIV (Fernandez et al. 2014), antiviral (Ouyang et al. 2008), antidepressant (Kaplancikli et al. 2010), antitumor (Lesyk et al. 2012), and antitubercular (Pathak et al. 2012, Khunt et al. 2012). Mebendazole

Fig. 1 Benzimidazole and pyrazoline containing marketed drugs



[Formula (I)] (Ingle and Magar 2011) and ibipinabant [Formula (II)] (Desai et al. 2013) both are well known drugs available in the market (Fig. 1). In the present paper, we have clubbed benzimidazole and pyrazoline moieties in one molecular structure for the synthesis of more potential antimicrobial agents. We have synthesized a series of 1-(3-(1*H*-benzoimidazol-2-yl)-5-aryl-4,5-dihydro-1*H*-pyrazol-1-yl)-2-(naphthalen-1-yloxy)ethanones (**5a–l**). The structures of targeted compounds were characterized on the basis of ^{13}C nuclear magnetic resonance (NMR), ^1H NMR, infrared (IR), and mass spectroscopy. These derivatives exhibited antimicrobial activity on various strains of bacteria and fungi.

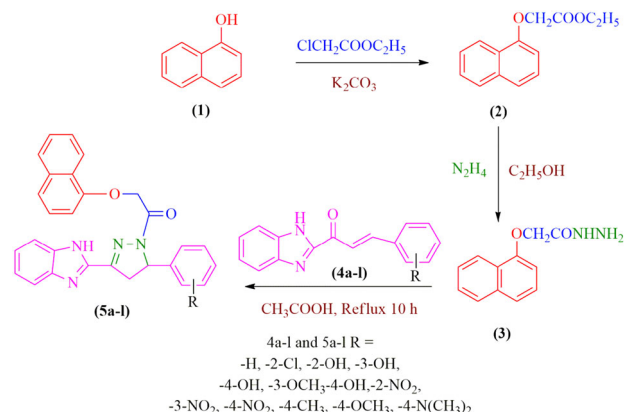
Experimental

Materials and methods

For determination of melting point open capillary method was used. Thin layer chromatography (TLC) on silica gel plates was used for reaction monitoring. Percentage of C, H, and N was checked by a Perkin-Elmer 2400 CHN analyzer. IR spectra of all compounds were recorded on a Shimadzu IR Prestige-21 (CE) Fourier transform infrared spectrophotometer in KBr; the frequencies were reported in cm^{-1} . ^1H NMR spectra were carried out on Varian Gemini 400 MHz and ^{13}C NMR spectra on Varian Mercury 400, 100 MHz in this dimethyl sulfoxide (DMSO)- d_6 as a used solvent, and tetramethylsilane used as a internal standard. ^1H data were given in multiplicity (s, singlet; d, doublet; t, triplet; m, multiple) and chemical shifts were interpreting in δ ppm. Mass spectroscopic data were scanned on a Shimadzu LCMS 2010 spectrometer. Büchi Rota vapor was used for the distillation.

Chemistry

The synthesized compounds (**5a–l**) were prepared in four steps. Compound (**2**) was synthesized from a mixture of α -naphthol, ethylchloro acetate, and refluxed in water bath. Dry acetone used as a solvent and anhydrous K_2CO_3 used as a catalyst. In second step, compound (**2**) and hydrazine



Scheme 1 Synthetic pathway of compounds (**5a–l**)

hydrate was refluxed in ethanol to yield intermediate *N*-amino-2-naphthyloxyacetamide (**3**). In the final step, intermediate (**3**) and 1-(1*H*-benzoimidazol-2-yl)-3-arylprop-2-en-1-ones (**4a–l**) were refluxed in acetic acid and cyclised to furnish final compounds (**5a–l**) (Scheme 1).

Synthesis of ethyl 2-naphthyloxyacetate (2), N-amino-2-naphthyloxyacetamide (3) and 1-(1H-benzoimidazol-2-yl)-3-arylprop-2-en-1-ones (4a–l)

Compound ethyl-2-naphthyloxyacetate (**2**) and *N*-amino-2-naphthyloxyacetamide (**3**) were prepared according to the method of (Rokade and Dongare 2010; Kumar et al. 2012). Similarly 1-(1*H*-benzoimidazol-2-yl)-3-arylprop-2-en-1-ones were also prepared (Behera et al. 2016).

Synthesis of 1-(3-(1H-benzoimidazol-2-yl)-5-aryl-4,5-dihydro-1H-pyrazol-1-yl)-2-(naphthalen-1-yloxy)ethanones (5)

A mixture of 1-(1*H*-benzoimidazol-2-yl)-3-phenylprop-2-en-1-one (**4**) (0.001 mol) and compound (**3**) (0.002 mol) were taken in 20 ml glacial acetic acid and refluxed at 130 °C for a period of 10 h. The mixture was concentrated under vacuum and diluted with ice cold water. On completion of the reaction, purity of compounds were checked by TLC using hexane-ethyl acetate (8:2 v/v) as mobile

phase and developed in an iodine chamber. All compounds (**5a–l**) of this series were prepared using the same method.

1-(3-(1*H*-benzimidazol-2-yl)-5-phenyl-4,5-dihydro-1*H*-pyrazol-1-yl)-2-(naphthalen-1-yloxy)ethanone (**5a**) Off white (MeOH) (yield 64%) mp 219–222 °C; IR (KBr, cm^{-1}): 3442 (N–H stretching, secondary amine), 3060 (C–H stretching, aromatic ring), 2928 (C–H stretching, $-\text{CH}_2$ group), 1680 (C=O stretching, aromatic ketone), 1500 ($-\text{C}=\text{N}$ stretching aromatic ring), 1457 (C=C stretching, aromatic ring), 1230, 1120 (C–O–C stretching); ^1H NMR (400 MHz, $\text{DMSO-}d_6$): δ = 12.73 (s, 1H, $-\text{NH}$), 6.54–8.51 (m, 16H, Ar–H), 5.23 (d, $J_{\text{AC}} = 3.09$ Hz, $J_{\text{BC}} = 11.08$ Hz, 1H, $>\text{CH}-\text{H}_\text{C}$), 4.92 (d, $J_{\text{AB}} = 17.41$ Hz, $J_{\text{BC}} = 11.02$ Hz, 1H, $\text{C}_5\text{-H}$ pyrazoline H_B), 4.74 (s, 2H, $-\text{O}-\text{CH}_2-$), 3.64 (d, $J_{\text{AB}} = 17.48$ Hz, $J_{\text{AC}} = 3.07$ Hz, 1H, $\text{C}_4\text{-H}$ pyrazoline H_A); ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$): δ = 169.7 ($>\text{C}=\text{O}$), 156.4 (1C, C_1 naphthalene ring), 155.1 (1C, C_3 pyrazoline ring), 151.7 (1C, C_2 benzimidazole ring), 141.1 (1C, C_1 aromatic ring), 134.4 (2C, C_8 and C_9 benzimidazole ring), 134.8 (1C, C_9 naphthalene ring), 134.7 (1C, C_{10} naphthalene ring), 128.3 (1C, C_3 and C_5 aromatic ring), 127.1 (1C, C_5 naphthalene ring), 126.0 (1C, C_6 naphthalene ring), 126.4 (1C, C_3 naphthalene ring), 126.6 (1C, C_4 aromatic ring), 126.7 (2C, C_2 and C_6 aromatic ring), 125.0 (1C, C_7 naphthalene ring), 123.8 (1C, C_8 naphthalene ring), 123.1 (2C, C_6 and C_5 benzimidazole ring), 120.7 (1C, C_4 naphthalene ring), 115.6 (2C, C_7 and C_4 benzimidazole ring), 107.0 (1C, C_2 naphthalene ring), 67.7 (1C, $-\text{O}-\text{CH}_2-$), 66.3 (1C, C_5 pyrazoline ring), 39.0 (1C, C_4 pyrazoline ring); MS (m/z): 446.02 (M^+); anal. calcd. for ($\text{C}_{28}\text{H}_{22}\text{N}_4\text{O}_2$): C, 75.32; H, 4.97; N, 12.55%; found: C, 75.40; H, 5.10; N, 12.62%.

