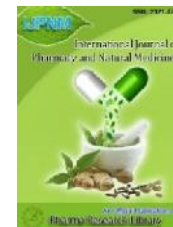




International Journal of Pharmacy and Natural Medicines

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Research Article

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Synthesis, Characterisation and Antimicrobial Activity of 1-(Morpholin-4-yl)-2-(1,3,4-Oxadiazol-2 Ylsulfanyl) Ethanone Derivatives

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ABSTRACT

Considering the biological and chemical relevance of Morpholine derivatives, we have devised novel derivatives of morpholine. The series of morpholine derivatives were synthesized in high yield and quality by reaction of 1-(Morpholin-4-Yl)-2-(1,3,4-Oxadiazol-2 yl-sulfanyl) Ethanone with various aromatic aldehyde giving Schiff base, The synthesized compounds were confirmed by ¹HNMR, IR, element analysis and Mass spectroscopy. All the compounds were screened invitro antibacterial and antifungal activities. 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. SMf 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). And for the antifungal activity MIC of the synthesized compounds ranges between 15.6-500 µg/ml. SMf was found moderately active compared with standard. Test compounds were found to be more sensitive towards *Aspergillus niger* and *Candida albicans*.

Keywords: *Saraca indica*, Soxhlet, Hexane extract, Steroid.

ARTICLE INFO

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Article History: Received 26 May 2015, Accepted 19 July 2015, Available Online 15 December 2015

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Manuscript ID: IJPNM2770



PAPER-QR CODE

Citation: M Somashekhar, et al. Synthesis, Characterisation and Antimicrobial Activity of 1-(Morpholin-4-yl)-2-(1,3,4-Oxadiazol-2 Ylsulfanyl) Ethanone Derivatives. *Int. J. Pharm. Natural Med.*, 2015, 3(2): 323-327.

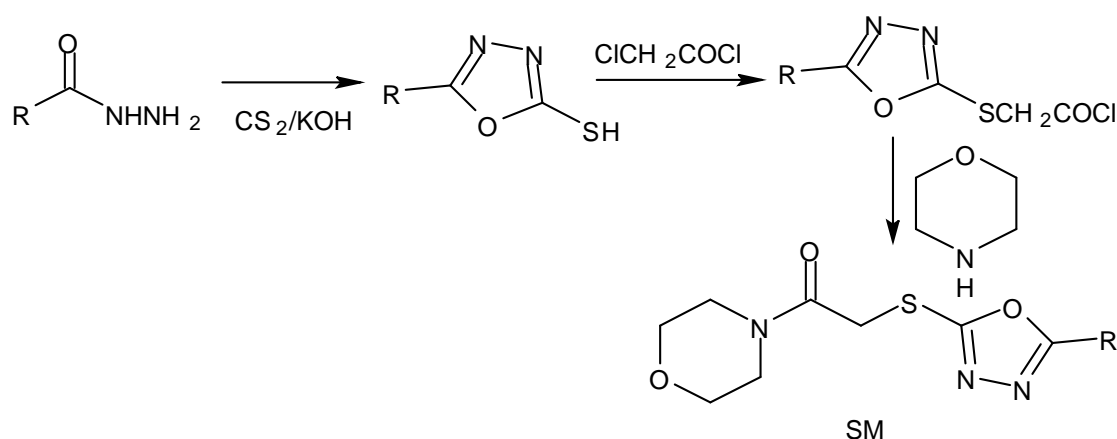
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1. Introduction

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. Its 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]

Oxadiazole a heterocyclic nucleus has attracted a wide attention for the researchers in search for the new therapeutic molecules. Among them, 1,3,4-oxadiazoles have exhibited a wide range of biological properties. The first mono-substituted 1,3,4-oxadiazoles were reported in 1955 by two independent laboratories. 1,3,4-oxadiazole considered as simple five membered Heterocyclic molecule possessing one oxygen and two nitrogen atoms at C-1, C-3 and C-4 respectively. 1,3,4-oxadiazole exhibited a wide range of biological activities which includes antimicrobial, anti-tubercular, anticonvulsant, hypoglycemic, anti-allergic, vasodilator, anti-inflammatory, analgesic, anthelmintic, anticancer, antiviral, antioxidant, hemolytic, antiproliferative activities etc. These synthesized compounds were subjected to preliminary biological evaluation. [8-15]



Scheme 1¹⁶⁻²²

Table 1: Different Aryl aldehydes [Schiff's bases] used for Morpholine derivatives.

