Research Article **ISSN:2321-2624**

International Journal of Medicine and Pharmaceutical Research
www.pharmaresearchlibrary.com/ijmpr

Synthesis and Antimicrobial activity of 5[4(morpholin-4-yl) phenyl] 1,3,4 Oxadiazole 2-yl Sulphonyl acetohydrazide Derivatives

M Somashekhar*[1], Basavraj Sonnad[4], Bharati Tare[1], R V Heralagi[2], Sachin Lokapure[3]

[1]Department Pharmaceutical Chemistry, Krupanidhi College of Pharmacy, Bangalore.
[4]Department Pharmacology, Krupanidhi College of Pharmacy, Bangalore.
[2]Department Pharmaceutical Chemistry, BLDEA'S College of Pharmacy, Bijapur. India
[3]Department Pharmaceutical Chemistry, Rajaram Bapu College of Pharmacy, Kasegaon, India
Received: 9 February 2014, Accepted: 10 March 2014, Published Online: 10 April 2014

Abstract

We have chosen molecule having moieties possessing antimicrobial activity, one of which is hydrazide skeleton, which is reported to have antibacterial and antitubercular activity and other morpholine ring attached to 4th position of the benzene ring which possess the antibacterial, antimycobacterial and antifungal activity. Present work deals with the preparation of morpholie And 4-chloro-benzonitrile on reflux gives 4-(morpholine-4-yl)benzonitrile. This upon treating with sodium hydroxide gives 4-(morpholin-4-yl)benzoicacid. Then this upon treating with thionyl chloride gives 4-(morpholin-4-yl)benzoyl chloride. This on further treatement with hydrazine-hydrate gives 4-(morpholin-4-yl) benzohydrazide. Which is treated with Carbon di sulphide gives 5[4(morpholin-4-yl) phenyl] 1,3,4 oxadiazole 2-thiol and it is treated with chloroacetyl chloride gives 5[4(morpholin-4-yl) phenyl] 1,3,4 oxadiazole 2-yl sulphonylacetylchloride and then it is further treated with hydrazine hydrate gives 5[4(morpholin-4-yl) phenyl] 1,3,4 oxadiazole 2-yl sulphonyl acetohydrazide and then it is treated with various substituted of aromatic aldehyde and to form morpholine derivatives. Hydrazides were synthesized so as to increase intracellular concentration and so as to try and decrease the resistant developed due to decrease intracellular concentration of the drug. These synthesized compounds were subjected to preliminary biological evaluation. The characterization of synthesized compounds was identified on the basis of IR, ^{1}HNMR, Mass spectroscopy. The compounds have been evaluated for antimicrobial activity.
Keywords: Morpholine, Antimicrobial activity, Intracellular concentration

Contents

1. Introduction 561
2. Experimental 563
3. Results and Discussion. 566
4. Conclusion 567
5. Acknowledgement. 568
6. References 568