Physical constant and characterization 1-(3-(1*H*-benzimidazol-2-yl)-5-(2-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)-2-(naphthalen-1-yloxy)ethanone (**5b**) Brown solid (MeOH) (yield 70%) mp 195–197 °C; IR (KBr, cm^{-1}): 3440 (N–H stretching, secondary amine), 3063 (C–H stretching, aromatic ring), 2923 (C–H stretching, $-\text{CH}_2$ group), 1683 (C=O stretching, aromatic ketone), 1504 ($-\text{C}=\text{N}$ stretching aromatic ring), 1456 (C=C stretching, aromatic ring), 1231, 1122 (C–O–C stretching), 895 (C–Cl stretching); ^1H NMR (400 MHz, $\text{DMSO-}d_6$): δ = 12.85 (s, 1H, $-\text{NH}$), 6.42–8.42 (m, 15H, Ar–H), 5.21 (d, $J_{\text{AC}} = 3.10$ Hz, $J_{\text{BC}} = 11.05$ Hz, 1H, $>\text{CH}-\text{H}_\text{C}$), 4.74 (s, 2H, $-\text{O}-\text{CH}_2-$), 3.70 (d, $J_{\text{AB}} = 17.42$ Hz, $J_{\text{BC}} = 11.09$ Hz, 1H, $\text{C}_5\text{-H}$ pyrazoline H_B), 3.22 (d, $J_{\text{AB}} = 17.43$ Hz, $J_{\text{AC}} = 3.05$ Hz, 1H, $\text{C}_4\text{-H}$ pyrazoline H_A); ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$): δ = 169.3 ($>\text{C}=\text{O}$), 156.1 (1C, C_1 naphthalene ring), 155.7 (1C, C_3 pyrazoline ring), 151.4 (1C, C_2 benzimidazole ring), 138.4 (1C, C_1 aromatic ring), 134.1 (1C, C_9 naphthalene ring), 134.2 (1C, C_{10} naphthalene ring),

134.9 (2C, C_8 and C_9 benzimidazole ring), 132.4 (1C, C_6 aromatic ring), 128.6 (1C, C_3 aromatic ring), 128.3 (1C, C_4 aromatic ring), 128.0 (1C, C_5 aromatic ring), 127.3 (1C, C_5 naphthalene ring), 126.2 (2C, C_3 aromatic ring and C_6 naphthalene ring), 126.9 (1C, C_3 naphthalene ring), 125.5 (1C, C_7 naphthalene ring), 123.8 (1C, C_8 naphthalene ring), 123.2 (2C, C_5 and C_6 benzimidazole ring), 120.7 (1C, C_5 naphthalene ring), 115.9 (2C, C_7 and C_4 benzimidazole ring), 107.8 (1C, C_2 naphthalene ring), 67.9 (1C, $-\text{OCH}_2-$), 61.6 (1C, C_4 pyrazoline ring), 39.0 (1C, C_5 pyrazoline ring); MS (m/z): 480.1 (M^+); anal. calcd. for ($\text{C}_{28}\text{H}_{21}\text{ClN}_4\text{O}_2$): C, 69.92; H, 4.40; N, 11.65%; found: C, 69.98; H, 4.48; N, 11.75%.

Physical constant and characterization 1-(3-(1*H*-benzimidazol-2-yl)-5-(2-hydroxyphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)-2-(naphthalen-1-yloxy)ethanone (**5c**) Yellowish white (MeOH) (yield 66%) mp 144–147 °C; IR (KBr, cm^{-1}): 3444 (N–H stretching, secondary amine), 3390 (O–H stretching), 3065 (C–H stretching, aromatic ring), 2925 (C–H stretching, $-\text{CH}_2$ group), 1681 (C=O stretching, aromatic ketone), 1508 ($-\text{C}=\text{N}$ stretching aromatic ring), 1452 (C=C stretching, aromatic ring), 1232, 1124 (C–O–C stretching); ^1H NMR (400 MHz, $\text{DMSO-}d_6$): δ = 12.81 (s, 1H, $-\text{NH}$), 6.45–8.40 (m, 15H, Ar–H), 5.32 (s, 1H, $-\text{OH}$), 5.25 (d, $J_{\text{AC}} = 3.11$ Hz, $J_{\text{BC}} = 11.04$ Hz, 1H, $>\text{CH}-\text{H}_\text{C}$), 4.75 (s, 2H, $-\text{O}-\text{CH}_2-$), 3.74 (d, $J_{\text{AB}} = 17.40$ Hz, $J_{\text{BC}} = 11.11$ Hz, 1H, $\text{C}_5\text{-H}$ pyrazoline H_B), 3.25 (d, $J_{\text{AB}} = 17.40$ Hz, $J_{\text{AC}} = 3.04$ Hz, 1H, $\text{C}_4\text{-H}$ pyrazoline H_A); ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$): δ = 169.3 (1C, $>\text{C}=\text{O}$), 156.7 (1C, C_1 naphthalene ring), 155.1 (1C, C_3 pyrazoline ring), 154.3 (1C, C_2 aromatic ring), 151.8 (1C, C_2 benzimidazole ring), 134.4 (2C, C_8 and C_9 benzimidazole ring), 134.0 (1C, C_9 naphthalene ring), 134.7 (1C, C_{10} naphthalene ring), 130.1 (1C, C_1 aromatic ring), 128.4 (1C, C_4 aromatic ring), 127.9 (1C, C_4 naphthalene ring), 126.8 (1C, C_6 naphthalene ring), 126.7 (1C, C_2 aromatic ring), 126.0 (1C, C_3 naphthalene ring), 125.4 (1C, C_7 naphthalene ring), 123.4 (2C, C_5 and C_6 benzimidazole ring), 121.4 (1C, C_3 aromatic ring), 120.4 (1C, C_4 naphthalene ring), 115.4 (2C, C_4 and C_7 benzimidazole), 107.1 (1C, C_2 naphthalene ring), 67.3 (1C, $-\text{OCH}_2-$), 66.8 (1C, C_5 pyrazoline ring), 39.4 (1C, C_4 pyrazoline ring); MS (m/z): 462.7 (M^+); anal. calcd. for ($\text{C}_{28}\text{H}_{22}\text{N}_4\text{O}_3$): C, 72.71; H, 4.79; N, 12.11%; found: C, 72.80; H, 4.81; N, 12.15%.

