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Research Article

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF SCHIFF BASES DERIVEDFROM NOVEL OXADIAZOLE DERIVATIVES

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ABSTRACT

Six novels Schiff base containing 1,3,4-oxadiazole (SB-1 to SB-6) were synthesized by the simple synthesis of benzohydrazide through nucleophilic acyl substitution reaction which involves a reaction between benzoic acid and hydrazine hydrate the compound is treated with POCl3and *p*-amino benzoic acid with the involvement of microwave irradiation (1-2 min) at 300 watts to obtain the 1,3,4-oxadiazole compound . An equimolar mixture of 0.01 mole of 1, 3, 4-oxadiazole and substituted benzaldehyde in the presence of glacial acetic acid resulted into respective Schiff base. The newly synthesized derivatives were characterized by spectroscopical methods using IR, 1HNMR spectroscopy and Mass spectrometry. All the synthesized compounds were screened for their antibacterial and antifungal activities. Anti-bacterial and anti-fungal activities were performed by using Agar well diffusion Results of the activities revealed that some of the derivatives showed potent anti-bacterial and anti-fungal activities and some other compounds shown mild to moderate activities when compared to the respective reference standard.

Keywords: 1, 3, 4-Oxadiazoles, Aromatic aldehydes, microwave irradiation Anti-bacterial Antifungal activity.

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INTRODUCTION

1,3,4-Oxadiazole: Oxadiazoles are five-membered heterocyclic compounds with two nitrogens and one oxygen atom. Depending upon the position of hetero atoms they are named as 1,2,3; 1,2,4; 1,2,5 and 1,3,4 oxadiazoles. The structures of the following compounds are as follows.

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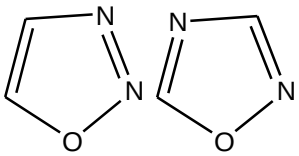
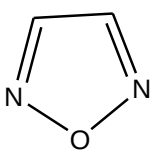
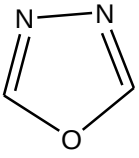


1, 2, 3-Oxadiazole

1, 2, 4-Oxadiazole



1, 2, 5-Oxadiazole

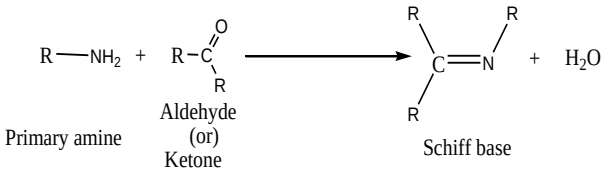


1, 3, 4-Oxadiazole

Chemistry of 1,3,4-Oxadiazoles: Oxadiazoles are very weak base due to the presence of two heteroatoms present on ring and the nitrogens show the inductive effect and oxadiazole ring are exhibit the dienecharacter. oxadiazoles are numbered as by designating the heteroatoms and the oxadiazoles have a special attention in pharmaceutical chemistry.

Schiff bases: Compounds containing Azomethine (or) imines are known as Schiff bases Generally, these compounds are formed by the condensation of primary amine with carbonyl compounds the aldehydes are aliphatic aldehydes they are unstable and the reacted aldehydes are aromatic aldehydes are having effective conjugation system, are more stable the formation of a Schiff base from an aldehyde (or)Ketone is a reversible reaction and generally takes place under acid (or) base catalysis (or) upon heating pH plays an important role in the process of condensation the chelating nature, moderate electron donor capacity, easily tunable electronic and steric parameters have proved the versatility nature of Schiff bases [1].

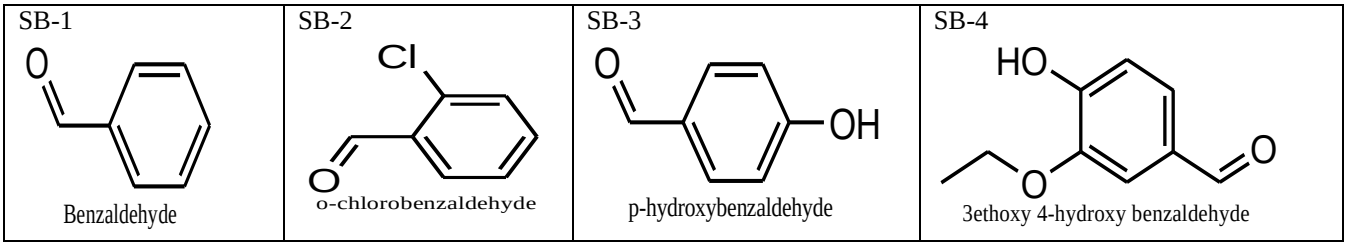
Formation of Schiff base:

