Innovare Academic Sciences

International Journal of Current Pharmaceutical Research

ISSN- 0975-7066 Vol 7, Issue 1, 2015

Original Article

SYNTHESIS AND INVITRO ANTIBACTERIAL SCREENING OF SOME NEW AZOMETHINES DERIVED FROM SULPHONAMIDES

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Received: 08 Oct 2014, Revised and Accepted: 12 Nov 2014

ABSTRACT

Objective: The purpose of research was to synthesize the better antimicrobial compounds using different substituted aromatic aldehydes containing allyl and allyl oxy group are chosen as the starting material for synthesis of imines with sulphonamides helps to formation in presence of alcohol and acidic reagent.

Methods: Reagents used in the present study were of analytical grade and solvents were used after distillation. All the melting points of the synthesized compounds were determined by open capillary and are uncorrected. The purity of the compounds was checked using pre coated TLC plates (MERCK) using n-hexane: ethyl acetate (8:2) solvent system. The developed chromatographic plates were visualized under UV at 254 nm. IR spectra were recorded using KBr on Perkin Elmer spectrophotometer. ^{1}HNMR spectra in DMSO on a BRUKER FT-NMR instrument using TMS as internal standard and chemical shift values were expressed in ppm. Elemental analysis (CHN) was performed on Carlo Erba 1108.

Results: A new series of azomethines was synthesized by condensation of different sulphonamide derivatives with substituted aromatic aldehydes containing allyl and allyloxy group. The structures of these products were confirmed by physical and spectral analysis. The compounds were assayed for antibacterial activity against different human pathogens such as *E. coli, P. aeruginosa, S. aureus, B. subtilis.* All the compounds exhibited considerable inhibition against the bacteria tested.

Conclusion: Antibacterial activity observed for the synthesized azomethine compounds through the disc diffusion assay. The reference antibacterial drug was Streptomycin and Penicillin-G for *E. coli*, *P. aeruginosa*, *S. aureus* and *B. subtilis.* Synthesized imines show good biological activity and have the good yield.

Keywords: Antibacterial screening, Azomethines, Disc diffusion, *P. aeruginosa, S. aureus, B. subtilis.*

INTRODUCTION

The increase in the mortality rate associated with infectious diseases is directly related to bacteria that exhibit multiple resistance to antibiotics. The lack of effective treatments is the main cause of this problem [1-2]. The development of new antibacterial agents with novel and more efficient mechanisms of action is definitely an urgent medical need [3]. Azomethine are some of the most widely used organic compounds. Sulfonamide derivatives have been subject to intensive studies, where a wide variety of those derivatives have been prepared and used in various biological and pharmacological fields. Azomethines are among the most studies sulfonamide derivatives which have been used for numerous biological application [4-5]. These types of derivatives are very important because of their varied structures and biological activities [6-7]. They are the important compound owing to their wide range of biological activities and industrial application. they have been found to posses the pharmacological activities such as antimicrobial [8-13], antipathogenic [14-15], antidepressant [16], antiviral [17-18], antitcancer [19-20], Fungicide [21-22], bactericide [23-24], Cytotoxicity [25], herbicide [26], insecticide [27-28], antioxidant agent [29-30], antiproliferative [31-32].

The development of bacterial resistance to existing drugs is a major problem in antibacterial therapy and necessitates continuing research into new classes of antibacterials. It is evident that in azomethine derivatives the C=N linkage is an essential structural requirement for biological activity. These compounds are readily hydrolyzed under acidic conditions leading to active aldehydes which can act as alkylating agents. Many attempts have been made to synthesize characterize and to study biological activity of azomethine. In view of the conclusions drawn from the previous work and looking to the antimicrobial efficacy of sulphonamides like sulphanilimide, sulphamethoxazole, sulphathiazole & sulphadimidine moieties attached to aryl ring it seems logical to combine all these moieties together in a parent molecule. This study was aimed at exploring the potential antimicrobial compounds containing an azomethine group (-CH=N).

