Asian Journal of Chemistry; Vol. 27, No. 4 (2015), 1326-1330

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2015.17807

Synthesis, Characterization and Biological Activities of 2-[(Methyl sulfonyl)]amino Benzoic Acid Derivatives and Their Metal Complexes

TANVEER HUSSAIN BOKHARI[1,*], NAVEEDA ASHRAF[1], MUHAMMAD SHAFIQ[1], MATLOOB AHMED[1], NASIR RASOOL[1], HAZOOR AHMAD SHAD[2], NABEELA ASHRAF[3], NADEEM ARSHAD[4] and MUHAMMAD NAWAZ TAHIR[5]

[1]Department of Chemistry, Government College University, Faisalabad-38000, Pakistan
[2]Department of Chemistry, University of Sargodha-60800, Pakistan
[3]Department of Applied Chemistry, UET, Lahore-54890, Pakistan
[4]Center of Excellence for Advanced Materials Research (CEAMR), Faculty of Science, King Abdulaziz University, Kingdom of Saudi Arabia
[5]Department of Physics, University of Sargodha-60800, Pakistan

*Corresponding author: E-mail: tanveer.bokhari@yahoo.com

Received: 12 April 2014; *Accepted*: 2 June 2014; *Published online*: 4 February 2015; AJC-16784

Sulfonamide derivatives and their metal complexes are acknowledged pharmaceutical moieties because this group has been played the key role as a functional part of the most of the drug structures due to constancy and for bearance in human beings. Sulfonamides have endowed great biological potential such as antibacterial, insulin releasing, carbonic anhydrase inhibitory, anti-inflammatory, antifungal and antitumor activities. In the present work, 2-[(methyl sulfonyl)] amino benzoic acid was N-alkylated using alkylating agent such as methyl. Due to the presence of electron donating groups like, -COOH, -SO_2, N-, the above mentioned molecules act as an excellent chelating agent. These substituted N-alkylated sulfonamide ligands were treated with a number of outer and inner transition metals such as Co(II), Cu(II), Ce(II), Pr(II), Dy(II) and Nd(II) to form coordinate complexes. These newly synthesized sulfonamides and their metal complexes were characterized by melting points, solubility, colour, FTIR analysis and XRD. These products were subjected for antimicrobial activities as well as other accessible applications.

Keywords: Sulfonamide derivatives, Pharmaceutical agent, Antibacterial, Antifungal.

INTRODUCTION

The transition metal complexes have gained attention of inorganic, metallo-organic as well as bio-organic chemists because of their extensive applications in wide ranging areas from material science to biological sciences[1]. Sulfonamide molecules have gained attention in pharmaceutical and agricultural areas[2] because of their extensive biological activities[3]. Metal complexes of sulfonamides are extensively studied due to synthetic flexibility, selectivity and sensitivity towards a variety of metal atoms[4]. Some of them are also used as organic compounds. These are used in the treatment of toxoplasmosis, nocardiasis, urinary tract infections, trachoma, chancroid, malaria, meningitis, streptococcal pharyngitis, bacillary dysentery and conjunctivitis[5-7]. A number of biological activities have been played by sulfonamide drugs such as antibacterial[8] antiinflammatory[9] carbonic anhydrase inhibitory[10-12] insulin releasing[13,14] and antitumor[15] activities[16]. Other available commercial drugs, having sulfonamide structure, are the antihypertensive agents like antiviral HIV protease inhibitor[17] and bosentan[18]. The various organic therapeutic agents'worth can often be boosted[19] up by coordination with suitable metal ions. In pharmacology, the activity has been found to be highly dependent on the identity of the donor sequence of the ligands, because different ligands show broadly different biological activities although they may differ only slightly in their molecular structure[20]. There is a real perceived need for the discovery of new compounds having strong antimicrobial activities. Sulfonamides and their metal complexes are known to be biologically significant and attractive because of their properties such as antidiabetic, antiinflammatory, antibacterial and antifungal[21,22].