Physical constant and characterization 1-(3-(1*H*-benzimidazol-2-yl)-5-(3-hydroxyphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)-2-(naphthalen-1-yloxy)ethanone (**5d**) Yellow (MeOH) (yield 69%) mp 224–227 °C; IR (KBr, cm^{-1}): 3448 (N–H stretching, secondary amine), 3395 (O–H stretching), 3069 (C–H stretching, aromatic ring), 2929 (C–H stretching, $-\text{CH}_2$ group), 1686 (C=O stretching, aromatic ketone),

1510 (C=N stretching aromatic ring), 1455 (C=C stretching, aromatic ring), 1235, 1126 (C–O–C stretching); ^1H NMR (400 MHz, DMSO- d_6): δ = 12.77 (s, 1H, $-\text{NH}$), 6.48–8.49 (m, 15H, Ar-H), 5.38 (s, 1H, $-\text{OH}$), 5.20 (d, J_{AC} = 3.13 Hz, J_{BC} = 11.04 Hz, 1H, $>\text{CH}-\text{H}_\text{C}$), 3.78 (d, J_{AB} = 17.41 Hz, J_{BC} = 11.12 Hz, 1H, C₅-H pyrazoline H_B), 4.80 (s, 2H, $-\text{O}-\text{CH}_2-$), 3.29 (d, J_{AB} = 17.43 Hz, J_{AC} = 3.01 Hz, 1H, C₄-H pyrazoline H_A); ^{13}C NMR (100 MHz, DMSO- d_6): δ = 169.3 (1C, $>\text{C}=\text{O}$), 156.0 (1C, C₁ naphthalene ring), 155.3 (1C, C₃ pyrazoline ring), 151.6 (1C, C₂ benzimidazole ring), 142.8 (1C, C₁ aromatic ring), 134.9 (2C, C₈ and C₉ benzimidazole ring), 134.6 (1C, C₉ naphthalene ring), 134.5 (1C, C₁₀ naphthalene ring), 127.0 (1C, C₅ naphthalene ring), 126.9 (1C, C₆ naphthalene ring), 126.8 (1C, C₃ naphthalene ring), 125.0 (1C, C₇ naphthalene ring), 123.8 (2C, C₅ and C₆ benzimidazole ring), 123.2 (1C, C₈ naphthalene ring), 120.7 (1C, C₄ naphthalene ring), 119.1 (1C, C₂ aromatic ring), 115.0 (2C, C₄ and C₇ benzimidazole ring), 113.0 (1C, C₄ aromatic ring), 112.4 (1C, C₆ aromatic ring), 107.4 (1C, C₂ naphthalene ring), 67.0 (1C, $-\text{OCH}_2-$), 66.4 (1C, C₅ pyrazoline ring), 39.0 (1C, C₄ pyrazoline ring); MS (m/z): 462.7 (M^+); anal. calcd. for (C₂₈H₂₂N₄O₃): C, 72.71; H, 4.79; N, 12.11%; found: C, 72.81; H, 4.84; N, 12.19%.

Physical constant and characterization 1-(3-(1*H*-benzimidazol-2-yl)-5-(4-hydroxy-4,5-dihydro-1*H*-pyrazol-1-yl)-2-(naphthalen-1-yloxy)ethanone (**5e**) Buff (MeOH) (yield 61%) mp 168–171 °C; IR (KBr, cm^{-1}): 3449 (N–H stretching, secondary amine), 3397 (O–H stretching), 3070 (C–H stretching, aromatic ring), 2926 (C–H stretching, $-\text{CH}_2$ group), 1685 (C=O stretching, aromatic ketone), 1509 (C=N stretching aromatic ring), 1457 (C=C stretching, aromatic ring), 1238, 1127 (C–O–C stretching); ^1H NMR (400 MHz, DMSO- d_6): δ = 12.74 (s, 1H, $-\text{NH}$), 6.44–8.42 (m, 15H, Ar-H), 5.35 (s, 1H, $-\text{OH}$), 5.23 (d, J_{AC} = 3.14 Hz, J_{BC} = 11.02 Hz, 1H, $>\text{CH}-\text{H}_\text{C}$), 4.85 (s, 2H, $-\text{O}-\text{CH}_2-$), 3.74 (d, J_{AB} = 17.42 Hz, J_{BC} = 11.11 Hz, 1H, C₅-H pyrazoline H_B), 3.25 (d, J_{AB} = 17.45 Hz, J_{AC} = 3.00 Hz, 1H, C₄-H pyrazoline H_A); ^{13}C NMR (100 MHz, DMSO- d_6): δ = 169.2 (1C, $>\text{C}=\text{O}$), 156.5 (1C, C₄ aromatic ring), 156.2 (1C, C₁ naphthalene ring), 155.4 (1C, C₃ pyrazoline ring), 151.9 (1C, C₂ benzimidazole ring), 134.8 (1C, C₁ aromatic ring), 134.2 (2C, C₈ and C₉ benzimidazole ring), 134.9 (1C, C₉ naphthalene ring), 134.7 (1C, C₁₀ naphthalene ring), 127.0 (2C, C₂ and C₆ aromatic ring), 127.5 (1C, C₅ naphthalene ring), 126.3 (1C, C₆ naphthalene ring), 126.0 (1C, C₃ naphthalene ring), 125.4 (1C, C₇ naphthalene ring), 123.4 (2C, C₅ and C₆ benzimidazole ring), 123.0 (1C, C₈ naphthalene ring), 120.1 (1C, C₄ naphthalene ring), 115.9 (2C, C₇ and C₄ benzimidazole ring), 115.0 (2C, C₃ and C₅ aromatic ring), 107.1 (1C, C₂ naphthalene ring), 67.7 (1C, $-\text{OCH}_2-$), 66.0

(1C, C₅ pyrazoline ring), 39.7 (1C, C₄ pyrazoline ring); MS (m/z): 462.9 (M^+); anal. calcd. for (C₂₈H₂₂N₄O₃): C, 72.71; H, 4.79; N, 12.11%; Found: C, 72.80; H, 4.88; N-12.19%.