***Corresponding author**
M Somashekhar
E-mail: csm.som@gmail.com
Manuscript ID: IJMPR2018

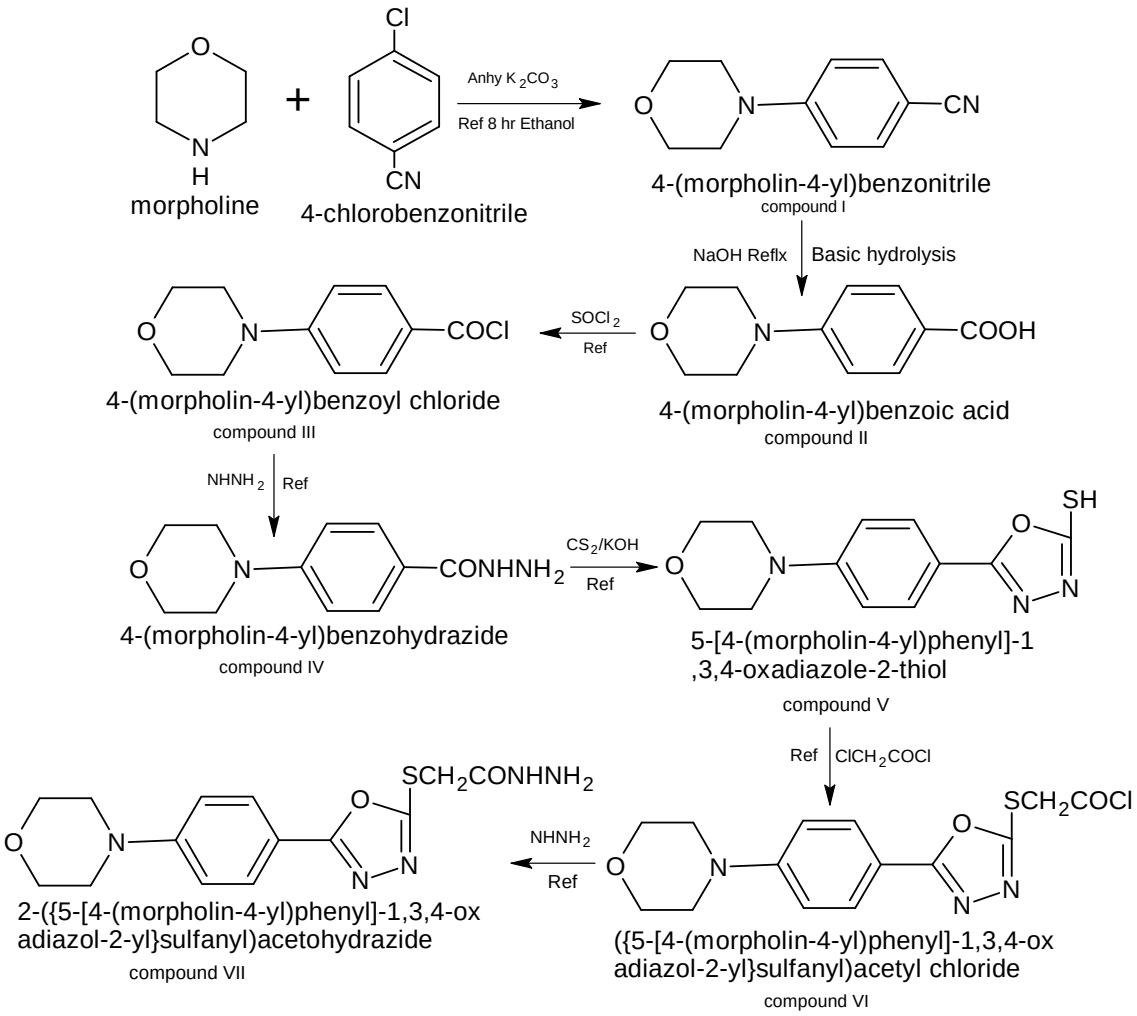
PAPER-QR CODE

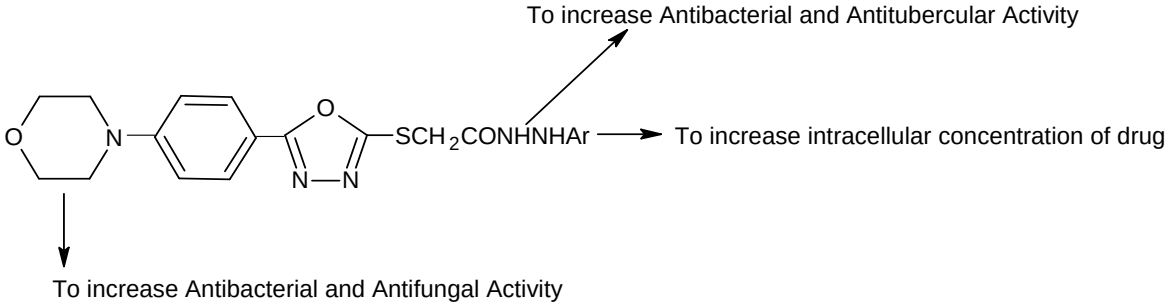
1. Introduction

Morpholine is an organic chemical compound having the chemical formula $O(CH_2CH_2)_2NH$.This heterocyclic structure features both amine and ether functional groups. Because of the amine group, morpholine is a base; its conjugate acid is called as morpholinium. Morpholine has great industrial importance and a wide range of applications; it is used as an anticorrosive agent in water boiling systems and as a chemical intermediate (catalyst, solvent, antioxidant, etc.) in the manufacture of rubber additives and in the textile industry. Till date, only strains belonging to the genus Mycobacterium have been reported to be able to use morpholine as a sole source of carbon, nitrogen, and energy. Morpholine is a common additive, in parts per million (ppm) concentrations, for pH adjustment in both fossil fuel and nuclear power plant steam systems.

