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Review Article

Schiff's Base of Different Sulfonamides

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ABSTRACT

Schiff's bases of sulfonamides represent a vital class of biologically active compounds with diverse pharmacological applications. Sulfonamides, initially developed as potent antibacterial agents, have been modified through Schiff's base formation to enhance their therapeutic potential while minimizing adverse effects. Schiff's bases, also known as azomethines (-C=N-), are synthesized by condensing sulfonamide derivatives with aldehydes or ketones under controlled reaction conditions. These compounds exhibit remarkable structural versatility, allowing them to form stable metal complexes with transition metals such as Cu, Co, Ni, and Zn. The chelation of Schiff's base ligands with metal ions often results in enhanced bioactivity, attributed to increased lipophilicity and improved interactions with biological targets. This Article comprehensively discusses the synthesis, structural characterization, and pharmacological significance of Schiff's bases derived from sulfonamides. Various synthetic strategies, including acid/base-catalyzed condensation and metal complexation, are explored alongside their spectroscopic characterization using FT-IR, NMR, and mass spectrometry. The biological activities of sulfonamide-based Schiff's bases are critically evaluated, highlighting their antimicrobial, anticancer, anti-inflammatory, antitubercular, and antiviral properties. Studies indicate that Schiff's bases exhibit superior pharmacological effects compared to their parent sulfonamides, particularly in their metal-coordinated forms. The findings underscore the potential of Schiff's base metal complexes as promising candidates for drug development. Further research into their mechanism of action, pharmacokinetics, and clinical applications is necessary to optimize their therapeutic efficacy. This Article aims to provide valuable insights into the expanding role of Schiff's bases in medicinal chemistry.

INTRODUCTION

The first class of clinically used, potent antibacterial medications were sulfonamides, or "sulfa-drugs," which paved the way for antibiotics

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in the medical field. Sulfa-drugs are still one of the most significant medication classes, and research has continued to harness their antibacterial capabilities by striking a balance between pharmacological efficacy and decreased toxicity. However, their use decreased in the early part of this decade due to some well-known adverse effects.[1-3] SCHIFF'S Base, a versatile substance discovered by physicist Hugo SCHIFF'S, is formed when important amines accumulate with carbonyl mixtures under clear-cut reaction circumstances. They are also known as azomethine (-C=N-) or imine. Aldehydes cause SCHIFF'S base ligands to form more quickly than ketones. Focus on SCHIFF'S basis has been completed due to its highly flexible personnel and diverse designs. Sturdy structures with metal particles make up SCHIFF'S basis. Many SCHIFF'S bases exhibit synergistic activity in various responses at very high temperatures and in the presence of moisture. SCHIFF'S bases containing sulfonamides also exhibit several organic qualities, such as antimicrobial, anticonvulsant, antitubercular, anticancer, cell reinforcement, antimalarial, antibacterial, antiviral, antitumor, anti-inflammatory, and anthelmintic.[4]

SYNTHESIS OF SCHIFF'S BASES

When an aldehyde or ketone reacts with an amine by base or corrosive catalysis, or after heat and water is ejected, a SCHIFF'S base is formed. Unlike aliphatic aldehydes, fragrant aldehydes have a structure that is persistent due to their strong formation.[4]

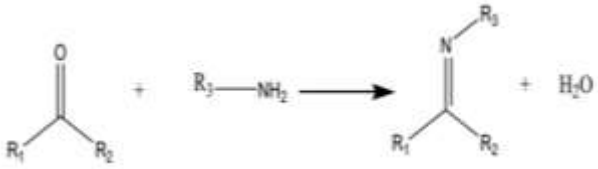


Figure 1:General synthesis of SCHIFF'S base

SYNTHESIS OF SOME SULFONAMIDES-BASED SCHIFF'S BASES :

By refluxing 3-aminobenzenesulphonamide with 2-hydroxy-7-methylquinoline-3-carbaldehyde and 2-hydroxy-7-methoxyquinoline-3-carbaldehyde in ethanol using con. H2SO4 as a catalyst for 5 hours at 75 °C, Athar et al. created the SCHIFF'S base ligands, 3-{[(1E)-(2-hydroxy-7-methylquinolin-3-yl)methylene]amino}benzenesulphonamide and 3-{[(1E)-(2-hydroxy-7-methoxyquinolin-3-yl)methylene]amino}benzenesulphonamide. For five to seven hours at 70 to 75 degrees Celsius, the resulting SCHIFF'S bases were refluxed with Cu, Co, Ni, and Zn salts in a 2:1 ratio. Gram-positive bacteria like Bacillus cereus and Streptococcus pneumoniae, as well as gram-negative bacteria like Escherichia coli and Klebsiella pneumoniae, were tested for the antibacterial activity of the synthesized ligand and complexes using the disc diffusion technique. The findings demonstrated that the metal chelates outperformed the SCHIFF'S base ligands in terms of antibacterial activity.[5]