MATERIALS AND METHODS

Chemistry

All chemicals and solvents, reagents used in the present study were of analytical grade and solvents were used after distillation. All the melting points of the synthesized compounds were determined by open capillary and are uncorrected. The purity of the compounds was checked using precoated TLC plates (MERCK) using n-hexane: ethyl acetate (8:2) solvent system. The developed chromatographic plates were visualized under UV at 254 nm. IR spectra were recorded using KBr on Perkin Elmer spectrophotometer. ^{1}HNMR spectra in DMSO on a BRUKER FT-NMR instrument using TMS as internal standard and chemical shift values were expressed in ppm. Elemental analysis (CHN) was performed on Carlo Erba 1108. Our general synthetic route leading to new azomethines involved the reaction between aromatic aldehydes containing allyl and allyloxy group with different sulphonamide derivatives is shown in scheme 1.

General procedure for the synthesis of azomethines

A solution of substituted aromatic aldehydes(0.01M: in 5 mL ethanol) was taken in a flask and sulphonamide derivatives (0.01M: : 5 mL ethanol) was slowly added with continuous stirring. The contents of the flask were refluxed for three hours and left over night. The reaction mixture was cooled in an ice bath and a drop of sulfuric acid was added to it The azomethines base separated out, collected and further purified by recrystallization from ethanol.

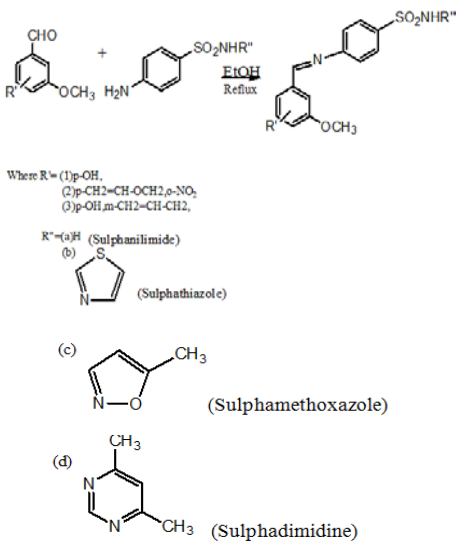
RESULTS

1(a) 4-{[(E)-(4-hydroxy-3-methoxyphenyl) methylidene] amino} benzenesulfonamide

Recrystallization from ethanol: $C_{14}H_{14}N_2O_4S$; M. wt 306; Yield 58%; m. p.200^{0}C; colour-whitsh yellow; IR (KBr) cm^{1}3400 cm^{-1}(O-H),

1670 cm^{-1} (CH=N), 1139 cm^{-1} (S=O); ^{1}HNMR(DMSO d_6) δ,ppm: 3.75 (s,3H,CH), 3.0 (s,1H,OH), 5.2-7.2 (m,3H,Ar-H), 8.4 (s,1H,CH=N), 7.6 (t,2H,CH), 7.9(t,2H,CH), 2.2(s,2H,SO_2NH_2). Anal. Calcd.(%):C=54.90, H=4.60, N=9.12, O=20.91, S=10.47.

1. General Scheme of the reaction



Scheme

1(b) 4-[(4-hydroxy-3-methoxybenzylidene)amino]-N-(1,3 thiazol-2-yl) benzenesulfonamide

Recrystallization from ethanol: $C_{17}H_{15}N_3O_4S_2$; M. wt 389; Yield 72%; m. p.150^{0}C; colour-yellow; IR (KBr) cm^{1}3420 cm^{-1}(O-H), 1650 cm^{-1} (CH=N), 1115 cm^{-1} (S=O); ^{1}HNMR(DMSO d_6) δ,ppm: 3.75 (s,3H,CH), 3.0 (s,1H,OH), 5.2-7.2 (m,3H,Ar-H), 8.4 (s,1H,CH=N),7.6 (t,2H,CH), 7.9 (t,2H,CH), 4.2(s,1H,SO_2NH), 6.5-7.5 (m,2H,CH). Anal. Calcd.(%):C=52.40, H=3.91, N=10.70, O=16.52, S=16.47.

