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Synthesis and Biological Activity of Novel 2, 5-Disubstituted Benzimidazole Derivatives

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ABSTRACT
A new series of 2, 5 di-substituted benzimidazole derivatives have been synthesized. The structures of the synthesized compounds were confirmed by IR, ^{1}H NMR and Mass spectral analysis and they were evaluated for their antibacterial; *Proteus vulgaris* (NCTC 4635), *Klesibella pneumonia* (ATCC 29655), *Bacillus cereus* (NL98), and *Enterococcus faecium* (ATCC 29212) and antifungal (*Aspergillus niger* and *Aspergillus fumigatus)* activities by disc diffusion method. All of the synthesized compounds showed good antibacterial and antifungal activity. However the antibacterial and antifungal activity of the synthesized compounds against the tested organisms was found to be less than that of respective standard drug at tested dose level.

Keywords: O-phenylene diamine, Benzimidazole, Antibacterial, Antifungal.

INTRODUCTION

Benzimidazole ring system known to be possess numerous antimicrobial [1-9], anti-inflammatory [9], anthelmintic [10], antiviral [11-13] and anti-tumour [14] properties. Therefore it was enabled that compounds containing benzimidazole nucleus would result in interesting of biological activities. In the present study 2-substituted benzimidazoles were synthesized by treating o-phenylene diamine with different carboxylic acids. Then they were subjected to nitration at room temperature to get 5-nitro 2-substituted benzimidazole derivatives. Finally they were reduced by using Zn/NaOH to get 5-amino 2-substituted benzimidazole derivatives. The structures of the synthesized compounds were confirmed by IR, ^{1}H NMR and Mass spectral analysis. The newly synthesized final compounds were screened for their antibacterial and antifungal activity.

MATERIALS AND METHODS

Melting points were determined in open capillary tubes on melting point apparatus (Sunbim, Guna enterprises) and are uncorrected. The ^{1}H NMR spectra were recorded on Bruker-NMR 500 mHZ using MeOD and DMSO – d_6 as solvent. Mass spectra were recorded on JEOL GC mate mass spectrometer. The IR spectra of the synthesized compounds were recorded on Perkin-Elmer FT-IR spectrophotometer with KBr pellets. The UV spectra were recorded by using Double beam SHIMADZU 1700 UV spectrometer. The purity of the compounds was checked by TLC on pre-coated silica gel G plates by using methanol: water as a mobile phase and visualized in iodine vapour.

General Method for the Synthesis of 2-substituted benzimidazole derivatives [14-15]

O-phenylene diamine (0.25 mol) and appropriate carboxylic acid (0.34 mol) was heated on a water bath at 100^{o}C for 6-8 h. The completion of reaction was monitored by TLC. After completion of reaction, the reaction mixture was cooled and basified to a pH of 7-8 by using 10% sodium hydroxide solution. The crude benzimidazole was filtered at the pump, washed with ice cold water. The crude product was dissolved in 400 ml of boiling water and 2 g of decolorizing carbon was added and digested for 15 min. The solution was filtered while hot, cooled the filtrate to about 10^{o}C. The pure product was filtered, washed with 25 ml of cold water and dried at 100^{o}C.

General Method for the Synthesis of 5-nitro 2-substituted benzimidazole derivatives [16]

Conc. HNO_3 (7.5 ml) was placed in three necked round bottom flask fitted with a mechanical stirrer. The flask was immersed in ice cold water and added slowly conc. H_2SO_4 (7.5 ml) down the condenser with slow stirring. After the addition, 2-substituted benzimidazoles (0.028 mol) were added in a portion over a period of 1 h at such a rate that the temperature did not exceed 35ºC. After continuous stirring for 12 h, the reaction mixture was poured very slowly over

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crushed ice with vigorous stirring. The formed product was filtered, washed with cold water and recrystallized from ethanol.