Physical constant and characterization 1-(3-(1*H*-benzimidazol-2-yl)-5-(4-hydroxy-3-methoxyphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)-2-(naphthalen-1-yloxy)ethanone (**5f**) Brown (MeOH) (yield 65%) mp 182–185 °C; IR (KBr, cm^{-1}): 3452 (N–H stretching, secondary amine), 3400 (O–H stretching), 3075 (C–H stretching, aromatic ring), 2930 (C–H stretching, $-\text{CH}_2$ group), 2820 (C–H stretching, $-\text{OCH}_3$ group), 1689 (C=O stretching, aromatic ketone), 1506 (C=N stretching aromatic ring), 1459 (C=C stretching, aromatic ring), 1231, 1129 (C–O–C stretching); ^1H NMR (400 MHz, DMSO- d_6): δ = 12.70 (s, 1H, $-\text{NH}$), 6.49–8.46 (m, 14H, Ar-H), 5.35 (s, 1H, $-\text{OH}$), 5.26 (d, J_{AC} = 3.19 Hz, J_{BC} = 11.09 Hz, 1H, $>\text{CH}-\text{H}_\text{C}$), 4.86 (s, 2H, $-\text{O}-\text{CH}_2-$), 3.85 (s, 3H, $-\text{OCH}_3$), 3.78 (d, J_{AB} = 17.46 Hz, J_{BC} = 11.17 Hz, 1H, C₅-H pyrazoline H_B), 3.26 (d, J_{AB} = 17.49 Hz, J_{AC} = 3.01 Hz, 1H, C₄-H pyrazoline H_A); ^{13}C NMR (100 MHz, DMSO- d_6): δ = 169.0 (1C, $>\text{C}=\text{O}$), 156.7 (1C, C₁ naphthalene ring), 155.7 (1C, C₃ pyrazoline ring), 151.7 (1C, C₂ benzimidazole ring), 147.0 (1C, C₃ aromatic ring), 146.0 (1C, C₄ aromatic ring), 134.4 (1C, C₁ aromatic ring), 139.0 (2C, C₈ and C₉ benzimidazole ring), 134.2 (1C, C₉ naphthalene ring), 134.7 (1C, C₁₀ naphthalene ring), 127.0 (1C, C₅ naphthalene ring), (2C, C₂ and C₆ aromatic ring), 126.7 (1C, C₆ naphthalene ring), 126.4 (1C, C₃ naphthalene ring), 127.0 (1C, C₇ naphthalene ring), 123.8 (2C, C₅ and C₆ benzimidazole ring), 123.4 (1C, C₈ naphthalene ring), 120.9 (1C, C₄ naphthalene ring), 115.8 (2C, C₇ and C₄ benzimidazole ring), 119.0 (1C, C₆ aromatic ring), 115.7 (1C, C₃ aromatic ring), 110.7 (1C, C₂ aromatic ring), 107.7 (1C, C₂ naphthalene ring), 67.0 (1C, $-\text{OCH}_2-$), 66.0 (1C, C₅ pyrazoline ring), 56.7 (1C, $-\text{OCH}_3$), 39.0 (1C, C₄ pyrazoline ring); MS (m/z): 492.5 (M^+); anal. calcd. for (C₂₉H₂₄N₄O₄): C, 70.72; H, 4.91; N, 11.38%; found: C, 70.82; H, 4.95; N, 11.45%.

Physical constant and characterization 1-(3-(1*H*-benzimidazol-2-yl)-5-(2-nitrophenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)-2-(naphthalen-1-yloxy)ethanone (**5g**) Dark yellow (MeOH) (yield 60%) mp 141–143 °C; IR (KBr, cm^{-1}): 3454 (N–H stretching, secondary amine), 3076 (C–H stretching, aromatic ring), 2932 (C–H stretching, $-\text{CH}_2$ group), 1691 (C=O stretching, aromatic ketone), 1535 (N=O stretching, aromatic ring), 1503 (C=N stretching aromatic ring), 1463 (C=C stretching, aromatic ring), 1230, 1130 (C–O–C stretching); ^1H NMR (400 MHz, DMSO- d_6): δ = 12.89 (s, 1H, $-\text{NH}$), 6.48–8.49 (m, 15H, Ar-H), 5.52 (d, J_{AC} = 3.21 Hz, J_{BC} = 11.06 Hz, 1H, $>\text{CH}-\text{H}_\text{C}$), 4.78 (s, 2H, $-\text{O}-\text{CH}_2-$), 3.75 (d, J_{AB} = 17.49 Hz, J_{BC} = 11.19 Hz, 1H,

C₅-H pyrazoline H_B), 3.26 (d, $J_{AB} = 17.52$ Hz, $J_{AC} = 3.05$ Hz, 1H, C₄-H pyrazoline H_A); ¹³C (100 MHz, DMSO-*d*₆): $\delta = 169.0$ (1C, >C=O), 156.7 (1C, C₁ naphthalene ring), 155.7 (1C, C₃ pyrazoline ring), 151.7 (1C, C₂ benzimidazole ring), 147.0 (1C, C₆ aromatic ring), 137.0 (1C, C₁ aromatic ring), 134.9 (2C, C₈ and C₉ benzimidazole ring), 134.3 (1C, C₉ naphthalene ring), 134.1 (1C, C₁₀ naphthalene ring), 134.0 (1C, C₃ aromatic ring), 127.4 (1C, C₂ aromatic ring), 127.3 (2C, C₅ naphthalene ring and C₂ aromatic ring), 127.0 (1C, C₄ aromatic ring), 126.7 (1C, C₆ naphthalene ring), 126.4 (1C, C₃ naphthalene ring), 125.0 (1C, C₇ naphthalene ring), 124.0 (1C, C₅ aromatic ring), 123.7 (2C, C₅ and C₆ benzimidazole ring), 123.1 (1C, C₈ naphthalene ring), 120.0 (1C, C₄ naphthalene ring), 115.0 (2C, C₇ and C₄ benzimidazole ring), 107.9 (1C, C₂ naphthalene ring), 67.4 (1C, -OCH₂-), 61.0 (1C, C₅ pyrazoline ring), 38.0 (1C, C₄ pyrazoline ring); MS (*m/z*): 491.2 (M⁺); anal. calcd. for (C₂₈H₂₁N₅O₄): C, 68.42; H, 4.31; N, 14.25%; found: C, 68.51; H, 4.41; N, 14.33%.

