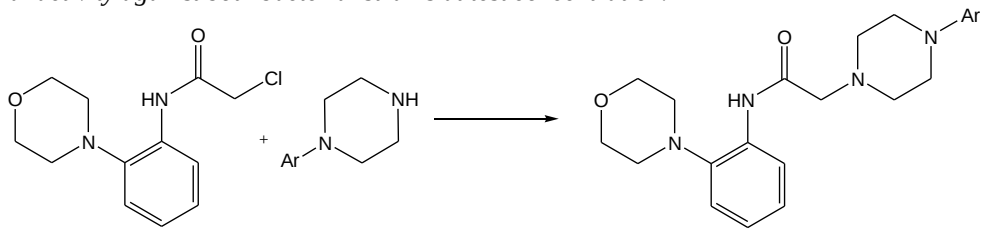
International Journal of Research in Engineering and Science (IJRES)
ISSN (Online): 2320-9364, ISSN (Print): 2320-9356
www.ijres.org Volume 9 Issue 2 ǁ 2021 ǁ PP. 69-74

Synthesis of new *N*1-(2-morpholinophenyl)-2-(4-arylpiperazino)-acetamide derivatives as potential antimicrobial agents

*Nagaraj, A., Raghuveer, S. and Amala, G.
Department of Chemistry, Telangana University, Nizamabad, Telangana-503322 India

Abstract:
*A series of new N1-(2-morpholinophenyl)-2-(4-arylpiperazino)-acetamide **8(a-j)** were synthesized and screened for their in vitro antimicrobial activities against bacterial strains of P. mirablilis, B. subtilis and fungal strains of C. albicans, A. fumigates and found that the antimicrobial activity of fluoro compounds (**8d**) is equal and (**8h**) is more than that of standard drugs. The compounds with 4-bromophenyl (**8e**) and 3-hydroxyphenyl (**8i**) group on piperazine ring showed considerable antifungal activity against C. albicans, compound **8a** did not show any antibacterial activity against both bacterial strains at test concentration.*



***Keywords**: Morpholine, Piperazines, Acetamide, Antibacterial Activity.*

Date of Submission: 06-02-2021 Date of acceptance: 20-02-2021

I. INTRODUCTION

Morpholine nucleus have aroused great interest in recent years due to their variety of biological activities [1], many morpholine based drugs showed significant biological/ pharmacological activities *viz.*, *Linezolid* is an antibiotic, commercially available antimicrobial drug [2]. *Aprepitant* is the first drug approved by FDA, acts as neurokinin 1 (NK1) receptor antagonist used for the treatment of chemotherapy-induced nausea and vomiting [3]. *Emorfazone* is an effective analgesic, anti-inflammatory and anti pyretic drug in animal models as well as in humans [4]. *Gefitinib* is a selective inhibitor of epidermal growth factor and clinically used for the treatment of chemoresistant non-small cell lung cancer patients [5] and *Timolol* is a non-selective *β*-adrenergic receptor antagonist, used for the treatment of glaucoma [6] (**Figure 1**).

Similar to morpholine, the piperazine is also an important heterocyclic compound, present in many pharmaceutically active molecule and possesses significant activities such antimalarial [7], antipsychotic [8], antifungal [9], antiinflammatory [10], dopamine receptor agonist [11]. The piperazine based drugs; HIV protease inhibitor *Crixivan* [12] and antibacterial agent *Ciprofloxacin* [13] are in clinical use.

Following the successful introduction of biological activities exhibited by morpholines, piperazines and development of hybrid molecules through the combination of different pharmacophores in one frame, may lead to compounds with interesting biological activities. We report herein the synthesis of new *N*1-(2-morpholinophenyl)-2-(4-arylpiperazino)-acetamide derivatives **8(a-j)** the antibacterial activities are also evaluated.