General Method for the Synthesis of 5-amino 2-substituted benzimdazole derivatives [17]

A solution of 0.5 g of 5-nitro, 2-substituted benzimidazoles in 15 ml of rectified sprit was taken in round bottom flask. To this, 5 ml of 20 % sodium hydroxide and 2.5 g of zinc dust powder was added. The reaction mixture was refluxed until colour of the solution changed from deep red to colourless (about 4.5 h), the hot mixture was filtered. The zinc residue was returned to the flask and extracted with 10 ml of hot rectified sprit for two times. The extracts were combined and the solvent was removed under vacuum, yielded the brown solid and recrystallized from methanol.

Spectral data of synthesized compounds

Compound SY_1: yield = 37.94%, mp 162°C, R_f = 0.79, λ_{max} (MeOH) 280.50, 242.5. IR (KBr) cm^{-1} 3369.99 (N-H str), 3100.50 (Ar C-H str), 2539.91 (S-H str), 1661.54 (Ar C=C ring str), 1556.06 (C=N str). ^{1}H NMR (MeOD) δ: 7.70 (m, 2H; Ar-H- C_4 & C_7,), 7.26 (m, 2H; Ar-H- C_5 & C_6), 5.0 (s, 1H; broad, NH), 3.82 (s, 2H; CH_2) 1.5 (s, 1H; SH). EI-MS *m/z* 163.82 (Calcd for $C_8H_8N_2S$: 164.22).

Compound SY_2: yield = 39.94%, mp 112°C, R_f = 0.85, λ_{max} (MeOH) 275.50, 210.0. IR (KBr) cm^{-1} 3363.57 (N-H str), 3032.10 (Ar C-H str), 2667.83 (C-H str), 1632.61 (C=C ring str), 1591.92 (C=N str), 1320.5 (C-H ben gem-dimethyl), 1272.31 (C-N str), 1114.79 (C-C skeletal str). ^{1}H NMR (MeOD) δ: 7.70 (m, 2H; Ar-H- C_4 & C_7), 7.26 (m, 2H; Ar-H- C_5 & C_6), 5.0 (s, 1H; broad, NH), 3.12 (m, 1H; CH of iso propyl), 1.29 (d, 6H; $2CH_3$ of iso propyl). EI-MS *m/z*: 159.90 (Calcd for $C_{10}H_{12}N_2$: 160.21).

Compound SY_3: yield = 54.02%, mp 114°C, R_f = 0.83, λ_{max} (MeOH) 293.50, 238.0. IR (KBr) cm^{-1} 3192.57 (C-H str), 3288.94 (N-H str), 3032.75 (Ar C-H str), 1632.86 (C=C ring str), 1590.16 (C=N str), 1272.45 (C-N str). ^{1}H NMR (MeOD) δ: 7.70 (m, 2H; Ar-H- C_4 & C_7), 7.26 (m, 2H; Ar-H- C_5 & C_6), 5.0 (s, 1H; broad, NH), 2.55(t, 2H; CH_2), 1.62 (m, 2H; CH_2), 1.33 (m, 2H; CH_2), 0.96 (t, 3H; methyl, C_{11}). EI-MS *m/z*: 174.24 (Calcd for $C_{11}H_{14}N_2$: 170.24).

Compound SY_4: yield = 35.37%, mp 248°C, R_f = 0.30, λ_{max} (MeOH) 294.50. IR (KBr) cm^{-1} 3514.74 (N-H asy str primary amine), 3463.63 (N-H sy str primary amine), 3358.60 (N-H str secondary amine), 2968.78 (Ar C-H str), 1621.12 (N-H ben), 1274.47 (C-N str). ^{1}H NMR (MeOD) δ: 7.70 (m, 2H; Ar-H- C_4 & C_7), 7.23-7.26 (m, 2H; Ar-H- C_5, C_6 & $C_{2'}$, $C_{6'}$), 6.52 (m, 2H; Ar–H- $C_{3'}$&$C_{5'}$), 5.0 (s, 1H; broad, NH), 4.0 (s, 2H; NH_2). EI-MS *m/z*: 209.18 (Calcd for $C_{13}H_{11}N_3$: 209.24).