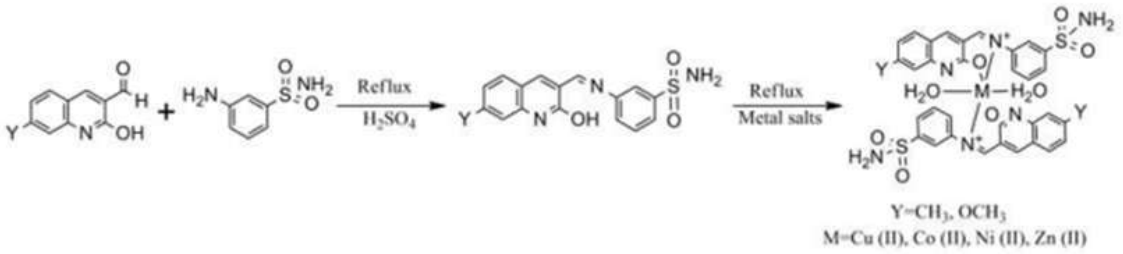


Figure 2: 3-{[(1E)-(2-hydroxy-7-methyl/methoxy quinolin 3yl)methylene]amino}benzenesulphonamide SCHIFF'S base

By refluxing 1 mmol of cephalexin and 1 mmol of sulphathiazole in hot methanol, Anacona et al. created a sulphathiazole-based SCHIFF'S base. The reaction mixture was then refluxed in a nitrogen environment at 70 °C for three hours. Metal acetate salts of manganese, cobalt, nickel, and zinc dissolved in water were gradually added to the ethanolic solution of SCHIFF'S base ligand while being constantly stirred. A potassium hydroxide solution was then added to bring the pH down to 7-8, and the reaction mixture was refluxed for four hours. When the SCHIFF'S base ligand and its metal chelates were tested against Staphylococcus aureus and E. coli, the results showed that the ligand had a zone of inhibition of 12.0 ± 1.0 and 15.0 ± 1.0 mm, while the metal complexes showed a zone of inhibition of 6.0 ± 1.0 and 18.0 ± 1.0 mm against the two bacteria.[6]

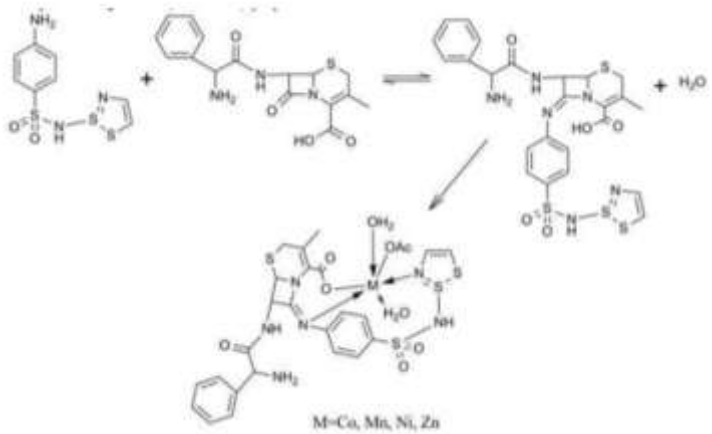


Figure 3:Synthesis of sulphathiazole-based SCHIFF'S base metal complexes

4-{[(Z)–(5-Bromo-2 hydroxyphenyl) methylidene] amino} was made by Chohan and associates. 4-(2-{[(E)–(5- Bromo-2-hydroxyphenyl) methylidene] amino}ethyl)-benzenesulphonamide SCHIFF'S bases by refluxing the ethanolic solution of sulphamethoxazole and 5-bromosalicylaldehyde for three hours while stirring continuously. Cu, Co, Ni, and Zn salts were added to a hot magnetically stirred dioxane SCHIFF'S base and refluxed for two hours. In vitro antibacterial and antifungal activity were assessed for SCHIFF'S base ligands and metal complexes against the following bacterial and fungal strains: Candida glabrata, A. flavus, Fusarium solani, Microsporum canis, Shigella flexneri, E. coli, and P. aeruginosa. The findings showed that ligand coordination enhanced their antibacterial and antifungal activities. By lowering the polarity of the transition metal ion by coordination with ligands, the chelation/coordination process makes the metal more lipophilic. The metal's ability to penetrate the lipoid layer of the microorganism's cell membrane was aided by its lipophilic nature. The Brine shrimp bioassay was used to assess the cytotoxicity of the SCHIFF'S base ligands and metal complexes. The results indicated that all of the complexes were more active, with the Zn complexes of 4-(2-[(E)–(5- Bromo-2-hydroxyphenyl)methylidene]aminoethyl)-benzenesulphonamide demonstrating exceptional cytotoxic activity against Artemia salina.[7]