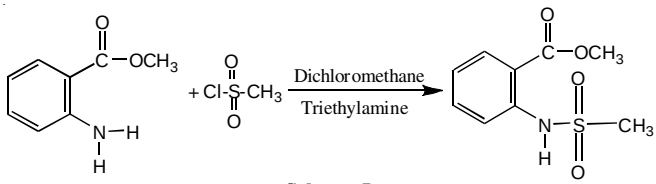
Compounds of benzoic acid derivative play an important role in many bio-chemical reactions[23,24]. The copper(II), cobalt(II), cerium(II), praseodymium(II), dysprosium(II) and neodymium(II) complexes of sulfonamide ligands have played a vital role in the development of coordination chemistry[25]. In view of the above considerations, we have synthesized and characterized Co(II), Cu(II), Ce(II), Pr(II), Dy(II) and Nd(II) complexes of sulfonamide derivatives and studied the biological activity of these complexes.

Main objectives of the present research work were, to develop reaction conditions for the successful synthesis of different kinds of derivatives of 2-[(methyl sulfonyl)amino]-benzoic acid and to check whether the new lead compounds were biologically active or not.

EXPERIMENTAL

All the commercially available reagents and chemicals were used as such without further purification for the preparation of ligands and metal complexes. All organic solvents were purchased from Merck. The IR spectra were recorded of (Thermo Nicolet FT-IR, Nicolet-200, USA) spectrometer in the 4000-400 cm^{-1} region using KBr pellets. A verity of glass-ware's were used which were oven and flame dried. The progress and completion of reactions was monitored by thin-layer chromatography. UV light at 254 nm was used to visualize the chromatograms. Melting points were determined in open capillary tubes on an electrothermal (Griffin 1090) melting point.

Synthesis of 2-[(methyl sulfonyl)]amino benzoic acid (L_1): It followed two step preparations. First step involved the conversion of methyl anthranilate to 2-[(methyl sulfonyl)]-amino benzoate. For this purpose, solution of methanesulfonyl chloride (0.8 mL) in dichloromethane (10 mL) was added to methyl anthranilate (0.9 mL) over 15-20 min at room temperature. The reaction mixture was stirred for 3.5 h (at room temperature) and maintained the pH of the mixture alkaline (8-12) by adding triethylamine. After complete conversion of reactant, the reaction mixture was neutralized with dilute hydrochloric acid. The separated organic layer was dried Na_2SO_4 and removed under vacuum (11 torr) to get yellow crude solid which gave white crystalline product after recrystallization from ethanol[26] (**Scheme-I**).

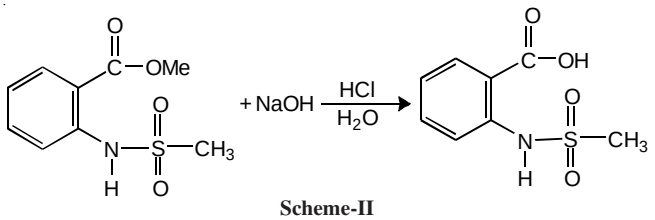


Scheme-I

This involved the preparation of 2-[(methyl sulfonyl)] amino benzoic acid by the addition of the mixture of 2-[(methyl sulfonyl)amino]benzoate (0.446 g, 1.930 mmol) and sodium hydroxide (0.083 g, 2.075 mmol) in aqueous media (10 mL distilled water) in a round bottom flask and stirred at room temperature for 7 h with the appearance of light yellow colour precipitates then stirred at 50 to 60 °C temperature for 2 h followed by addition of dilute hydrochloric acid until the appearance of off white precipitates. Then precipitates were filtered, washed with cold water and dried under vacuum followed by recrystallization in ethanol[27] (**Scheme-II**).

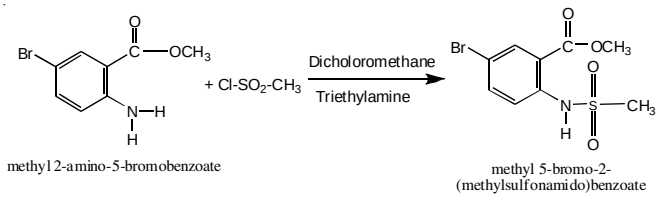
Synthesis of 5-bromo-2-(N-methyl sulfonamido)-benzoic acid (L_2): It was synthesized in three steps *i.e.*, the N-sulfonation, N-alkylation and simple hydrolysis.