1(c)4-[(4-hydroxy-3-methoxybenzylidene)amino]-N-(5-methylisoxazol-2-yl)benzenesulfonami de

Recrystallization from ethanol: $C_{18}H_{17}N_3O_5S$; M. wt 387; yield 98%; m. p.190^{0}C; colour-pale yellow; IR (KBr) cm^{1}3440 cm^{-1}(O-H), 1670 cm^{-1} (CH=N), 1149 cm^{-1} (S=O); ^{1}HNMR(DMSO d_6)δ,ppm: 3.75(s,3H,CH), 3.0(s,1H,OH), 5.2-7.2(m,3H,Ar-H), 8.4(s,1H,CH=N), 7.6(t,2H,CH), 7.9(t,2H,CH), 4.2(s,1H,SO_2NH), 5.2(s,1H,CH), 2.5(s,3H,CH_3). Anal. Calcd.(%):C=52.30, H=4.01, N=10.70,O=16.52, S=16.47.

1(d)N-(4,6-dimethylpyrimidin-2-yl)-4-{[(E)-(4-hydroxy-3-methoxyphenyl)methylidene] amino }benzene sulfonamide

Recrystallization from ethanol: $C_{20}H_{20}N_4O_4S$; M. wt 412; Yield 50%; m. p.110^{0}C; colour-yellow; IR (KBr) cm^{1}3450 cm^{-1}(O-H), 1660 cm^{-1} (CH=N), 1153 cm^{-1} (S=O); ^{1}HNMR(DMSO d_6) δ,ppm: 3.75(s,3H,CH), 3.0(s,1H,OH), 5.2-7.2(m,3H,Ar-H), 8.4(s,1H,CH=N), 7.6(t,2H,CH), 7.9(t,2H,CH), 4.2(s,1H,SO_2NH), 3.8(s,1H,CH), 2.8-3(s,6H,CH_3). Anal. Calcd.(%):C=58.20, H=4.93, N=13.50,O=15.60, S=7.77.

2(a) 4-[(5-Methoxy-2-nitro-4-vinyloxymethyl-benzylidene)-amino] -benzenesulfonamide:

Recrystallization from ethanol: $C_{17}H_{17}N_3O_6S$; M. wt 391; Yield 66%; m. p.120^{0}C; colour-yellow; IR (KBr) cm^{1}1617 cm^{-1} (CH=N), 1598 cm^{-1} (NO_2),1139 cm^{-1} (S=O); ^{1}HNMR(DMSO d_6) δ,ppm: 3.75(s,3H,CH), 5.2-7.2(m,2H,Ar-H), 5.4(s,2H,CH), 6.5(t,1H,CH), 4.2(d,2H,CH), 8.4(s,1H,CH=N), 7.6(t,2H,CH), 7.9(t,2H,CH), 4.2(s,2H,SO_2NH_2). Anal. Calcd.(%): C=52, H=4.55, N=10.70, O=24.57,S=8.19.

2(b)4-[(5-Methoxy-2-nitro-4-vinyloxymethyl-benzylidene)-amino]-N-thiazol-2-yl-benzene sulfonamide

Recrystallization from ethanol: $C_{20}H_{18}N_4O_6S_2$; M. wt 474; Yield 70%; m. p.110^{0}C; colour- brown yellow; IR (KBr) cm^{1}1627 cm^{-1} (CH=N), 1588 cm^{-1} (NO_2),1190 cm^{-1} (S=O);^{1}HNMR(DMSO d_6) δ,ppm: 3.75(s,3H,CH), 5.2-7.2(m,2H,Ar-H), 5.4(s,2H,CH), 6.5(t,1H,CH), 4.2(d,2H,CH), 8.4(s,1H,CH=N), 7.6(t,2H,CH), 7.9(t,2H,CH), 4.2(s,1H,SO_2NH), 6.5-7.5(m,2H,CH). Anal. Calcd.(%): C=50.30%, H=3.82, N=11.81, O=20.55, S=13.51.