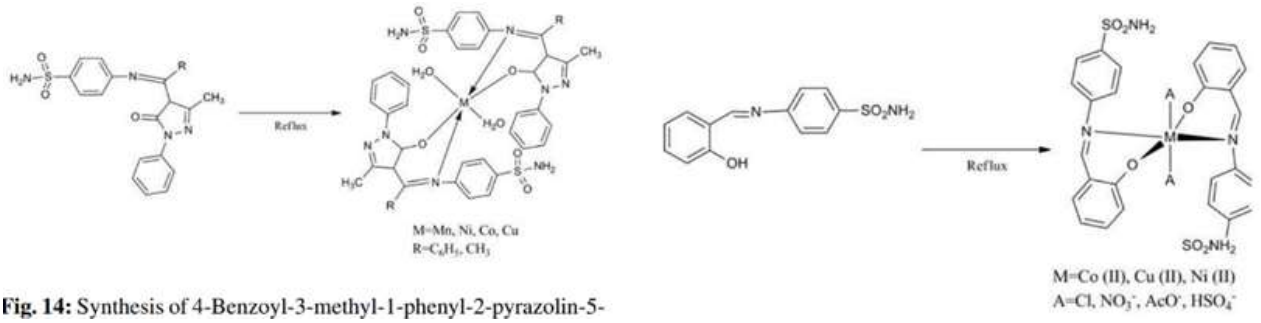


Fig. 14: Synthesis of 4-Benzoyl-3-methyl-1-phenyl-2-pyrazolin-5-

Figure 4:Synthesis of Sulphamethoxazole-5-bromosalicylaldehyde SCHIFF'S base

By refluxing sulfanilamide and salicylaldehyde, Ul-Hassan et al. created SCHIFF'S base based on sulfanilamide. An aqueous solution of copper, cobalt, and nickel was refluxed with the hot ethanolic solution of SCHIFF'S base for three hours in order to create the metal complexes. The SCHIFF'S base metal complexes demonstrated a higher affinity for binding to the isoenzymes hCA I, II, and IV than the parent form, and the carbonic anhydrase inhibitory action of SCHIFF'S base was found to be mild-moderate against these vital physiological processes.[8]

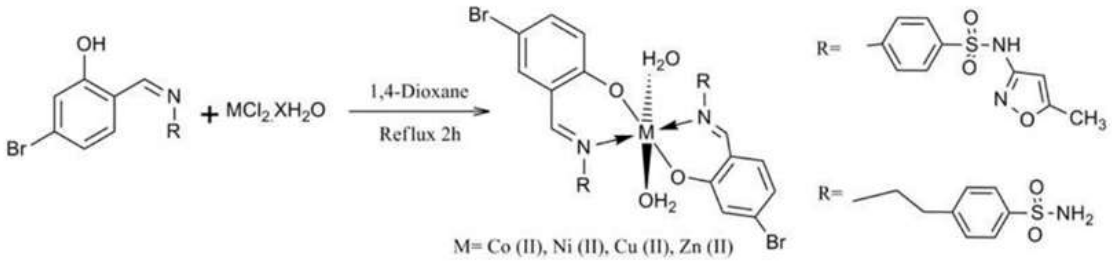
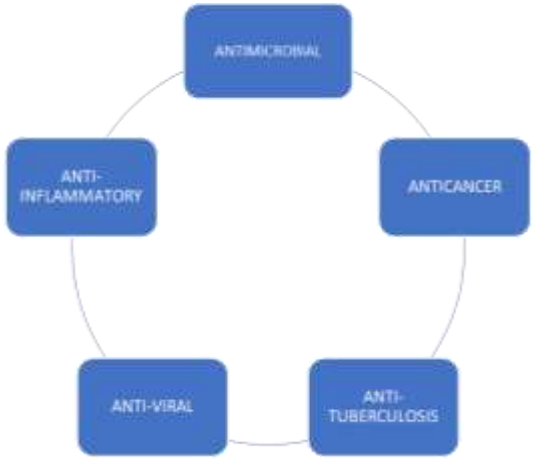


Figure 5:Synthesis of sulphanilamide-salicylaldehyde SCHIFF'S base metal complexes

BIOLOGICAL ACTIVITIES SHOWN BY SULFONAMIDES-BASED SCHIFF'S BASES:

Schiff's bases exhibit antimicrobial, anticancer, antituberculosis, antiviral, and anti-inflammatory biological activities.[9-15]



CONCLUSION

Because SCHIFF'S bases include azomethine nitrogen, they are an important class of ligands in coordination chemistry and are easy to synthesize with inexpensive catalysts. In coordination chemistry, SCHIFF'S base ligands have garnered a lot of interest due to their easy synthesis, broad availability, and advantageous electronic properties. Sulphonamides' efficient oral absorption and urine excretion make them an important class of drug-like chemical compounds with wide biological importance. The production and pharmacological uses of SCHIFF'S base metal complexes made from sulfanilamide are discussed in this article. There are many medicinal uses for the sulphonamide SCHIFF'S base metal complexes because of its reduced toxicity, increased reactivity, and reduced cost. According

to the study, the metal complexes and SCHIFF'S bases made from sulphonamide derivatives had superior pharmacological activities with fewer adverse effects. In particular, the pharmacological effects of the coordinated metal complexes were better than those of the uncoordinated SCHIFF'S bases. Consequently, it would be advantageous to take sulphonamides into account while creating new organic and inorganic molecules.

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