Compound name	Aryl aldehydes [Schiff's bases]
SMA	Benzaldehyde
SMB	4-MethoxyBenzaldehyde
SMC	4-Methyl Benzaldehyde
SMd	4-Bromo Benzaldehyde
SMe	(2E)-3-Phenylprop-2-enal
SMf	4-Hydroxy Benzaldehyde

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 (ν -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. [23-31]

General procedure for Synthesis of 1-(morpholin-4-yl)-2-(1,3,4-oxadiazole-2-yl sulfanyl) ethanone[SM].

To the mixture of alkyl/aromatic hydrazide (0.01 mmol) 10 ml and carbon di-sulphide 0.6 ml added a solution of KOH 0.56 gm in 50 ml water and 50 ml ethanol was refluxed on water bath for about 3hrs then the reaction mixture was acidified with con HCl. The solid product was filtered and washed with water recrystallized from 50% ethanol. To this mixture chloroacetyl chloride was added drop wise with constant stirring the reaction mixture was refluxed gently at 120⁰ C for 5 hours and poured on crushed ice and filtered and recrystallized from ethanol 70%. To this mixture morpholine (4 gm, 0.14 mol) in ethanol (25 ml) in 250 ml round bottom flask and added anhydrous potassium carbonate (3gm) for the purpose of increasing rate of reaction. It was heated at 120⁰C. The reaction was complete after 12 hours. Water (25 ml) 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 2856 cm⁻¹ N-H stretch of primary amine, 2594 cm⁻¹ aromatic C-H stretch, 2569 cm⁻¹ aliphatic C-H stretch, 1398 cm⁻¹ aromatic C=C cm⁻¹ stretch, 1595 cm⁻¹ C = O Stretch, 1163 cm⁻¹ C-N stretch, 1633 cm⁻¹, 680 C-S cm⁻¹ stretch. 1H-NMR spectrum: 1H-NMR (DMSO-d₆, 300 MHz), (ppm): 2.87(s, 4H, N (CH₂)₂), 7.1-7.79 (m, 6H, Ar-H). Element analysis is C-41.91, H-4.84, N-18.33, O-20.94, and S-13.99. LC-MS (m/z): 229.05 (M+ 1). Melting points is 263.61°C.

General procedure for Synthesis of 1-(morpholin-4-yl)-2-(1,3,4-oxadiazole-2-yl)sulfanyl ethanone derivatives[SMA-f].

Take a mixture of 1-(morpholin-4-yl)-2-(1,3,4-oxadiazole-2-yl)sulfanyl ethanone 0.01 mole and add a Aromatic aldehyde 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 SMA–SMf derivatives compounds.

1-(morpholin-4-yl)-2-[[5-(phenyl carbonyl)-1,3,4-oxadiazole-2-yl]sulfanyl] ethanone[SMA].

The compound SMA was confirmed by IR KBr plate method. 2966 cm⁻¹ N – H Stretch of 2° amine, 2891cm⁻¹ Aromatic C-H Stretch, 2716 cm⁻¹ Aliphatic C-H Stretch, 1655 cm⁻¹ C = O Stretch, 1457 cm⁻¹ C = N Stretch, 998 cm⁻¹ C – N Stretch, 676 cm⁻¹ C - S Stretch. 1H-NMR spectrum: 1H-NMR (DMSO-d₆, 300 MHz), (ppm): 2.87(s, 4H, N (CH₂)₂), 7.26-7.89 (m, 6H, Ar-H). Element analysis is C-54.04, H-4.54, N-12.60, O-19.20, and S-9.62. LC-MS (m/z): 333.08 (M+ 1). Melting points is 431.37°C.