Compound SY_5: yield = 31.38%, mp 254°C, R_f = 0.58, λ_{max} (MeOH) 273.0, IR (KBr) cm^{-1} 3114.22 (N-H str), 3062.21 (Ar C-H str), 1604.17 (C-C skeletal str), 1541.85 (N-O asy str), 1349.62 (N-O sym str), 1288.31 (C-N str). ^{1}H NMR (MeOD) δ: 8.25 (m, 2H; Ar-H- $C_{3'}$ & $C_{5'}$), 7.74 (m, 2H; Ar-H- $C_{2'}$&$C_{6'}$), 7.70 (m, 2H; Ar-H- C_4 & C_7), 7.26 (m, 2H; Ar-H- C_5 & C_6), 5.0 (s, 1H; broad, NH). EI-MS *m/z*: 238.95 (Calcd for $C_{13}H_9N_3O_2$: 239.23).

Compound SY_6: yield = 54.79%, mp 185°C, R_f = 0.81, λ_{max} (MeOH) 280.0, IR (KBr) cm^{-1} 3072.23 (Ar C-H str), 2933.61 (S-H str), 1683.23 (C=C ring str), 1584.92 (N-O asy str), 1348.72 (N-O sym str), 1537.17 (C=N str), 846.68 (C-N str), 763.10 (N-O ben), 715.23 (C-S str). ^{1}H NMR (MeOD) δ: 8.63 (s, 1H; Ar-H- C_4), 8.19 (d, 1H; Ar-H- C_6), 7.96 (d, 1H; Ar-H- C_7), 5.0 (s, 1H; broad, NH), 3.82 (s, 2H; CH_2), 1.5 (s, 1H; SH). EI-MS *m/z*: 209.11 (Calcd for $C_8H_7N_3O_2S$: 209.22).

Compound SY_7: yield = 31.53%, mp 96°C, R_f = 0.69, λ_{max} (MeOH) 233.0, IR (KBr) cm^{-1} 3384.19 (N-H str), 3098.25 (Ar C-H str), 1612.71 (N-H ben), 1538.03 (N-O asy str), 1348.03 (N-O sym str), 1217.67 (C-N str), 883.21 (C=C ring str). ^{1}H NMR (MeOD) δ: 8.63 (s, 1H; Ar-H- C_4), 8.19 (d, 1H; Ar-H- C_6), 7.96 (d, 1H; Ar-H- C_7), 5.0 (s, 1H; broad, NH), 3.12 (m, 1H; CH of isopropyl), 1.29 (d, 6H; $2CH_3$ of isopropyl). EI-MS *m/z*: 204.88 (Calcd for $C_{10}H_{11}N_3O_2$: 205.21).

Compound SY_8: yield = 26.59%, mp 124°C, R_f = 0.84, λ_{max} (MeOH) 244.0, IR (KBr) cm^{-1} 3651.02 (N-H str), 3098.41 (Ar C-H str), 1541.67 (N-O asy str), 1344.16 (N-O sym str), 1209.52 (C-N str), 892.90 (C=C ring str). ^{1}H NMR (MeOD) δ: 8.63 (s, 6H; Ar-H- C_4), 8.19 (d, 1H; Ar-H- C_5), 7.96 (d, 1H; Ar-H- C_7), 5.0 (s, 1H; broad, NH), 2.55 (t, 2H; CH_2), 1.62 (m, 2H; CH_2), 1.33 (m, 2H; CH_2), 0.96 (t, 2H; CH_3). EI-MS *m/z*: 219.04 (Calcd for $C_{11}H_{13}N_3O_2$: 219.24).