2(c)N-(4,6-Dimethyl-pyrimidin-2-yl)-4-[(5-methoxy-2-nitro-4-vinyloxymethyl-benzylidene)-amino]-benzenesulfonamide

Recrystallization from ethanol: $C_{23}H_{23}N_5O_6S$; M. wt 520; yield 60%; m. p.130^{0}C; colour- brown yellow; IR (KBr) cm^{1}1620 cm^{-1} (CH=N), 1542 cm^{-1} (NO_2), 1139 cm^{-1} (S=O);^{1}HNMR(DMSO d_6)δ,ppm: 3.75(s,3H,CH), 5.2-7.2(m,3H,ArH), 5.4(s,2H,CH), 6.5(t,1H,CH),. 2(d,2H,CH), 8.4(s,1H,CH=N), 7.6(t,2H,CH), 7.9(t,2H,CH), 4.2(s,1H,SO_2NH), 3.8(s,1H,CH), 2.8-3 (s, 6H, CH_3). Anal. Calcd. (%):C=55.50, H=4.68, N=14, O=19.37, S=6.44.

2(d)4-[(4-Allyloxy-5-methoxy-2-nitro-benzylidene)-amino]-N-(5-methyl-isoxazol-3-yl)-benzene sulfonamide

Recrystallization from ethanol: $C_{21}H_{20}N_4O_7S$; M. wt 472; Yield 70%; m. p.120^{0}C; colour- brown yellow; IR (KBr) cm^{1}1640 cm^{-1} (CH=N), 1540 cm^{-1} (NO_2), 1120 cm^{-1} (S=O);^{1}HNMR(DMSO d_6)δ,ppm: 3.75(s,3H,CH), 5.2-7.2(m,2H,Ar-H), 5.4(s,2H,CH), 6.5(t,1H,CH), 4.2(d,2H,CH), 8.4 (s,1H,CH=N), 7.6(t,2H,CH), 7.9(t,2H,CH), 4.2(s,1H,SO_2NH), 5.2(s,1H,CH), 2.5(s,3H,CH_3). Anal. Calcd.: C=53.30, H= 4.35, N=11.80, O= 23.76, S= 6.79.

3(a)4-[(3-Allyl-4-hydroxy-5-methoxy-benzylidene)-amino]-benzenesulfonamide

Recrystallization from ethanol: $C_{17}H_{18}N_2O_4S$; M. wt 346;Yield 72%; m. p.75^{0}C; colour- yellow; IR (KBr) cm^{1}3430 cm^{-1}(O-H), 1630 cm^{-1} (CH=N);^{1}HNMR(DMSO d_6) δ,ppm: 3.75(s,3H,CH), 3.0(s,1H,OH), 5.2-7.2(m,2H,Ar-H), 4.96(d,2H,CH), 6.4(p,1H,CH), 3.5(d,2H,CH), 8.4(s,1H,CH=N), 7.6(t,2H,CH), 7.9(t,2H,CH), 2.2(s,2H,SO_2NH_2). Anal. Calcd.(%):C=58.90, H=5.28, N=8.09, O=18.47, S=9.27.