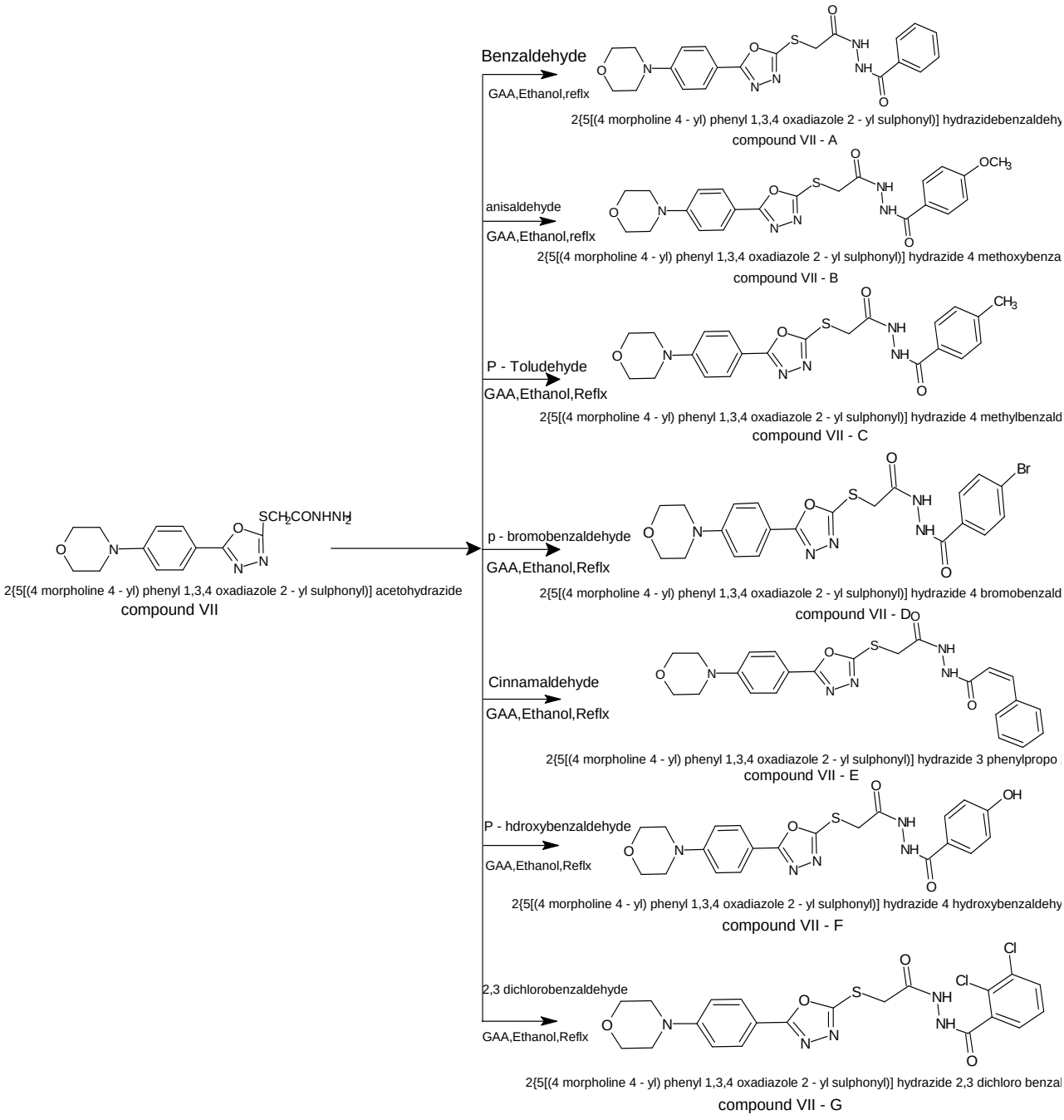
Morpholine is used because its volatility is same as water, so once it is added to the water, its concentration becomes distributed rather evenly in both the water and steam phases. It's pH adjusting qualities then become distributed throughout the steam plant to provide protection against corrosion. Morpholine is often used in conjunction with low concentrations of hydrazine or ammonia to provide comprehensive all-volatile treatment chemistry for protection against corrosion for the steam systems of such plants [1-7]. We have chosen molecule having moieties possessing antimicrobial activity, one of which is hydrazine skeleton, which is reported to have antibacterial, antifungal andanti-tubercular activity and the other is morpholine ring attached to 4th position of the benzene ring which possess the antimicrobial activity. Hydrazines were synthesized so as to increase intracellular concentration and so as to try and decrease the resistant developed due to decrease intracellular concentration of the drug. These synthesized compounds were subjected to preliminary biological evaluation.

Scheme –1[8-17]





Scheme-2[18-23]



2. Materials and Method

The melting points were determined in open capillary tube using Precision melting point apparatus and uncorrected. Thin-layer chromatography was performed with fluorescent silica gel plates HF254 (Merck), plates were viewed under UV 254 and 265 light. Infrared spectra's (v-cm-1) were recorded on a Shmadzu FT-IR 4000; using KBr disks.1H-NMR spectra were recorded on Bruker Spectrophotometer at 300MHz frequency in CDCl3 as well as DMSO using TMS as internal standard reference. Peaks are reported in ppm downfield of TMS. Mass spectra were recorded in 'GCMSQP2010s' instrument by direct injection method [8-17].

Step-1: Synthesis of 4-Morpholin-4-yl-benzonitrile.

A mixture of morpholine (4gm, 0.14 mol) in ethanol (25ml) and 4-chloro-benzonitrile (3.2gm, 0.05 mol) in 250ml round bottom flask and added anhydrous potassium carbonate (3gm) for the purpose of increasing rate of reaction. It was heated at 120˚C. The conversion of 4-chloro-benzonitrile (2) was complete after 12hours.Water (25ml) was added into the reaction mixture. The precipitate was filtered off, washed with water and dried under vacuum (30˚C) to give title compound. It was recrystallized from 50% aqueous ethanol. Infrared spectroscopy of this product was 3181cm^{-1} aromatic C-H stretch, 2924 cm^{-1} aliphatic C-H stretch, 1620 cm^{-1} aromatic C=C stretch, 1220 cm^{-1} C-N stretch.Melting point is 82˚C.

