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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF SCHIFF BASE

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Abstract – Schiff bases are heterocyclic compounds and heterocyclic compounds have hetero-atoms like Nitrogen, Sulphur, and Oxygen with Carbon structure. Similarly, Schiff bases, along with carbon and hydrogen, have nitrogen and oxygen in their structure. Schiff bases show multiple activities in the field of science and biological activity is one of them. In the present study, 2TMBAMP Schiff base shows its biological activities like antibacterial and antifungal activity. Schiff base was synthesized and depicted with elemental analysis, FTIR, and ^{1}H-NMR spectroscopy. Here, Schiff base was evaluated for its antimicrobial activity with agents such as E. coli, S. aureus, C. albicans, A. flavus.

Key Words: Heterocyclic compounds, Schiff base, Antimicrobial activity, Antibacterial activity, Antifungal activity.

1. Introduction –

Heterocyclic compounds are essential to life in various ways and distributed across nature. According to the heterocyclic compound investigation, heterocyclic makes up 69 percent of drugs in the late stages of development that are already on the market (1-2). Schiff base was named after Hugo Schiff, who discovered them in 1864, a German chemist and Nobel Prize winner. Schiff base ligands are considered as privileged as they are synthesized by condensation of primary amines and carbonyl compounds as aldehydes or ketones (3). Schiff bases are considered as important class of compounds because it had abilities to form complexes with transition metal ions (4).

Schiff bases play vital roles in modern coordination chemistry and bioinorganic chemistry. Schiff base has pharmacological properties because it shows broad application in medicine. The main reason is >C=N— in azomethine derivatives is essential for biological activities and they were reported to possess antimicrobial (antibacterial, antifungal), anticancer, and diuretic activities (6).

Schiff base ligands mainly have some specific properties as easily synthesized, available, and electronic properties so it became the cause of their extensive studies. Schiff base coordination chemistry has attracted attention due to its significant role in analytical chemistry, organic synthesis, refining of metal, electroplating, metallurgy, and photography (5). Food and dye industry, analytical chemistry, catalysis, fungicidal, and agrochemical activities are wide applications of Schiff bases [7]. Schiff base complexes have unusual properties and structures so they have been showing importance in supramolecular chemistry, catalysis & material science, and the separation and encapsulation process, biomedical applications and formation of compounds with unusual structures and properties have been recognized as well as reviewed [8].

According to the study in biological systems, the nitrogen of Schiff base provides binding sites for metal ions to be attached with various biomolecules (proteins, amino acids, etc.) for anti-germ activities. Our body catalyzes many metabolic reactions in the form of enzymes, which show activities against various microbes. Various research on the bio-functions of Schiff bases and their metal complexes described that they have anti-bacterial, antifungal, antiulcer, antiviral, and anticancer activities depending upon the transition metal ions present in Schiff bases [9].

Last few decades studies on Schiff bases and their metal ligands complexes have been many reports on their applications specifically in biological fields including antibacterial, antifungal, anticancer, anti-inflammatory, anti-malarial, antioxidant, and antiviral activities [10-17]. This review highlights the Schiff bases and their biological aspects, especially among their versatile applications from 2000 to the present day.

2. EXPERIMENTAL SECTION –

Each chemical and reagent, which is used in reactions, was procured from their retail outlets. To determine the melting points, the open capillary technique was used and the obtained data were not modified in any way. For thin-layer chromatography (TLC), iodine vapors were used to analyze the spots, while it was observed on the silica gel-coated glass plates. FTIR and ^{1}H-NMR spectroscopy were used to test the characterization of the 2TMBAMP Schiff base. A Bruker Advance Neo 500MH$_z$ NMR spectroscopy helped to generate the ^{1}H-NMR spectra by using tetramethyl silane (TMS) internal standard and DMSO as the solvent. FTIR was performed using Perkin Elmer Spectrum version 10.4.00 and a universal sampling system for measurements in the range of 4100-400 cm^{-1} for solid sample in KBr pellet.