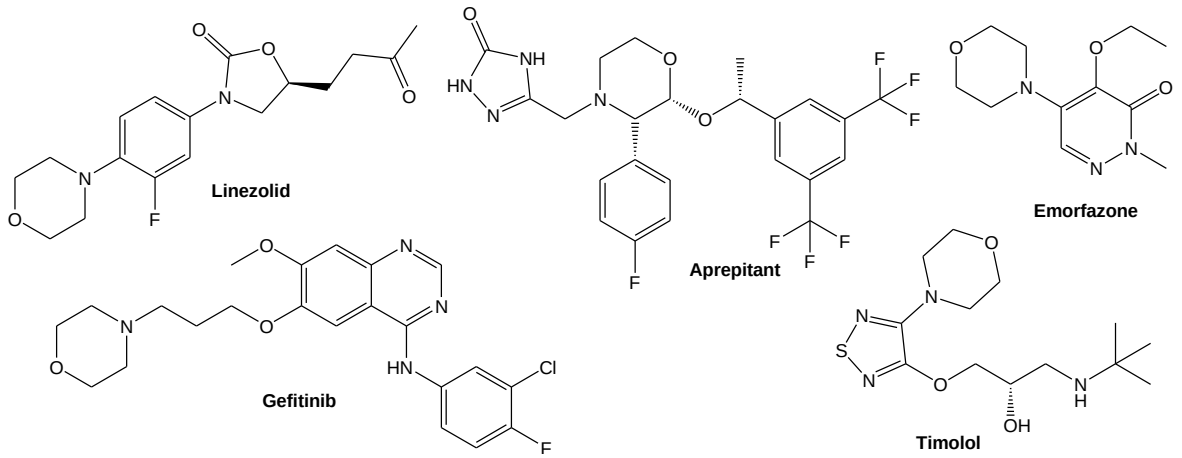
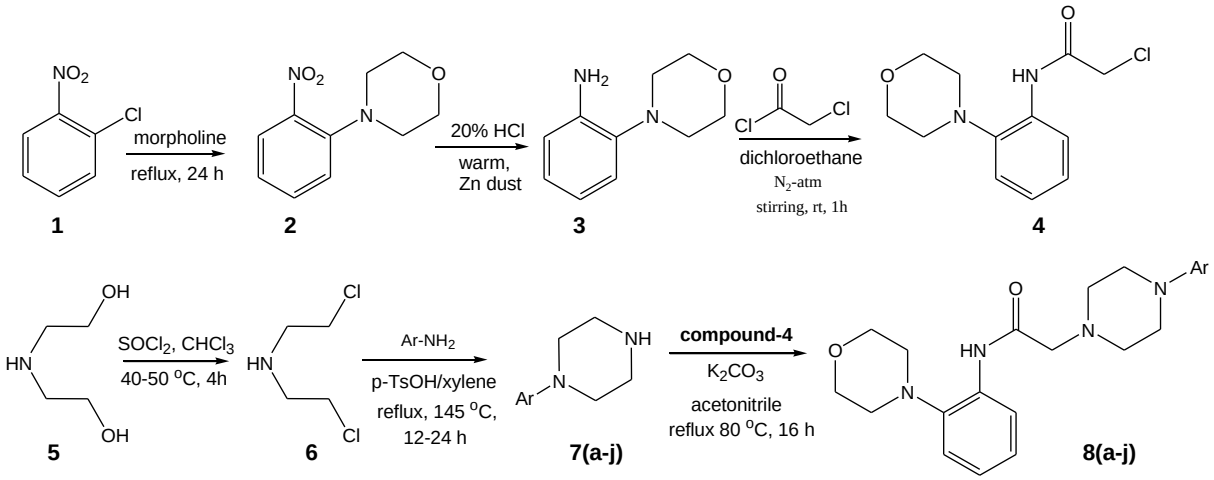