2-[[5-[(4-methoxy phenyl) carbonyl]-1,3,4-oxadiazole-2-yl]sulfanyl]-1-(morpholin-4-yl) ethanone[SMb].

The compound SMb was confirmed by IR KBr plate method. 2913cm⁻¹ N – H Stretch of 2° amine, 2856 cm⁻¹ Aromatic C-H Stretch, 2812 cm⁻¹ Aliphatic C-H Stretch, 1598 cm⁻¹ C = O Stretch, 1531cm⁻¹ C = N Stretch, 1012cm⁻¹ C – N Stretch, 692 cm⁻¹ C - S Stretch. 1H-NMR spectrum: 1H-NMR (DMSO-d₆, 300 MHz), (ppm): 2.87(s, 4H, N (CH₂)₂), 7.18-7.26 (m, 6H, Ar-H). Element analysis is C-52.88, H-4.72, N-11.56, O-22.01, and S-8.82. LC-MS (m/z): 363.09 (M+ 1). Melting points is 477.39°C.

2-[[5-[(4-methyl phenyl) carbonyl]-1,3,4-oxadiazole-2-yl]sulfanyl]-1-(morpholin-4-yl) ethanone[SMc].

The compound SMc was confirmed by IR KBr plate method. 2880 cm⁻¹ N – H Stretch of 2° amine, 2908 cm⁻¹ Aromatic C-H Stretch, 2853 cm⁻¹ Aliphatic C-H Stretch, 1603 cm⁻¹ C = O Stretch, 1655 cm⁻¹ C = N Stretch, 1042 cm⁻¹ C – N Stretch, 650cm⁻¹ C - S Stretch. 1H-NMR spectrum: 1H-NMR (DMSO-d₆, 300 MHz), (ppm): 1.37-3.65(s, 4H, N (CH₂)₂), 7.26-7.77 (m, 6H, Ar-H). Element analysis is C-55.32, H-4.93, N-12.10, O-18.42, and S-9.23. LC-MS (m/z): 347.09 (M+ 1). Melting points is 455.16°C.

2-[[5-[(4-bromo phenyl) carbonyl]-1,3,4-oxadiazole-2-yl]sulfanyl]-1-(morpholin-4-yl) ethanone[SMd].

The compound SMd was confirmed by IR KBr plate method. 2947 cm⁻¹ N – H Stretch of 2° amine, 2915 cm⁻¹ Aromatic C-H Stretch, 2875 cm⁻¹ Aliphatic C-H Stretch, 1615 cm⁻¹ C = O Stretch, 1577 cm⁻¹ C = N Stretch, 1054 cm⁻¹ C – N Stretch, 723 cm⁻¹ C - S Stretch C-Br Stretch 810 cm⁻¹. 1H-NMR spectrum: 1H-NMR (DMSO-d₆, 300 MHz), (ppm): 2.87-3.67(s, 4H, N (CH₂)₂), 7.26-7.79 (m, 6H, Ar-H). Element analysis is C-43.70, H-3.42, Br-19.38, N-10.19, O-15.52, and S-7.78. LC-MS (m/z): 410.99 (M+ 1). Melting points is 503.69°C.

(2)-1-[5-[(2-(morpholin-4-yl)-2-oxoethyl) sulfanyl]-1,3,4-oxadiazole-2-yl]-3-phenylprop-2-en-1-one[SMe].

The compound SMe was confirmed by IR KBr plate method. 2940 cm⁻¹ N – H Stretch of 2° amine, 2903 cm⁻¹ Aromatic C-H Stretch, 2835 cm⁻¹ Aliphatic C-H Stretch, 1612 cm⁻¹ C = O Stretch, 1623 cm⁻¹ C = N Stretch, 1063 cm⁻¹ C – N Stretch, 710 cm⁻¹ C - S Stretch. 1H-NMR spectrum: 1H-NMR (DMSO-d₆, 300 MHz), (ppm): 2.87-3.65(s, 4H, N (CH₂)₂), 7.26-7.60 (m, 6H, Ar-H). Element analysis is C-56.81, H-4.77, N-11.69, O-17.81, and S-8.92. LC-MS (m/z): 359.09 (M+ 1). Melting points is 448.83°C.