2.1 Antimicrobial activity –

Micro-organisms are widely stretched in the environment and have become a part of our daily lives. They play a significant role in the ecosystem on the earth. Some of the microbes provide comprehensive and crucial benefits. An antimicrobial activity of an agent is the tendency to destroy micro-organisms like bacteria, and fungi or to stop further growth. The action against micro-organisms can be classified as antibiotics against bacteria or antifungals against fungi. The incorporation of hetero atoms of Schiff base has made it an antimicrobial agent. These compounds reflect impressive antimicrobial activity.

2.1.1 Antibacterial assay by well diffusion method -

The Agar Well Diffusion method, which is also known as the Standard microbial technique **(Perez and Anesini,1994),** is used for in-vitro antibacterial assay. The different samples were diluted by using 10% dimethyl sulphoxide (DMSO) and 3 different concentrations of 50 µg/ml, 100 µg/ml, and 150 µg/ml of Schiff base were prepared. The nutrient agar (NA) medium held via disinfected petri dishes was used for the inoculation of test microorganisms, this inoculum was spread all over the dish using a spreader and kept to stand for 30 min. In the seeded agar plates, wells of 6 mm diameter were prepared. Control well was also prepared at an equal distance. Various concentrations of all the samples and standard drug (30 µl) were poured into the preorganized wells of seeded plates. The plates were kept for incubation for 24 hrs at 37ºC temperature. The antibacterial spectrum of the test sample was determined via the inhibition zone (IZ) around each prepared well. The comparison of diameters of the inhibition zone developed by the test sample was done via the commercial control antibiotics cipro (1 µg/ml).[22]

2.1.2 Antifungal assay by well diffusion method -

We used the Agar Well Diffusion method for in-vitro antifungal assay. The various samples were diluted by using 10% dimethyl sulphoxide (DMSO) and 3 different concentrations of 50 µg/ml, 100 µg/ml, and 150 µg/ml of Schiff base were prepared. The potato dextrose agar (PDA) medium held in disinfected Petri dishes was used for the inoculation of test microorganisms, this inoculum spread all over the dish using a spreader and was kept to stand for 30 min. In the seeded agar plates wells of 6 mm diameter were prepared. Control well was also prepared at an equal distance. Various concentrations of Schiff base and standard drug (30 µl) were poured into the preorganized wells of seeded plates. The plates were kept for incubation for 24 hrs at 37ºC temperature. The antibacterial spectrum of the test sample was determined by measuring the inhibition zone (IZ) around each prepared well. We compared the diameters of the inhibition zones produced by the test sample with those produced by the commercial control antibiotic ketoconazole (1 mg/ml).[23]

3. SYNTHESIS AND CHARACTERIZATION OF SCHIFF BASES –

Schiff bases are formed by the condensation of an amine with a carbonyl compound and that compound contains an azomethine group (-CH=N-).

Yield: 78%,

m.p. - 68°C,

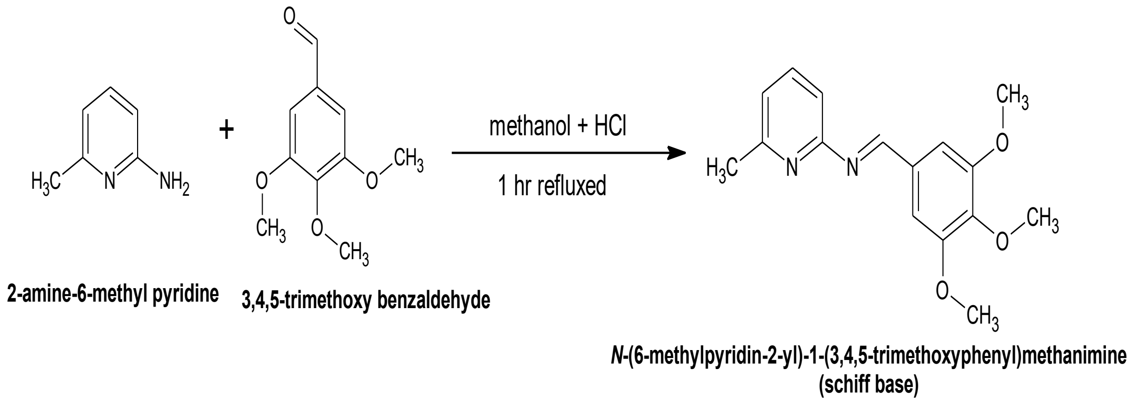


Fig 3.1 Reaction scheme for Schiff base (E)-N-(6-methylpyridin-2-yl)-1-(3,4,5-trimethoxyphenyl)methanimine (2TMBAMP) formation