In 1st step, solution of methanesulfonyl chloride (8 mL) in dichloromethane (10 mL) was taken in round bottom flask and stirred it for 15-20 min at room temperature with the drop



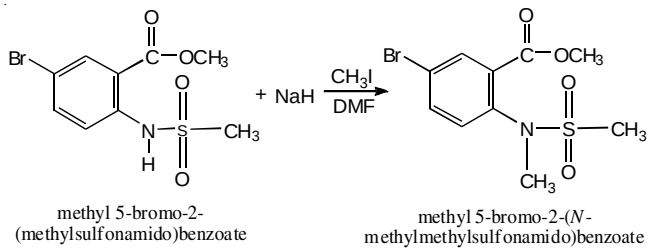
Scheme-II

wise addition of the mixture of methyl-2-amino-5-bromobenzoate (0.9 mL) and dichloromethane (10 mL) in it. The reaction mixture was stirred for 3.5 h (at room temperature) keeping the pH of the mixture alkaline (8-12) by adding triethylamine. After completion of reaction, the mixture was neutralised with the help of dilute hydrochloric acid. The separated organic layer was dried by using sodium sulphate and removed under vacuum (11 torr) to get yellow crude solid which gave white crystalline product after recrystallization from ethanol[26] (**Scheme-III**).



Scheme-III

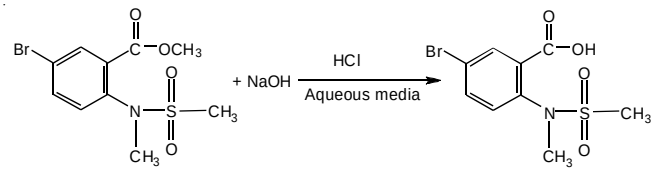
This step involved the N-alkylation. Methyl 5-bromo-2-(methyl sulfonamido)benzoate (33 mmol) was dissolved in DMF (10 mL) and added to *n*-hexane washed suspension of NaH (66 mmol) in DMF (10 mL). After stirring the suspension for 45 min, alkyl iodide was added (66 mmol) and the resulting mixture was stirred at room temperature for 12-16 h. TLC (*n*-hexane:ethyl acetate in 4:1 ratio) was used to monitor the progress of reaction. The mixture was poured into cold 3 N hydrochloric acid and potassium carbonate was used to neutralize the pH. The resultant mixture was extracted with ethyl acetate and the combined organic layers were dried over K_2SO_4 and evaporated under reduced pressure to get methyl 5-bromo-2-(N-methyl methylsulfonamido)benzoate[27] (**Scheme-IV**).



Scheme-IV

In third step involved the hydrolysis of methyl 5-bromo-2-(N-methyl methyl sulfonamido)benzoate. For this, the mixture of methyl 5-bromo-2-(N-methyl methyl sulfonamido)benzoate (0.446 g, 1.38 mmol) and sodium hydroxide (0.083 g, 2.075 mmoles) was added in aqueous media (10 mL distilled water) in a round bottom flask and stirred at room temperature for 7 h until the appearance of light yellow precipitates then refluxed it for 2 h followed by addition of dilute

hydrochloric acid until the appearance of brownish yellow precipitates. The progress of reaction was monitored by TLC (*n*-hexane:ethyl acetate in 4:0.75 ratios). After completion of reaction; precipitates were filtered, washed with cold water and dried under vacuum followed by recrystallization in ethanol (**Scheme-V**).



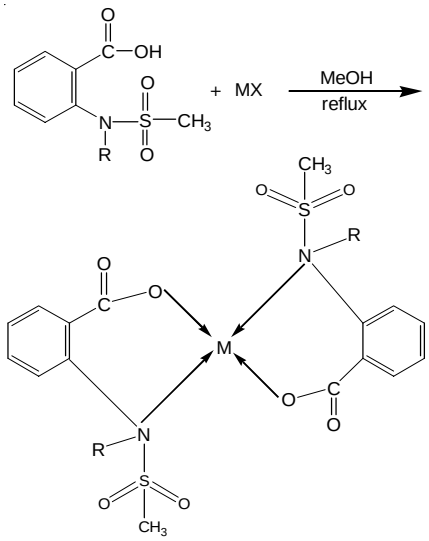
Methyl 5-bromo-2-(*N*-methylmethylsulfonamido)benzoate — 5-Bromo-2-(*N*-methylmethylsulfonamido)benzoate

