CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187
https://doi.org/10.5281/zenodo.18732672

Available online at: http://www.iajps.com Research Article

SYNTHESIS AND BIOLOGICAL EVALUATION OF 1-SUBSTITUTED IMIDAZOLE DERIVATIVES

Ms. Harshada Patil*, Lecturer, Ms. Asmita D Vasaikar, Lecturer,
Department of Pharmaceutical Chemistry, Shatabdi Institute of Pharmacy,
Bamdod-425412, Nandurbar

Abstract:
A novel series of 1-substituted imidazole derivatives was created in this investigation using various anilines.and the substitution of sulfonamides. IR, 1H-NMR, and mass spectrometry were used to confirm the chemical structures.spectral information. The compounds' antimicrobial and anticancer properties were examined. N-3-chloro-4-When it came to cervical cancer, fluorophenyl)-4-(1H-imidazol-1-yl)benzamide showed the strongest activity. 4-(1H-imidazol-1-Good antifungal activity was demonstrated by yl)-N-(4-(N-(5-methylisoxazol-4-yl) sulfamoyl) phenyl) benzamide. 4-(1H-Good antibacterial activity was demonstrated by imidazol-1-yl)-N-(4-(N-thiazol-4-ylsulfamoyl) phenyl) benzamide.

Key words: *Imidazole, Aniline, Sulfonamide, Anticancer, Antibacterial and Antifungal.*

Corresponding author:
Harshada Patil,
Department of Pharmaceutical Chemistry
Shatabdi Institute of pharmacy,
Bamdod-425412,Nandurbar
e-mail: Yakubpasha 786@gmail.com
https://orcid.org/0009-0007-8799-6064

QR CODE

Please cite this article in press Harshada Patil et al., Synthesis And Biological Evaluation Of 1-Substituted Imidazole Derivatives, Indo Am. J. P. Sci, 2026; 13(02).

INTRODUCTION:

The imidazole moiety is known to play an important role in biological systems as a part of the histidyl residue in peptides and proteins1 . Imidazole is an important aromatic heterocycle in organic compounds because of its variable biological activities. The amino acid histidine and its decomposition product histamine have the imidazole structure, biotin as a growth factor for both humans and yeast. Imidazole derivatives pose a diverse range of pharmacological activities such as antibacterial, antifungal, antitumor, antiulcer, anticonvulsant, antiprotozoal, antitubercular, antihypertensive, analgesic, antiinflammatory, antiviral, antideprassant and anti-HIV2-6 . The literature reveals that anticancer and antimicrobial properties of imidazole were associated with substitutions at 1 position2,5 . Therefore it was envisaged that a new series of 1- substituted imidazole derivatives with an amide group for good penetration into the BBB (Blood Brain Barrier) would result in compounds of potent biological activities. In the present study, a new series of imidazole derivatives have been synthesized by a four step procedure. Different anilines and sulfonamides have been taken as substitutions. The chemical structures were confirmed by means of IR, 1H NMR and Mass spectral data. The compounds were screened for acute oral toxicity, anticancer and antimicrobial activities.

MATERIALS AND METHODS:

The melting points were taken in open capillary tube and are uncorrected. The IR spectra of the compounds were recorded on ABB Bomem FT-IR spectrometer MB 104 with potassium bromide pellets. The 1H-NMR spectra of the synthesized compounds were recorded on a JOEL GSX 400 NMR spectrometer in DMSO unless otherwise stated. Mass spectra were recorded on Shimadzu GCMS QP 5000. The purity of the compounds was checked by TLC on pre – coated SiO2 gel (HF254 200 mesh) aluminium plates (E-merk) using (4:1) Chloroform: Methanol as eluent and visualized by iodine vapours. The IR, 1H-NMR and mass spectra were consistent with the assigned structure.

Synthesis of 4-(1H-Imidazol-1-yl) benzonitrile (3)7,8:

A mixture of imidazole(1) (0.5 mol), 4-Chlorobenzonitrile(2) (0.15 mol) and 50ml of ethanol are heated at 95oC. The conversion of 4-Chlorobenzonitrile is completed after 12 hr and then add water to the reaction mixture. The precipitate is filtered off, washed with water and dried under vaccum. The dried product is recyrstallized with ethanol.

