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NOVEL SULFONAMIDE SCHIFF'S BASES AND THEIR ANTIMICROBIAL ACTIVITY

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ABSTRACT: In the vision of chemistry, Schiff bases are excellent ligands and play a very important role in drug discovery and development. The Schiff bases and their complexes have been reported in the literature possessing wide applications in biological, clinical, and analytical fields. In outlook of this, new Schiff bases of Sulfonamide drug were synthesized by a very simple reaction and in good yield. The purity of the newly synthesized bases was confirmed by performing TLC in a suitable solvent system. The functional groups present in the targeted Schiff bases were confirmed by FT-IR spectroscopy. Further, all the synthesized compounds were successfully screened for their antimicrobial activity. Among these Schiff bases, the compound containing nitro and fluoro groups shows greater activity than standard drugs. By considering this, there is a need to design more analogs of sulfonamide Schiff bases and correlate the structural modifications with their respective antimicrobial activity to develop a Structure activity relationship.

INTRODUCTION: Schiff's bases are an important class of organic compounds. A Schiff base is a functional group that contains a carbon-nitrogen double bond with the nitrogen atom connected to an aryl or alkyl group, but not hydrogen. Schiff's bases are condensation products of primary amines with carbonyl compounds. Schiff bases are well-known important intermediates for the synthesis of various bioactive compounds [1, 2]. They are reported to show a variety of biological activities, including antibacterial [3], antifungal [4], anticonvulsant [5], anti- HIV [6], anti-inflammatory [7], antitumor [8], anti-tubercular [9], analgesics [10], insecticidal and herbicidal [11] activities. Also, they are fundamental material for synthesis of various Schiff base ligands, which are used as chiral auxiliaries in asymmetric synthesis [12].

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Structurally, a Schiff's base (also known as imine or azomethine) is a nitrogen analogue of an aldehyde or ketone in which the carbonyl group (>C = O) is replaced by an imine or azomethine group. Imine or azomethine groups are present in various natural, naturally derived, and non-natural compounds. The amine group present in such compounds has been shown to be critical to their biological activities [13, 14].

In view of this, the present investigation involves the synthesis of Schiff bases of Sulfonamide through condensation of the amine group and substituted aldehyde in search of more potential antimicrobial complexes.

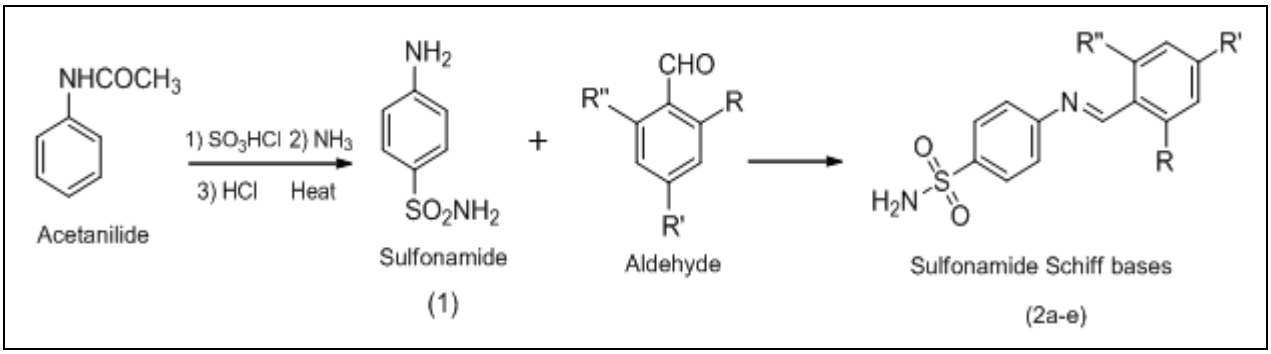
MATERIALS AND METHODS: The starting materials and solvents used for each reaction are of synthetic grade procured from Sigma Aldrich. All the chemicals and synthesized products were characterized for their purity by physical constant and thin-layer chromatography (TLC). All the reactions were monitored by using thin-layer chromatography on pre-coated TLC plates (Silica gel 60-120#) by using solvent system Benzene:

Ethanol [8:2] for Sulfonamide and Dichloro-methane: Ethyl acetate [9:1] for Sulfonamide complexes. The obtained TLC plates were observed under a long UV lamp in the UV chamber and also in the iodine chamber for detection of spots. The synthesized compounds were characterized by the spectroscopic method FT-IR for elucidation and confirmation of their structures.

Synthesis of Sulfonamide: Sulfonamide was synthesized from acetanilide by following the various steps. Acetanilide refluxed with an excess of chlorosulphonic acid which gives p-acetamido-benzensulphonyl chloride, which readily converted into corresponding p-acetamidobenzenesulfonamide upon reaction with ammonia on heating. Further acetamido group easily undergoes hydrolysis by acid-catalyzed reaction, and it forms p-amino-benzenesulfonamide (Sulfonamide) [15, 16].