Scheme-V

Synthesis of metal complexes by sulfonamide ligands: The metal complexes were synthesized by the following general procdure, appropriate metal salt wasdissolved in methanol (7 mL) in 100 mL round bottom flask and stirred until the clarity of the solution. Then to this solution, corresponding ligand (L_1, L_2) (0.05 g) was added and refluxed it for 6 to 7 h for the synthesis of L_1M_1, L_1M_2, L_1M_3 and L_1M_4 complexes while 5 to 46 h for L_2M_5 and L_2M_6 at a temperature of 50-60 °C. Metal to ligand ratio was 0.5:1. Mixture appeared coloured. TLC was performed to monitor the progress of reaction. Then mixture was filtered and product was appeared in the filtrate on slow evaporation by washing with ethanol (**Scheme-VI**).

RESULTS AND DISCUSSION

Two new bidentate sulfonamides, 2-[(methyl sulfonyl)] amino benzoic acid and 5-bromo-2-[(N-methyl sulfonamido)]-benzoic acid have been synthesized by N-sulfonation, N-alkylation and simple hydrolysis of anthranilate and methyl-2-amino-5-bromobenzoate, respectively. The metal complexes of Cu(II), Co(II), Ce(II), Pr(II), Dy(II) and Nd(II) were obtained by the reaction of metal chloride/acetate/nitrate with bidentate ligand in 0.5:1 molar ratios. The physical data, shown in Tables 1 and 2, of ligands and complexes, are consistent with the proposed molecular formulae. Thecomplexesare of bright colour and soluble in DMF, DMSO and other common organic solvents like methanol, ethanol and ethyl acetate.



Where M = Ce, Pr, Nd, Dy, Cu or Co and X = acetate, chloride or nitrates

Scheme-VI

Single crystal X-rays studies for 5-bromo-2-(N-methyl-sulfonamido)benzoic acid: This compound consists of two molecules in the crystallographic asymmetric unit which differs from each other geometrically. The molecular structure of the compound, 5-bromo-2-(N-methylsulfonamido)benzoic acid with atom number arrangement is given in Fig. 1. The crystallographic data is shown in Table-3. In one molecule, the 4-bromobenzoic acid moiety, group A (C1-C7/O1/O2/Br1) and N-methylmethanesulfonamide, groups B (C8/C9/N1/S1/O3/O4) are non-linear to each other and showed bond angle deviation of 117.5(7)°. The dihedral angle between A/B groups is 87(1)°. The bond length (C4-Br1) in title molecule is 1.88(1), which is little bit smaller than the bond length, 1.894(2) as reported by Shafiq *et al.*[27]. All other bond lengths and angles are approximately same as reported by Shafiq *et al.*[27], with small variation. In second molecule, both of the groups, C (C10-C16/O5/O6/Br2) and N-methylmethanesulfonamide, D (C17/C18/N2/S2/O7/O8) are shown approximately same deviation from their planar behavior as exhibited by the first molecule, with opposite direction. The dihedral angle between C and D is -85(1)°. The bond length (C13-Br2) of second molecule is slightly larger, 1.89(1) than the bond length 1.88(1) of first

TABLE-1
PHYSICAL CHARACTERISTIC DATA OF SULFONAMIDE LIGANDS

Sulfonamide ligands	Sulfonating agent	Amino benzoate	Physical state	m.f.	m.w. (g/mol)	m.p. (°C)
L_1	Methyl sulfonylchloride	Methyl anthranilate	Off white solid	$C_8H_9O_3NS$	215	186-189
L_2	Methyl sulfonylchloride	Methy 2-amino-5-bromo benzoate	Light yellowish brown solid	$C_9H_{10}O_4BrSN$	308	143-147