Physical constant and characterization 1-(3-(1*H*-benzoimidazol-2-yl)-5-(3-nitrophenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)-2-(naphthalen-1-yloxy)ethanone (**5h**) Yellowish orange (MeOH) (yield 68%) mp 154–156 °C; IR (KBr, cm⁻¹): 3458 (N–H stretching, secondary amine), 3078 (C–H stretching, aromatic ring), 2933 (C–H stretching, -CH₂ group), 1690 (C=O stretching, aromatic ketone), 1530 (N=O stretching, aromatic ring), 1507 (C=N stretching aromatic ring), 1468 (C=C stretching, aromatic ring), 1234, 1136 (C–O–C stretching); ¹H NMR (400 MHz, DMSO-*d*₆): $\delta = 12.80$ (s, 1H, -NH), 6.45–8.45 (m, 15H, Ar-H), 5.50 (d, $J_{AC} = 3.18$ Hz, $J_{BC} = 11.02$ Hz, 1H, >CH–H_C), 4.78 (s, 2H, -O–CH₂-), 3.72 (d, $J_{AB} = 17.56$ Hz, $J_{BC} = 11.15$ Hz, 1H, C₅-H pyrazoline H_B), 3.20 (d, $J_{AB} = 17.54$ Hz, $J_{AC} = 3.00$ Hz, 1H, C₄-H pyrazoline H_A); ¹³C (100 MHz, DMSO-*d*₆): $\delta = 169.3$ (1C, >C=O), (1C, C₄ aromatic ring), 156.0 (1C, C₁ naphthalene ring), 155.3 (1C, C₃ pyrazoline ring), 151.1 (1C, C₂ benzimidazole ring), 147.1 (1C, C₃ aromatic ring), 144.0 (1C, C₁ aromatic ring), 134.7 (2C, C₈ and C₉ benzimidazole ring), 134.6 (1C, C₉ naphthalene ring), 134.5 (1C, C₁₀ naphthalene ring), 133.4 (1C, C₆ aromatic ring), 129.4 (1C, C₅ aromatic ring), 127.1 (1C, C₅ naphthalene ring), 126.6 (1C, C₆ naphthalene ring), 126.0 (1C, C₃ naphthalene ring), 125.1 (1C, C₇ naphthalene ring), 123.7 (1C, C₈ naphthalene ring), 123.2 (2C, C₅ and C₆ benzimidazole ring), 121.2 (1C, C₅ aromatic ring), 120.7 (1C, C₄ naphthalene ring), 107.0 (1C, C₂ naphthalene ring), 115.8 (2C, C₇ and C₄ benzimidazole ring), 67.6 (1C, -OCH₂-), 65.7 (1C, C₅ pyrazoline ring), 39.1 (1C, C₄ pyrazoline ring); MS (*m/z*): 491.5 (M⁺); anal. calcd. for (C₂₈H₂₁N₅O₄): C, 68.42; H, 4.31; N, 14.25%; found: C, 68.50; H, 4.38; N, 14.31%.

Physical constant and characterization 1-(3-(1*H*-benzoimidazol-2-yl)-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)-2-(naphthalen-1-yloxy)ethanone (**5i**) Light orange (MeOH) (yield 62%) mp 150–152 °C; IR (KBr, cm⁻¹): 3457 (N–H stretching, secondary amine), 3077 (C–H stretching, aromatic ring), 2928 (C–H stretching, -CH₂ group), 1693 (C=O stretching, aromatic ketone), 1525 (N=O stretching, aromatic ring), 1511 (C=N stretching aromatic ring), 1466 (C=C stretching, aromatic ring), 1240, 1139 (C–O–C stretching); ¹H NMR (400 MHz, DMSO-*d*₆): $\delta = 12.83$ (s, 1H, -NH), 6.49–8.44 (m, 15H, Ar-H), 5.58 (d, $J_{AC} = 3.23$ Hz, $J_{BC} = 11.07$ Hz, 1H, >CH–H_C), 4.72 (s, 2H, -O–CH₂-), 3.75 (d, $J_{AB} = 17.58$ Hz, $J_{BC} = 11.13$ Hz, 1H, C₅-H pyrazoline H_B), 3.25 (d, $J_{AB} = 17.52$ Hz, $J_{AC} = 2.99$ Hz, 1H, C₄-H pyrazoline H_A); ¹³C (100 MHz, DMSO-*d*₆): $\delta = 169.1$ (1C, >C=O), 156.0 (1C, C₁ naphthalene ring), 155.0 (1C, C₃ pyrazoline ring), 151.0 (1C, C₂ benzimidazole ring), 147.4 (1C, C₁ aromatic ring), 145.0 (1C, C₄ aromatic ring), 134.7 (2C, C₈ and C₉ benzimidazole ring), 134.3 (1C, C₉ naphthalene ring), 134.2 (1C, C₁₀ naphthalene ring), (2C, C₂ and C₆ aromatic ring), 127.0 (1C, C₅ naphthalene ring), 126.4 (1C, C₆ naphthalene ring), 126.2 (1C, C₂ naphthalene ring), 125.0 (1C, C₇ naphthalene ring), 123.7 (2C, C₅ and C₆ benzimidazole ring), 123.4 (1C, C₈ naphthalene ring), 123.5 (2C, C₂ and C₆ aromatic ring), 123.2 (2C, C₃ and C₅ aromatic ring), 120.0 (1C, C₄ naphthalene ring), 115.2 (2C, C₇ and C₄ benzimidazole ring), 107.0, (1C, C₂ naphthalene ring), 67.7 (1C, -OCH₂-), 66.4 (1C, C₅ pyrazoline ring), 39.2 (1C, C₄ pyrazoline ring); MS (*m/z*): 491.9 (M⁺); anal. calcd. for (C₂₈H₂₁N₅O₄): C, 68.42; H, 4.31; N, 14.25%; found: C, 68.49; H, 4.40; N, 14.34%.

Physical constant and characterization 1-(3-(1*H*-benzoimidazol-2-yl)-5-(4-methylphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)-2-(naphthalen-1-yloxy)ethanone (**5j**) Pale yellow (MeOH) (yield 60%) mp 190–192 °C; IR (KBr, cm⁻¹): 3453 (N–H stretching, secondary amine), 3079 (C–H stretching, aromatic ring), 2930 (C–H stretching, -CH₂ group), 2889 (C–H stretching, -CH₃ group), 1694 (C=O stretching, aromatic ketone), 1512 (C=N stretching aromatic ring), 1471 (C=C stretching, aromatic ring), 1239, 1141 (C–O–C stretching); ¹H NMR (400 MHz, DMSO-*d*₆): $\delta = 12.89$ (s, 1H, -NH), 6.48–8.48 (m, 15H, Ar-H), 5.60 (d, $J_{AC} = 3.20$ Hz, $J_{BC} = 11.01$ Hz, 1H, >CH–H_C), 4.75 (s, 2H, -O–CH₂-), 3.78 (d, $J_{AB} = 17.54$ Hz, $J_{BC} = 11.14$ Hz, 1H, C₅-H pyrazoline H_B), 3.20 (d, $J_{AB} = 17.57$ Hz, $J_{AC} = 3.06$ Hz, 1H, C₄-H pyrazoline H_A), 2.40 (s, 3H, -CH₃); ¹³C (100 MHz, DMSO-*d*₆): $\delta = 169.7$ (1C, >C=O), 156.0 (1C, C₁ naphthalene ring), 155.8 (1C, C₃ pyrazoline ring), 151.0 (1C, C₂ benzimidazole ring), 138.4 (1C, C₁ aromatic ring), (1C, C₄ aromatic ring), 134.8 (2C, C₈ and C₉ benzimidazole ring), 134.8 (1C, C₉ naphthalene ring), 134.2 (1C, C₁₀ naphthalene ring), 128.4 (2C, C₃ and C₅ aromatic ring),