Figure 1: Morpholine based commercial drugs

II. RESULTS AND DISCUSSION

The starting material, 4-(2-nitrophenyl)morpholine **2** was obtained *via* reaction of 1-chloro-2-nitrobenzene **1** with morpholine under heating at reflux temperature for 24 hours, which on reduction using zinc dust in the presence of hydrochloric acid resulted 2-morpholinoaniline **3** which further reacted with chloroacetyl chloride in dichloreethane under nitrogen atmosphsphere at stirring for 1 hour, afforded *N*1-(2-morpholinophenyl)-2-chloroacetamide **4**. The chlorination of diethanolamine **5** with thionyl chloride at 40-50 ^{o}C in chloroform for 4 h, led to the formation of *N*,*N*-di(2-chloroethyl)amine **6**, which on cyclization and condensation with corresponding aromatic amines in the presence of *p*-TsOH in xylene at reflux temperature for 12-24 h, to afford 4-arylpiperazines **7(a-j)**. The title compounds *N*1-(2-morpholinophenyl)-2-(4-arylpiperazino)-acetamide **8(a-j)** has been synthesized by reacting compound **4** with the corresponding compound **7(a-j)** in the presence of potassium carbonate in acetonitrile under reflux for 16 hours (**Scheme 1**). The structures of all the synthesized compounds were confirmed by their spectral data.



7/8: Ar = a) phenyl; b) 4-methylpenyl; c) 4-methoxyphenyl; d) 4-fluorophenyl; e) 4-bromophenyl; f) 2-nitrophenyl; g) 4-nitrophenyl; h) 2,5-difluorophenyl; i) 3-hydroxyphenyl; j) 4-hydroxyphenyl

Scheme 1

The IR spectrum of **2** the characteristic absorption band for -NO_2 group was observed at 1540, 1370 and C-N band at 1286 cm^{-1}. Its ^{1}H NMR spectrum, the aryl proton signals appeared as multiplet and singlet under two groups in the range of δ 6.80-6.90 and 7.86 ppm, the methylne protons of morpholine ring appeared as a multiplets in the region of δ 3.50-3.67 and 3.30-3.40.

The IR spectrum of compound **3**, the disappearance of NO_2 absorption band and appearance of absorption at 3370-3310 indicated presence of NH_2 the other absorption band for C-N and C-O of morpholine was observed at 1284 and 1074 cm^{-1}. Its proton NMR spectrum, the methylene proton signals of morpholine

ring was appeared as multiplets at δ 2.80-2.90 and 3.50-3.60 ppm, a broad singlet for amine protons appeared at 3.90-4.00 ppm, the aryl protons appeared as multiplets between δ 6.20-6.30 and 6.75-6.80 ppm.

The IR spectrum of **4**, the absorption band for N-H and C=O of amide group was observed at 3441 and 1702, the C-Cl absorption band appeared at 686 cm^{-1}. Its proton NMR spectrum, the methylene protons of morpholine appeared as multiplets at δ 3.12-3.20 and 3.82-3.90, the methylene protons of acetamide group appeared at δ 4.17 as singlet, a broad singlet δ 8.80 was assigned to the NH proton, aryl proton signals was appeared as multiplets at δ 6.40-6.45 and 7.00-7.10 ppm. Its 13C NMR spectrum, the signals for carbons of morpholine ring appeared at δ 64.3 and 57.1 ppm, the signal of amide carbonyl group is appeared at δ 160.8 ppm.

The IR spectrum of compound **7a**, the characteristic absorption of amide N-H and C=O bands was observed at 3213 and 3072 cm^{-1}. Its proton NMR spectrum, the methylene proton signals of piperazine ring appeared as multiplets in the region of δ 3.10-3.15 and 3.20-3.25 ppm, the aryl proton signals appeared at δ 6.90-6.95 as multiplet and a doublet at δ 7.34 ppm The IR spectrum of compound **8a**, the amide carbonyl (C=O) and (N-H) absorption appeared at 1705 and 3433 cm^{-1}. Its proton NMR spectrum, the methylene proton of acetamide moiety appeared at δ 3.05 as singlet, the methylene protons of both piperazine and morpholine ring was appeared as multiplets in the range of δ 3.10-4.00 and aryl protons as multiplets at δ 6.60-6.70 and 7.00-7.10.

III. ANTIMICROBIAL ACTIVITY

All newly synthesized compound **8(a-j)** were screened for their *in vitro* antimicrobial activities against bacterial strains of *P. mirabilis*, *B. subtilis* and fungal strains of *C. albicans* and *A. fumigates* using the disc diffusion method[14]. The zone of inhibition (mm) at 500 μg/mL of the test compound were determined and compared with the standard antibacterial drug ciprofloxacin and antifungal drug amphotericin-B, the results have been reported in **Table 1**.