TABLE-2
PHYSICAL CHARACTERISTICS DATA OF METAL COMPLEXES

Complex	Sulfonamide ligands	Metal salt	Physical state	m.f.	m.w. (g/mol)	m.p. (°C)
L_1M_1	L_1	Cerium nitrate	Dark purple solid	$C_{16}H_{18}O_8N_2S_2Ce$	566.0	184-188
L_1M_2	L_1	Praseodymium chloride	Dark purple solid	$C_{16}H_{18}O_8N_2S_2Pr$	567.0	143-147
L_1M_3	L_1	Dysprosium nitrate	Dark purple solid	$C_{16}H_{18}O_8N_2S_2Dy$	588.5	168-172
L_1M_4	L_1	Neodymium chloride	Pinkish purple solid	$C_{16}H_{18}O_8N_2S_2Nd$	570.0	89-94
L_2M_5	L_2	Copper acetate	Blackish green solid	$C_{18}H_{18}O_8N_2S_2Br_2Cu$	677.5	> 300
L_2M_6	L_2	Cobalt acetate	Brownish black solid	$C_{18}H_{18}O_8N_2S_2Br_2Co$	673.0	> 300

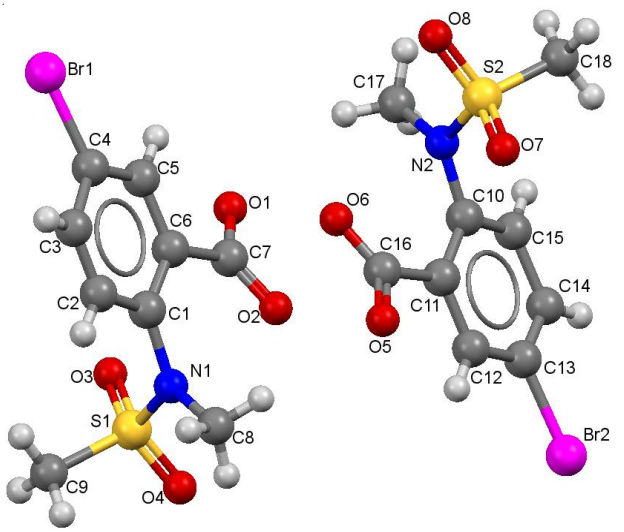


Fig. 1. Single crystal X-ray structure of compound 5-bromo-2-(N-methyl-sulfonamido)benzoic acid

TABLE-3
CRYSTAL STRUCTURE PARAMETERS FOR COMPOUND 5-BROMO-2-(N-METHYLSULFONAMIDO)BENZOIC ACID

Chemical formula	$C_9H_{10}BrNO_4S$	c(Å)	19.3428 (9)
Formula weight	308.15	α(°)	90
Crystal system	Orthorhombic	β(°)	90
Space group	$Pna2_1$	γ(°)	90
a (Å)	16.5633 (9)	Cell volume	2375.7 (2) Å^3

molecule. Similarly, other bond lengths and angles are also shown a small variation with respect to the first molecule.

Infrared spectroscopy: The infrared spectra of newly formed ligands and their metal complexes were charactrized as KBr pellets in the broad range of 4000-400 cm^{-1}. These spectra of sulfonamides and their metal complexes showed remarkable broad bands as shown in Table-4. The values of different vibrational frequencies were assigned to different bonds by comparing spectra of ligands with the literature values. The calculated IR bands of the Ce(II), Pr(II), Dy(II), Nd(II), Cu(II), and Co(II), metal complexes are different from their free ligand and provide significant indications regarding the coordination and binding sites of the ligand to the metal ion. The ν(C-O) vibrational mode for free ligand (L_1, L_2) was observed at 1253.73, 1296.16 cm^{-1}, shifted to 1166.93, 1172.72, 1166.93, 1166.08, 1068.56 and 1070.49 cm^{-1} in the spectra of Ce(II), Pr(II), Dy(II), Nd(II), Cu(II) and Co(II) complexes of metals respectively, indicating the coordination of carboxyl oxygen to the metal. While the IR bands of ligands (L_1, L_2) showed spectral peaks at 1338.10 and 1325.10 cm^{-1} which was contributed to ν(C-N) vibration. In case of Ce(II), Pr(II), Dy(II), Nd(II), Cu(II) and Co(II) complexes, this peak was shifted slightly downwards to 1257.59, 1247.94, 1253.73, 1259.52, 1151.50 and 1151.50 cm^{-1}, respectively, which indicate the presence of ν(C-N) vibration and suggesting the participation of amino nitrogen in complexation. Sulfonyl functional group shows absorption bands at 1168.86 and 1157.29 cm^{-1} in the spectra of free ligands (L_1, L_2) but showed slight shifts of 1028.06, 1031.92, 1022.27, 1037.70, 1336.67 and 1332.81 cm^{-1} in the complexes of Ce(II), Pr(II), Dy(II), Nd(II), Cu(II) and Co(II), respectively, which indicate that this group does not participate in bonding. The spectral bands, which are not appeared in the ligand spectrum but appeared in the metal complexes spectra within the range of 557.43, 522.71, 518.85, 522.71, 540.07 and 538.14 cm^{-1}, corresponding to ν(M-N) and 435.43, 414.70, 422.41, 415.71, 424.34 and 451.34 cm^{-1} to ν(M-O)[28-30] vibrations, respectively. Appearance of ν(M-N) and ν(M-O) vibrations indicates the involvement of N and O atoms in complexation with metal ions under investigation.