Synthesis of 4-(1H-Imidazol-1-yl) benzoic acid (4):

A mixture of 4-(1H-imidazo-1-yl) benzonitrile (0.07 mol), sodium hydroxide (0.3 mol) and water (100ml) are refluxed for 5 hr. It is then cooled down to room temperature and acidify with HCl (5%) with efficient stirring (Alkali-Acid Hydrolysis). The precipitate is filtered off, washed with water and dried under vaccum.

Synthesis of 4-(1H-Imidazol-1-yl) benzoylchloride (5):

A mixture of 4-(1-H-imidazol-1-yl) benzoic acid (0.05mol) and thionyl chloride (0.06mol) are refluxed on water bath for 7 hr. Excess of thionyl chloride is removed under reduced pressure and the dried product is recrystallised.

General procedure for the synthesis of compounds (P1-P14)9 :

To a well-stirred solution of 4-(1Himidazol-1-yl)benzoyl chloride (0.01mol) and triethylamine (0.01mol) in benzene, substituted anilines (P1-P10) and sulphonamides (P11-P14) (0.01mol) in benzene was added in dropwise for about half an hour, and stirring was continued in cool condition. After the completion of reaction, it was poured into water and extracted with ether. The collected etheral extracts were then washed well with 3% sodium bicarbonate solution, dried and then recrystallised.

Structural Data:

4-(1H-imidazol-1-yl)-N-(4-nitrophenyl)benzamide (P1): Yield 65%, mp 176-178ºC, Rf value 0.55. IR (KBr) (cm-1): 2975.79(Ar-H), 1593.60(C=C), 1364.65(C-N), 1474.65(C=N), 1643.63(AmideC=O), 3433.85(AmideNH), 1512.42(Ar-NO2). 1H NMR (δ ppm): 7-8.5 [m, 11H, Ar-H], 9.2 [s, 1H, NH]. Mass: m/z 308(5%)M+ , (M.F: C16H12N4O3), 69(100%), 151(29%), 172(21%), 188(15%), 252(7%), 264(18%), 293(10%).

4-(1H-imidazol-1-yl)-N-(2,4-dinitrophenyl) benzamide (P2): Yield 63%, mp 180-182ºC, Rf value 0.396. IR (KBr) (cm-1): 3330.77(Ar-H), 1584.55(C=C), 1388.83(C-N), 1494.04(C=N), 1628.53(AmideC=O), 3445.45(AmideNH), 1520.58 (Ar-NO2). 1H NMR (δ ppm): 7-8.9 [m, 10H, Ar-H], 9.2 [s, 1H, NH]. Mass: m/z 353(6%) M+ , (M.F: C16H11N5O5), 144(100%), 91(58%), 153(22%), 188(32%), 252(6%), 264(22%), 308(35%), 338(27%).

N-(3-chloro-4-fluorophenyl)-4-(1H-imidazol-1-yl) benzamide (P3): Yield 60%, mp 166-168ºC, Rf value 0.477. IR (KBr) (cm-1): 3094.52(Ar-H), 1592.10 (C=C), 1366.64(C-N), 1492.01(C=N), 1682.6 (AmideC=O), 3447.53(AmideNH), 1282.80 (C-F), 761.24(C-Cl). 1H NMR (δ ppm): 7-8 [m, 10H, ArH], 9.2 [s, 1H, NH]. Mass: m/z 315(8%) M+ , (M.F: C16H11ClFN3O) 128(100%), 316(7%),

M+1, 66(75%), 91(61%), 144(20%), 158(43%), 171(19%), 188(15%), 252(9%), 265(17%), 281(27%).

N-(4-fluorophenyl)-4-(1H-imidazol-1-yl)benzamide (P4): Yield 50%, mp 172-174ºC, Rf value 0.425. IR (KBr) (cm-1): 2918.71(Ar-H), 1588.80(C=C), 1329.85(C-N), 1508.63(C=N), 1629.02(AmideC=O), 3149.61(AmideNH), 1217.31(C-F). 1H NMR (δ ppm): 7-8 [m, 11H, Ar-H], 9.2 [s, 1H, NH]. Mass: m/z 282(4%)M+ , (M.F: C16H12FN3O), 144(100%), 68(75%), 79(34%), 96(19%), 128(15%), 171(23%), 186(12%), 252(7%), 264(17%).