3(b)4-[(3-Allyl-4-hydroxy-5-methoxy-benzylidene)-amino]-N-thiazol-2-yl-benzenesulfonamide

Recrystallization from ethanol: $C_{20}H_{19}N_3O_4S$; M. wt 429;Yield 80%; m. p.65^{0}C; colour- cremish yellow; IR (KBr) cm^{1}3410 cm^{-1}(O-H), 1650 cm^{-1} (CH=N); ^{1}HNMR(DMSO d_6) δ,ppm: : 3.75(s,3H,CH), 3.0(s,1H,OH), 5.2-7.2(m,2H,Ar-H), 4.96(d,2H,CH), 6.4(p,1H,CH), 3.5(d,2H,CH), 8.4(s,1H,CH=N), 7.6(t,2H,CH), 7.9(t,2H,CH), 4.2(s,1H,SO_2NH), 6.5-7.5(m,2H,CH). Anal. Calcd.(%): C=55.90, H=4.49, N=9.70, O=14.98,S=14.93.

3(c) 4-[(3-Allyl-4-hydroxy-5-methoxy-benzylidene)-amino]-N-(5-methyl-isoxazol-3-yl)-benzene sulfonamide

Recrystallization from ethanol: $C_{21}H_{21}N_3O_5S$; M. wt 427; Yield 95%; m. p.70^{0}C; colour- cremish white; IR (KBr) cm^{1}3400 cm^{-1}(O-H), 1670 cm^{-1} (CH=N);^{1}HNMR(DMSO d_6) δ,ppm: 3.75(s,3H,CH), 3.0(s,1H,OH), 5.2-7.2 (m,2H,Ar-H), 4.96(d,2H,CH), 6.4 (p,1H,CH),3.5 (d,2H,CH), 8.4 (s,1H,CH=N), 7.6 (t,2H,CH),7.9 (t,2H,CH), 4.2 (s,1H,SO_2NH),5.2 (s,1H,CH), 2.5 (s,3H,CH_3). Anal. Calcd.(%): C=59.00, H=4.98%, N=9.80, O=18.70, S=7.51.

3(d)4-[(3-Allyl-4-hydroxy-5-methoxy-benzylidene)-amino]-N-(4,6-dimethyl-pyrimidin-2-yl)-benzene sulfonamide

Recrystallization from ethanol: $C_{23}H_{24}N_4O_4S$; M. wt 452;Yield 80%; m. p.72^{0}C; colour- cremish white; IR (KBr) cm^{1}3450 cm^{-1}(O-H), 1640 cm^{-1} (CH=N),;^{1}HNMR(DMSO d_6) δ,ppm: 3.75(s,3H,CH), 3.0(s,1H,OH), 5.2-7.2(m,2H,Ar-H), 4.96(d,2H,CH), 6.4(p,1H,CH), 3.5(d,2H,CH), 8.4(s,1H,CH=N), 7.6(t,2H,CH),7.9(t,2H,CH), 4.2(s,1H,SO_2NH), 3.8(s,1H,CH), 2.8-3(s,6H,CH_3). Anal. Calcd.(%):C, C=61.10, H=5.30, N=12.38, O=14.14, S=7.09.

DISCUSSION

All the compounds were screened for their in vitro antibacterial activity at Birla Institute of Medical Research and College of Life Sciences, Gwalior, against 24h old cultures of bacterial pathogens. Antibacterial activity was determined against Gram–ve bacteria i. e. *Escherichia coli & Pseudomonas aeruginosa* and Gram+ve bacteria i. e. *Staphylococcus aureus* & *Bacillus subtilis,* bacterial strains using

disc diffusion assay. For this sterile filter paper disc (8 mm) impregnated with fixed doses (500 µg/mL, 1000 µg/mL) of synthesized compounds under investigation were placed upon the seeded petri dishes. Similar plates were prepared for the standard drugs, the reference antibacterial drug was Streptomycin for Gram – ve bacteria and Penicillin-G was used for Gram+ve bacteria. Dimethyl formamide is used as control solvent. The plates were allowed to stay for 24h at 37^{0}C for bacterial strains. The zone of inhibition, observed around the disc after incubation were measured. The compounds show less activity at 500 µg/disc concentrations and exhibited promising activities at 1000 µg/disc concentration, are presented in table 1.