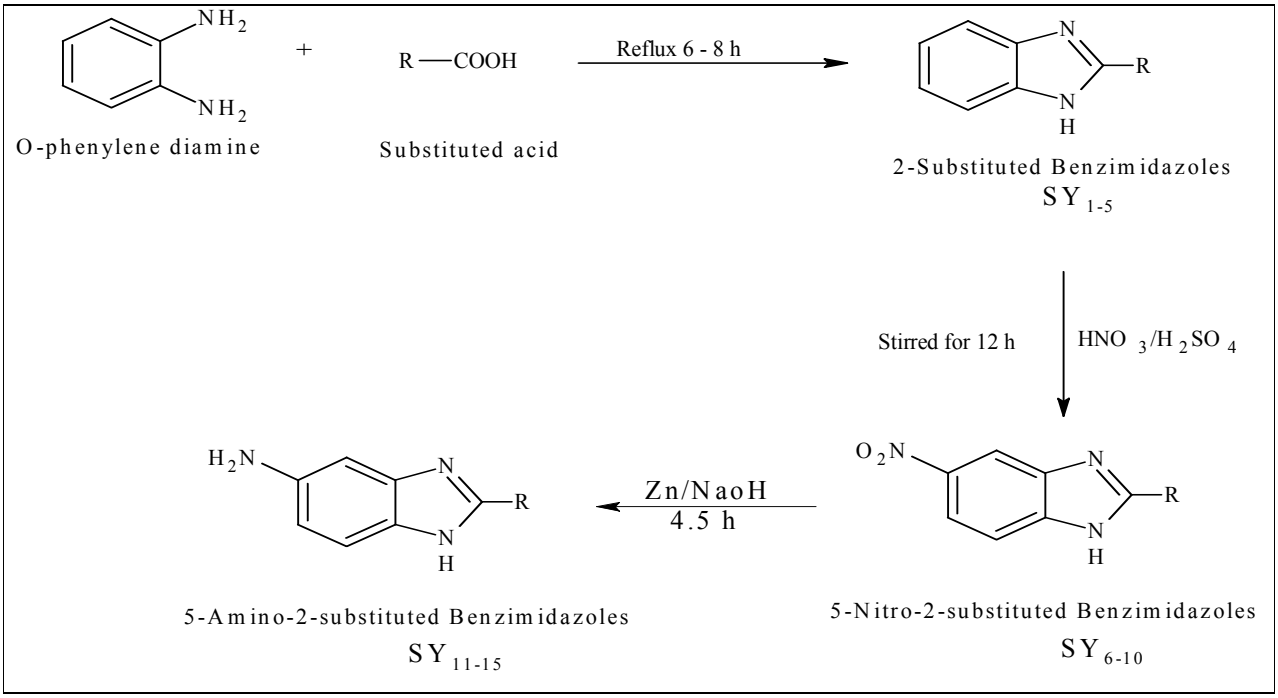
Compound SY_9: yield = 30.09%, mp 216°C, R_f = 0.81, λ_{max} (MeOH) 313.0, IR (KBr) cm^{-1} 3418.50 (N-H sym str primary amine), 3322.70 (N-H str secondary amine), 3072.36 (Ar C-H str), 1644.22 (N-H ben), 1532.92 (N-O asy str), 1344.12 (N-O sym str), 1231.34 (C-N str). ^{1}H NMR (MeOD) δ: 8.63 (s, 1H; Ar-H- C_4), 8.19 (d, 1H; Ar-H- C_6), 7.96 (d, 1H; Ar-H- C_7), 7.23 (m, 2H; Ar-H- $C_{2'}$ & $C_{6'}$), 6.52 (m, 2H; Ar-H- $C_{3'}$ & $C_{5'}$), 5.0 (s, 1H; broad, NH), 4.0 (s, 1H; NH_2). EI-MS *m/z*: 254.12 (Calcd for $C_{13}H_{10}N_4O_2$: 254.24).

Compound SY_{10}: yield = 39.54%, mp 226°C, R_f = 0.58, λ_{max} (MeOH) 267.5, IR (KBr) Cm^{-1} 3114.32 (N-H str), 3061.87 (Ar C-H str), 1698.28 (N-O asy str), 1604.29 (N-H ben), 1349.69 (N-O sym str), 877.69 (C-N str). ^{1}H NMR (MeOD) δ: 8.63 (s, 1H; Ar-H- C_4), 8.25 (m, 2H; Ar-H- $C_{3'}$ & $C_{5'}$), 8.19 (d, 1H; Ar-H- C_6), 7.96 (d, 1H; Ar-H- C_7), 7.74 (m, 1H; Ar-H- $C_{2'}$ & $C_{6'}$), 5.0 (s, 1H; broad, NH). EI-MS *m/z*: 284.12 (Calcd for $C_{13}H_8N_4O_4$: 284.22).