N-(4-chlorophenyl)-4-(1H-imidazol-1-yl)benzamide (P5): Yeild 55%, mp 168-170ºC, Rf value 0.461. IR (KBr) (cm-1): 3094.52(Ar-H), 1592.11(C=C), 1322(C-N), 1491.91(C=N), 1682.44(AmideC=O), 3447.53(AmideNH), 761.43(C-Cl). 1H NMR (δ ppm): 7-8 [m, 11H, Ar-H], 9.2 [s, 1H, NH]. Mass: m/z 297(5%), M + (M.F C16H12ClN3O) 69(100%), 298(6%), M+1, 92(44%), 114(29%), 129(20%), 144(24%), 153(36%), 172(26%), 183(8%), 251(15%), 263(19%).

N-(2-chlorophenyl)-4-(1H-imidazol-1-yl)benzamide (P6): Yeild 54%, mp 160-162ºC, Rf value 0.541. IR (KBr) (cm-1): 2975.79(Ar-H), 1593.60(C=C), 1364.65(C-N), 1474.65(C=N), 1643.63(Amide C=O), 3433.85(Amide NH), 763.35(C-Cl). 1H NMR (δ ppm): 7-8 [m, 11H, Ar-H], 9.2 [s, 1H, NH]. Mass: m/z 297(8%) M + , (M.F C16H12ClN3O), 145(100%)B, 298(5%), 90(58%), 122(23%), 128(33%), 153(35%), 173(16%), 189(10%), 252(11%), 264(18%).

4-(1H-imidazol-1-yl)-N-(4-methoxyphenyl) benzamide (P7): Yield 58%, mp 184-186ºC, Rf value 0.381. IR (KBr) (cm-1): 3148.53(Ar-H), 1586.57(C=C), 1385.23(C-N), 1457.63(C=N), 1654.04(Amide C=O), 3418.68(Amide NH), 1078.71(Ar-OCH3). 1H NMR (δ ppm): 6.8-8 [m, 11H, Ar-H], 9.2 [s, 1H, NH], 3.8 [s, 3H, CH3]. Mass: m/z 294(5%), M + (M.F C17H15N3O2), 124(100%), 91(60%), 92(10%), 110(27%), 144(13%), 153(36%), 172(23%), 188(9%), 252(6%), 263(14%), 280(25%).

4-(1H-imidazol-1-yl)-N-P-tolylbenzamide (P8): Yield 57%, mp 190-192ºC, Rf value 0.521. IR (KBr) (cm-1): 2918.71(Ar-H), 1588.80(C=C), 1329.85(CN), 1508.63(C=N), 1629.02(Amide C=O), 3149.61(Amide NH), 2918.71 (Ar-CH3). 1H NMR (δ ppm): 7-8 [m, 11H, Ar-H], 9.2 [s, 1H, NH], 2.5 [s, 3H, CH3]. Mass: m/z 278(5%), M + (M.F C17H15N3O), 68(100%), 90(56%), 108(20%), 122(23%), 144 (14%), 153(38%), 172(19%), 188(16%), 252(8%), 263(17%).

4-(1H-imidazol-1-yl)-N-(pyridin-2-yl)benzamide (P9): Yield 56%, mp 196-198ºC, Rf value 0.482. IR (KBr) (cm-1): 2839.95(Ar-H), 1543.05(C=C), 1325.91(C-N), 1474.76(C=N), 1667.37(Amide C=O), 3424.68(Amide NH). 1H NMR (δ ppm): 6.4-8 [m, 11H, Ar-H], 9.2 [s, 1H, NH]. Mass: m/z 264(5%)M+ , (M.F C15H12N4O), 68(100%), 78(35%), 94(58%), 144(24%), 158(27%), 175(30%), 188(6%), 202 (10%), 215(9%), 242(7%).

N-(4-bromophenyl)-4-(1H-imidazol-1-yl)benzamide (P10): Yeild 51%, mp 174-176ºC, Rf value 0.465. IR (KBr) (cm-1): 2975.74(Ar-H), 1591.9(C=C), 1398.56(C-N), 1474.83(C=N), 1650.85(Amide C=O), 3448.78(Amide NH), 521.87(C-Br). 1H NMR (δ ppm): 7-8 [m, 11H, Ar-H], 9.2 [s, 1H, NH]. Mass: m/z 342(7%)M+ , (M.F C16H12BrN3O), 188(100%), 344(5%)M+2, 92(40%), 128(20%), 144(15%), 153 (36%), 171(18%), 263(16%).