The results of antimicrobial screening revealed that all tested compounds exhibited moderate to excellent activity against both bacteria and both fungi. The antimicrobial activity of fluoro compounds (**8d**) is equal and (**8h**) is more than that of standard drugs. The compounds with 4-bromophenyl (**8e)** and 3-hydroxyphenyl (**8i**) group on piperazine ring showed considerable antifungal activity against C. albicans, compound **8a** did not show any antibacterial activity against both bacterial strains at test concentration.

Table 1: Antimicrobial Activity of Compounds **8**(**a-j**)

Compound	Zone of inhibition (mm) at 500 μg/mL			
	Antibacterial Activity		Antifungal Activity	
	P. mirabilis	***B. subtilis***	***C. albicans***	***A. fumigatus***
8a	—	—	6	8
8b	17	16	14	11
8c	20	19	15	14
8d	21	23	20	14
8e	12	10	19	12
8f	7	6	10	7
8g	13	14	13	13
8h	25	25	22	16
8i	17	16	18	9
8j	—	6	—	5
Ciprofloxacin	25	23	—	—
Amphotericin-B	—	—	20	16

IV. MATARIALS AND METHODS

All reagents are commercial grade and were used as supplied. Reactions were monitored by thin-layer chromatography (TLC) on pre-coated silica gel F254 plates from Merck, and compounds visualized by exposure to UV light. Chromatographic columns 70–230 mesh silica gel for separations were used. IR spectra were recorded using KBr disk on a Perkin–Elmer FTIR spectrometer. The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Gemini spectrometer (300 MHz for ^{1}H and 75 MHz for ^{13}C). Chemical shifts are reported in δ ppm units with respect to TMS as internal standard and coupling constants (*J*) are reported in Hz units. Mass spectra were recorded on a VG micro mass 7070H spectrometer.

Synthesis of 4-(2-nitrophenyl)morpholine (2): A mixture of 1-chloro-2-nitrobenzene **1** (0.01 mol) and morpholine (0.2 mol) was heated on a water bath at reflux temperature with occasional stirring for 24 h. The obtained solid was cooled and collected on a filter paper and recrystallized from methanol to gave a orange crystals of compound **2** in 96% yield, melting point 148-150 ^{o}C. IR (KBr) ν_{max}: 3071 (CH-Ar), 1540, 1370 (NO_2), 1286 (C-N) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.30-3.40 (m, 4H, morpholine-H), 3.50-3.67 (m, 4H, morpholine-H), 6.80-6.90 (m, 3H, ArH), 7.86 (m, 1H, ArH); MS: *m/z* 208 (M^+).

Synthesis of 2-morpholinoaniline (3): A solution of compound **2** (0.01 mol) in 20% hydrochloric acid (75 mL) was treated with small portion of zinc dust with stirring and gentle warming until all the orange colour of nitro compound had disappeared. The mixture was filtered to remove the excess zinc and the filtrate was neutralized with NaOH. The crude product obtained was filtered, dried and crystallized from methanol to give pure compound **3** in 84% yield, melting point 128-130 ^{o}C. IR (KBr) ν_{max}: 3370-3310 (O-H), 3056 (CH-Ar), 1284 (C-N), 1074 (C-O) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.80-2.90 (m, 4H, morpholine-H), 3.50-3.60 (m, 4H, morpholine-H), 3.90-4.00 (bs, 2H, NH_2), 6.20-6.30 (m, 2H, ArH), 6.75-6.80 (m, 2H, ArH); MS: *m/z* 178 (M^+).