Table 1: Results of *in-vitro* antibacterial activity observed for the synthesized imine compounds through disc diffusion assay

S. No.	Compound	Zone of Inhibition	*E. coli*	*P. aeruginosa*	*S. aureus*	*B. subtilis*
1.	1(a)	1	-	-	-	-
		2	16	-	12	14
2.	1(b)	1	-	-	-	-
		2	10	-	14	10
3.	1(c)	1	10	-	14	12
		2	20	12	**28**	14
4.	1(d)	1	-	-	-	-
		2	16	-	16	16
5.	2(a)	1	-	-	-	-
		2	10	-	12	-
6.	2(b)	1	-	-	-	-
		2	16	-	16	16
7.	2(c)	1	11	-	-	10
		2	22	16	16	16
8.	2(d)	1	-	-	-	-
		2	16	-	16	16
9.	3(a)	1	10	-	16	-
		2	16	14	22	12
10.	3(b)	1	-	-	14	-
		2	10	14	20	12
11.	3(c)	1	12	10	14	12
		2	24	20	28	24
12.	3(d)	1	-	-	-	-
		2	15	14	14	12
	Control (Std-Streptomycin)		28	24		
	Penicillin-G				38	32
	Blank(DMF)		-	-	-	-

1= 500µg/mL, 2=1000 µg/mL, (-)= No effect

CONCLUSION

In the present work, 12 new compounds were synthesized. The synthetic route for the compounds is outlined in scheme-1. Equimolar quantities of these aromatic amines and sulphonamides derivatives was reacted for the first time in presence of mild acidic condition give azomethine in good to excellent yield. All the synthesized compounds were purified by successive recrystallization using ethanol. The purity of the synthesized compounds was checked by performing TLC. The structures of the synthesized compounds were determined on the basis of their FTIR, ^{1}HNMR data and elemental analyzer. The IR spectra of the synthesized compounds showed the presence azomethine group of C=N stretching bands at 1600-1690 cm^{-1}. In ^{1}HNMR spectra, all the compounds were characterized by the presence of imino proton (CH=N) at 8.1-8.5 ppm. All compounds gave satisfactory elemental analysis.

In table 1 show result of *in-vitro* antibacterial activity observed for the synthesized azomethine compounds through disc diffusion assay. The reference antibacterial drug was Streptomycin for Gram – ve bacteria i. e. *E. coli*, and *P. aeruginosa*. Penicillin-G was used as reference antibacterial drug for Gram+ve bacteria i. e. *S. aureus* and *B. subtilis*. The inhibition depends on type of bacterial strain, solvent as well as the structure of compound. All the azomethine compounds contain the same central moiety with different side chains. So in a particular solvent, for a particular effect side chains play important role in inhibition. Azomethines containing sulphamethoxazole as moiety in (1c,2c,3c) show excellent yield and exhibited remarkable inhibition in all bacterial strains. The presence of electron withdrawing substitution on aromatic ring increases the antibacterial activity of different derivatives. Azomethines containing sulphathiazole (1b,2b,3b) and sulphanilimide (1a,2a,3a) as moiety show average yield and moderate inhibition activity while azomethines containing sulphadimidine (1d,2d,3d) as moiety show minimum yield and less inhibition activity.

ACKNOWLEDGEMENT

Sincere thanks are due to the Dean, BIMR College of Life Science Gwalior, For providing antibacterial sceening and to the SOS chemistry for providing lab facility.