4-(1H-imidazol-1-yl)-N-(4-(N-(5-methylisoxazol-4- yl)sulfamoyl) phenyl) benzamide (P11): Yield 66%, mp 302-304ºC, Rf value 0.441. IR (KBr) (cm-1): 3094.21(Ar-H), 1592.87(C=C), 1377.79(C-N), 1491.68(C=N), 1682.46(Amide C=O), 3476.80 (Amide NH), 1324.0(SO2), 897.94(S-N), 2982.62(ArCH3), 1015.21(C-O). 1H NMR (δ ppm): 7-8.2 [m, 12H, Ar-H], 9.2 [s, 1H, NH], 2.5 [s, 3H, CH3], 4 [, 1H, S-NH]. Mass: m/z 423(4%), M + (M.F C20H17N5O4S), 174(100%), 82(30%), 111(50%), 145 (35%), 156(79%), 157 (8%), 190(6%), 266(26%), 262(12%), 342(24%), 397(22%), 409(20%).

4-(1H-imidazol-1-yl)-N-(4-(N-pyrimidin-2-ylsulfamoyl)phenyl)benzamide (P12): Yield 65%, mp 296-298ºC, Rf value 0.372. IR (KBr) (cm-1): 3095.58(Ar-H), 1592.70(C=C), 1401.06(C-N), 1491.74(C=N), 1683.11(Amide C=O), 3430.41 (Amide NH), 1323.86(SO2), 939.82(S-N). 1H NMR (δ ppm): 7-8.5 [m, 14H, Ar-H], 9.2 [s, 1H, NH], 4 [, 1H, S-NH]. Mass: m/z 420(4%), M + (M.F C20H16N6O3S), 65(100%), 420(4%)M+ , 79(25%), 111 (48%), 144(6%), 156(78%), 175(18%), 252(19%), 263(35%), 278(12%), 343(10%), 354(29%).

4-(1H-imidazol-1-yl)-N-(4-(N-thiazol-4-ylsulfamoyl) phenyl)benzamide (P13): Yield 67%, mp 308-310ºC, Rf value 0.510. IR (KBr) (cm-1): 3094.51(Ar-H), 1592.39(C=C), 1400.96(C-N), 1492.25(C=N), 1682.79(Amide C=O), 3470.75(Amide NH), 1321.99(SO2), 929.53(S-N), 761.71(C-S). 1H NMR (δ ppm): 7-8.9 [m, 13H, Ar-H], 9.2 [s, 1H, NH], 4 [, 1H, S-NH]. Mass: m/z 425(7%)M+ , (M.F C19H15N5O3S2), 106(100%), 67(80%), 86(22%), 136(15%), 144(8%), 152(12%), 176(9%), 224(25%), 255(24%), 276(20%),

283(35%), 342(6%), 357 (19%), 372(23%), 416(10%).

4-(1H-imidazol-1-yl)-N-(4-(N-(5-methylpyrazin-2-yl)sulfamoyl)phenyl)benzamide (P14): Yield 64%, mp 292-294ºC, Rf value 0.360. IR (KBr) (cm-1): 3094.58(Ar-H), 1594.04(C=C), 1372.23(C-N), 1491.66(C=N), 1634.96(Amide C=O), 3482.17 (Amide NH), 1325.50(SO2), 930.14(S-N), 2959.30 (Ar-CH3). 1H NMR (δ ppm): 7-8.2 [m, 13H, Ar-H], 9.2 [s, 1H, NH], 2.4 [s, 3H, CH3], 4 [, 1H, S-NH]. Mass: m/z 434(4%)M+ , (M.F C21H18N6O3S), 121(100%), 92(22%), 111(50%), 97(5%), 172(17%), 179(8%), 227(7%), 277(20%), 343(9%), 355(19%), 368(48%), 390(42%), 401(22%), 422(21%).

Pharmacological Activity:

The synthesized compounds were evaluated for acute oral toxicity, anticancer and antimicrobial activities. Statistical analysis (ANOVA followed by Dunnet's ttest) was performed for anticancer activity to ascertain the significance of the exhibited activity. The test compounds were administered in the form of a suspension (1% carboxy methyl cellulose as vehicle). The animals used in the present study swiss albino mice weighing 20-25 g were kept in colony cages at 25±2oC, relative humidity of 45-55% under 12 hr light and dark cycle. All the animals were fed with standard animal feed and water ad libitum.