Step-2: Synthesis of 4-morpholin-4-yl-benzoic acid.

To 4-morpholin–4-yl-benzonitrile (3gm, 0.01mol), water (120ml) and sodium hydroxide (6gm, 0.3mol) were added. Small amount of methanol was added to increase the rate of the reaction. The reaction mixture was refluxed on water bath for 5 hours; it was cooled to room temperature and make acidic by the addition of HCl (10%) with efficient stirring. The precipitate was filtered off, washed with water and dried under vacuum (60˚C) to give the title compound. It was recrystallized from ethanol. Infrared spectroscopy of this product was 2925cm^{-1} aromatic C-H stretch, 2850 cm^{-1} aliphatic C-H stretch, 1593 cm^{-1} aromatic C=C stretch, 1321 cm^{-1} C-N stretch, 1683 cm^{-1} C=O stretch.Melting point is 275˚C.

Step-3: Synthesis of 4-Morpholin-4-yl-Benzoylchloride

A mixture of 4-morpholin-4-yl-benzoic acid (6gm, 1 mol) in ethanol (25ml) and thionyl chloride ($SOCl_2$) (3.3ml, 0.5 mol) was refluxed on water bath for 6 hours. Excess of thionyl chloride was removed by distillation under reduced pressure or by adding formic acid drop wise as required and the residue so collected was used for the next step. Infrared spectroscopy of this product was 2926 cm^{-1} aromatic C-H stretch, 2675 cm^{-1} aliphatic C-H stretch, 1424 cm^{-1} aromatic C=C cm^{-1} stretch, 1246 cm^{-1} C-N stretch, 1683 cm^{-1} C=O stretch, 1088C-Cl cm^{-1} stretch .Melting point is 130˚C.

Step-4: Synthesis of (4-morpholin-4-yl) benzohydrazide

To the solution of 4-morpholin-4-yl-benzoyl chloride (6gm, 0.01mol) in 15ml of methanol, 99% hydrazine hydrate (1.94ml, 0.03mol) was added and the mixture was refluxed with on water bath for 4hours. After cooling the precipitate was collected, washed with distilled water, and it was recrystallized from ethanol. Infrared spectroscopy of this product was 3150 cm^{-1} N-H stretch of primary amine, 2851 cm^{-1} aromatic C-H stretch, 2676 cm^{-1} aliphatic C-H stretch, 1424 cm^{-1} aromatic C=C cm^{-1} stretch, 1130 cm^{-1} C-N stretch, 1686 cm^{-1} C=O stretch, 1088C-Cl cm^{-1} stretch, 852 cm^{-1} N-H bending. 1H-NMR spectrum: 1H-NMR (DMSO-d6, 300 MHz), δ (ppm): 2.27(s, 4H, N (CH2)2), 6.8-7.9 (m, 6H, Ar-H).LC-MS (m/z): 206.29 (M+ 1) .Melting points is 282˚C.

Step-5: Synthesis of 5[4-Morpholin-4-yl-Phenyl)1,3,4oxadiazole 2 thiol.

To the mixtureof (4-morpholin-4-yl)benzohydrazide (0.01mmol) 10ml and carbon di sulphide 0.6ml added a solution of KOH 0.56gm in 50ml water and 50ml ethanol was refluxed on water bath for about 3hrs then the reaction mixture was acidified with concHCl.The solid product was filtered and washed with water recrystalised from 50% ethanol. Infrared spectroscopy of this product was 2843 cm^{-1} N-H stretch of primary amine, 2634 cm^{-1} aromatic C-H stretch, 2557 cm^{-1} aliphatic C-H stretch, 1416 cm^{-1} aromatic C=C cm^{-1} stretch, 1134 cm^{-1} C-N stretch, 1681 cm^{-1} C=O stretch, 680 C-S cm^{-1} stretch. 1H-NMR spectrum: 1H-NMR (DMSO-d6, 300 MHz), δ (ppm): 2.26(s, 4H, N (CH2)2), 6.7-7.8 (m, 6H, Ar-H).LC-MS (m/z): 263.31 (M+ 1) .Melting points is 293˚C.

Step-6: Synthesis of {5[4-Morpholin-4-yl-Phenyl)] 1,3,4 oxadiazole-2yl} Sulfonyl acetyl chloride.