Antibacterial activity: The antibacterial activity of the synthesized ligand (L_1, L_2) and its complexes[31] (L_1M_1), (L_1M_2), (L_1M_3), (L_1M_4), (L_2M_5) and (L_2M_6) tested using agar diffusion technique against *Staphylococcus aureus*, *Bacillus subtilis*, *Pasteurella multocida*, *Escherichia coli* using streptomycin as positive control[32]. Both ligands (L_1, L_2) showed the moderate activity against the *P. multocida* and *E. coli* while the least activity against the *B. subtilis*. In case of complexes, L_2M_5 complex was found to be highly active against all the bacterial strains. L_1M_1, L_1M_2, L_1M_3 and L_2M_6 complexes exhibited moderate activity against all the bacteria. While L_1M_4 showed the least activity against *Staphylococcus aureus* and *Bacillus subtilis*.

Antifungal activity: The antifungal activity was performed using fluconazole as positive control, against *Aspergillus niger*, *Aspergillus flavus*, *Helmenthosporium medis*, *Alternaria alternate*. Results are given in Table-4. Both ligands (L_1, L_2) showed the moderate activity against the *Helmenthosporium medis* and *Alternaria alternate* while the least activity against the *Aspergillus flavus*. In case of complexes, L_2M_5 complex was found to be highly active against all the fungal strains especially against *Aspergillus flavus*. All the other complexes exhibited moderate activity against all the bacteria, except L_1M_4 which showed the least activity against *Aspergillus niger* and *Aspergillus flavus*.

TABLE-4
ANTIFUNGAL ACTIVITY OF SULFONAMIDE LIGANDSAND THEIR METALCOMPLEXES

Sample No.	Fungal inhibition zone (mm)			
	Aspergillus niger	*Aspergillus flavus*	*Helmenthosporium medis*	*Alternaria alternate*
L_1	13	12	14	13
L_2	13	12	16	14
L_1M_1	15	13	11	13
L_1M_2	14	14	12	13
L_1M_3	12	13	13	12
L_1M_4	11	10	15	13
L_2M_5	22	25	23	24
L_2M_6	11	12	12	13
Fluconazole	23	24	27	28

Minimum inhibitory concentration for antibacterial activity: The minimum inhibitory concentration method was used to investigate the efficacy of listed sulfonamides and metal complexes against four bacteria *S. aureus*, *B. subtilis*, *P. multocida*, *E. coli* by using streptomycin as positive control. These results showed that the values of ligands and complexes were satisfying. Results are summarized in Table-5.