2-[[5-[(4-hydroxy phenyl) carbonyl]-1,3,4-oxadiazole-2-yl]sulfanyl]-1-(morpholin-4-yl) ethanone[SMf].

The compound SMf was confirmed by IR KBr plate method. 2895 cm⁻¹ N – H Stretch of 2° amine, 2880 cm⁻¹ Aromatic C-H Stretch, 2810 cm⁻¹ Aliphatic C-H Stretch, 1595 cm⁻¹ C = O Stretch, 1593 cm⁻¹ C = N Stretch, 995 cm⁻¹ C – N Stretch, 687 cm⁻¹ C - S Stretch. 1H-NMR spectrum: 1H-NMR (DMSO-d₆, 300 MHz), (ppm): 2.87-3.65(s, 4H, N (CH₂)₂), 5.35-6.12 (-OH) 6.89-7.72 (m, 6H, Ar-H). Element analysis is C-51.57, H-4.33, N-12.03, O-22.90, and S-9.18. LC-MS (m/z): 349.07 (M+ 1). Melting points is 543.09°C.

Table 2: Physicochemical properties of derivatives compound SMA-SMf.

Sl. no	Compound Code	Molecular Formula	Molecular Weight	M.P. (°C)	% Yield	Re-crystallization Solvent
1	SMA	C ₁₅ H ₁₅ N ₃ O ₄ S	333.36	431-432	72.30	Ethanol
2	SMb	C ₁₆ H ₁₇ N ₃ O ₅ S	363.39	477-478	78.55	Ethanol
3	SMc	C ₁₆ H ₁₇ N ₃ O ₄ S	347.39	455-457	81.62	Ethanol
4	SMd	C ₁₅ H ₁₄ N ₃ O ₄ BrS	412.26	503-504	79.90	Ethanol
5	SMe	C ₁₇ H ₁₇ N ₃ O ₄ S	359.40	448-449	88.50	Ethanol
6	SMf	C ₁₅ H ₁₅ N ₃ O ₅ S	349.36	543-544	81.30	Ethanol

3. Results and Discussion

All the derivatives of 1-(morpholin-4-yl)-2-(1,3,4-oxadiazole-2-yl)sulfanyl)ethanone were assayed in vitro for their antibacterial activity against *Staphylococcus aureus* (Gram-positive bacteria) and *Escherichia coli* (Gram-negative bacteria) and antifungal activity against *Aspergillusniger* 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 standard are given in Table No. 3 and 4 respectively.

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. SMf 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 during the test procedures as references. MIC of the synthesized compounds ranges between 15.6-500 µg/ml. SMf was found moderately active compared with standard. Test compounds were found to be more sensitive towards *Aspergillusniger* and *Candida albicans*.

Table 3: Zone of inhibition of synthesized compounds [SMa-SMf]. (Against Bacteria)

Sl. no	compound	Zone of Inhibition(mm)	
		<i>E.coli</i>	<i>S.Aureus</i>
1	SMa	10	06
2	SMb	06	07
3	SMc	14	11
4	SMd	16	17
5	SMe	18	18
6	SMf	23	21
7	S	29	31
8	C	-	-

Note: 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 [SMa-SMf]. (Against Fungi)

Sl. no	compound	Zone of Inhibition(mm)	
		<i>C.albicans</i>	<i>A.niger</i>
1	SMa	14	12
2	SMb	12	11
3	SMc	13	14
4	SMd	19	18
5	SMe	20	19
6	SMf	24	22
7	S	35	34
8	C	-	-

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

4. Conclusion

Most compounds exhibited significant antibacterial and antifungal activity. A remarkable activity was found in compound SMf 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 SMf may be considered promising for the development of new antibacterial and antifungal agent.