Compound SY_{11}: yield = 44.04%, mp 261°C, R_f = 0.78, λ_{max} (MeOH, DMSO) 275.0, IR (KBr) cm^{-1} 3552.00 (N-H asy str primary amine), 3416.86 (N-H sym str primary amine), 3376.18 (N-H str secondary amine), 2468.00 (S-H str), 1622.56 (N-H ben), 1225.49 (C-N str), 746.41 (C-S str). ^{1}H NMR (DMSO – d_6) δ: 7.31 (d, 1H; Ar-H- C_7), 6.70 (s, 1H; Ar-H- C_4), 6.62 (d, 1H; Ar-H- C_6), 5.0 (s, 1H; NH), 4.03 (s, 2H; CH_2), 3.48 (s, 2H; NH_2), 1.68 (s, 1H; SH). EI-MS *m/z*: 179.14 (Calcd for $C_8H_9N_3S$: 179.24).

Compound SY_{12}: yield = 91.96%, mp 220°C, R_f = 0.79, λ_{max} (MeOH, DMSO) 272.5, IR (KBr) cm^{-1} 3587.00 (N-H asy str primary amine), 3218.00 (N-H str secondary amine), 2343.00 (C-H str), 1635.00 (N-H ben), 1385.00 (C-N str), 1129.00 (C-H inplane ben). ^{1}H NMR (DMSO – d_6) δ: 7.31 (d, 1H; Ar-H- C_7), 6.69 (s, 1H; Ar-H- C_4), 6.61 (d, 1H; Ar-H- C_6), 5.0 (s, 1H; NH), 3.48 (s, 2H; NH_2), 3.40 (m, 1H; CH of isopropyl), 1.24 (m, 6H; CH_3 of isopropyl). EI-MS *m/z*: 175.18 (Calcd for $C_{10}H_{13}N_3$: 175.23).

Compound SY_{13}: yield = 93.02%, mp 238°C, R_f = 0.80, λ_{max} (MeOH, DMSO) 366.0, IR (KBr) cm^{-1} 3573.00 (N-H asy str primary amines), 3393.00 (N-H str secondary amines), 2175.00 (C-H str), 1648.00 (N-H ben), 1397.00 (C-N str). ^{1}H NMR (DMSO – d_6) δ: 7.31 (d, 1H; Ar-H- C_7), 6.69 (s, 1H; Ar-H- C_4), 6.61 (d, 1H; Ar-H- C_6), 5.0 (s, 1H; NH), 3.48 (s, 2H; NH_2), 2.86 (t, 2H; CH_2), 1.72 (m, 2H; CH_2), 1.30 (m, 2H; CH_2), 0.90 (t, 3H; CH_3). EI-MS *m/z*: 189.22 (Calcd for $C_{11}H_{15}N_3$: 189.25).



Synthetic Scheme

Scheme 1: Synthetic scheme of 5-amino 2-substituted benzimidazole derivatives.

Compound	R
SY_1, SY_6, SY_{11}	CH_2SH
SY_2, SY_7, SY_{12}	$CH(CH_3)_2$
SY_3, SY_8, SY_{13}	$CH_2CH_2CH_2CH_3$
SY_4, SY_9, SY_{14}	C_6H_6N
SY_5, SY_{10}, SY_{15}	$C_6H_4NO_2$

