SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF SUBSTITUTED SALICYALDEHYDE SCHIFF BASE DERIVATIVE

Shere Priti H.*,1, Shaikh Amreen S.2 and Khobragade Chandrakasya N.3

School of Life Sciences, Swami Ramanand Teerth Marathwada University, Nanded, India-431606.

*Corresponding Author: Shere Priti H.
School of Life Sciences, Swami Ramanand Teerth Marathwada University, Nanded, India-431606.

ABSTRACT

The new Substituted salicyaldehyde Schiff base derivative was synthesized by condensing 3,5-dibromosalicylaldehyde with 4-chloroaniline in ethanol in the presence of glacial acetic acid. Forming new substituted Schiff base derivative 2,4-dibromo-6-[(4-methylphenyl)imino[methyl]phenol]. Synthesis was ascertained with 1H NMR, FTIR, and Mass Spectroscopic studies. Substituted Schiff base derivatives were evaluated for their antimicrobial potential. Schiff derivative investigated have shown significant antimicrobial activity against bacteria Escherichia coli, Staphylococcus aureus and fungus candida albicans.

KEYWORD: Schiff derivatives, 1H NMR, FTIR, Mass Spectroscopy, Antimicrobial activity.

1. INTRODUCTION

The status of Schiff base complex for catalysis, bioinorganic chemistry, biomedical applications, encapsulation processes, and formation of compounds with unusual properties and structures has been well recognized. When the primary amines and carbonyl compounds were subjected for condensation it forms Schiff base.[2,19] Schiff base contains the azomethine group with general formula RHC=N=NR1 where R and R1 is any functional group like alkyl, cyclo alkyl or aryl.

Schiff bases have huge advances in medicine as some of them are biologically active. They have been used as antibacterials,[2,3] antifungals,[13] and antitumor.[7,14] Several Schiff bases which are reported to be therapeutically active possess anticancer activity.[4,6] The metal complexes of Schiff bases have been used as active drugs against tuberculosis.[11,16] Schiff bases derived from sulpha drugs and salicylaldehyde have been found to be good chelating agents.[10,17] Recently the research field dealing with Schiff base application has extended immensely.

The Schiff’s bases are synthesized by condensation of primary amine with compound containing carbonyl group. Compounds containing azomethine group are basic in nature, as N atom of this group has a lone pair electrons and the double bond has electron donating character. Compounds have been evaluated for their antibacterial activity and the biological activities compared with standard drugs.

2. MATERIALS AND METHODS

2.1. Chemistry

A Schiff base is a nitrogen analogue of an aldehyde or ketone in which the C=O group is replaced by C=N-R group.[22] It is usually formed by condensation of an aldehyde or ketone with a primary amine. The synthesis of substituted salicyaldehyde Schiff base derivative was carried out as shown in figure 1.

2.2. Synthesis of substituted Schiff base derivatives

The Schiff base 3,5-dibromosalicylaldehyde was condensed with 4-chloroaniline and bromine substituted Schiff bases in ethanol in presence of glacial acetic acid forming the substituted Schiff bases. The completion of reaction was checked by thin layer chromatography. 0.01 mole of bromide substituted salicylaldehyde was dissolved in 15 ml of ethanol at room temperature. Then 0.01 mole of substituted aniline and 0.5 mole glacial acetic acid was added. The reaction mixture was refluxed in water bath for 1-2 hours. After reaction completion it was allowed to cool down. The separated solid was filtered, dried and recrystallized by ethanol.[23] The structures of substituted Schiff base was analysed by 1H NMR, FTIR and Mass Spectroscopy. The Structure of compounds analysed is given below:
2.3. Nuclear Magnetic Resonance (¹H NMR Spectroscopy)
¹H NMR spectra were recorded on a Bruker DPX 300 MHz in chloroform-d₆. Chemical shifts are reported in ppm with the internal TMS signal at 0.0 ppm as a standard. Chemical shifts are the most easily measured NMR parameters and carry important structural information.

5A Compound yield 70%, orange, 130°C; 2.2-3 (2.398 Ar-C-H), 2.5-4 (3.518 HC-Br), 3.4-4 (3.518 HC-OH), 3.3-4 (HC-OR), 2.2-6 (HC-COOH), 2-2.7 (HC-C=O), 2.4-(R-OH), 4-12-1.5-5-8.5 [8.539, 7.745, 7.737, 7.482, 7.474, 7.227, 7.206, 7.198 AR OH, R-NH₂, RNHC(=O)R'] (Figure 2)

2.4. Fourier Transform Infrared Spectroscopy (FTIR Spectroscopy)
5A Compound: 3135.05 (S) C=H stretch-COOH; 1565.98 (m) C-C stretch (in ring)-Ar; 1400.43 (m) C=O stretch (in ring)-Ar; 1213.92 (s) C-O stretch, -OH, -COOH, -R-O-R, COOR; 1161.27, 1114.35 (m) C-N stretch, aliphatic amines, 1069.24 (m) C-N stretch, aliphatic amines, 991.79, 912.93 (m) O-H bend –COOH; 853.83 (s, b) N-H wag 1° & 2° amines; 808.06 (s, b) N-H wag 1° & 2° amines; 690.14 (s, b) N-H wag 1° & 2° amines; 613.95 (m) C-Br stretch, aliphatic amines, 529.69 (m), C-Br stretch, alkyl halides (Figure 3)

