Synthesis and evaluation of antimicrobial activity of new sulfonamide Schiff's base

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Abstract: **Synthetic chemistry is the most frequently used in the preparation of organic compounds from smaller entities. The process of establishing a new drug exceedingly complexioned involves the talents of people from a variety of disciplines, including chemistry, biochemistry, physiology, pharmacology, pharmaceutics and medicine. On through literature survey we found that the Schiff base containing sulphonamide compound having wide range of pharmacological and biological actions, reported that the Schiff base containing sulphonamide compounds having various variety of pharmacological and microbial actions. In our present work we are planning to synthesis some of the Schiff base containing sulphonamides by using different aromatic aldehydes, to obtain pharmacologically or biologically useful compounds. The synthesised compounds were subjected to in-vitro anti-microbial evaluation. The zone of inhibition at various concentrations of synthesised compounds against gram positive bacteria were determined by disc diffusion method.**

Index Terms: **Sulphonamides, Schiff's base, disc diffusion method, antibacterial activity**

I. INTRODUCTION

The synthetic and medicinal chemistry is concerned mainly with the organic, analytical and biological aspects of this process. It occupies a strategic position at the interface of chemistry and biology. Together computer aided drug design (CADD), x-ray crystallography, metabolism and pharmacokinetics, legal and regulating affairs, clinical franchise management, and pharmaceutics and process research chemistry uses sophisticated analytical techniques to synthesis and test new drug products and to develop the most effective and environmentally friendly means of production. The sulphonamide antimicrobial drugs were the first effective chemotherapeutic agents that could be used systemically for the cure of bacterial infections in humans. Structural similarity between sulphonamide and PABA is the basis for the inhibitory activity of sulfa drugs on dihydrofolate biosynthesis. The sulphonamides are having pharmacological activities like Anti-inflammatory bowel diseases, Antimicrobial, Intestinal infections, Ulcerative colitis, Haemophilusvaginalis, Local management of ophthalmic infections and Anti-tumour activity. Schiff's base is a compound, considered a sub-class of imines, being either secondary ketimines or secondary aldimines depending on their structure. It is also known as Hugo (Ugo) Schiff base and synonymous with azomethine.
Schiff's bases can be synthesised from a reaction of an aromatic amine and a carbonyl compound by a nucleophilic addition forming a hemiaminal followed by a dehydration to generate an imine. These are having antimicrobial, antiviral and anticancer activity. After observing number of literature, it is found that sulphonamide having more importance to treat the bacterial infections. Based on this present work is designed to synthesise sulphonamide with Schiff's base and evaluated their anti-microbial activity.

II. METHOD:

Synthesis of Sulphonamide containing Schiff's base derivatives:

Step - 1: Preparation of P- Acetamido benzene sulfonyl chloride
In a fume cupboard 10gms of acetamide was placed in 250ml round bottomed flask fitted with a dropping funnel containing 25ml of chlorosulfonic acid .The acid was added drop by drop with constant stirring after that it was subjected to reflux for 1 hour and then the reaction mixture was cooled and poured into 150ml of ice cold water with stirring, para- acetamido benzene sulfonyl chloride was precipitated and filtered in a Buncher funnel with solution. The residue was washed with ice cold water about 9gms of product was used for next step.

Step-2: Preparation of para-acetamido benzene sulfanilamide
To the entire para- acetamido benzene sulfonyl chloride obtained in the 1st step 35ml of liquid ammonia and 35ml of water were added in a 250ml of round bottomed flask in a fume cupboard. The contents were mixed by shaking and the mixture was heated just below the B.P. for 15min and the flask was cooled in the ice bath and the reaction mixture was filtered in a buncher funnel with suction washed with water. Dried well in an oven at 100c the yield of p- acetamido benzene sulfonilamide was noted.

Step-3: Preparation of sulphanilamide
In a 250ml round bottomed flask 6gms of p-acetamido benzene sulphanilamide, 10ml of dil.HCl & 10ml of water were taken, reflux condenser was fixed & boiled under reflux for 40-50 min until solid was separated on cooling .The solution was decolourised by adding 1gm of animal charcoal & boiled & then it is immediately filtered to the filtrate 6gms of $NaHCO_3$ was added slowly in

portions with stirring until effervescence of CO_2 was obtained. Sulfanilamide was repeated and filtered in a Buncher funnel and dried.