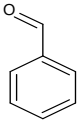
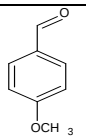
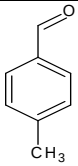
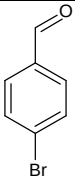
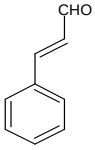
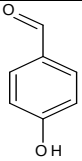
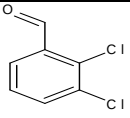
The suspension of 5[4-Morpholin-4-yl-Phenyl)1,3,4 oxadiazole 2 thiol in glacial acetic acid 30 ml and chloroacetyl chloride was added dropwise with constant stirring the reaction mixture was refluxed gentaly at 120^0 C for 5 hours and poured on crushed ice and filtered and recrystalised from ethanol 70%.Infrared spectroscopy of this product was 3320 cm^{-1} N-H stretch of primary amine, 2846 cm^{-1} aromatic C-H stretch, 2635 cm^{-1} aliphatic C-H stretch, 1533 cm^{-} aromatic C=C cm^{-1} stretch, 1134 cm^{-1} C-N stretch, 1089 cm^{-1} C-Cl stretch, 670 C-S cm^{-1} stretch. 1H-NMR spectrum: 1H-NMR (DMSO-d6, 300 MHz), δ (ppm): 2.28(s, 4H, N (CH2)2), 6.7-7.86 (m, 6H, Ar-H).LC-MS (m/z): 339.79 (M+ 1) .Melting points is 282˚C.

Step-7: Synthesis of 2{5[4-Morpholin-4-yl-Phenyl)] 1,3,4 oxadiazole-2yl} Sulfonylacetohydrazide.

To the mixture of{5[4-Morpholin-4-yl-Phenyl)] 1,3,4 oxadiazole-2yl} Sulfonyl acetyl chloride.(6gm, 0.01 mol) in15ml of methanol, 99% hydrazine hydrate (1.94ml, 0.03 mol) was added and themixture was refluxed with on water bath for 4hrs. After cooling the precipitate wascollected, washed with distilled water, and recrystallized from

ethanol.Infrared spectroscopy of this product was 2845 cm^{-1} N-H stretch of primary amine, 2676 cm^{-1} aromatic C-H stretch, 2559 cm^{-1} aliphatic C-H stretch, 1586 cm^{-1} aromatic C=C cm^{-1} stretch, 1133 cm^{-1} C-N stretch, 1686 cm^{-1} C=O stretch, 670 C-S cm^{-1} stretch. 1H-NMR spectrum: 1H-NMR (DMSO-d6, 300 MHz), δ (ppm): 1.69-4.7(s, 4H, N (CH2)2), 6.7-7.8 (m, 6H, Ar-H).LC-MS (m/z): 335.38 (M+ 1) .Melting points is 285˚C.

Table 1. Different Aryl aldehyde attaches with the Hydrazides

Compound	-Ar	MP ° C
VII-a	 benzaldehyde	290°C
VII-b	 4-methoxybenzaldehyde	295°C
VII-c	 4-methylbenzaldehyde	280°C
VII-d	 4-bromobenzaldehyde	282°C
VII-e	 (2*E*)-3-phenylprop-2-enal	288°C
VII-f	 4-hydroxybenzaldehyde	292°C
VII-g	 2,3-dichlorobenzaldehyde	295°C

Scheme 2: Preparation of 2{5[4-Morpholin-4-yl-Phenyl)] 1,3,4 oxadiazole-2yl} Sulfonyl hydrazide derivatives. (VIIa–VIIg).

Take a mixture of 2{5[4-Morpholin-4-yl-Phenyl)] 1,3,4 oxadiazole-2yl} Sulfonylacetohydrazide 0.01mole and add a Aromaticaldehyde 0.01 mole and add few drops of glacial acetic acid in ethanol 30 ml and reflux for 5 hours the residue was stirred with ice cold water 50 ml and filtered off the solid mass and recrystallized from ethanol. This method of preparation gives the VIIa–VIIg derivatives compounds.The compound VII fwas confirmed by IR KBr plate method. 2926cm $^{-1}$N – H Stretch of 2˚ amine, 2851cm $^{-1}$Aromatic C-H Stretch, 2676cm $^{-1}$ Aliphatic C-H Stretch, 1685 cm $^{-1}$ C = O Stretch, 1424cm $^{-1}$C = N Stretch, 1013cm $^{-1}$C – N Stretch, 681 cm $^{-1}$C - S Stretch.LC-MS (m/z): 455.48 (M+ 1) .Melting points is 292˚C.it shows moderate antibacterial and antifungal activity.

Table 2. Physicochemical properties of derivatives compoundVIIa-VIIg.

S.NO	Compound Code	Molecular Formula	Molecular Weight	M.P. (^oC) (uncorrected)	% Yield	Recrystallization Solvent
1	VII-a	$C_{21}H_{21}N_5O_4S$	439.48	288-290	70.00	Ethanol
2	VII-b	$C_{22}H_{23}N_5O_5S$	469.51	294-295	83.35	Ethanol
3	VII-c	$C_{22}H_{23}N_5O_4S$	453.51	280-282	79.88	Ethanol
4	VII-d	$C_{21}H_{20}N_5O_4BrS$	518.38	282-284	82.50	Ethanol
5	VII-e	$C_{23}H_{23}N_5O_4S$	465.52	288-290	90.00	Ethanol
6	VII-f	$C_{21}H_{21}N_5O_5S$	455.48	290-292	84.38	Ethanol
7	VII-g	$C_{21}H_{19}N_5O_4SCl_2$	508.37	293-295	76.50	Ethanol