Acute Oral Toxicity:

In the present study the acute oral toxicity of the synthesized compounds were performed by acute toxic class method10,11 as per organization of economic co-operation and development (OECD) guidelines. In this methods the toxicity of the synthesized compounds were tested using a step wise procedure, each step using three mice of a single sex. The mice were fasted prior to dosing (food but notwater should be with held) for three to four hours. Then the animals were weighed and the synthesized compounds were administered orally at a dose of 2000 mg/Kg body weight. Animals were observed individually after dosing at least once during the first 30 min; periodically during the first 24 h with special attention given during the first 4 h and daily thereafter, for a total of 14 day.

Anticancer Activity12:

Anticancer activity was carried out by MTT [(3-(4,5- dimethylthiazol-2yl)-2,5-diphenyltetrazolium bromide] assay using HELA cell lines against cervical cancer. 0.1ml of the cell suspension (containing 5 106 cells/100 l) and 0.1ml of the test solution (6.25 g - 100 g in 1% DMSO such that the final concentration of DMSO in media is less than 1%) were added to the 96 well plates and kept in 5% CO2 incubator at 370 C for 72 hours. Blank contains only cell suspension and control wells contain 1% DMSO and cell suspension. After 72 hours, 20 l of MTT was added and kept in carbondioxide incubator for 2 hours followed by propanol 100 l. The plate was covered with aluminium foil to protect it from light. Then the 96 well plates are kept in rotary shaker for 10-20 minutes. After 10-20 minutes, the 96 well plates were processed on ELISA reader for absorption at 562nm. The readings were averaged and viability of the test samples was compared with DMSO control. Anticancer activity was carried out for compounds P2, P3, P4, P6, and P7. The data was presented in Table 1.

Antimicrobial Activity13:

The activity was carried paper disc diffusion method. The sterilized (autoclaved at 120°C for 30min) medium (40-50°C) was inoculated (1mL/100mL of medium) with the suspension (105 cfu mL-1) of the micro-organism (matched to McFarland barium sulphate standard) and poured into a petridish to give a depth of 3-4 mm. The paper impregnated with the test compounds (25, 50 and 100 µg mL-1 in dimethyl formamide) was placed on the solidified medium. The plates were pre-incubated for 1 h at RT and incubated at 37°C for 24 and 48 h for anti-bacterial and anti-fungal activities, respectively. Ciprofloxacin (100 µg/disc) and Ketoconazole (100 µg/disc) were used as standard for anti-bacterial and anti-fungal activities, respectively. Antibacterial activity was carried out against Staphylococcus aureus, Staphylococcus epidermids(Gram +ve), Escherichia coli, Klebsiella pneumonia(Gram –ve) organisms. Antifungal activity was tested against Aspergillus niger, Candida Albicans organisms. The zone of inhibition observed was presented in the Table 2, 3, 4, 5 and 6.

RESULTS AND DISCUSSION:

Compounds P1-P14 did not cause mortality up to 2000mg/kg and were considered as safe (xunclassified). Compound P-3 was found to exhibit good anticancer activity, the compound P-6 showed moderate activity and compounds P-2, P-4 had mild activity. Compounds P-1, P-3, P-5, P-6, P-8, P-11, were possessed good activity against Gram-positive and Gram-negative bacteria in comparison with standard (Ciprofloxacin 50 µg/ml). Compound P-13 showed significant antibacterial activity, when compared to Ciprofloxacin. Compounds P-2, P-3, P4, P-6, P-9, P-10, P-13 and P-14 showed good antifungal activity and Compound P-11 has showed significant antifungal activity compared to Ketaconazole. The present study reveals that introduction of sulfinyl group showed anticancer and antimicrobial activities. Therefore may serve as lead molecule for further modification to obtain therapeutically useful novel entities in this series.