Synthesis of Sulfonamide Schiff bases: Sulfonamide (0.0107 mole) dissolved in a mixture of Tetrahydrofuran and Ethanol (1:4 v/v) was mixed with an aldehyde (0.0107 mole) already dissolved mixture of the same solvent. To this, glacial acetic acid was added, and the reaction mixture was refluxed on a water bath at 80 °C for 6 h. The progress of the reaction was monitored by TLC. The mixture was cooled and poured into ice-cooled water to precipitate Schiff base. The resulting colored precipitate was filtered and recrystallized from ethanol and dried in a desiccator [17, 18].

Reaction Scheme:



Antimicrobial Activity:

Antimicrobial Activity of Sulfonamide Schiff Bases: The antibacterial activity of all the synthesized compounds 2a-e were screened against different Gram-positive (*Staphylococcus aureus* and *Streptococcus pyogenes)* and Gram-negative (*Escherichia coli* and *Pseudomonas aeruginosa*) bacteria by measuring the zone of inhibition. The antibacterial activity was performed by the Agar diffusion method at the concentration level of 50µg/ml. Ciprofloxacin was used as a standard drug at a concentration of 50µg/ml. Nutrient agar was used as culture media, and DMSO was used as solvent [19, 20].

RESULTS AND DISCUSSION: All chemicals and products have shown a single spot on the TLC plate when observed under UV light and iodine chamber. The melting points were taken in open capillaries on the melting point apparatus and were found uncorrected.

TABLE 1: PHYSICAL CHARACTERISTICS DATA OF SYNTHESIZED SULFONAMIDE COMPLEXES

Comp. No.	R	R'	R''	M. P. (°C)	% Yield
2a	NO_2	NO_2	H	156	84
2b	OCH_3	OCH_3	OCH_3	172	77
2c	H	NO_2	H	164	80
2d	H	OH	H	187	86
2e	H	F	H	192	67

Spectral Data: The Infrared spectroscopy was carried out by using the potassium bromide (KBr) pellet method on the Shimadzu IR Affinity-1. The characterization with IR spectra of the synthesized compounds confirmed the anticipated Functional group in structure. The spectral data of synthesized Schiff bases are as follows;

Spectral Data of Synthesized Sulfonamide Schiff Bases:

Compound 2a: 4-[2,4-Dinitro-benzylidene)-amino]-benzenesulfonamide

IR (KBr cm^{-1}): 3284 (NH_2), 1612 (C=N), 1342 (S=O), 1143(C-N); aromatic), 834 (C-S-C),

Compound 2b: 4-[2,4,6-trimethoxy-benzylidene)-amino]-benzenesulfonamide

IR (KBr cm^{-1}): 3323 (NH_2), 1618 (C=N), 1337 (S=O), 1148 (C-N); aromatic), 822 (C-S-C),

Compound 2c: 4-[4-Nitro-benzylidene)-amino]-benzenesulfonamide

IR (KBr cm^{-1}): 3296 (NH_2), 1593 (C=N), 1353 (S=O), 1131 (C-N); aromatic), 841 (C-S-C),

Compound 2d: 4-[4-Hydroxy-benzylidene)-amino]-benzenesulfonamide

IR (KBr cm^{-1}): 3310 (NH_2), 1602 (C=N), 1344 (S=O), 1127 (C-N); aromatic), 811 (C-S-C),

Compound 2e: 4-[4-Fluoro-benzylidene)-amino]-benzenesulfonamide

IR (KBr cm^{-1}): 3290 (NH_2), 1609 (C=N), 1322 (S=O), 1114 (C-N); aromatic), 829 (C-S-C).

Antimicrobial Activity: Though we have many synthetic drugs in the market, the bacterial mutations are making them resistant. In view of this, the synthesized intermediate compounds in the present investigation (2a-e) were evaluated for their antimicrobial activity.

Antimicrobial Activity of Sulfonamide Schiff Bases: It is observed that the Sulfonamide Schiff bases 2a-e showed antibacterial activity. From the result, it has been concluded that compounds 2e and 2d have shown a similar potential to that of standard. In general, it is worth noting that compounds having fluorine and chlorine groups in the scaffold exhibited excellent activity while the compounds having other substituents showed good to moderate activity. Antibacterial activity data (Zone of inhibition) of the synthesized Schiff bases 2a–e is presented in **Table 2**.

TABLE 2: ANTIMICROBIAL ACTIVITY OF COMPOUNDS 2a-e

Compound	Zone of inhibition (mm)			
	Gram-positive bacteria		Gram-negative bacteria	
	S. aureus	***S. pyogenes***	***E. coli***	***P. aeruginosa***
4-[2,4-Dinitro-benzylidene)-amino]-benzenesulfonamide (a)	9	11	12	14
4-[2,4,6-trimethoxy-benzylidene)-amino]-benzenesulfonamide (b)	10	12	13	14
4-[4-Nitro-benzylidene)-amino]-benzenesulfonamide (c)	10	12	15	17
4-[4-Hydroxy-benzylidene)-amino]-benzenesulfonamide (d)	11	10	11	13
4-[4-Fluoro-benzylidene)-amino]-benzenesulfonamide (e)	11	10	14	15
Standard: Ciprofloxacin	13	14	18	19
Solvent: DMSO	-	-	-	-

CONCLUSION: Some of the new Sulfonamide Schiff bases were synthesized *via* a simple conventional method, and these complexes were characterized by analytical methods. Spectral data confirm the structure of the synthesized complexes as expected. These are successfully evaluated for their anti-microbial activity. From the results, it can be concluded that the modified complexes show remarkable anti-microbial action and having the potential in view to study their structural activity relationship for the discovery of more potential and selective complexes.