Step- 4: Preparation of sulphonamide containing Schiff's base
To the above sample formed in the step – 3 add 1ml Schiff's base. And then heat it for 20mins and then dried in oven at 50^0c for 20mins.

Procedure for preparation of Schiff's base:
Mix 1ml of aromatic aldehyde and 1ml of sample in a small evaporating- basin, place the latter on a boiling water bath and stir the mixture gently with a glass rod. Globules of water soon appear on the oily layer. After about 20 minutes place the basin in ice-water, and stir the content well, where upon solidification should rapidly occur. If the material does not solidify, replace the basin on the boiling water bath for a further 10minutes. Break up the solid material in the basin, transfer to conical flask, re-crystallise from rectified spirit.
The total scheme for the synthesis of Sulphonamide containing Schiff's base and their derivatives was represented in fig 1. The synthesized compounds were allowed for the calculation of molecular weight based upon molecular formula and determined the melting point. The values were presented in table-1. The synthesised derivatives were characterised by using IR –spectrum and the result was tabulated in table-2.

Anti-bacterial activity:
The synthesized compounds were subjected for anti bacterial study by paper disc diffusion method against the organisms Bacillus subtils, Bacillus aureus. Nutrient agar was used as media for the study. Nutrient agar (composition) is Peptic digest of animal tissue, Beef extract, Sodium chloride, Agar.

DISC DIFFUSION METHOD
A suspension of organism were added to sterile nutrient agar media at 45^o C and the mixture transferred to sterile petri dishes and allowed to solidify sterile discs 6mm in diameter (made from Whatmann filter paper previously sterilised in UV lamp) dipped in a specified concentrations. solutions of synthesised compounds and standards were placed on the surface of agar plates. A disc dipped in DMF was allowed to used as control. The plates were left for 1 hr at room temperature as a period of pre- incubation diffusion to minimize the effects of variation in the between the application of different solutions. The plates were then incubated at 37^oC ($\pm$ 1^oC) for 18 hrs and observed for antibacterial activity. The diameter of zone of inhibition were measured and calculated the area of inhibition zone compared with that of standard. The result was presented in table-3.