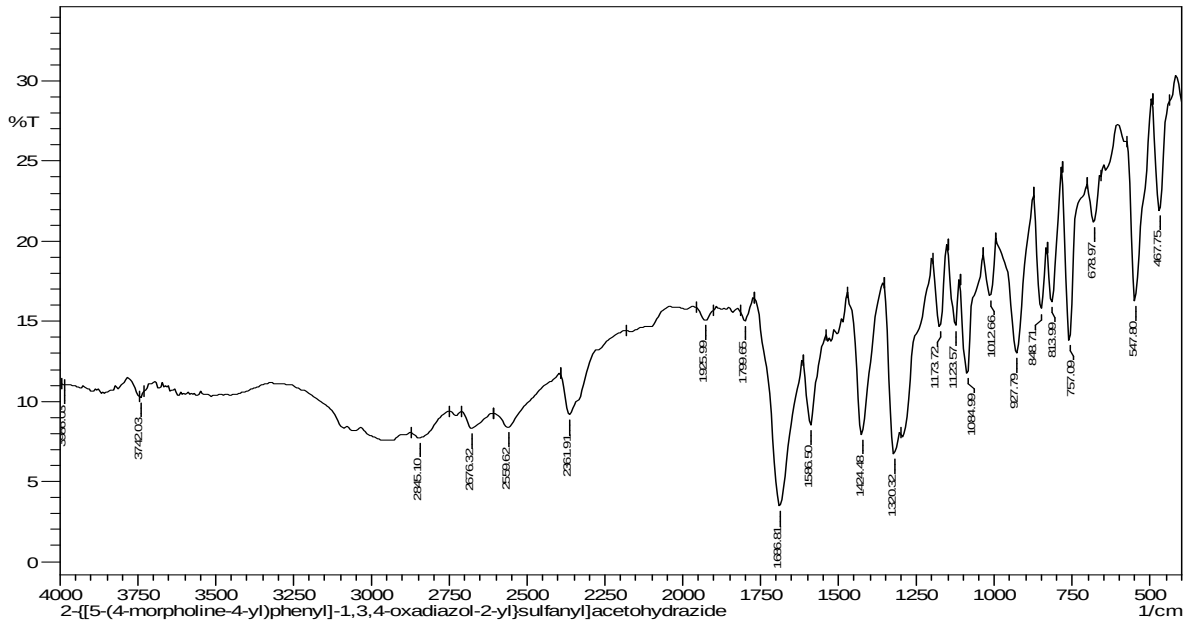


Figure 1. FT-IR spectrum of compound VII

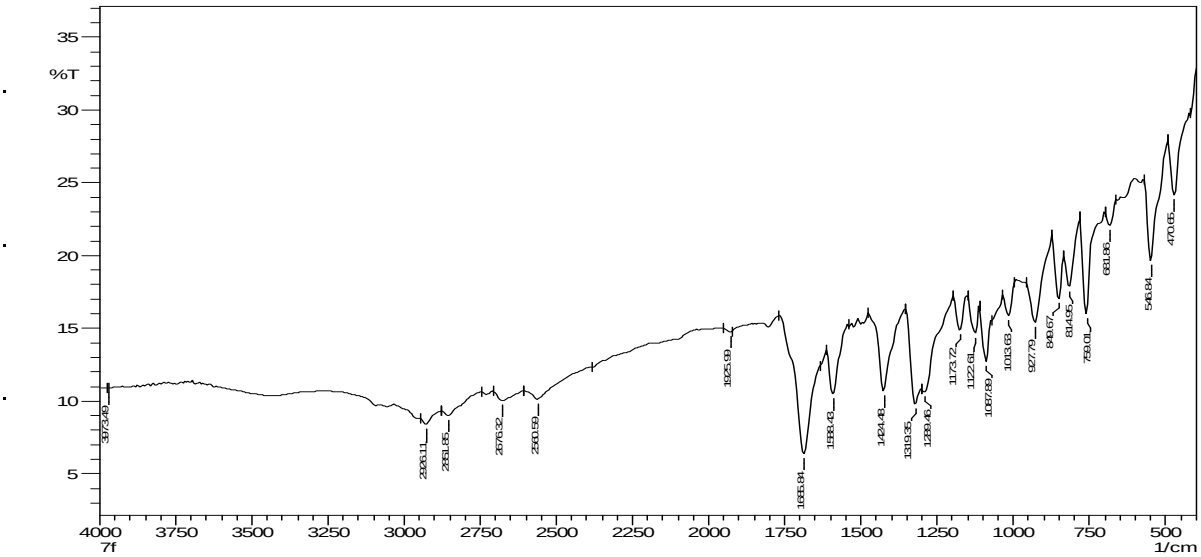


Figure 2. FT-IR spectrum of compound VIIf

3. Results and Discussion

All the derivatives of 4-morpholin-4-yl-benzohydrazidewere assayed in vitro for their antibacterial activity against *Staphylococcus aureus* (Gram-positive bacteria) and *Escherichia coli* (Gram-negative bacteria) and antifungal activity against *Aspergillus niger* and *Candida albicans*. The minimum inhibitory concentration (MIC) value for antibacterial activity of compounds was determined by the cup plate method by using nutrient agar media (NAM). The minimum inhibitory concentration (MIC) values for antifungal activity were determined by using broth double dilution method (Serially diluted method) in Potato dextrose broth at pH 7.4. For comparison, Ciprofloxacin was used as the reference antibacterial agents; Ketoconazole was employed as the reference antifungal agent. The antibacterial and antifungal MIC values for test compound as well as reference standardare given in Table No.3 and 4 respectively.

Table 3. Zone of inhibition of synthesized compounds [VIIa-VIIg].(Against Bacteria)

S. No	compound	Zone of Inhibition (mm)	
		E.coli	***S.Aureus***
1	VIIa	09	05
2	VIIb	07	04
3	VIIc	14	10
4	VIId	18	16
5	VIIe	22	21
6	VIIf	23	22
7	VIIg	08	06
9	S	29	32
10	C	-	-

0-15 mm poor activity,
15-25 mm moderate activity,
25 above good.
Standard(S) = Ciprofloxacin Control (C) = DMF

Table 4. Zone of inhibition of synthesized compounds [VIIa-VIIg].(Against Fungi)

S.NO	Compound	Zone of inhibition in diameter (mm)	
		C.albicans	***A. niger***
1	VIIa	13	11
2	VIIb	11	10
3	VIIc	14	10
4	VIId	09	11
5	VIIe	23	20
6	VIIf	22	21
7	VIIg	07	09
10	S	35	33
11	C	-	-

0-15 mm poor activity,
15-25 mm moderate activity,