FTIR: IR (KBr, cm^{-1}): 2976.54 (Ar-H stretch); 1685.39 (s), 1587.40(s) (υC=N); 1424.85 (w), 1380.41 (w), 1330.05 (w) (υC-N); 1235.53 (C-O stretching); 1504.97(s), 1461.51(m) (C=C vibration); 1127.24(w)(C-H in plane); 991.74(m), 845.14(w), 729.81(m)(C-H out of plane);

^{1}H-NMR: δ 3.7690 [6H,m-OCH_3(s), J=3.43]; 3.8581 [3H,p-OCH_3(s), J=6.50]; 7.051 [1H,dd]; 7.2352 [1H,dd, J=2.01]; 9.8713[1H,s,J=1.00]; 2.3274, 2.5076[3H,s]; 7.668[1H,t]; 7.079[d, 2H].

4. BIOLOGICAL ASPECTS OF SCHIFF BASES –

Schiff bases are the most widely used organic compounds in chemistry. They have been shown to exhibit a broad range of biological activities including antifungal, antibacterial, antimalarial, antiproliferative, anti-inflammatory, antiviral, and antipyretic properties, etc. In this paper, we have to summarize the biological activities of the 2TMBAMP Schiff base.

Antimicrobial Activity –

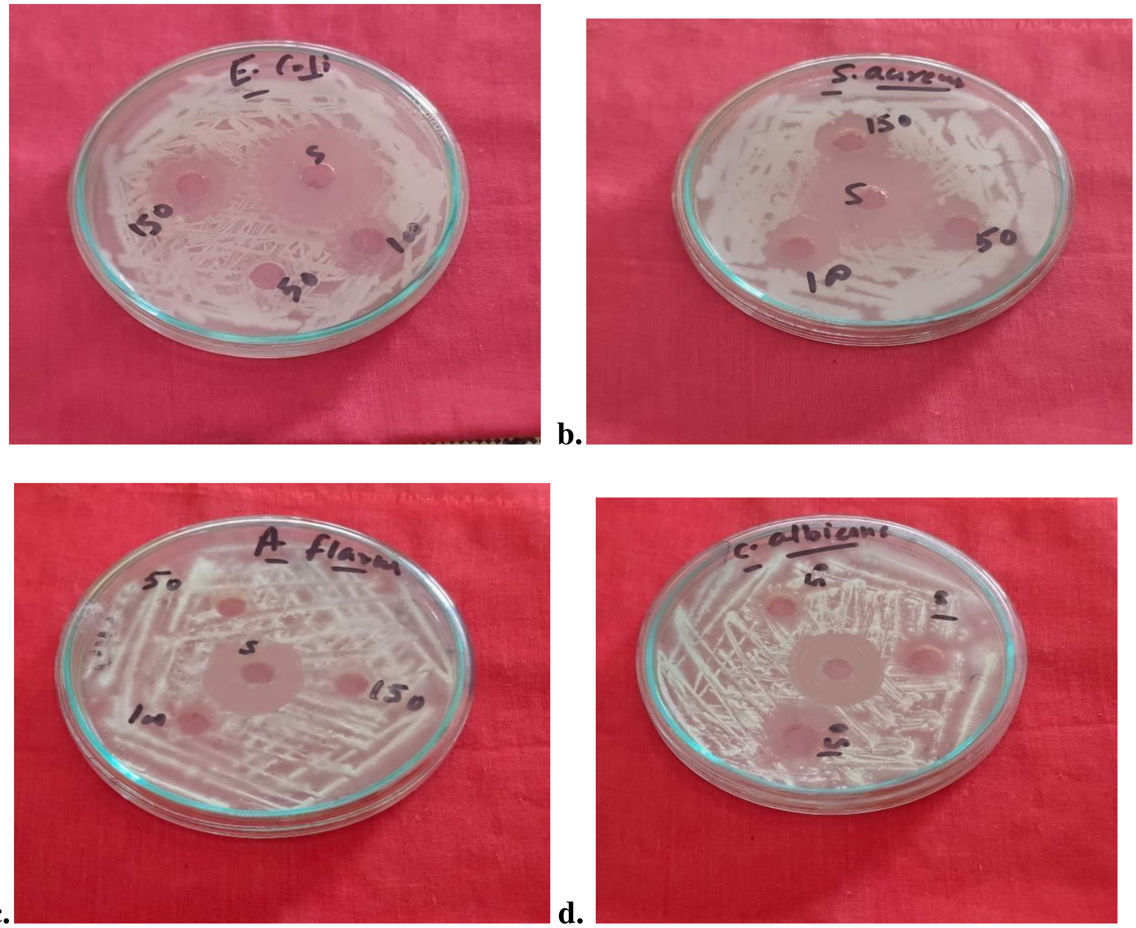
An antimicrobial activity agent tends to reduce their growth or kill microorganisms like bacteria, fungi, etc. Based on their action against micro-organisms, these can be classified as antibiotics that work against bacteria and antifungals used against fungi. Schiff bases have this specific application and their metal complexes can also make them antimicrobial agents. These compounds contain impressive antimicrobial activity [18]. The tendency to kill bacteria or reduce their growth rate is called anti-bacterial activity. Many Schiff bases are chemically stable and mostly fight against infectious diseases.