2.5. MASS Spectroscopy
The substituted salicyaldehyde Schiff base derivatives were ionized with 20-140 eV where substituent at meta and ortho position peaks were observed in the base peaks. It represents ion having specific mass to charge ratio (m/z) and the length of the bar indicated the relative abundance of the ion (Figure 4). The Mass spectrometry analysis shows the (m/z) ratio at each peak by calculating this we get the molecular weight of substituted salicyaldehyde Schiff base derivatives and was found to be (m/z) 369 Daltons. It also confirms the structure of substituted salicyaldehyde Schiff base derivative as C₁₄H₁₃ONBr₂ with Br-43.36; N-3.79.
3. Antimicrobial Activity/Disk diffusion Assay

In a Kirby-Bauer test, the size of the zone of inhibition indicates the degree of sensitivity of microbes to a compound. In general, a bigger area of microbe-free media surrounding the disk means the microbes are more sensitive to the compound the disk contains. Bacterial culture of Gram positive *Staphylococcus aureus* and Gram negative *Escherichia coli* were enriched in nutrient broth and was allowed to incubate overnight at 37°C with 150 rpm. Mueller Hinton agar was prepared and autoclaved at 121 lbs for 10 minutes. Mueller Hinton agar plates were prepared and allowed to solidify at room temperature. The Bacterial inoculum was prepared in the 0.1N saline, a loopful of suspension was taken by using sterile nichrome wire loop and it was suspended in 3ml of sterile saline. Vortexes slightly to create a smooth suspension as per 0.5Mac farland standard. The suspension culture of fungus *Candida albicans* was prepared in 3ml of saline and tween 20 is added to this suspension. Sterile swab was used to spread the inoculum/suspension on the sterile petriplates. Each culture was inoculated on the dried surface of Mueller Hinton agar plate by spreading the swabs over the entire agar plate. For the even distribution of the inoculum or suspension swab was spreaded by rotating the agar plated.

Figure 3: Fourier Transform Infra-red Spectroscopy analysis of compound 5A.

Figure 4: Mass spectroscopic analysis of compound 5A with the molecular weight of 369Dalton.

The stock solution of Compound 5A was prepared by mixing of 1mg of compound in 1ml of DMSO solution. Then different concentrations such as 50µg/ml, 100µg/ml, 250µg/ml, and 500µg/ml were prepared. After the placing sterile disk on MHA plate, different concentrations of compounds was added with the help of micropipette on MHA plates with Standard drugs used penicillin, streptomycin and fluconazole. These plates were incubated at 37°C for 24 hours for bacterial culture and 72 hours for fungal culture. After incubation results were observed. The zone inhibition was measured with the help of Himedia measuring scale. It includes the diameter of the disk in the measurements. The zone in which the growth is up to the edge of the disk is noted as 0 mm (Table.1).
The synthesis of substituted salicylaldehyde Schiff base derivative 2,4-dibromo-6-[(4-chlorophenyl) imino]methyl] phenol was carried out. Compound was characterized with 1HNMR, FTIR and Mass Spectroscopy. The Mass spectral analysis shows molecular weight of 369 Dalton and the structure was also confirmed. The substituted salicylaldehyde Schiff’s derivative exhibits antibacterial as well as antifungal activities. The Kirby-Bauer Disk diffusion assay studies shows that bacteria Staphylococcus aureus and Escherichia coli are sensitive to the compounds 2,4-dibromo-6-[(4-chlorophenyl)imino]methyl]phenol. As the concentration of compound increases, zone size is also increases. Compound shows antifungal activity against Candida albicans and zone of inhibition was found to be higher than that of bacterial zones.

5. CONCLUSION
Schiff base compounds have been widely explored for industrial applications however, the biological activity of this class of compounds deserves further investigation. New substituted Schiff base derivative was synthesized by condensation of 3,5,-dibromosalicylaldehyde with 4-chloro aniline in ethanol along with glacial acetic acid. Further evaluation laid by 1HNMR, FTIR and Mass spectroscopy. Schiff base compounds have been shown to be promising leads for design of more efficient antimicrobial agents. Advances in this field will require analyses of structure activity relationship of the Schiff base as well as the mechanism of these compounds. The synthesized compound possesses antibacterial and antifungal activity. The synthesized substituted salicylaldehyde derivatives were shown to exhibit biological activity when subjected for antimicrobial studies Staphylococcus aureus, Escherichia coli are found to be sensitive to this compound. The Fungus Candida albicans is also susceptible to the substituted salicylaldehyde Schiff base derivatives.

ACKNOWLEDGMENT
I would like to thank Indian Institute of Chemical Technology, Hyderabad for Mass Spectroscopic analysis. I also thank Vishnu Chemicals, Hyderabad for 1HNMR, FTIR spectral studies.

REFERENCES
5. Karthikeyan MS, Prasad DJ, Poojary B, Subrahmanya Bhat K, Holla BS, Kumari NS, Synthesis and biological activity of Schiff and Mannich bases bearing 2,4-dichloro-5-fluorophenyl.