25 above good.
Standard(S) = Ketoconazole
Control (C) = DMF

Antibacterial activity:
The minimum inhibitory concentration (MIC) was determined by the cup plate method. Ciprofloxacin was employed during the test procedures as reference. The MIC of the synthesized compounds ranges between 25-200 µg/ml. VIIf were found moderately active compared with standard. Test compounds were found to be more sensitive towards *Staphylococcus aureus* (Gram-positive bacteria) and *Escherichia coli* (Gram-negative bacteria).
Antifungal activity:
The minimum inhibitory concentration (MIC) was determined by the broth dilution method (Serially diluted method). Ketoconazole was employed du6d ring the test procedures as references.MIC of the synthesized compounds ranges between 15.6-500µg/ml. VIIf was found moderately active compared with standard. Test compounds were found to be more sensitive towards *Aspergillus niger*and *Candida albicans.*

4. Conclusion

Most compounds exhibited significant antibacterial and antifungal activity. A remarkable activity was found in compound VIIf having good antibacterial and antifungal activity. From the detailed analysis of the results of above studies, we conclude that antibacterial and antifungal activity of the synthesized compounds is significantly depends on the lipophilicity. The results obtained show that some of the synthesized and tested compounds, especially VIIf may be considered promising for the development of new antibacterial and antifungal agent.

5. Acknowledgement

The authors thank the Chairman, Director, Principal, colleagues and non-teaching staff KCP Bangalore and BLDEA'S college of pharmacy Bijapur, for providing laboratory facilities and encouragement and Director IISc Bangalore and Oxygen health care Ahmadabad, provided for spectral studies.