Compound SY_{14}: yield = 86.36%, mp 255°C, R_f = 0.72, λ_{max} (MeOH, DMSO) 366.0, IR (KBr) cm^{-1} 3579.00 (N-H asy str primary amine), 3369.00 (N-H str secondary amine), 1645.00 (N-H ben), 1429.00 (C-N str), 866.00 (C-H ben). ^{1}H NMR (DMSO – d_6) δ: 7.85 (m, 2H; Ar-H- $C_{2'}$ & $C_{6'}$), 7.43 (d, 1H; Ar-H- C_7), 6.85 (s, 1H; Ar-H- C_4), 6.76 (d, 1H; Ar-H- C_6), 6.59 (m, 2H; Ar-H- C_{10} & C_{12}), 5.0 (s, 1H; NH), 3.99 (s, 2H; NH_2), 3.58 (s, 2H; NH_2). EI-MS *m/z*: 224.20 (Calcd for $C_{13}H_{12}N_4$: 224.26).

Compound SY_{15}: yield = 39.14%, mp 277°C, R_f = 0.76, λ_{max} (MeOH, DMSO) 270.0, IR (KBr) cm^{-1} 3559.00 (N-H asy str primary amine), 3432.00 (N-H sym str primary amine), 3206.00 (N-H str secondary amine), 1632.00 (N-H ben), 1596.00 (N-O str). ^{1}H NMR (DMSO – d_6) δ: 8.28 (m, 2H; Ar-H- $C_{3'}$ & $C_{5'}$), 8.02 (m, 2H; Ar-H- $C_{2'}$ & $C_{6'}$), 7. 44 (d, 1H; Ar-H-C_7), 6.91 (s, 1H; Ar-H-C_4), 6.82 (d, 1H; Ar-H- C_6), 5.0 (s, 1H; NH), 3.58 (s, 2H; NH_2). EI-MS *m/z*: 254.12 (Calcd for $C_{13}H_{10}N_4O_2$: 254.24).

Antimicrobial Activity [2]

The synthesized compounds were tested for antimicrobial activity by disc diffusion method. They were dissolved in DMSO and sterilized by filtering through 0.45µm millipore filter. Final inoculums of 100µl suspension containing 10^8 CFU/ ml of each bacterium and fungus used. Nutrient agar (antibacterial activity) and sabouraud's dextrose agar medium (antifungal activity) was prepared and sterilized by an autoclave (121°C and 15 Ibs for 20 min) and transferred to previously sterilized petridishes (9 cm in diameter). After solidification, petriplates were inoculated with bacterial organisms in sterile nutrient agar medium at 45°C, and fungal organisms in sterile sabouraud's dextrose agar medium at 45°C in aseptic condition. Sterile Whatmann filter paper discs (previously sterilized in U.V. lamp) were impregnated with synthesized compounds at a concentration of 25; 100 mg/disc were placed in the organism-impregnated petri plates under sterile condition. The plates were left for 30 min to allow the diffusion of compounds at room temperature. Antibiotic discs of ciprofloxacin (100µg /disc) and ketaconazole (100µg /disc) were used as positive control, while DMSO used as negative control. Then the plates were incubated for 24 h at 37 ± 1°C for antibacterial activity and 48 h at 37±1°C for antifungal activity. The zone of inhibition was calculated by measuring the minimum dimension of the zone of no microbial growth around the each disc.

RESULTS AND DISCUSSION

The structure of the synthesized compounds were established by spectral (IR, ^{1}H NMR and Mass) analysis data. The NH band (3463-3114 cm^{-1}) and NH proton signal (5.0 ppm) of 2-substituted benzimidazole in IR and ^{1}H NMR spectrum respectively in the synthesized compounds, (SY_1-SY_5) confirmed the formation of benzimidazole nucleus. In SY_1, ^{1}H NMR spectrum showed a 2 proton singlet at δ 1.5 and δ 3.82 for 3 protons confirmed the presence of methane thiol group. In SY_2, multiplet at δ 3.12 for 1 proton and doublet at δ 1.29 for 6 protons indicated the formation of iso-propyl group. In SY_3, two triplets at δ 2.55 and 0.96 for 5 protons and two multiplet at δ 1.62 and δ 1.37 for 4 protons indicated the presence of butyl group. In SY_4, two multiplet at δ 7.23-7.26 and δ 6.52 for 4 protons and a singlet at δ 4.0 for 2 protons indicated the presence of amino phenyl group. In the case of SY_5, two multiplet at δ 8.25 and δ 7.74 for 4 protons indicated the substitution of nitro phenyl group at C_2 of benzimidazole nucleus. The presence of nitro group in SY_6-SY_{10} was ascertained from strong bands at 1584 -1532 cm^{-1} and 1345 cm^{-1} corresponding to asymmetric and symmetric O=N=O stretch respectively.