127.4 (1C, C₅ naphthalene ring), 126.7 (1C, C₆ naphthalene ring), 126.5 (1C, C₃ naphthalene ring), 125.4 (1C, C₇ naphthalene ring), 125.2 (2C, C₃ and C₅ aromatic ring), 123.4 (2C, C₅ and C₆ benzimidazole ring), 123.1 (1C, C₈ naphthalene ring), 120.4 (1C, C₄ naphthalene ring), 115.1 (2C, C₇ and C₄ benzimidazole ring), 107.2 (1C, C₂ naphthalene ring), 67.1 (1C, -OCH₂-), 66.7 (1C, C₅ pyrazoline ring), 39.9 (1C, C₄ pyrazoline ring), 21.4 (1C, -CH₃); MS (*m/z*): 460.7 (M⁺); anal. calcd. for (C₂₉H₂₄N₄O₂): C, 75.63; H, 5.25; N, 12.17%; found: C, 75.74; H, 5.36; N, 12.26%.

Physical constant and characterization 1-(3-(1*H*-benzimidazol-2-yl)-5-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)-2-(naphthalen-1-yloxy)ethanone (**5k**) Brown (MeOH) (yield 65%) mp 242–244 °C; IR (KBr, cm⁻¹): 3454 (N–H stretching, secondary amine), 3080 (C–H stretching, aromatic ring), 2927 (C–H stretching, -CH₂ group), 2888 (C–H stretching, -OCH₃ group), 1695 (C=O stretching, aromatic ketone), 1514 (-C=N stretching aromatic ring), 1468 (C=C stretching, aromatic ring), 1245, 1138 (C–O–C stretching); ¹H NMR (400 MHz, DMSO-*d*₆): δ = 12.85 (s, 1H, -NH), 6.43–8.38 (m, 15H, Ar-H), 5.62 (d, *J*_{AC} = 3.26 Hz, *J*_{BC} = 11.05 Hz, 1H, >CH-H_C), 4.83 (s, 2H, -O-CH₂-), 3.89 (s, 3H, -OCH₃), 3.58 (d, *J*_{AB} = 17.62 Hz, *J*_{BC} = 11.18 Hz, 1H, C₅-H pyrazoline H_B), 3.12 (d, *J*_{AB} = 17.50 Hz, *J*_{AC} = 3.10 Hz, 1H, C₄-H pyrazoline H_A); ¹³C (100 MHz, DMSO-*d*₆): δ = 169.6 (1C, >C=O), 158.4 (1C, C₄ aromatic ring), 156.4 (1C, C₁ naphthalene ring), 155.1 (1C, C₃ pyrazoline ring), 151.8 (1C, C₂ benzimidazole ring), 147.1 (1C, C₃ aromatic ring), (1C, C₁ aromatic ring), 134.0 (2C, C₈ and C₉ benzimidazole ring), 134.8 (1C, C₉ naphthalene ring), 134.5 (1C, C₁₀ naphthalene ring), 127.0 (1C, C₅ aromatic ring), 127.1 (1C, C₅ naphthalene ring), 126.1 (1C, C₆ naphthalene ring), 126.0 (1C, C₆ aromatic ring), 126.0 (1C, C₃ naphthalene ring), 125.7 (1C, C₇ naphthalene ring), 123.7 (1C, C₈ naphthalene ring), 123.4 (2C, C₅ and C₆ benzimidazole ring), 120.4 (1C, C₄ naphthalene ring), 115.1 (2C, C₇ and C₄ benzimidazole ring), 114.4 (1C, C₃ aromatic ring), 107.3 (1C, C₂ naphthalene ring), 67.4 (1C, -OCH₂-), 66.4 (1C, C₅ pyrazoline ring), 55.1 (1C, -OCH₃), 39.3 (1C, C₄ pyrazoline ring); MS (*m/z*): 476.5 (M⁺); anal. calcd. for (C₂₉H₂₄N₄O₃): C, 73.09; H, 5.08; N, 11.76%; found: C, 73.14; H, 5.11; N, 11.85%.

Physical constant and characterization 1-(3-(1*H*-benzimidazol-2-yl)-5-(4-(dimethylamino)phenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)-2-(naphthalen-1-yloxy)ethanone (**5l**) Brownish yellow (MeOH) (yield 63%) mp 170–172 °C; IR (KBr, cm⁻¹): 3458 (N–H stretching, secondary amine), 3086 (C–H stretching, aromatic ring), 2925 (C–H stretching, -CH₂ group), 2886 (C–H stretching, -CH₃ group), 1690 (C=O stretching, aromatic ketone), 1515 (-C=N stretching aromatic ring), 1473 (C=C stretching, aromatic ring),

1247, 1133 (C–O–C stretching); ¹H NMR (400 MHz, DMSO-*d*₆): δ = 12.85 (s, 1H, -NH), 6.50–8.47 (m, 15H, Ar-H), 5.63 (d, *J*_{AC} = 3.24 Hz, *J*_{BC} = 11.03 Hz, 1H, >CH-H_C), 4.79 (s, 2H, -O-CH₂-), 3.81 (d, *J*_{AB} = 17.61 Hz, *J*_{BC} = 11.20 Hz, 1H, C₅-H pyrazoline H_B), 3.26 (d, *J*_{AB} = 17.53 Hz, *J*_{AC} = 3.07 Hz, 1H, C₄-H pyrazoline H_A), 3.08 (s, 6H, -N (CH₃)₂); ¹³C (100 MHz, DMSO-*d*₆): δ = 169.3 (1C, >C=O), 156.2 (1C, C₁ naphthalene ring), 155.2 (1C, C₃ pyrazoline ring), 151.1 (1C, C₂ benzimidazole ring), 149.2 (1C, C₄ aromatic ring), 134.5 (2C, C₈ and C₉ benzimidazole ring), 134.8 (1C, C₉ naphthalene ring), 134.9 (1C, C₁₀ naphthalene ring), 131.5 (1C, C₁ aromatic ring), 129.3 (2C, C₂ and C₆ aromatic ring), 129.6 (2C, C₂ and C₆ aromatic ring), 127.5 (1C, C₇ naphthalene ring), 127.7 (1C, C₅ naphthalene ring), 126.4 (1C, C₆ naphthalene ring), 126.1 (1C, C₃ naphthalene ring), 125.5 (1C, C₇ aromatic ring), 123.3 (2C, C₅ and C₆ benzimidazole ring), 123.0 (1C, C₈ naphthalene ring), 120.1 (1C, C₄ naphthalene ring), 115.5 (2C, C₇ and C₄ benzimidazole ring), 112.5 (2C, C₃ and C₅ aromatic ring), 107.5 (1C, C₂ naphthalene ring), 67.1 (1C, -OCH₂-), 66.7 (1C, C₅ pyrazoline ring), 41.7 (2C, -CH₃), 39.4 (1C, C₄ pyrazoline ring); MS (*m/z*): 489.2 (M⁺); anal. calcd. for (C₃₀H₂₇N₅O₂): C, 73.60; H, 5.56; N, 14.31%; found: C, 73.71; H, 5.61; N, 14.38%.