Synthesis of *N*1-(2-morpholinophenyl)-2-chloroacetamide (4): A solution of compound **3** (30 mmol) in dichloroethane (25 mL) was placed into an ice bath and stirred for 10 min under nitrogen. Chloroacetyl chloride (2.6 mL, 33 mmol) was added dropwise into the solution, and it was stirred at room temperature for 1 h. After stirring for 1 h, the reaction mixture was adjusted to *p*H = 9 with a solution of saturated sodium hydroxide in water and extracted two times with dichloroethane. The organic layer was dried over anhydrous sodium sulfate. Removal of the solvent by using a rotary evaporator and recrystallization from acetonitrile gave compound **4** in 48% yield. IR (KBr) ν_{max}: 3441 (N-H), 3078 (CH-Ar), 2987 (CH-Ali), 1702 (C=O), 1282 (C-N), 686 (C-Cl cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.12-3.20 (m, 4H, morpholine-H), 3.82-3.90 (m, 4H, morpholine-H), 4.17 (s, 2H, CH_2), 8.80 (bs, 1H, NH), 6.40-6.45 (m, 2H, ArH), 7.00-7.10 (m, 2H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 49.2, 57.1, 64.3, 115.9, 116.4, 117.0, 122.7, 126.4, 136.2, 160.8; MS: *m/z* 254 (M^+).

Preparation of *N,N*-di(2-chloroethyl)amine 6: To a stirred solution of diethanolamine **5** (0.1 mol) in 15 mL of $CHCl_3$, a mixture of thionylchloride (28 mL) and $CHCl_3$ (15 mL) was slowly added dropwise for 1 h and the reaction was continued for 2 more hours. The excess of solvent was removed under reduced pressure to give a pale yellow solid, which was purified by crystallization from ethylacetate.

General procedure for the synthesis 1-arylpiparazines 7(a-j): To a solution of compound **6** (2 mmol) in xylene (5 mL), corresponding arylamine (2 mmol) and *p*-toluenesulphonic acid (PTSA) (3%) was added and then heated the mixture to reflux at 140-145 ^{o}C for 12-24 h. After the completion of the reaction, crystalized the product by cooling to rt and purified by recrystallization to give the corresponding compounds **7(a-j)**.

1-Phenylpiperazine (7a): IR (KBr) ν_{max}: 3213 (NH), 3072 (CH-Ar), 2918 (CH-Ali), 1288 (C-N) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.12 (s, 1H, NH), 3.10-3.15 (m, 4H, piperazine-H), 3.20-3.25 (m, 4H, piperazine-H), 6.90-6.95 (m, 3H, ArH), 7.34 (d, *J* = 8.2 Hz, 2H, ArH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 48.1, 51.2, 114.6, 119.3, 130.7, 148.3; MS: *m/z* 162 (M^+).

General procedure for the synthesis of *N*1-(2-morpholinophenyl)-2-(4-arylpiperazino)- acetamide 8(a-j): A solution of corresponding arylpipearazines **7(a-j)** (5.9 mmol) in acetonitrile (5 mL) was added dropwise into a solution of compound **4** (1.0 g, 6 mmol) and K_2CO_3 (1.6 g, 12 mmol) in acetonitrile (25 mL). The mixture was heated under reflux (80 °C) for about 16 h and cooled to room temperature. The resulting mixture was dissolved in water, extracted with dichloromethane (two times). The organic layer was washed successively with water and brine, dried over anhydrous sodium sulfate. Evaporation of the solvent gave the crude product, which was purified by a column chromatography.

***N*1-(2-morpholinophenyl)-2-(4-phenylpiperazino)acetamide (8a):** IR (KBr) ν_{max}: 3433 (NH), 3089 (CH-Ar), 2947 (CH-Ali), 1705 (C=O), 1278 (C-N) cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 3.05 (s, 2H, CH_2), 3.10-3.15 (m, 4H, piperazine-H), 3.40-3.50 (m, 8H, piperazine-H & morpholine-H), 3.90-4.00 (m, 4H, morpholine-H), 6.60-6.70 (m, 5H, ArH), 7.00-7.10 (m, 4H, ArH), 8.24 (s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 46.9, 52.7, 55.3, 62.9, 64.8, 115.0, 116.1, 116.3, 119.0, 120.7, 121.5, 128.0, 130.1, 134.5, 149.6, 166.4; MS: *m/z* 380 (M^+).