REFERENCES

1. Baquero F. Gram-positive resistance: challenge for the development of new antibiotics. J Antimicrob Chemother 1997;39:1–6.
2. Alekshun MN, Levy SB. Molecular mechanisms of antibacterial multidrug resistance. Cell 2007;128:1037–50.
3. Rice LB. Unmet medical needs in antibacterial therapy. Biochem Pharmacol 2006;71:991–5.
4. Hadi JS. Alsalami BK, Essa AH. Microwave assisted one-pot synthesis and screening of some schiff's bases of sulfanilamide. J Sci Res 2009;3:563-8.
5. Abbas SA, Munir M, Fatima A, Naheed S, Ilyas Z. Synthesis, characterization and biocidal studies of some transition metal complexes containing tetra dentate and neutral bi dentate schiff base. E-J Life Sci 2010;1:37-40.
6. Kumar S, Niranjan MS, Chaluvaraju KC, Jamakhandi CM, Kadadevar D. Synthesis and antimicrobial study of some schiff bases of sulfonamides. J Curr Pharm Res 2010;01:39-42.
7. Singh UK, Pandeya SN, Sethia SK, Pandey M, Singh A, Garg A, *et al*. Synthesis and biological evaluation of some sulfonamide schiff's bases. IJPSDR 2010;2:216-8.
8. Kratky M, Sova JV, Volkova M, Buchta V, Trejtnar FS, Rikova J. Antimicrobial activity of sulfonamides containing 5-chloro-2-

hydroxybenzaldehyde and 5-chloro-2-hydroxybenzoic acid scaffold. Eur J Med Chem 2012;50:433-40.