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CONFLICTS OF INTEREST: No conflict of interest.

REFERENCES:

1. Mohamed NI and Hazem KAL–Deeb: Synthesis, Characterization and Study of the Biological Activity of Some Aldimines Derivative. E-Journal of Chemistry 2006; 3(13): 257-61.

2. Mohammad MY: Synthesis and Characterization of Schiff Base Aniline with 5-bromo-2-hydroxyl benzaldehyde and their metal complexes. International Journal of Recent Scientific Research 2018; 9 (4): 26026-30.
3. Shah NN and Baseer MA: Synthesis and Antimicrobial Studies of Some Novel Schiff bases. Asian J Pharm Clin Res 2012; 5(3): 228-32.
4. Lijie Wei and Wenqiang Tan: Synthesis, Characterization, and Antifungal Activity of Schiff Bases of Inulin Bearing Pyridine ring. Polymers 2019; 11: 371.
5. Batra N, Batra S and Badri P: Design, Synthesis and Evaluation of Schiff bases & Thiazolidinone Derivatives for Anticonvulsant Activity. Journal of Applied Pharmaceutical Science 2014; 4(1): 105-12.
6. Gadada N, Reinout M and Petsom A: Synthesis and Antimicrobial Activity of New Schiff Base Compounds Containing 2-Hydroxy-4-pentadecylbenzaldehyde Moiety. Advances in Chemistry 2014; 1-10.
7. Krátký M: Sulfadiazine Salicylaldehyde-Based Schiff Bases: Synthesis, Antimicrobial Activity and Cytotoxicity. Molecules 2017; 22: 1573.
8. Villar R, Encio I, Migliaccio M: Synthesis and Cytotoxic Activity of Lipophilic Sulphanamide Derivatives of the Benzo [b] thiophene 1, 1-dioxode. Bioorg Med Chem 2004; 12: 963-68.
9. Racha U: Synthesis and Anti-Inflammatory Activity of Some New Schiff's Bases and Azetidinones. IJSRM 2016; 4(3): 1-6.
10. Muzammil K, Trivedi P and Khetani DB: Synthesis and Characterization of Schiff base m-nitro aniline and their complexes. Research Journal of Chemical Sciences 2015; 5(5): 52-55.
11. Nirmal R: Synthesis and Pharmacological Evaluation of Novel Schiff Base Analogues of 3-(4-amino) Phenylimino) 5-fluoroindolin-2-one. J Young Pharm 2010; 2(2): 162-68.
12. Anu K and Kamboj S: Schiff Bases: A Versatile Pharmacophore. Journal of Catalysts 2013; 14.
13. Shahare HV, Mugdiya YN and Kharabe GP: Synthesis and Antimicrobial Activity of New Series of Schiff Bases. WJPR 2014; 3(2): 2120-24.
14. Khan MN and Khan AM: Synthesis and Antibacterial Activity of the Sulfonamide based Schiff Base and its Transition Metal (II) Complexes. Pak J Pharm Sci 2018; 31(1): 103-111.
15. Furniss BS, Hannafod AJ, Smith PWG and Tatchell AR: Vogels Textbook of Practical Organic Chemistry. Pearson Education, New Delhi, 5th edition 1989.
16. Kumar S and Niranjan MS: Synthesis and Antimicrobial Study of Some Schiff Bases of Sulfonamides. Journal of Current Pharmaceutical Research 2010; 01: 39-42.
17. Singh P and Raj R: 1, 2, 3-Triazole tethered beta lactam-Chalcone bifunctional hybrids: Synthesis and anticancer evaluation. European J of Med Chem 2011; 30: 1-7.
18. Manivannan C and Santhi N: Synthesis, Characterization, Molecular Docking Studies and Antibacterial Evaluation of Chalcone based Pyrazolines as DNA Gyrase Inhibitors. Int J Modn Res Revs 2015; 3(5): 679-87.
19. Wasfi A: The NMR Study and Antimicrobial Activity of Some Schiff Bases Derived From Sulphonamide Drug. Journal of Advances in Chemistry 2015; 12(2): 1-6.
20. Mustafa M, Elias RS and Munther A: Synthesis, Characterization and Antibacterial Evaluation of some Sulfonamide Schiff base Derivatives. International Journal of Research in Pharmaceutical Sciences 2019; 1(4): 1729.

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