Table 1: Antimicrobial activity of the synthesized compounds by disc diffusion method (SY_{11} – SY_{15})

Organisms	Diameter of Zone of inhibition in mm											
	SY_{11}		SY_{12}		SY_{13}		SY_{14}		SY_{15}		Ket	Cip
	25 (mg)	100 (mg)	25 (mg)	100 (mg)	25 (mg)	100 (mg)	25(mg)	100 (mg)	25 (mg)	100 (mg)	100 (µg)	100 (µg)
B. cereus	11	17	17	25.5	12	14	10	14.8	18	26	----	30
P. vulgaris	12	18.5	12	15	21	25	11	16.4	12	17	-----	28
K.pneumonia	13	15	14	17	18	22.5	21	26	22	26.5	-----	29
E. faecium	15	18	14	17.6	11	14	17	21	17	24	-----	28
A. niger	14	17.5	19	22	14	26	15	19.5	12	16.4	30	----
A. fumigatus	15	17	20	21	15	16	11	16.7	13	18	27	-----

(Ket = Ketoconazole, Cip = Ciprofloxacin, *P. vulgaris = Proteus vulgaris, K. pneumonia = Klesibella pneumonia, B. Cereus = Bacillus cereus, E. faecium = Enterococcus faecium, A. niger = Aspergillus niger* and *A. fumigatus = Aspergillus fumigatus)*

Further a strong intensity signal at 1231-846 cm^{-1} was attributed to the C-N stretching for aromatic nitro compounds. Spectrum of SY_6-SY_{10} in the aromatic region indicated that the three chemical environments at δ 8.63, 8.19 and 7.96, instead of two regions which were present in SY_1-SY_5. The presence of primary amino group in SY_{11}-SY_{15} was ascertained from strong bands at 3500 cm^{-1} and 3400 cm^{-1} corresponding to asymmetric and symmetric H-N-H stretch respectively. Further a strong signal at 1648-1622 cm^{-1} was attributed to N-H bending for primary amino group. In SY_{11} – $SY_{15,}$ a singlet at δ 3.48 for 2 protons indicated the presence of primary amino group. In the mass spectrum of the synthesized compounds produced (M^+) molecular ion peaks at 163.82, 159.90, 174.24, 209.18, 238.95, 209.11, 204.88, 219.04, 254.12, 284.12, 179.24, 175.23, 189.25, 224.26, 254.24 values for SY_1 - SY_{15} respectively corresponds to their molecular formulas.

The synthesized compounds were evaluated for *in-vitro* anti-bacterial activity against gram negative bacteria *Proteus vulgaris* (NCTC 4635), *Klesibella pneumonia* (ATCC 29655) and gram positive bacteria *Bacillus cereus* (NL98), *Enterococcus faecium* (ATCC 29212). These are the agents commonly causes urinary tract infection, nosocomial infection, biliary tract infection. The gram negative organism *Klesibella pneumonia* causes pneumonia, bronco pneumonia and bronchitis infection. The gram negative organisms *Bacillus cereus* and *Enterococcus faecium* cause endocarditis, bacteremia, meningitis and septicaemia. From the biological data, it was evident that the compound SY_{15} was found to be more active against *Klesibella pneumonia* (ATCC 29655), *Bacillus cereus* (NL98), and *Enterococcus faecium* (ATCC 29212); where as compound SY_{13} was found to be more active aganist *Proteus vulgaris* (NCTC 4635). Compound SY_{12} was found to be more active against *Aspergillus niger* and *Aspergillus fumigatus.* However the antimicrobial activity of the synthesized compounds against the tested organisms was found to be less than that of respective standard drug at tested dose level. In future study the activity of the compounds may be manipulated by introducing unsaturation or heterocyclic ring at C_2 of benzimidazole.