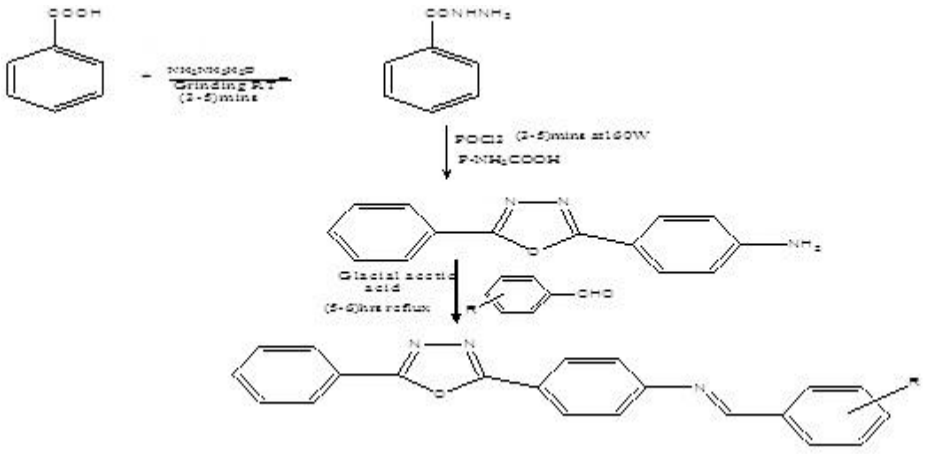


MATERIALS AND METHODS:

All chemicals used were of analytical grade and purchased from SD Fine. Melting points of all the synthesized compounds were determined by open capillary tube method. The purity of all compounds was checked by TLC technique and spots were visualized using UV radiation/iodine chamber. IR spectra were recorded on Shimadzu IR spectrophotometer by using KBr pellets technique. 1H- NMR was recorded on Bruker AMX 60 MHz spectrophotometer by using DMSO as solvent [2].

Scheme





EXPERIMENTAL METHODOLOGY

Step-1: Preparation of Benzohydrazide

The carboxylic acids(3.0mmol) was ground with hydrazine hydrate (80%3.75mmol) by a pestle in a mortar for 3-5 minutes and left for digestion (10 minutes) when the reaction mixture set into a solid mass. The completion of the reaction was checked by a thin layer chromatography. The solid mass was crystalized from ethanol to give hydrazides [2].

Step-2: Preparation of 1, 3, 4-oxadiazoles

The mixture of Benzohydrazide (0.002 mole) glacial acetic acid (0.003 mole) and phosphorus oxychloride (1ml) was ground to get a homogenous mixture and then heated in a beaker under microwave irradiation at for 1-2 mints.

Completion of the reaction was monitored by TLC. The contents were cooled to RT and added to excess ice-cold water. The solid product separated was collected by filtration. Further purification was done by recrystallization using ethanol.

Step-3: Preparation of Schiffbase (III) The secondstep product(0.01 mole) was dissolved in 30 ml ethanol containing few drops of GAA The appropriate aromatic aldehyde(0.01 mole) was added and reaction mixture was refluxed 5 hrs at 70°c.The reaction mixture was cooled. Poured in crushed ice .filtered and the separated product were purified by recrystallized from ethanol [3].

Characterization

Compound (SB-1)

IR (KBr in cm^{-1}): 1099.43 (C-O-C stretch), 1481.93(C=N), 3050(aromatic stretching)

^1H NMR($CDCl_3$+DMSO)(δppm) 7.5(m,14H,Ar H),3.8(S,1H,CH)2.5(Solvent peak)and Base peak = 106 $[M+H]^+$=326

Compound (SB-2)

IR (KBr in cm^{-1}): 1080(C-O-C stretch), 1490(C=N), 844 (Cl stretch) 2980 (Aromatic Stretch) ^1H NMR($CDCl_3$+DMSO) (δppm) (7.3-8.2M,13H,Ar-H), 3.8 (CH), 2.5 (Solvent peak), 0(TMS). Base peak=106 $[M+H]^+$=360

Compound (SB-3)

IR (KBr in cm-1):3618.46(Phenolic CH Stretch), 3008.95(Aromatic CH stretch), 2920.23 (Aliphatic CH stretch), 1492.90 (C=N),1157.92 (C-O-C stretch), 1H NMR(CDCl3+DMSO) (δppm) 9.0 (S,1H,OH) 7.38. (4M, 13H,ArH), 3.8 (S,1H=CH), 2.5 (Solvent DMSO), 0(TMS).and Base peak=106 $[M+H]^+$= 341.