5. Acknowledgments

The authors thank the Chairman, Director, Principal, colleagues and non-teaching staff KCP Bangalore and BLDEA'S college of pharmacy Vijaypur, 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 Chikhaliya. Synthesis of novel aliphatic thiourea derivatives S-triazine moiety as potent antimicrobial agents. *Ind.Jr. of Chem.*, **2007**, 46(B): 1169-1173.
- [2] TA Naik, KH Chikhaliya. Studies on Synthesis of Pyrimidine Derivatives and their Pharmacological Evaluation. *E-Jr. of Chem.*, **2007**, 4(1): 60-66.
- [3] OArpacıa, A Ozdemira, I smail, I Yıldıza, E Akı, NAltanlarb. Synthesis and Antimicrobial Activity of Some 5-[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] A Ozdem, G lhan, ZA Kaplancikli. Novel Analogues of 2-Pyrazoline: Synthesis, Characterization, and Antimycobacterial Evaluation. *Turk Jr. Chem.*, **2008**, 32: 529–538.
- [5] S Batra, Z Tusi, SM adappaa. Medicinal Chemistry of ureido derivatives as Antiinfectives. *Anti-Infective Agents in Med. Chem.*, **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 cells of leukemia lines. *Exp. Oncol.*, **2008**, 30(2): 139-142.
- [7] MA Rode, SS Rindhe, KB Karale. Synthesis and biological activities of some indoline derivatives. *Jr. Serb. Chem. Soc.*, **2009**, 74(12): 1377–1387.
- [8] PP Naik, RR Somani, SO Waghulde, P Juvatkar, PY Shirodkar, MK Kale. Synthesis And Biological Activities of Some 1, 3, 4-Oxadiazole Based Schiff's Bases. *Int. Jr. of Pharm. And Phyto. pharmaco. Rech.*, **2015**: 1-10.
- [9] R Naik. Synthesis And Characterization Of 1, 3, 4-Oxadiazole And 1,3,4- Thiadiazole Ind. *Jr. of Rech. In Pharm. and Biotech.*, **2013**, 1(3): 413-420.
- [10] AK Singh, VK Sahu, D Yadav. Biological Activities of 2, 5-Disubstituted-1,3,4 Oxadiazoles. *Int. Jr. of Pharma. Sci. and Rech.*, **2011**, 2(6): 135-147.
- [11] VK Sahu, AK Singh, D Yadav. Review Article on 1,3,4-Oxadiazole Derivatives & its Pharmacological Activities. *Int. Jr. of Chem. Rech.*, **2011**, 3(3): 1362-1372.
- [12] K Ajay Kumar, P Jayaropa, G Vasanth Kumar. Comprehensive Review On The Chemistry Of 1,3,4-Oxadiazoles And Their Applications. *Int. Jr. of Chem. Rech.*, **2012**, 4(4): 1782-1791.
- [13] H Rajak, MD Kharya, P Mishra. Biologically Active 2,5-Disubstituted 1,3,4-Oxadiazoles. *Int. Jr. of Pharma. Sci. and Nano tech.*, **2009**, 2(1): 390-406.
- [14] S Sanchit, SN Pandeya. Various Approaches for Synthesis of Oxadiazole Derivatives. *Int. Jr. of Rech. In Ayu. And Pharm.*, **2011**, 2(2): 459-468.
- [15] A Pangal, JA Shaikh. Various Pharmacological Aspects Of 2, 5-Disubstituted 1,3,4-Oxadiazole Derivatives: A Review. *Rech. Jr. of Chem. Sci.*, **2013**, 3(12): 79-89.
- [16] IKJ Al-Joubory, TFK Albayati, KAJ Albayati, TSM Al-Joubory. Synthesis, Characterization and Biological Activity of Some Oxadiazoles Derivatives and Thiadiazoles Derivatives. *Diyala Jr. For Pure Sci.*, **2013**, 9(3): 47-56.
- [17] AA Kharche, SH. Bairagi, NK Gord, SS Laddha. 1,3,4-Oxadiazole: A New Profile Of Biological Activities. *Asian Jr. Res. Chem.*, 20114, (1): 1-12.