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REFERENCES

1. Gupta SK, Pancholi SS, Gupta MK, Agarwal D, Khinchi MP. Synthesis and biological evaluation of some 2-substituted derivatives of benzimidazoles. J. Pharm. Sci. & Res. 2010; 2(4): 228-231.
2. Vijaya B, Rajeev K, Varadaraj G, Gautham G. Synthesis and antimicrobial studies of some novel benzimidazole derivatives. Asian. J. Research Chem. 2009; 2(2): 162-167.
3. Jadhav SB, Shastri RA, Bagul KR, Gaikwad KV. Synthesis and antimicrobial activity of N-substituted benzimidazoles. Indian J. Heterocyclic Chem. 2009; 18: 319-320.
4. Ganesh R, Mohammad U, Rajesh P, Deepak R. Synthesis of fluorobenzimidazoles as antimicrobial agents. Indian J. Heterocyclic Chem. 2009; 18: 419-420.
5. Gulgun A, Nurten A. Synthesis and antifungal properties of some benzimidazole deriovatives. Turk J. Chem. 2006; 30: 223-228.
6. Oztekin A, Nizami D, Gulay G. synthesis and evaluation of antimicrobial activity of some 1, 5(6)-H/or–Methyl-2-substituted benzimidazole derivatives. Asian J. Chem. 2007; 19(4): 3085-3092.
7. Shanmugapandian P, Denshing KS, Ilavarasan R, Anbalagan N, Nirmal R. Synthesis and biological activity of 2-(Thiazolidine-4-one) phenyl]-1h-phenylbenzimidazoles and 2-[4-(Azetidin-2-one)-3-chloro-4-Phenyl] - 1h-Phenylbenzimidazoles. International Journal of Pharmaceutical Sciences & Drug Research 2010; 2(2): 115-119.
8. Hasan K, Riza D, Nihat S, Selami. Synthesis, antibacterial and antifungal activities of new bis-5(6)-nitrobenzimidazoles. Asian J. Chem. 2010; 22(4): 2816-2824.
9. Leonard JT, Rajesh OS, Jeyaseeli L, Murugesh K. Synthesis, antiinflammatory and antibacterial activities of substituted phenylbenzimidazoles. Asian J. Chem. 2007; 19(1): 116-120.
10. Sreena K, Ratheesh R, Rachana M, Poornima M, Shyni C. Synthesis and anthelmenitic activity of benzimidazole derivatives. HYGEIA 2009; 1(1): 21, 22.
11. Simone B, Mariola K, Agata G, Zygmunt K, Henning E, Paolo C, Frank S. Substituted benzimidazoles: antiviral activity and synthesis of nucleosides. ARKIVOC 2009; 3: 225-250.
12. Ashish kumar T, Mishra A. Synthesis and antiviral activities of N-substituted-2-substituted-benzimidazole derivatives. Indian J. Chem. 2006; 45B: 489-493.
13. Starcevic K, Kralj M, Ester K, Sabol I, Grce M. Synthesis, antiviral and antitumor activity of 2-substituted-5-amidino benzimidazoles. Bioorg Med Chem 2007; 15(13): 4419-4426.
14. Vogel. Text book of Practical Organic Chemistry. Dorling Kindersley Publishers, 2006, 1162-1163.
15. Ahuluwalia VK, Agarwal R. Comprehensive Practical Organic Chemistry, University Press India Ltd, 2010, 120-121.
16. Singh J, Grover P, Pathak DP. Synthesis and Comparatrive QSAR study of some novel benzimidazole derivatives. Acta. Pharm. Sci. 2010; 52: 510-521.
17. Raju B, Rahul R, Sivasankar BN. A New reagent for selective reduction of amino group. Indian J. Chem. 2009; 45B: 1315-1318.