***N*1-(2-morpholinophenyl)-2-[4-(4-methylphenyl)piperazino]acetamide (8b):** IR (KBr) ν_{max}: 3423 (NH), 3062 (CH-Ar), 2932 (CH-Ali), 1706 (C=O), 1281 (C-N) cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 2.32 (s, 3H, CH_3), 3.07 (s, 2H, CH_2), 3.10-3.15 (m, 4H, piperazine-H), 3.40-3.50 (m, 8H, piperazine-H & morpholine-H),

3.90-4.00 (m, 4H, morpholine-H), 6.60-6.70 (m, 6H, ArH), 7.00-7.10 (m, 2H, ArH), 8.24 (s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 27.9, 46.7, 52.2, 55.9, 62.8, 65.2, 111.9, 115.3, 115.9, 119.6, 122.5, 128.7, 129.4, 130.8, 134.8, 144.8, 166.2; MS: *m/z* 394 (M^+).

***N*1-(2-morpholinophenyl)-2-[4-(4-methoxyphenyl)piperazino]acetamide (8c):** IR (KBr) ν_{max}: 3418 (NH), 3083 (CH-Ar), 2947 (CH-Ali), 1710 (C=O), 1282 (C-N), 1072 (C-O) cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 3.10 (s, 2H, CH_2), 3.10-3.15 (m, 4H, piperazine-H), 3.40-3.50 (m, 8H, piperazine-H & morpholine-H), 3.80 (s, 3H, CH_3), 3.90-4.00 (m, 4H, morpholine-H), 6.60-6.70 (m, 6H, ArH), 7.00-7.10 (m, 2H, ArH), 8.27 (s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 45.8, 53.5, 56.1, 58.2, 62.7, 65.4, 112.0, 115.3, 116.9, 119.0, 122.4, 125.4, 128.4, 135.1, 140.2, 155.8, 165.2; MS: *m/z* 410 (M^+).

***N*1-(2-morpholinophenyl)-2-[4-(4-fluorophenyl)piperazino]acetamide (8d):** IR (KBr) ν_{max}: 3435 (NH), 3042 (CH-Ar), 2968 (CH-Ali), 1705 (C=O), 1410 (C-F), 1288 (C-N) cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 3.02 (s, 2H, CH_2), 3.10-3.15 (m, 4H, piperazine-H), 3.40-3.50 (m, 8H, piperazine-H & morpholine-H), 3.90-4.00 (m, 4H, morpholine-H), 6.60-6.70 (m, 4H, ArH), 7.00-7.10 (m, 4H, ArH), 8.25 (s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 46.3, 52.4, 55.9, 62.7, 64.5, 114.6, 115.2, 116.3, 119.2, 121.4, 125.0, 128.5, 133.7, 145.8, 164.4, 165.3; MS: *m/z* 398 (M^+).

***N*1-(2-morpholinophenyl)-2-[4-(4-bromophenyl)piperazino]acetamide (8e):** IR (KBr) ν_{max}: 3433 (NH), 3057 (CH-Ar), 2987 (CH-Ali), 1707 (C=O), 1288 (C-N), 589 (C-Br) cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 3.09 (s, 2H, CH_2), 3.10-3.15 (m, 4H, piperazine-H), 3.40-3.50 (m, 8H, piperazine-H & morpholine-H), 3.90-4.00 (m, 4H, morpholine-H), 6.60-6.70 (m, 4H, ArH), 7.00-7.10 (m, 4H, ArH), 8.21 (s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 46.5, 51.6, 54.7, 62.3, 64.6, 115.2, 116.2, 117.0, 118.8, 122.6, 123.8, 128.3, 130.8, 134.1, 147.0, 165.1; MS: *m/z* 459 (M^+).

***N*1-(2-morpholinophenyl)-2-[4-(2-nitrophenyl)piperazino]acetamide (8f):** IR (KBr) ν_{max}: 3429 (NH), 3056 (CH-Ar), 2971 (CH-Ali), 1705 (C=O), 1572 (NO_2), 1286 (C-N) cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 3.04 (s, 2H, CH_2), 3.10-3.15 (m, 4H, piperazine-H), 3.40-3.50 (m, 8H, piperazine-H & morpholine-H), 3.90-4.00 (m, 4H, morpholine-H), 6.60-6.70 (m, 3H, ArH), 7.00-7.10 (m, 4H, ArH), 8.04 (m, 1H, ArH), 8.24 (s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 45.3, 52.5, 55.1, 61.8, 64.3, 115.2, 116.7, 119.1, 121.0, 122.4, 123.8, 126.0, 128.1, 133.8, 134.3, 140.8, 143.8, 164.9; MS: *m/z* 425 (M^+).