Biological evaluation

Antimicrobial screening assay

1-(3-(1*H*-benzimidazol-2-yl)-5-aryl-4,5-dihydro-1*H*-pyrazol-1-yl)-2-(naphthalen-1-yloxy)ethanones (**5a–l**) were screened for their antibacterial activity against *Escherichia coli* (MTCC-442), *Pseudomonas aeruginosa* (MTCC-441), *Staphylococcus aureus* (MTCC-96), and *Streptococcus pyogenes* (MTCC-443). MICs of the titled compounds were compared with ampicillin (for bacteria) and griseofulvin (for fungi) was standards and the results are displayed in Table 1. Antifungal activity was screened against three fungi *Candida albicans* (MTCC-227), *Aspergillus niger* (MTCC-282) and *Aspergillus clavatus* (MTCC-1323). Titled compounds were screened in six sets against bacteria and fungi. The MIC of titled compounds was determined as per the National Committee for Clinical Laboratory Standards protocol using Mueller-Hinton Broth (Becton-Dickinson, USA) dilution method (Rattan 2000).

Antibacterial activity

The data of compounds **5a–l** are displayed in Table 1. The data of antibacterial activity clearly showed that compound **5i** (-4-NO₂) exhibited very good activity (MIC = 25 µg/ml) against *E. coli*, *S. aureus*, and *S. pyogenes* and showed

Table 1 Antibacterial and antifungal activity of compounds (**5a–l**)

Sr. no.	-R	Minimum bactericidal concentrations (MIC _B) in µg/ml				Minimum fungicidal concentrations (MIC _F) in µg/ml		
		<i>E. c.</i>	<i>P. a.</i>	<i>S. a.</i>	<i>S. p.</i>	<i>C. a.</i>	<i>A. n.</i>	<i>A. c.</i>
5a	-H	250	250	200	250	100	100	100
5b	-2-Cl	50	50	100	12.5	500	500	500
5c	-2-OH	100	100	100	100	100	100	100
5d	-3-OH	500	500	500	100	500	100	>1000
5e	-4-OH	500	250	100	100	100	500	100
5f	-3-OCH ₃ -4-OH	250	250	250	500	100	500	500
5g	-2-NO ₂	500	250	500	500	500	100	>1000
5h	-3-NO ₂	500	500	250	500	500	1000	>1000
5i	-4-NO ₂	25	12.5	50	25	250	100	250
5j	-4-CH ₃	100	500	500	500	500	50	>100
5k	-4-OCH ₃	50	50	100	50	100	50	25
5l	-4-N(CH ₃) ₂	250	250	500	500	100	500	500
Ampicillin		100	100	250	100	–	–	–
Griseofulvin		–	–	–	–	500	100	100

E.c. Escherichia coli (MTCC-442), *P.a.* Pseudomonas aeruginosa (MTCC-441), *S.a.* Staphylococcus aureus (MTCC-96), *S.p.* Streptococcus pyogenes (MTCC-443), *C.a.* Candida albicans (MTCC-227), *A.n.* Aspergillus niger (MTCC-282), *A.c.* Aspergillus clavatus (MTCC-1323)

excellent activity (MIC = 12.5 µg/ml) against *P. aeruginosa*. Compound **5k** (-4-OCH₃), showed good activity (MIC = 50 µg/ml) against *E. Coil*, *P. aeruginosa*, and *S. pyogenes*. The remaining compounds of the series possessed moderate antibacterial activity against responsible bacterial strains.

Antifungal activity

Antifungal activity was performed using *C. albicans*, *A. niger*, and *A. clavatus* at various concentrations and MIC values are displayed in Table 1. Synthesized compounds were diluted to 1000 µg/ml concentration, as a stock solution. According to the screening results it was indicated that, Compounds **5j** and **5k** exhibited good antifungal activity against *A. niger* at MIC = 50 µg/ml and compound **5k** possessed very good activity against *A. clavatus* at MIC = 25 µg/ml. Other derivatives showed moderate activity against responsible fungal strains.

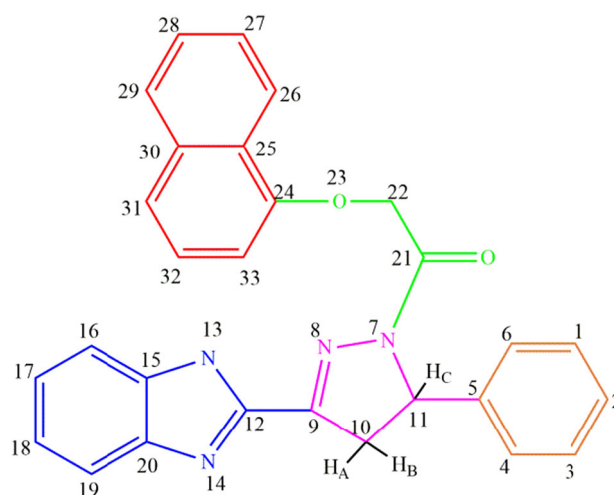
Results and discussion

Characterization of newly synthesized compounds was carried out by standard spectroscopic methods.

Interpretation of data was reported in the experimental section. Infrared spectrum of compound **5h** showed stretching vibration at 3458 cm⁻¹ indicating the presence of N–H stretching of secondary amines. The absorption band at 3078 cm⁻¹ indicated the presence of Ar–H stretching vibration. Stretching at 2933 cm⁻¹ had proved the presence of –CH₂ group in compound **5h**. The absorption band at 1690 cm⁻¹ showed the presence of a >C=O stretching vibration. Absorption bands at 1507, 1468, and 1530 cm⁻¹ showed the presence of >C=N, >C=C<, and –N=O– stretching of the aromatic ring. Stretching at 1136 and 1234 cm⁻¹ showed the presence of C–O–C bending vibrations.

The ¹H NMR spectra of final compound **5h** showed that protons attached to C-22, gave singlet at δ = 4.78 (–O–CH₂–). In pyrazoline ring one proton showed chemical shift at δ = 5.50 (>CH–H_C) as a doublet, one proton of pyrazoline H_B and pyrazoline H_A gave doublet of doublet at δ = 3.72 and 3.20. Secondary amine displayed chemical shift at δ = 12.80 as a singlet while the protons of phenyl ring furnished multiple signals at δ = 6.45–8.45 (m, 15H, Ar–H) (Fig. 2).