Minimum inhibitory concentration for antifungal activity: Ligands and their metal complexes efficacy was investigated by using minimum inhibitory concentration method against four fungal strains *A. niger*, *A. flavus*, *G. lucidum*, *A. alternata*

TABLE-5
MINIMUM INHIBITORY CONCENTRATION FOR ANTIBACTERIAL ACTIVITY OF SULFONAMIDE LIGANDS AND THEIR COMPLEXES

Sample No.	Minimum inhibitory concentration (µg/mL)			
	S. aureus	*B. subtilis*	*P. multocida*	*E. coli*
$3L_1$	265	262	285	250
$3L_2$	251	262	255	225
$3L_1M_1$	224	249	278	250
$3L_1M_2$	225	234	265	248
$3L_1M_3$	250	251	251	262
$3L_1M_4$	285	276	224	285
$3L_2M_5$	124	28	125	115
$3L_2M_6$	262	274	250	251
Streptomycin	74	98	30	57

using fluconazole as positive control. These results were helpful to conclude that the values of sulfonamides and their complexes were satisfactory. Results are summarized in Table-6.

TABLE-6
MINIMUM INHIBITORY CONCENTRATION FOR ANTIFUNGAL ACTIVITY OF SULFONAMIDE LIGANDS AND THEIR COMPLEXES

Sample No.	Minimum inhibitory concentration (µg/mL)			
	Aspergillus niger	*Aspergillus flavus*	*Helmenthosporium medis*	*Alternaria alternate*
$3L_1$	261	275	251	261
$3L_2$	260	275	225	250
$3L_1M_1$	215	261	284	261
$3L_1M_2$	250	251	274	258
$3L_1M_3$	275	260	261	275
$3L_1M_4$	285	301	185	259
$3L_2M_5$	151	115	135	125
$3L_2M_6$	284	275	275	260
Fluconazole	130	125	85	75

Cytotoxicity: Sample's toxicity analysis was performed and Statistix MINITAB 13 was used to obtain the results. The significance of samples was compare with the help of two standers. The erthrocytic membrane mechanical stability is a good indicator for the screening of cytotoxicity. It is also dependent upon their physical and structural properties. Haemolysis is a infectious disease which occurs due to presence of parasites (*Plasmodium falciparum*) and other microbes[33]. The given figure showed the observed values of % haemolysis with selected values of ligands and complexes. On y-axis lysis of human blood is compared. With the selected sample compounds on x-axis comparing with positive control having (100 %) lysis. While PBS used as a negative control have (0.0 %) lysis. Samples showed good haemolytic activity by comparing them with positive control. Results are summerized in Table-7.

TABLE-7
HAEMOLYTIC VALUES FOR SULFONAMIDE LIGANDS AND THEIR COMPLEXES

Sample No.	Hemolytic activity (mean % ± S.D.)	Sample No.	Hemolytic activity (mean % ± S.D.)
$3L_1$	3.52 ± 0.72	$3L_1M_4$	5.09 ± 1.06
$3L_2$	4.34 ± 1.18	$3L_2M_5$	4.03 ± 1.04
$3L_1M_1$	4.21 ± 0.69	$3L_2M_6$	3.35 ± 1.18
$3L_1M_2$	1.15 ± 0.34	PBS	0.00 ± 0.0
$3L_1M_3$	1.46 ± 0.49	Triton (toxicity)	100 ± 0.0