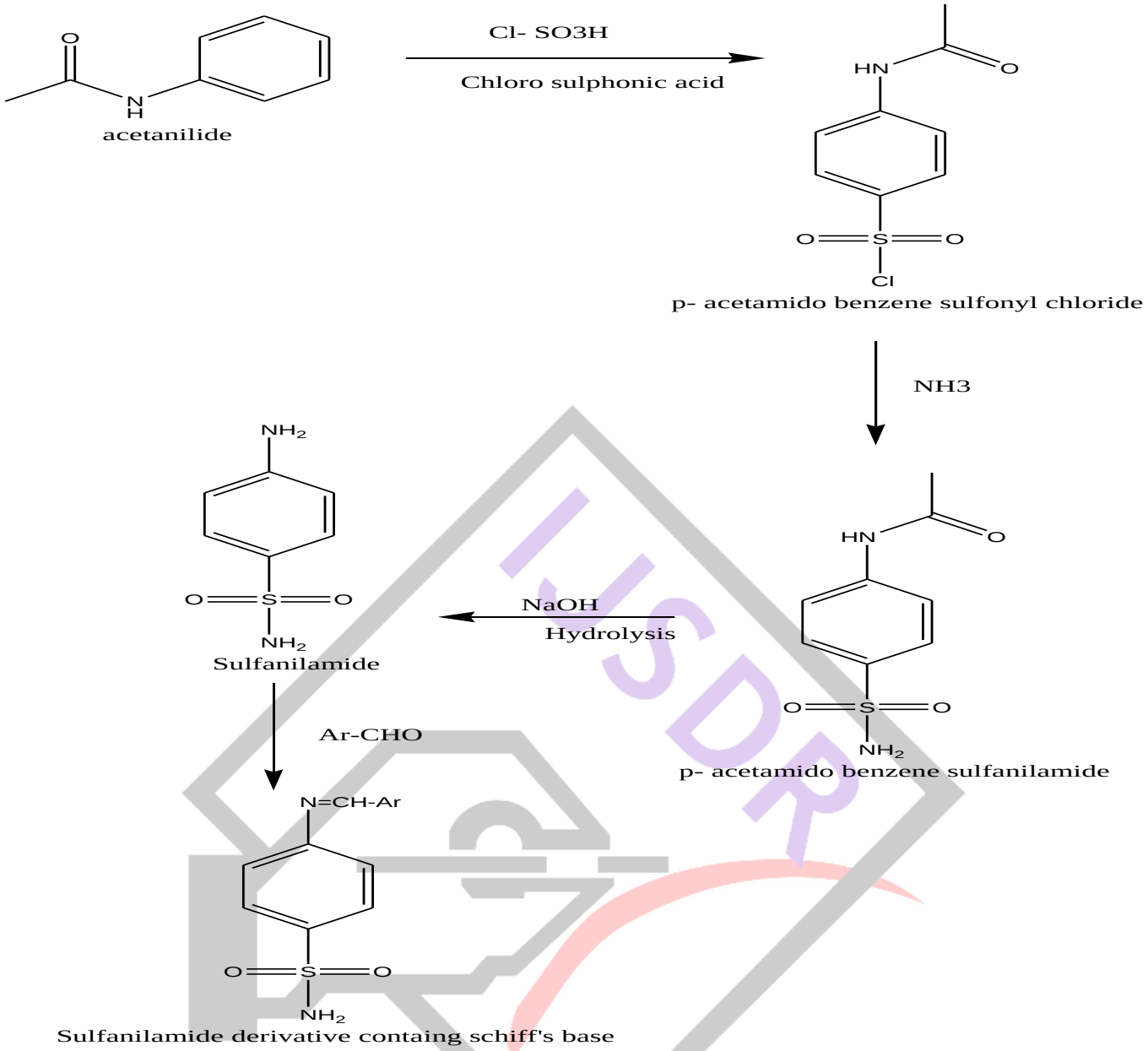
III. RESULT AND DISCUSSION:
All the synthesized compounds prepared from standard procedure. The Schiff's bases were synthesized from different substituted benzaldehyde in the presence of solvent or free solvent conditions. All the synthesized compounds in the present study subjected to determine the physical constituents like M.P &I.R spectrum values were reported in table-1 & table-2.

ANTIMICROBIAL ACTIVITY
All the synthesized compounds were screened for in-vitro antibacterial activity against bacteria by the disc diffusion method using various concentrations. All the synthesised compounds shows the antibacterial activity. Among these compound A and B shows the siginificant activity when comparing with the standard. After calculating the area of inhibition zone the compound B having more activity than the standard.

IV. CONCLUSION:
In our present study certain N-substituted sulphonamide derivatives were synthesised. The synthesised compounds were subjected to in-vitro anti-microbial evaluation. The zone of inhibition at various concentrations of synthesised compounds against gram-positive bacteria were determined by disc diffusion method. From the above results the anti-bacterial activities revelled that the substitution of amino group shows significant anti-bacterial activity.

Further studies can be done to get biologically more useful compounds in the series.

SCHEME



AROMATIC ALDEHYES (Ar-CHO):

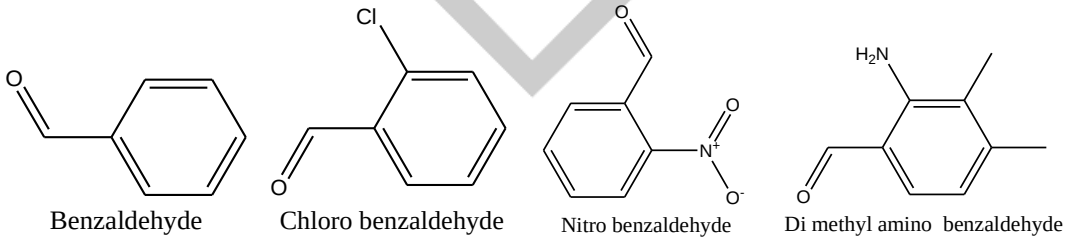


Fig-1: Synthesis of Sulphonamide containing Schiff's base and their derivatives.