Compound (SB-4)

IR (KBr in cm^{-1}):3440.71(Phenolic OH stretch), 3062.96(Aromatic CH stretch),2981.95(Aliphatic CH stretch), 1509.91 (C=N),1072.42 (C-O-C stretch), ^1H NMR ($CDCl_3$+DMSO)(δppm) 9.0(S,1H,OH)7.4-8.5(M.12HAr-H),4.2(S,1H-CH_2),2.5 (Solvent DMSO), 1.4(S,3H-CH_3)Base peak=385 $[M+H]^+$=386 [4].

RESULTS AND DISCUSSION:

Antibacterial activity: The antibacterial activity of synthesized derivatives performed by using Agar well diffusion method.

In this present research work, based on the wide literature survey, novel derivatives of oxadiazole containing Schiff bases were synthesized in three-step facile procedure and six in number [5]. All the reactions were monitored by TLC and purification was done by recrystallization process. All the derivatives were characterized using spectral studies like FT-IR spectroscopy, ^1H-NMR spectroscopy and Mass spectrometry [6].

All the six derivatives were screened for their Anti-fungal and Antibacterial activities.

Anti-fungal activity: The Anti-fungal activity of the synthesized derivatives SB-1 to SB-4 was carried out using Agar well diffusion method against Griseofulvin as a standard drug at various concentrations (250µg, 500µg and 1mg) out of all the four synthesized derivatives SB-2 and SB-3 are showing good activity the results are compared with standard drug Griseofulvin the order of antifungal activity results of the synthesized compound is as follows:

Test derivatives: SB-2> SB-4>SB>3>SB>1.

Standard drug: Griseofulvin.

Anti-bacterial activity: The Anti-bacterial activity of the synthesized derivatives SB-1 to SB-4 was carried out using Agar well diffusion method against Ampicillin as a standard drug at various concentrations (250µg, 500µg and 1mg) Out of all the four synthesized derivatives SB-1 and SB-4 are showing good activity the results are compared with the standard drug Ampicillin the order of antibacterial activity results of synthesized compounds is as follows:

Test derivatives: SB-1> SB-4>SB>3>SB>2.

Standard drug: Griseofulvin.

Table 1: Results of Antibacterial Activity

Sample code	Type of Organism	Zone of Inhibition(c.m)		
		250µg	500 µg	1mg
SB-1	Gr Negative *(E.Coli)*	1.4	1.9	2.8
	Gr Positive *(S.aureus)*	0.9	1.5	2.2
SB-2	Gr Negative *(E.Coli)*	1	1.4	2.4
	Gr Positive *(S.aureus)*	1.4	1.6	2.2
SB-3	Gr Negative *(E.Coli)*	1.2	1.9	2.5
	Gr Positive *(S.aureus)*	1.1	1.6	2.1
SB-4	Gr Negative *(E.Coli)*	1.4	1.9	2.7
	Gr Positive *(S.aureus)*	1.1	1.6	2.3

Table 2. Anti-fungal activity: Anti-fungal activity is performed by using Agar well diffusion method. The results of the synthesized derivatives as follows,

Samplecode	Fungi	Zone of Inhibition(mm.)		
		25µg	50µg	100µg
SB-1	Candida	5	7	10
SB-2		3	6	8
SB-3		4	7	11
SB-4		6	10	13
Griseofulvin		6.8	10.6	13.4