Table 1: antimicrobial activity of the given compound –

Name of compound	Concentrations (µg/ml)			
	50	100	150	
	IZ	IZ	IZ	Standard
E. coli	3	11	15	36

S. aureus	11	14	17	32
C. albicans	6	9	13	30
A. flavus	NA	3	5	28

note: NA-No activity, IZ- Inhibition zone (mm),



a. b. c. d.

Fig. 4.1 Antibacterial activity of Schiff base 2AMBTBP against a.) E. coli, b.) S. aureus and Antifungal activity of Schiff base 2TBMAMP against c.) A. flavus, d.) C. albicans

The disc-diffusion technique was employed to assess the newly synthesized Schiff base for its potential to prevent bacterial growth in vitro. In addition, these tests were carried out to determine the capabilities of the substance. Depending on the specific type of pathogen used, 50, 100, and 150 µg/ml was the concentration of Schiff base used for the pathogens. This collection of pathogens comprised both Gram-positive and negative strains of the bacterium S. aureus and E. coli.

Using this technique mentioned above, the size of the zone of inhibition in the nutritious agar media was calculated in millimeters. To produce the concentration solutions for the Schiff base, the compound was first allowed to dissolve in DMSO before being mixed. When the common antibiotic Cipro was used, it revealed an inhibitory zone of 15 millimeters for E. coli (36 standards) and 17 millimeters for S. aureus (32 standards) at 150 milligrams per milliliter concentration. The findings are outlined in Table 1, which may be seen further down on this page.

In a manner analogous to this, the disc diffusion technique was utilized to evaluate the Schiff base for its ability to inhibit fungal growth. A. flavus and Candida albicans, separate fungus species, were tested at levels of 50, 100, and 150 µg/ml concentration of Schiff base, respectively. In the experiment, which used the medication ketoconazole as a point of comparison, the zone of inhibition for A. flavus measured 5 millimeters (28 standards), while the zone for C. Albicans measured 13 millimeters (30 standards). The findings are summarized in Table 1, which may be seen below.

5. Conclusion –

Antibacterial activities of Schiff base are studied on E. coli and S. aureus, where S. aureus shows the maximum antibacterial activity at 150µg/ml concentration of 2TMBAMP Schiff base compound. While E. coli reflects the minimum control at 50µg/ml concentration of 2TMBAMP Schiff base compound. Antifungal activities of Schiff base are studied on C. albicans and A. flavus, where C. albicans represents the maximum antifungal activity at 150µg/ml concentration of 2TMBAMP Schiff base compound. While A. flavus presents the minimum control at 50µg/ml concentration of 2TMBAMP Schiff base compound. Hence we can conclude that the Schiff base effectively controls the microbial activities against these three microbes (E. coli, S. aureus, and C. albicans) while ineffective when it comes to A. flavus. The present research can support the new researchers for further characterization and estimating different Schiff base compounds for developing new useful antimicrobial agents.

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