Table 1: **GI_{50} of synthesized compounds**

Compounds	Hela		
	GI_{50}(μm)	TGI(μm)	LC_{50}(μm)
P_2	20.5	52.7	>100
P_3	18.8	42.7	88.2
P_4	21	43.6	>100
P_6	19.5	35.4	79.2
P_7	20.8	47.2	>100
DOXO	0.05	0.41	0.88

Table 2: **Zone of Inhibition of Synthesized Compounds against Gram +Ve Bacteria**

Compounds	ZONE OF INHIBITION					
	S.Aureus			*S.Epidermis*		
	25 μg/ml	50 μg/ml	100 μg/ml	25 μg/ml	50 μg/ml	100 μg/ml
P_1	8	16	28	23	29	30
P_2	8	15	26	21	26	28
P_3	10	17	26	25	30	25
P_4	10	13	25	25	28	28
P_5	10	15	28	22	25	27
P_6	12	16	28	24	27	32
P_7	8	13	27	22	23	34
P_8	8	15	26	23	25	30
P_9	7	15	23	18	25	33
P_{10}	10	17	25	22	26	30
P_{11}	12	18	26	10	22	32
P_{12}	8	17	23	10	27	28
P_{13}	10	18	22	18	25	32
P_{14}	8	16	27	20	26	30
Std	23	23	23	31	31	31
Control	-	-	-	-	-	-

Table 3: **Zone of Inhibition of Synthesized Compounds against Gram –Ve Bacteria**

Compounds	ZONE OF INHIBITION					
	E.Coli			*K.Pneumonia*		
	25 µg/ml	50 µg/ml	100 µg/ml	25 µg/ml	50 µg/ml	100 µg/ml
P_1	10	23	28	12	14	20
P_2	12	18	22	15	16	27
P_3	16	22	30	11	20	25
P_4	11	20	22	11	10	30
P_5	11	21	25	10	23	28
P_6	16	29	32	8	15	26
P_7	11	15	20	10	14	25
P_8	8	17	22	10	16	26
P_9	9	14	22	8	20	25
P_{10}	10	16	25	12	10	28
P_{11}	20	20	28	15	16	26
P_{12}	18	22	32	12	14	26
P_{13}	20	25	30	12	20	25
P_{14}	18	22	25	10	20	26
Std	27	27	27	24	24	24
Control	-	-	-	-	-	-

Table 4: **Minimum Inhibitory Concentration of Synthesized Compounds against Gram (+) Ve and Gram (-) Ve Bacteria**

Compounds	MINIMUM INHIBITORY CONCENTRATION (µg/ml)			
	S.Aureus	*S.Epidermis*	*E.Coli*	*K.Pneumonia*
P_1	9	7	8	10
P_2	10	6	10	9
P_3	9	6	7	9
P_4	10	7	6	6
P_5	9	6	7	10
P_6	10	6	6	6
P_7	10	8	9	7
P_8	9	6	10	7
P_9	10	8	6	10
P_{10}	9	7	10	8
P_{11}	10	9	8	7
P_{12}	9	8	7	10
P_{13}	9	9	6	10
P_{14}	10	8	7	10
Std	0.2	0.39	0.2	0.1

Table 5: **Zone of Inhibition of synthesized compounds against fungi**

Compounds	ZONE OF INHIBITION					
	Candida Albicans			*Aspergillus Niger*		
	25 µg/ml	50 µg/ml	100 µg/ml	25 µg/ml	50 µg/ml	100 µg/ml
P_1	10	16	20	8	10	16
P_2	15	22	25	7	12	17
P_3	20	21	24	6	12	13
P_4	20	24	26	8	11	15
P_5	15	17	20	2	10	16
P_6	20	22	25	7	8	13
P_7	10	15	15	8	10	14
P_8	20	22	22	5	8	16
P_9	15	20	26	8	13	13
P_{10}	20	20	22	6	12	16
P_{11}	10	24	23	6	15	11
P_{12}	20	18	20	8	13	14
P_{13}	20	22	26	8	13	12
P_{14}	20	20	25	6	11	10
Std	23	23	23	20	20	20
Control	-	-	-	-	-	-

Table 6: **Minimum Inhibitory Concentration of Synthesized Compounds against Fungi**

Compounds	MINIMUM INHIBITORY CONCENTRATION (µg/ml)	
	Candida Albicans	***Aspergillus Niger***
P_1	6	10
P_2	6	9
P_3	9	10
P_4	6	9
P_5	10	10
P_6	10	10
P_7	7	9
P_8	7	10
P_9	6	9
P_{10}	7	9
P_{11}	7	8
P_{12}	8	9
P_{13}	6	8
P_{14}	6	10
Ketaconazole	1	6.1

ACKNOWLEDGEMENT:
The authors are thankful to the principal and management of Shatabdi Institute of Pharmacy, Bamdod , Nandurbar 425412 for their generous support for the work.