Figure(1):Anti-Bacterial activity of synthesized derivatives

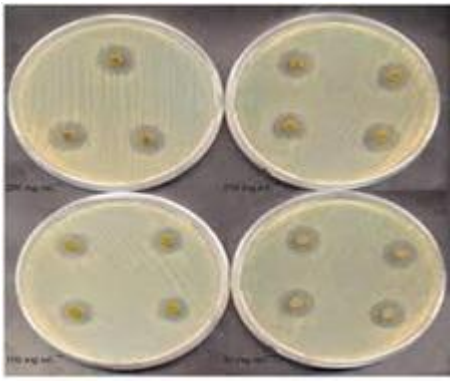
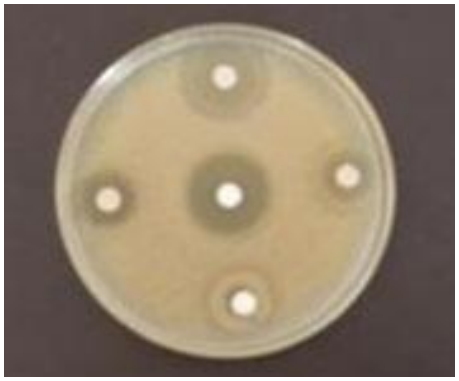


Figure: **(2) Anti-Fungal activity of synthesized derivatives**



CONCLUSION:

Novel derivatives of Oxadiazole containing Schiff bases were synthesized using conventional methods. All the synthesized compounds were identified by performing their melting point and TLC check and characterized by IR, ^{1}H-NMR, and Mass spectrometry. Later all the derivatives were screened for their Anti-fungal and Antibacterial activity by using Agar Well diffusion method [7].

In vitro anti-bacterial activity performed the four derivatives that are SB-1 SB-2 andSB-3,SB-4 by taking standard Ampicillin Among the four derivatives SB-1 and SB-4 Showing good activity compared to SB-3 and SB-4. *In vitro Anti-fungal activity* performed the four derivatives SB-1,SB-2 and SB-3,SB-4 derivatives by taking the standard Griseofulvin among the four derivatives SB-2 possess Chlorine group SB-4 possess ethoxy group which might showing better activity compare than SB-2 and SB-3 derivatives [8].

This promising *in-vitro* anti-fungal and anti-bacterial activity results also give scope to study other molecular descriptors like electronic and steric parameters. It gives a scope for further comparing the selected derivatives [9].

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REFERENCES

1. Ashish kumar, Anshujakhar, and Makrandi J.k. A Highly efficient solvent free synthesis of hydrazides using grinding technique. *Heterocyclic Letters.* 2(4), 2012, 401-404.
2. Alaa jawad H. Jawad Shneine K, Ahmed Ahmed and Mustafa Abdulrasool Synthesis M, Characterization and Evaluation of biological activity of Some heterocyclic compounds containing 1,2,4 Triazole ring. *International journal of research in pharmacy and chemistry*, (IJRPC). (2012), 1102-1123.
3. GhoneimAA, Assy MG ,Synthesis and Characterization of Antimicrobial activity of Azoles and Azine derivatives from tertiary butyl carbazatel. *Organic Chem Curr Res,* 4 (3), 2015, 1-5.
4. Giuseppe Daidone, DemetrioRaffa, FabianaPlescia. Benedetta Maggio and Angela Roccaro, Synthesis of Pyrazole-4-carbohydrazide derivatives of Pharmaceutical interest, *ARKIVOC*, 2002, 227-235.
5. Abdel-Aal MT[1], Abdel-Aleem AA, Ibahim LI, Zein AL. Synthesis and antimicrobial activity of novel 5-amino-4-cyano-1H-pyrazole and quinazolin-4(3H)-one derivatives. *Arch Pharm Res*. 33(12), 2010, 1891-900
6. TarekAboul-Fadl, HatemA.Abdel-Aziz, Adnan Kadi, Ahmed Bari. Pervez Ahmad, Tilal Al-Samani. *Arch. Pharm. Res.* 16, 2011, 3544-3551.
7. Meshram Vishskhap, Y. K. Bodade Rohini R.Dharmakar Synthesis of Some Substitued Schiff bases by Microwave irradiation: Astep to Eco-friendly Synthesis. *Indian journal of Applied Synthesis*, 4(3), 2014, 34-36.

8. Thirugnanasambandhan, A. Venkatraman, S. Senthilpalaniappan, M. Synthesis and antimicrobial Screening of some substituted 1,3,4-Oxadiazole derivatives. *Journal of chemical and pharmaceutical research*, 4(2), 2012, 1217-1221.
9. Arfan M, Khan R, Khan MA, Anjum S, Choudhary MI, Ahmad M. Synthesis and antileishmanial and antimicrobial activities of some 2,3-disubstituted 3H-quinazolin-4-ones. *J Enzyme Inhib Med Chem.* 25(4) 2010, 451-8.