Looking to the ¹³C NMR spectra, the chemical shifts of the final compound **5h** have carbons that varied from δ = 169.3–39.1 ppm. Carbon of ketone (>C=O) group has chemical shift at δ = 169.3. The carbon of –OCH₂ group at C-22 attached to the ketone group has a chemical shift value at δ = 67.6. The carbons of pyrazoline ring, C-9, C-10, and C-11 showed chemical shifts at δ = 155.3, 39.1, and 65.7, respectively. The benzimidazole carbons C-12 showed peak at 151.1 ppm, C-15, C-20 appeared at 134.0 ppm. Similarly C-16, C-19 exhibited chemical shifts at 115.8, C-17 while C-18 showed at 123.7 ppm. The carbons of naphthalene ring, C-24, C-26, C-27, and C-29 appeared at 156.0, 123.7,

**Fig. 2** Carbon enumerations of compound **5h**

125.1, 126.0, and 127.1. Carbons of C-25 and C-30 exhibited peaks at 134.7, 134.4 while C-31, C-32, and C-33 appeared at 120.6, 126.6, and 107.0. The nitro group in the phenyl ring gave a chemical shift at $\delta = 147.1$.

Structure–activity relationship (SAR) studies

SAR studies revealed that the presence of the benzimidazole ring is essential for a broad spectrum antimicrobial activity. Substitution pattern on the benzimidazole clubbed pyrazoline derivatives was carefully selected for considering electronic environments of the structures. Antimicrobial data of targeted compounds in Table 1 has clearly shown that diverse electronic varieties are responsible for broad spectrum activity. Compound **5i** containing nitro group at *para* position and in compound **5b** group at *ortho* position showed the highest inhibition against bacterial strains. On the other hand the results exhibited that compounds **5j** and **5k** substituted with methyl and methoxy group at *para* position was found to be the most promising antifungal agents. SAR studies indicates that compounds containing electron withdrawing groups at the *para* position increased antibacterial activity while the presence of the electron releasing group at the *para* position enhanced antifungal activity.

Conclusion

The titled compounds were screened for their in vitro antibacterial and antifungal activities. It is clearly concluded from Table 1 that structural and electronic variety of the targeted compounds affected their biological activities. On the basis of results of biological activity we have concluded that *para* nitro and *para* chloro are the most distinctive derivatives in the present study because of their prominent in vitro antibacterial potency. For antifungal activity it is proved that *para* position of methoxy and methyl group showed most incremental antifungal activity. SAR studies revealed that *para* position of substituent is essential for potential antimicrobial activity.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

References

- Alaqeel SI (2017) Synthetic approaches to benzimidazoles from o-phenylenediamine: a literature review. *J Saudi Chem Soc* 21:229–237
- Behera AK, Panda J, Padhy GK (2016) Synthesis and characterization of novel benzimidazole chalcones as antibacterial agents. *Der Pharma Chem* 8:235–241
- Desai NC, Joshi VV, Rajpara KM, Satodiya HM, Vaghani HV (2013) Synthesis of quinoline-pyrazoline-based thiazole derivatives endowed with antimicrobial activity. *Indian J Chem Sect B* 52:1191–1201
- Desai NC, Joshi VV, Rajpara KM, Vaghani HV, Satodiya HM, Bhatt KA (2014a) Synthesis and evaluation of *N*-substituted thiazolidine-2,4-dione containing pyrazole as a potent antimicrobial agents. *Anti-infective agents* 12:85–94
- Desai NC, Shihory NR, Kotadiya GM (2014b) Facile synthesis of benzimidazole bearing 2-pyridone derivatives as potential antimicrobial agents. *Chin Chem Lett* 25:305–307
- Fernandez R, Goya P, Elguero J (2014) A review of recent progress (2002–2012) on the biological activities of pyrazoles. *ARKIVOC* 02:233–293
- Garuti L, Roberti M, Malagoli M, Rossi T, Castelli M (2000) Synthesis and antiproliferative activity of some benzimidazole-4,7-dione derivatives. *Bioorg Med Chem Lett* 10:2193–2195
- Gawad NM, Hassan GS, Georgey HH (2012) Design and synthesis of some pyrazole derivatives of expected anti-inflammatory and analgesic activities. *Med Chem Res* 21:983–994
- Ingle RG, Magar DD (2011) Heterocyclic chemistry of benzimidazoles and potential activities of derivatives. *Int J Drug Res Technol* 01:26–32
- Kaplancikli ZA, Ozdemir A, Turan-Zitouni G, Altintop MD, Can OD (2010) New pyrazoline derivatives and their antidepressant activity. *Eur J Med Chem* 45:4383–4387
- Khunt RC, Khedkar VM, Chawda RS, Chauhan NA, Parikh AR, Coutinho EC (2012) Synthesis, antitubercular evaluation and 3D-QSAR study of *N*-phenyl-3-(4-fluorophenyl)-4-substituted pyrazole derivatives. *Bioorg Med Chem Lett* 22:666–678
- Kumar RS, Arif IA, Ahamed A, Idhayadhulla A (2015) Anti-inflammatory and antimicrobial activities of novel pyrazole analogs. *Saudi J Biol Sci*, doi:10.1016/j.sjbs.2015.07.005
- Kumar S, Kumar P, Sati N (2012) synthesis and biological evaluation of Schiff base and azetidinones of 1-naphthol. *J Pharm Bioallied Sci* 04:246–249
- Lesyk R, Havrylyuk D, Zimenkovsky B, Vasylenko O, Gzella A (2012) Synthesis of new 4-thiazolidinone, pyrazoline and isatin based conjugates with promising antitumor activity. *J Med Chem* 55:8630–8641
- Mckellar QA, Scott EW (1990) The benzimidazole anthelmintic agents—a review. *J Vet Pharmacol Ther* 13:223–247
- Ouyang G, Cai XJ, Chen Z, Song BA, Bhadury PA, Yang S, Jin LH, Xue W, Hu DY, Zeng S (2008) Synthesis and antiviral activities of pyrazole derivatives containing an oxime moiety. *J Agric Food Chem* 56:10160–10167
- Padmaja A, Rajasekhara C, Muralikrishna A, Padmavathi V (2011) Synthesis and antioxidant activity of oxazolyl/thiazolyl sulfonyl methyl pyrazoles and isoxazoles. *Eur J Med Chem* 6:5034–5038
- Pathak RB, Chovatia PT, Parekh HH (2012) Synthesis, antitubercular and antimicrobial evaluation of 3-(4-chlorophenyl)-4-substituted pyrazole derivatives. *Bioorg Med Chem Lett* 22:5129–5133

- Rattan A (2000) Antimicrobials in laboratory medicine. Churchill BI. Livingstone, New Delhi, 85
- Rokade Y, Dongare N (2010) Synthesis and antimicrobial activity of some azetidinone derivatives with the β -naphthol. Rasayan J Chem 4:641–645
- Sekar UN, Padalkar BBN, Gupta VD, Pharangare KR, Patil VS, Umape PG (2016) Synthesis and antimicrobial activity of novel 2-substituted benzimidazole, benzoxazole and benzothiazole derivatives. Arab J Chem 9:S1125–S1130