REFERENCES

1. Z.A. Siddiqi, M. Khalid, S. Kumar, M. Shahid and S. Noor, *Eur. J. Med. Chem*., **45**, 264 (2010).
2. G.F. Yang and H. Z. Yang, *Chin. J. Chem*., **17**, 650 (1999).
3. B.R. Stranix, J.-F. Lavallée, G. Sévigny, J. Yelle, V. Perron, N. LeBerre, D. Herbart and J.J. Wu, *Bioorg. Med. Chem. Lett*, **16**, 3459 (2004).
4. S. Cezar and K. Angela, *Acta Chim. Slov*., **47**, 179 (2000).
5. P. Selvam, D.F. Smee, B.B. Gowen, C.W. Day, D. Barnard and J. Morrey, *Antiviral Res*., **74**, 81 (2007).
6. H.S. Patel and H.J. Mistry, *Phosphorous, Sulfur, Silicon Rel. Elem*., **179**, 1085 (2004).
7. C.T. Supuran, A. Casini, A. Mastrolorenzo and A. Scozzafava, *Mini Rev. Med. Chem*., **4**, 625 (2004).
8. T.H. Maren, *Annu. Rev. Pharmacol. Toxicol*., **16**, 309 (1976).
9. J.J. Li, D. Anderson, E.G. Burton, J.N. Cogburn, J.T. Collins, D.J. Garland, S.A. Gregory, H.C. Huang, P.C. Isakson, C.M. Koboldt, E.W. Logusch, M.B. Norton, W.E. Perkins, E.J. Reinhard, K. Seibert, A.W. Veenhuizem, Y. Zang and D.B. Reitz, *J. Med. Chem*., **38**, 4570 (1995).
10. A.K. Gadad, C.S. Mahajanshetti, S. Nimbalkar and A. Raichurkar, *Eur. J. Med. Chem*., **35**, 853 (2000).
11. V.S. Misra, V.K. Saxena and R. Srivastava, *J. Indian Chem. Soc*., **59**, 781 (1982).
12. F. Zani and P. Vicini, *Arch. Pharm*., **331**, 219 (1998).
13. C.T. Supuran, A. Scozzafava, B.C. Jurca and M.A. Ilies, *Eur. J. Med. Chem*., **33**, 83 (1998).
14. G. Renzi, A. Scozzafava and C.T. Supuran, *Bioorg. Med. Chem. Lett*., **10**, 673 (2000).
15. H. Yoshino, N. Ueda, J. Niijima, H. Sugumi, Y. Kotake, N. Koyanagi, K. Yoshimatsu, M. Asada and T. Watanabe, *J. Med. Chem*., **35**, 2496 (1992).
16. D.J. Abraham, W.S. John and N.J. Hoboken, Burger's Medicinal Chemistry and Drug Discovery, John Wiley & Sons, New Jersey (2003).
17. E.D. Clercq, *Curr. Med. Chem*., **8**, 1543 (2001).
18. C. Wu, E.R. Decker, G.W. Holland, F.D. Brown, F.D. Stavros, T.A. Brock and R.A.C. Dixon, *Drugs Today*, **37**, 441 (2001).
19. J.K. Barton, J.M. Goldberg, C.V. Kumar and N.J. Turro, *J. Am. Chem. Soc*., **108**, 2081 (1986).
20. S. Delaney, M. Pascaly, P.K. Bhattacharya, K. Han and J.K. Barton, *Inorg. Chem*., **41**, 1966 (2002).
21. A.P. Mishra and S.K. Gavtarm, *J. Indian Chem. Soc*., **81**, 324 (2004).
22. N.A.Venkariya, M.D. Khunt and A.P. Parikh, *Indian J. Chem*., **42B**, 421 (2003).
23. N.M. Sivasankaran and S.T. David, *J. Indian Chem. Soc*., **77**, 220 (2000).
24. R.K. Murray and D.K. Granner, Haper Biochemistry, Appleton and Lange, Stamford (1996).
25. N. Raman, S. Ravichandran and C. Thangaraja, *J. Chem. Sci*., **116**, 215 (2004).
26. J.G. Lombardino, *J. Chem*., **9**, 315 (1971).
27. M. Shafiq, M. Zia-ur-rehman, I.U. Khan, M.N. Arshad and I. Ahmad, *Acta Crystal*., **E65**, o2453 (2009).
28. C. Tang, R. Tang, C. Tang and Z. Zeng, *Bull. Korean Chem. Soc*., **31**, 1283 (2010).
29. K. Nakamoto, IR and Raman Spectra of Inorganic and Coordination Complexes, Part A: Theory and Applications in Inorganic Chemistry, edn 5, Wiley, New York (1997).
30. M. Thomas, M.K.M. Nair and P.K. Radhakrishnan, S*ynth. React. Inorg. Met-Org. Chem*., **25**, 471 (1995).
31. M.M. Ali, M.M.F. Ismail, M.S.A. El-Gaby, M.A. Zahran and Y.A. Ammar, *Molecules*, **5**, 864 (2000).
32. K. Jamil, M. Bakhtiar, A. Khan, F. Rubina, R. Rehana, R. Wajid and M. Qaisar, *Afr. J. Pure Appl. Chem*., **3**, 71 (2009).
33. M.A. Neelakantan, M. Esakkiammal, S.S. Mariappan, J. Dharmaraja and T. Jeyakumar, *Indian J. Pharm. Sci*., **72**, 216 (2010).