9. Suresh R, Kamalakkannan D, Ranganathan K, Arulkumaran R, Sundararajan R, Sakthinathan SP, *et al*. Solvent-free synthesis, spectral correlations and antimicrobial activities of some aryl imines. Spectrochim Acta Part A 2013;101:239–48.
10. Vijesh AM, Isloor AM, Shetty P, Sundershan S, Fun HK. New pyrazole derivatives containing 1,2,4-triazoles and benzoxazoles as potent antimicrobialand analgesic agents. Eur J Med Chem 2013;62:410-5.
11. Pudota PT, Purohit RSM, Pujar GV. Synthesis, *in vitro* antimicrobial and cytotoxic activities of some novel bis-1,3,4-oxadiazoles. J Appl Chem Res 2013;7:7-18.
12. Naganagowda G, Meijboom R, Petsom A. Synthesis and antimicrobial activity of new schiff base compounds containing 2-hydroxy-4-pentadecylbenzaldehyde moiety. Hindawi Publishing Corporation Advances in Chemistry; 2014.
13. Hussain Z, Yousif E, Altaie A. Synthesis and characterization of Schiff's bases of Sulfamethoxazole. Org Med Chem Lett 2014;4:1.
14. Soleiman H, Leena Al-Kaabi, Suad A, Yaser T, Rabah I, Na'il S, *et al*. Antipathogenic effects of structurally-related Schiff base derivatives: Structure–activity relationship. Arabian J Chem 2013;4(1):15.
15. Hu S, Huang Y, Wu Y, He H, Katherine A, Young G, *et al*. Structure activity relationship studies of 3-arylsulfonyl-pyrido [1,2-a] pyrimidin-4-imines as potent 5-HT6 antagonists. Bioorg Med Chem 2014;22:1782–90.
16. Asha BT, Rabindra KN, Lata PK, Sunil CH. Synthesis and biological evaluation of Schiff's bases and 2-azetidinones of isonocotinyl hydrazone as potential antidepressant and nootropic agents. Arabian J Chem. [article in press DOI: 10.1016/j.arabjc.2011.02.015].
17. Shaoyong K, Yanhong W, Ziwen Y, Kaimei W, Ying L, Liqiao S. Novel cycloalkylthiophene–imine derivatives bearing benzothiazole scaffold: synthesis, characterization and antiviral activity evaluation. Bioorg Med Chem Lett 2013;23:5131–4.
18. Sriram D, Yogeeswari P, Myneedu NS, Saraswat V. Abacavir prodrugs: microwave-assisted synthesis and their evaluation of anti-HIV activities. Bioorg Med Chem Lett 2006;16:2127-9.
19. Kumar M, Narasimhan B, Kumar P, Ramasamy K, Mani V, Mishra RK, *et al*. 4-(1-Aryl-5-chloro-2-oxo-1,2-dihydro-indol-3-ylideneamino)-N-substitutedbenzene sulfonamides: Synthesis, antimicrobial, anticancer evaluation and QSAR studies. Arabian Journal of Chemistry 2013;7(4):436–47.
20. Monteiro A, Gonçalves LM, Maria MM, Santos. Synthesis of novel spiropyrazoline oxindoles and evaluation of cytotoxicity in cancer cell lines. Eur J Med Chem 2014;79:266-72.
21. Aggarwal N, Kumar R, Dureja P, Diwan S, Rawat DS. Schiff bases as potential fungicides and nitrification inhibitors. J Agric Food Chem 2009;57:8520-5.
22. Isloor AM, Kalluraya B, Shetty P. Regioselective reaction: synthesis, characterization and pharmacological studies of some new Mannich bases derived from 1,2,4-triazoles. Eur J Med Chem 2009;44:3784-7.
23. Shi L, Ge HM, Tan SH, Li HQ, Song YC, Zhu HL, Tan RX. Synthesis and antimicrobial activities of Schiff bases derived from 5-chloro-salicylaldehyde, Eur J Med Chem 2007;42:558-64.
24. Wang X, Yin J, Shi L, Zhang G, Song B. Design, synthesis, and antibacterial activity of novel Schiff base derivatives of quinazolin-4(3H)-one. Eur J Med Chem 2014;77:65-74.
25. Kolundz B, Markovic V, Stanojkovic T, Joksovic L, Matic I, Todorovic N, *et al*. Novel anthraquinone based chalcone analogues containing an imine fragment: Synthesis, cytotoxicity and anti-angiogenic activity. Bioorg Med Chem Lett 2014;24:65–71.
26. Ward CE, Berthold RV, Koerwer JF, Tomlin JB, Manning DT. Synthesis and herbicidal activity of 1,2,3,4-tetrahydro-1,3,5-triazino[1,2-a]benzimidazoles. J Agric Food Chem 1986;34:1005-10.
27. DeMilo AB, Redfern RE. New insect juvenile hormone mimics: aromatic Schiff bases and related compounds against the large milkweed bug and yellow mealworm. J Agric Food Chem 1979;27:760-2.
28. Gautam N, Chourasia OP. Synthesis, antimicrobial, insecticidal and anthelmintic activity studies of some new alkyl/aryl 6-(4-(4-methyl-1H-1,2,3-triazol-1 yl)phenyl amino) phenyl)-N^2,N^4-bis(4-methoxyphenyl)-1,3,5-triazin-2,4 diamine carbamic acid ester derivatives. Indian J Chem 2012;51:1020-6.
29. Gumrukcuoglu N, Sokmen BB, Ugras S, Ugras HI, Yanardag R. Synthesis, antibacterial, antielastase, antiurease and antioxidant activities of new 1, 4-butylene bridged bis-1,2,4-triazole derivatives. J Enzyme Inhib Med Chem 2013;28:89-94.
30. Bhosale JD, Shirolkar AR, Pete UD, Zade CM, Mahajan DP, Hadole CD, *et al*. Synthesis, characterization and biological activities of novel substituted formazans of 3,4-dimethyl-1Hpyrrole-2-carbohydrazide derivatives, J Pharm Res 2013;7:582-7.
31. Sztanke K, Maziarka A, Osinka A, Sztanke M. An insight into synthetic Schiff bases revealing antiproliferative activities *in vitro*. Bioorg Med Chem 2013;21:3648-66.
32. Mohana KN, Mallesha L. Synthesis and antiproliferative activity of some new fluorinated Schiff bases derived from 1,2,4-triazoles. J Fluorine Chem 2013;156:15-20.