6. References

1. AD Desai; DH Mahajan; KH Chikhalia. Synthesis of novel aliphatic thiourea derivatives S-triazine moiety as potent antimicrobial agents. Indian Journal of Chemistry, 2007, 46(B).
2. TA Naik; KH Chikhalia. Studies on Synthesis of Pyrimidine Derivatives andtheir Pharmacological Evaluation. E-Journal of Chemistry, 2007, 4(1), 60-66.
3. OT-Arpacıa; AOzdemira; I smail; I Yıldıza; E Akı-S; NAltanlarb. Synthesis and Antimicrobial Activity of Some5-[2-(Morpholin-4-yl)acetamido] and/or 5-[2-(4-Substituted piperazin-1-yl)acetamido]-2-(*p*-substituted phenyl)benzoxazoles. Arch Pharm Chem Life Sci, 2005, 338, 105−111.
4. AOzdem; G lhan; ZAsımKaplancikli. Novel Analogues of 2-Pyrazoline: Synthesis, Characterization, and Antimycobacterial Evaluation. Turk J Chem, 2008, 32, 529–538.
5. S Batra;Z Tusi; SMadappaa. Medicinal Chemistry of ureido derivatives as Antiinfectives. Anti-Infective Agents in Medicinal Chemistry, 2006, 5, 135-160.
6. S Jantova; ARepicky; E Paulovicova; S Letasiova; L Cipak. Antiproliferative activity and apoptosis induced by 6-bromo-2-(morpholin-1-yl)-4-anilinoquinazoline on cellsofleukemia lines. ExpOncol, 2008, 30(2), 139-142.
7. MA Rode; SS Rindhe; K BhausahebKarale. Synthesis and biological activities of some indoline derivatives. J. Serb. Chem. Soc,2009,74(12), 1377–87.
8. M Somashekhar;AR Mahesh; BSonnad. Synthesis and antimicrobial activity of of 4-(morpholin-4-yl) benzohydrazide derivatives. World journal of pharmacy and pharmaceutical sciences, 2013, 2(4), 2011-2020.
9. P Venkatesh; SN Pandeya. Synthesis and Anti-oxidant activity of Some n-(anilinocarbonothioyl) benzamide and Heterocyclic based Thiourea Derivatives. International Journal of ChemTech Research, 2009, 1(3), 733-741.
10. GM Sreenivasa;E Jayachandran; B Shivakumar;K Jayaraj; V Kumar. Synthesis of Bioactive Molecule FluoroBenzothiazole Comprising PotentHeterocyclic Moieties for Anthelmentic Activity. Arch Pharm Sci & Res, 2009, 1(2), 150-157.
11. P. Panneerselvam;M GnanarupaPriya; N Ramesh Kumar; GSaravanan. Synthesis and Pharmacological Evaluation of Schiff Bases of 4-(2-Aminophenyl)-Morpholines. Indian J Pharm Science, 2009,71(4), 428–432.
12. AK Shaukath; BA Begum; V Girish; N Fatima Khanum. Synthesis and Evaluation of Benzophenone-N-ethyl Morpholine Ethers as Anti-inflammatory Agents. International journal ofBiomedical science, 2010, 6(1), 60-65.
13. HS Basavaraja;KVJayadevaiah; MM Hussain; V Kumar; BPadmashali. Synthesis of novel piperazine and morpholine linked substitutedpyrimidine derivatives as antimicrobial agents. J. Pharm. Sci. & Res, 2010, 2(1), 5-12.
14. DP Kardile;NV Kalyane. Synthesis and antimicrobial activity of 4 thiomorpholine -4ylbenzohydrazide derivatives. IJABPT, 2010, 1(3), 1021-1031.
15. D Singh; G Bansal. Synthesis of Morpholine Containing Sulfonamides: Introduction of Morpholine Moiety on Amine Functional Group. E-Journal of Chemistry, 2004, 1(2), 164-169.
16. MK Piestrzeniewicza; D Wilmanskaa; J Szemrajb; K Studziana; M Gniazdowskia. Interactions of Novel Morpholine and Hexamethylene Derivatives of Anthracycline Antibiotics with DNA.Z. Naturforsch, 2004, 59(9-10), 739-748.
17. N Upmanyu; S Kumar; M Kharya; K Shah; P Mishra. Synthesis and anti-microbial evaluation of some novel 1, 2, 4 -triazole derivatives. ActaPoloniae Pharmaceutical Drug Research, 2011, 68(2), 213-221.
18. E Wyrzykiewicz; MWendzonka; BKędzia. Synthesis and antimicrobial activity of new (E)-4-[piperidino (4'-methylpiperidino-, morpholino-) N-alkoxy]stilbenes. European Journal of Medicinal Chemistry, 2006,41(4), 519-525.
19. S Upinder; B Raju; S Lam; J Zhou; RC Gadwood; CW Ford; GE Zurenko; RD Schaadt; SE Morin; WJ Adams.New Antibacterial tetrahydro-4(2*H*)-thiopyran and thiomorpholineS-oxide and S,S-dioxide phenyloxazolidinones. Bio-organic & Medicinal Chemistry Letters, 2003,13(23), 4209-4212.
20. V Raparti;TChitre;K Bothara;V Kumar;S Dangre;C Khachane;S Gore;BDeshmane. Novel 4-(morpholin-4-yl)-N′-(arylidene) benzohydrazides: Synthesis, antimycobacterial activity and QSAR investigations. European Journal of Medicinal Chemistry, 2009,44(10), 3954-3960.

21. J Mirzaei; F Siavoshi; S Emam; F Safari; MR Khoshayand; A Shafiee; A Foroumadi.Synthesis and in vitro anti-Helicobacter pylori activity of *N*-[5-(5-nitro-2-heteroaryl) - 1, 3, 4-thiadiazol-2-yl] thiomorpholines and related compounds. European Journal of Medicinal Chemistry, 2008,43(8), 1575-1580.
22. S Kumar; DN Dhar; PN Sexena. Application of Metal Complexes of Schiff Bases- A Review. Journal of Science & Industrial Research, 2009, 68, 181-187.
23. GRPriya. Synthesis, Characterisation and Antibacterial, Antifungal activities of schiff bases of 4 – (2-aminphenyl) Morpholines. International Journal ofPharma and Bio Sciences, 2011,1(2), 267-272.