***N*1-(2-morpholinophenyl)-2-[4-(4-nitrophenyl)piperazino]acetamide (8g):** IR (KBr) ν_{max}: 3434 (NH), 3089 (CH-Ar), 2972 (CH-Ali), 1701 (C=O), 1578 (NO_2), 1286 (C-N) cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 3.08 (s, 2H, CH_2), 3.10-3.15 (m, 4H, piperazine-H), 3.40-3.50 (m, 8H, piperazine-H & morpholine-H), 3.90-4.00 (m, 4H, morpholine-H), 6.60-6.70 (m, 2H, ArH), 7.00-7.10 (m, 4H, ArH), 7.85 (d, J = 8.9 Hz, 2H, ArH), 8.24 (s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 46.9, 52.7, 55.3, 62.9, 64.8, 113.2, 115.0, 116.1, 119.0, 121.5, 126.9, 128.0, 134.5, 139.0, 152.7, 166.4; MS: *m/z* 425 (M^+).

***N*1-(2-morpholinophenyl)-2-[4-(2,5-difluorophenyl)piperazino]acetamide (8h):** IR (KBr) ν_{max}: 3437 (NH), 3038 (CH-Ar), 2972 (CH-Ali), 1706 (C=O), 1407 (C-F), 1289 (C-N) cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 3.10 (s, 2H, CH_2), 3.10-3.15 (m, 4H, piperazine-H), 3.40-3.50 (m, 8H, piperazine-H & morpholine-H), 3.90-4.00 (m, 4H, morpholine-H), 6.60-6.70 (m, 4H, ArH), 7.00-7.10 (m, 3H, ArH), 8.22 (s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 46.9, 52.7, 55.3, 62.9, 64.8, 104.8, 106.4, 115.0, 116.1, 118.0, 119.0, 121.5, 128.0, 129.7, 134.5, 156.8, 160.9,166.4; MS: *m/z* 416 (M^+).

***N*1-(2-morpholinophenyl)-2-[4-(3-hydroxyphenyl)piperazino]acetamide (8i):** IR (KBr) ν_{max}: 3447 (NH/OH), 3078 (CH-Ar), 2989 (CH-Ali), 1702 (C=O), 1291 (C-N) cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 3.10 (s, 2H, CH_2), 3.10-3.15 (m, 4H, piperazine-H), 3.40-3.50 (m, 8H, piperazine-H & morpholine-H), 3.90-4.00 (m, 4H, morpholine-H), 6.60-6.70 (m, 6H, ArH), 7.00-7.10 (m, 3H, ArH & OH), 8.21 (s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 46.9, 52.7, 55.3, 62.9, 64.8, 100.2, 106.2, 110.0, 115.0, 116.1, 119.0, 121.5, 128.0, 130.1, 134.5, 137.7, 156.8, 166.4; MS: *m/z* 396 (M^+).

***N*1-(2-morpholinophenyl)-2-[4-(4-hydroxyphenyl)piperazino]acetamide (8j):** IR (KBr) ν_{max}: 3457 (NH/OH), 3072 (CH-Ar), 2981 (CH-Ali), 1704 (C=O), 1292 (C-N) cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 3.12 (s, 2H, CH_2), 3.10-3.15 (m, 4H, piperazine-H), 3.40-3.50 (m, 8H, piperazine-H & morpholine-H), 3.90-4.00 (m, 4H, morpholine-H), 6.60-6.70 (m, 6H, ArH), 7.00-7.10 (m, 2H, ArH), 8.24 (s, 1H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 46.9, 52.7, 55.3, 62.9, 64.8, 114.9, 115.0, 116.1, 119.0, 121.5, 122.4, 128.0, 134.5, 141.4, 153.0, 166.4; MS: *m/z* 396 (M^+).