- [18] V Modi, P Modi. Oxadiazole: Synthesis, Characterization and Biological Activities. *Jr. of Saudi Chem. Soc.*, **2012**, 16: 327–332.
- [19] SJ Gilani, O Alam, SA Khan, N Siddiqui, H Kumar. Synthesis Of Some Derived Thiazolidin-4-One, Azetidin-2-One And 1,3,4-Oxadiazole Ring Systems From Isonicotinic Acid Hydrazide: A Novel Class Of Potential Anticonvulsant Agents. *Der Pharmacia Lettre.*, **2009**, 1(2): 1-8.
- [20] S Gul, AU Rehman, MA Abbasi, KM Khan, K Nafeesa, ASiddiq, MN Akhtar, M Shahid, Z Subhani. Synthesis, Antimicrobial Evaluation And Hemolytic Activity Of 2-[[5-Alkyl/Aralkyl Substituted-1,3,4-Oxadiazol-2-Yl]Thio]-N-[4-(4-Morpholinyl)Phenyl]Acetamide Derivatives. *Jr. of Saudi Chem. Soc.*, **2014**.
- [21] M Somashekhar, AR Mahesh, B Sonnad. Synthesis and antimicrobial activity of 4-(morpholin-4-yl) benzohydrazide derivatives. *World Jr. of pharm. and pharma. Sci.*, **2013**, 2(4): 2011-2020.
- [22] M Somashekhar, B Sonnad, B Tare, RV Heralagi, S Lokapure. Synthesis and Antimicrobial activity of 5-[4(morpholin-4-yl) phenyl] 1,3,4Oxadiazole 2-yl Sulphonylacetohydrazide Derivatives. *Int. Jr. Med. Pharm. Rech.*, **2014**, 2(2): 462-471.
- [23] P Venkatesh, SN Pandeya. Synthesis and Antioxidant activity of some n-(anilinothioyl) benzamide and Heterocyclic based Thiourea Derivatives. *Int. Jr. of Chem. Tech Rech.*, **2009**, 1(3):733-741.
- [24] GM Sreenivasa, E Jayachandran, B Shivakumar, K Jayaraj, V Kumar. Synthesis of Bioactive Molecule Fluoro Benzothiazole Comprising Potent Heterocyclic Moieties for Anthelmintic Activity. *Arch Pharm. Sci. & Rech.*, **2009**, 1(2): 150-157.
- [25] P. Panneerselvam, MG Priya, NR Kumar, G Saravanan. Synthesis and Pharmacological Evaluation of Schiff Bases of 4-(2-Aminophenyl)-Morpholines. *Ind. Jr. Pharm. Sci.*, **2009**, 71(4): 428–432.
- [26] AK Shaukath, BA Begum, V Girish, NF Khanum. Synthesis and Evaluation of Benzophenone-N-ethyl Morpholine Ethers as Anti-inflammatory Agents. *Int. Jr. of Biomed. Sci.*, **2010**, 6(1): 60-65.
- [27] HS Basavaraja, KV Jayadevaiah, MM Hussain, V Kumar, B Padmashali. Synthesis of novel piperazine and morpholine linked substituted pyrimidine derivatives as antimicrobial agents. *Jr. Pharm. Sci. & Rech.*, **2010**, 2(1): 5-12.
- [28] DP Kardile, NV Kalyane. Synthesis and antimicrobial activity of 4 thiomorpholine -4yl benzohydrazide derivatives. *IJABPT*, **2010**, 1(3): 1021-1031.
- [29] D Singh, G Bansal. Synthesis of Morpholine Containing Sulfonamides: Introduction of Morpholine Moiety on Amine Functional Group. *E-Jr. of Chem.*, **2004**, 1(2): 164-169.
- [30] MK Piestzeniewicz, DW skaa, J Szemrajb, K Studziana, M Gniazdowska. Interactions of Novel Morpholine and Hexamethylene Derivatives of Anthracycline Antibiotics with DNA. *Z. Naturforsch.*, 2004, 59(9-10): 739-748.
- [31] N Upmanyu, S Kumar, M Kharya, K Shah, P Mishra. Synthesis and anti-microbial evaluation of some novel 1, 2, 4 -triazole derivatives. *Acta Poloniae Pharma. Drug Rech.*, **2011**, 68(2): 213-221.