MELTING POINTS

Table – 1: computation of molecular weight and melting point of synthesised compounds

COMPOUND NAME	MOL. FORMULA	MOL. WEIHT	AVG.MP(^{O}C)
Compound – A	$C_{13}H_{12}O_2N_2S$	260	240- 250
Compound – B	$C_{13}H_{11}O_4N_3S$	305	210- 220
Compound – C	$C_{15}H_{11}O_2N_3S$	303	102- 105
Compound – D	$C_{13}H_{11}O_2N_2SCl$	294.5	200- 210

I.R. SPECTRUM RESULTS

Table – 2: computation of I.R value of synthesised compounds

S.NO	COMPOUND	IR cm^{-1}
1	COMPOUND - A	C-N - 1310,C=N – 1656, C –S - 721, SO_2 – 1365 N –H – 3345, S-N – 935.
2	COMPOUND – B	C-N - 1286,C=N – 1703,C –S - 645,SO_2 – 1343, N –H – 3442,S-N – 910,C-NO_2 – 1592
3	COMPOUND – C	C-N - 1280,C=N – 1623,C –S - 775,SO_2 – 1331, N –H – 3286,S-N – 893,C-Cl – 698
4	COMPOUND – D	C-N - 1333,C=N – 1687,C –S - 775,SO_2 – 1330, N –H – 3288,S-N – 894

Table-3: antimicrobial activity of synthesized compounds

S.NO	Compound	Concentration (ug/ml)	Distance in mm	Area of zone of inhibition
1	Compound- A	700	3	7.065
		1000	5	19.625
2	Compound- B	700	3	7.065
		1000	12	113.04
3	Compound- C	700	1	0.0785
		1000	2	3.14
4	Compound- D	700	1	0.785
		1000	0	0

REFERENCES

[1] Y. Rajendra Prasad, P.Praveen kumar, Oriental,Chem Vol 23(3) 2007, 1069-1072
[2] Y. Rajendra Prasad, P.Praveen kumar,E.J.CemVol 5, No.1,2008, 144-148
[3] Tewari A K, Mishral, Verma HN & Misra A, Indian journal of chem.,41 B,2002,664.
[4] M E Abd EI- Fattah, *Indian journal of chemVol* 45 b 2523-2533
[5] Craiga. Zifcask and Dennis j. HLasta tetrahedron letters 46 (2005) 4789-4792.
[6] S SMahajan& R G Nandreindian journal of Chemvol 45-B 1756-1758.
[7] G.Ayhan, k, N.Altanlar Turk j Chem 30(2006) 223-228.
[8] NidaIqbal, JavedIqbal, Mummad Imran, journal of scientific research, vol. XXXIX No.1,june, 2009
[9] Erglu, E.Some QSAR studies for a group of sulphonamide Schiff base as carbonic anhydrase CA II inhibitors, int.J.Mol.Sci.2, 181-197.
[10] Ashish Kumar Tewari, Anil Mishra Indian Jan Chem 45 B, 2006, 489-493.
[11] Vogels text book of practical organic chemistry
[12] Walksman, S.A.Microbial antagonism and antibiotic substance, 2nd edition, commonwealth fund, 27, 1947.
[13] Maood- Ul- Hassan,Coan ZH, Scozzaifava A, Supuran CT., J Enzyme Inhib Med Chem. 2004 Jun; 19(3)263-7.
[14] - Ul- Hassan M, Scozzaifava A Coan ZH, Supuran CT., J Enzyme Inhib. 2001 Dec; 16(6): 499-505.
[15] Bhat MA. Imran M. Khan S A and siddiqui N. Biological activities of sulphonamides. Indian journal of pharmaceutical science 2005; 67: 151-159.
[16] Patel A. Bari S, Telele G, pate J. Saraangapani M. Synthesis and antimicrobial activity of some new isatin derivatives. Iran. J. Parm.Sci. 2006; 4: 249-254.

[17] Wang L, Feng Y. Xue J and Li Y. Synthesis and characterisation of novel pophyrin Schiff bases, J Serb Chem Soc. 2008; 73: 1-6.
[18] Santhosh Kumar, Niranjan MS, Caluvaraju KC, Jamakhandi CM and DayanandKadadevar.J.Curr.Pharm.Res. 2010; 1 (1): 39-42.
[19] Evans, D.A.; Nelson, S.G.J. Am. Chem.Soc.1997, 119, 6452-6453.
[20]Calligaris, M.; Nardin, G.; Randaccio, L. Coord. Chem. Rev. 1972, 385-403.