V. CONCLUSION

A series of new *N*1-(2-morpholinophenyl)-2-(4-arylpiperazino)-acetamide **8(a-j)** were synthesized and screened for their *in vitro* antimicrobial activities against bacterial strains of *P. mirablilis*, *B. subtilis* and fungal strains of *C. albicans*, *A. fumigates* and found that the antimicrobial activity of fluoro compounds (**8d**) is equal and (**8h**) is more than that of standard drugs. The compounds with 4-bromophenyl (**8e)** and 3-hydroxyphenyl (**8i**) group on piperazine ring showed considerable antifungal activity against *C. albicans*, compound **8a** did not show any antibacterial activity against both bacterial strains at test concentration.

ACKNOWLEDGEMENTS

The authors are thankful to the Director, Indian Institute of Chemical Technology, Hyderabad, India, for providing NMR and mass spectral data.

REFERENCES

[1]. V. A. Palchikov, Russian J. Org. Chem. 49, 787 (2013)..
[2]. H. S. Sader, A. C. Gales, R. N. Jones, Brazilian J. Infec. Dis. 5, 171 (2001).
[3]. C. Girish, S. Manikandan, Indian J. Can. 44, 25 (2007).
[4]. M. Takaya, M. Sato, K. Terashima, H. Tanizawa, Y. Maki, J. Med. Chem. 22, 53 (1979).
[5]. Y. Nakamura, K. Sano, H. Soda, H. Takatani, M. Fukuda, S. Nagashima, T. Hayashi, M. Oka, K. Tsukamoto, S. Kohno, J. Thor. Oncol. 5, 1404 (2010).
[6]. S. C. Sacca, S. La Maestra, R. T. Micale, P. Larghero, G. Travaini, B. Baluce, A. Izzotti, Arch. Ophthal. 129, 48 (2011).
[7]. A. Ryckebusch, R. Poulain, L. Maes, M. A. Debreu-Fontaine, E. Mouray, P. Grellier, C. Sergheraert, J. Med. Chem. 46, 542 (2003).
[8]. J. P. Yevich, J. S. New, D. W. Smith, W. G. Lobeck, J. D. Catt, J. L. Minielli, M. S. Eison, D. P. Taylor, L. A. Riblet, D. L. Temple, J. Med. Chem. 29, 359 (1986).
[9]. R. S. Upadhayaya, N. Sinha, S. Jain, N. Kishore, R. Chandra, S. K. Arora, Bioorg. Med. Chem. 12, 2225 (2004).
[10]. H. Y. Li, C. Morisseau, B. D. Hammock, Y. Q. Long, Bioorg. Med. Chem. 14, 6586 (2006).
[11]. M. A. Matulenko, A. A. Hakeem, T. Kolasa, M. Nakane, M. A. Terranova, M. E. Uchic, L. N. Miller, R. Chang, D. L. Donnelly-Roerts, M. T. Namovic, R. B. Moreland, J. D. Brioni, A. O. Stewart, M. Kimara, T. Masuda, K. Yamada, Bioorg. Med. Chem.12, 3471 (2004).
[12]. J. P. Vacca, B. D. Dorsey, W. A. Schleif, R. B. Levine, S. L. McDaniel, P. L. Darke, J. Zugay, J. C. Quintero, O. M. Blahy, B. B. Sardana, A. J. Schlabach, P. L. Graham, J. H. Condra, L. Gotlib, M. K. Holloway, J. Lin, I. W. Chen, K. Vastag, D. Ostovic, P. S. Anderson, E. A. Emini, J. R. Huff, J. Med. Chem. 37, 3443 (1994).
[13]. R. J. Kerns, M. J. Rybak, G. W. Kaatz, F. Vaka, R. Cha, R. G. Grucz, V. U. Diwadkar, Bioorg. Med. Chem. Lett. 13, 2109 (2003).
[14]. H. W. Seely, D. P. J. Van, Microbes in action: A laboratory manual of microbiology, D. B. Taraporevala Sons & Co Pvt. Ltd. Bombay, **1975**, pp. 55.