REFERENCES:

1. Sigel H, Saha A, Saha N, Carloni P, Kapinos LE, Griesser R. Evaluation of intramolecular equilibria in complexes formed between substituted imidazole ligands and nickel(II), copper(II) or zinc(II). J. Inorg. Biochem., 2000; 78 ((2): 129-37.

2. Sabrina C, Giorgio S, Annalisa Ch, Graziella P. Synthesis and antimicrobial properties of 3-aryl-1- -biphenyl-4-yl)-2-(1H-imidazol-1-yl)propanes as 'carba-analogues' of the Narylmethyl-N-[(1,1-biphenyl)- 4-ylmethyl])-1H-imidazol-1-amines, a new class of antifungal agents. II Farmaco, 2003; 58(8): 563-8.

3. Rodrıguez-Arguelles MC, Lopez-Silva EC, Sanmartın J, Bacchi A, Pelizzi C, Zani F. Cobalt and nickel complexes of versatile imidazole- and pyrrole-2-carbaldehyde thiosemicarbazones. Synthesis, characterization and antimicrobial activity. Inorg. Chimica Acta. 2004; 357(9): 2543-52.

4. Magdy WS, Nadia AM, Riham RM, Neveen MK, Soliman MA El L. Synthesis, characterization and antimicrobial activity of poly (N-vinyl imidazole) grafted carboxymethyl chitosan. Carbohydrate Polymers, 2010; 79(4): 998-1005.

5. Sabbir A, Imran S, Sachin D, Caroline PO. Synthesis and biochemical evaluation of a range of sulfonated derivatives of 4-hydroxybenzyl

imidazole as highly potent inhibitors of rat testicular 17a-hydroxylase/17, 20-lyase (P-45017a). Bioorg. Med. Chem. Lett., 2009; 19(16): 4698-701.
6. Ulrike EH, Qingzhong H, Carsten V, Matthias N, Marc B, Ursula Mu¨ ller-Vieira, Thomas L, Rolf WH. Novel CYP17 inhibitors: Synthesis, biological evaluation, structure–activity relationships and modelling of methoxy- and hydroxy-substituted methyleneimidazolyl biphenyls. Eur. J. Med. Chem., 2009; 44(7), 2765- 75.
7. Tian W, US Patent Office, Serial No. 6,689,882 B2, 2004.
8. Raparti V, Chitre T, Bothara K, Kumar V, Dangre S, Khachane C, Gore S, Deshmane B. Novel 4-(morpholin-4-yl)-N'-(arylidene) benzohydrazides: synthesis, anti mycobacterial activity and QSAR investigations. Eur. J. Med. Chem. 2009; 44(10): 3954-60.
9. Aridoss G, Balasubramanian S, Parthiban P, Kabilan S. Synthesis, stereochemistry and antimicrobial evaluation of some N-morpholinoacetyl-2,6-diarylpiperidin-4-ones. Eur. J. Med. Chem., 2007; 42(6): 851- 60.
10. OECD 1996. Report of the SETAC/OECD Workshop on Avian Toxicity Testing, OECD/GD (96) 166.
11. Rang HP, Dale MM, Ritter JM, Flower RJ, Henderson G. Rang & Dale's Pharmacology, 5th Ed., Elsevier Publications, 2003, pp.244-248; 550-554; 574-6.
12. Collins L, Franzblau SG. Microplate alamar blue assay versus BACTEC 460 system for high-throughput screening of compounds against Mycobacterium tuberculosis and Mycobacterium avium. Antimicrob. Agents Chemother., 1997; 41(5): 1004-9.
13. National Committee for Clinical Laboratory Standards; 2003. Performance standards for antimicrobial disk susceptibility tests, 8th ed. Approved standard M2-A8. National Committee for Clinical Laboratory Standards, Wayne, PA.
14. Pharma Scholars Library 2011 ; 1(2);92-98Internationl journal of Pharmacy ISSN 2249-1848 Reserch Article Journal Homepage: http://www.pharmascholars.com