AN UPDATE OF APPLICATIONS OF AZOMETHINE DERIVATIVES AND SCHIFF BASES

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Abstract
Schiff bases, defined by their characteristic azomethine group (–C=N–), have become central to contemporary chemical research due to their synthetic flexibility and broad functional scope. These compounds exhibit notable biological activity and serve as key intermediates in the development of pharmaceuticals, agrochemicals, and industrial materials. Their ability to coordinate with transition metals enhances their therapeutic potential, leading to applications in antimicrobial, anticancer, anti-inflammatory, and antiviral treatments. In analytical chemistry, SBs are employed as chelating agents and sensor components, enabling precise detection of metal ions through spectroscopic and electrochemical techniques. Industrially, they contribute to dye production, corrosion inhibition, and catalysis, particularly in oxidation and polymerization reactions. The donor properties of azomethine nitrogen, often complemented by oxygen or sulfur atoms, allow SBs to function as versatile ligands—ranging from bidentate to polydentate configurations—supporting diverse metal complex geometries. Recent innovations in green synthesis, hybrid molecule design, and nanomaterial integration continue to expand their relevance across scientific disciplines. This review highlights the multifaceted roles of SB derivatives, emphasizing their enduring significance and potential for future advancements in both applied and theoretical chemistry.
Keywords: *Azomethine, medicinal applications, metal complexes, analytical sensors, catalysis.*

Introduction:
Schiff bases (SB) compounds are condensation products of primary amines and carbonyl compounds, having the general structure $R_2C{=}NR'$. Since R, R′ is an alkyl or aryl group, the first to prepare and isolate it was the German scientist Nobel Prize winner Hugo Joseph Schiff, were discovered in 1864 from the condensation of the carbonyl group (aldehyde, ketone) with a primary amine compound (aliphatic, aromatic) [1]. SB are organic substances with an imine or azomethine (-C=N-) functional group. They are frequently utilized in several industries including organic synthesis, medicinal chemistry, pharmaceutical chemistry, and coordination chemistry. SBs have been produced using green chemistry principles focuses on reducing or eliminating the use of hazardous reagents and solvents, minimizing waste generation, and improving overall process efficiency [2]. Selection of Starting Materials: Choose starting materials that are non-toxic, readily available, and easily handled. These can include primary amines (aliphatic or aromatic) and carbonyl compounds such as aldehydes or ketones [3]. A condensation process occurs when the nucleophilic nitrogen atom of an amine attacks the electrophilic carbon atom of an aldehyde or ketone. This reaction results in the replacement of the C=O group with a C=N group in the final product. This product is known as a SB, imine, azomethine, or anil. SBs, characterized by the -N=CH- (imine) group, have been extensively used as chelating ligands in coordination chemistry. Their metal complexes are of significant interest due to their diverse chemical, structural, and biological properties. These complexes have industrial, antifungal, antibacterial, anticancer, and herbicidal applications. Chelating ligands with N, S, and O donor atoms are particularly interesting for their biological activity and versatility in bonding to metal ions, which can enhance their effectiveness [3]. SBs have experienced significant advancements, resulting in innovative applications across various scientific fields. These developments underscore their versatility in addressing contemporary challenges. SBs have been utilized to create advanced drug delivery systems, enabling the controlled encapsulation and release of therapeutic agents [4]. Incorporated into nanomaterials, SBs play a role in nanotechnology applications such as Nano catalysis, Nano sensors, and drug delivery platforms. SBs are used in biological imaging to accurately visualize cellular processes and structures including pharmaceuticals, sensors, corrosion inhibitors, crucial intermediates in biochemical reactions [5]. SBs are explored in Supramolecular Chemistry, photodynamic therapy for cancer treatment to target and destroy cancer cells, antihistamine, antineoplastic, leveraging their photosensitive properties [6]. Over the last couple of years, numerous reports have highlighted their applications in biology in terms of their antioxidant,

antibacterial, antifungal, anthelminthic, antitubercular, anti-inflammatory, antiviral, and antimalarial activities [7]. SB imparts distinctive properties, such as electronic and steric effects, to the resulting complexes. These SB ligands, when coordinated with metal ions, form metal complexes, which demonstrate enhanced characteristics, including improved reactivity, stability, and special spectroscopic properties [8]. SB have a wide range of applications, extending the shelf life of the dispersion, sorbents, adhesives or toners, waterborne coating compositions. SB derivatives have also found applications as composite electroactive materials for charge storage devices, polymers and resins and organo-catalysts [9]. Bis-SB compositions are reported as thermosetting elastomers with improved thermal barrier properties. It promotes secondary battery using a non-aqueous electrolyte solution additive with a thiophen based organic compound, a SB, to increase energy density and improve performance. SBs have been important ligands for decades because they are easily synthesized and can be linked with a wide range of metal ions. Compounds with amine groups are vital for studying transformation and racemization reactions in biological systems due to their structural resemblance to natural biological molecules [10].

Applications of Azomethine Derivatives and SBs

Azomethine derivatives, particularly SBs, have become indispensable in modern chemical research due to their structural adaptability, ease of synthesis, and wide-ranging functionality. The azomethine group (–C=N–), formed through the condensation of primary amines with aldehydes or ketones, serves as a key reactive center that imparts both biological activity and coordination potential. These compounds have found extensive use across medicinal, analytical, industrial, and catalytic domains, reflecting their interdisciplinary significance.

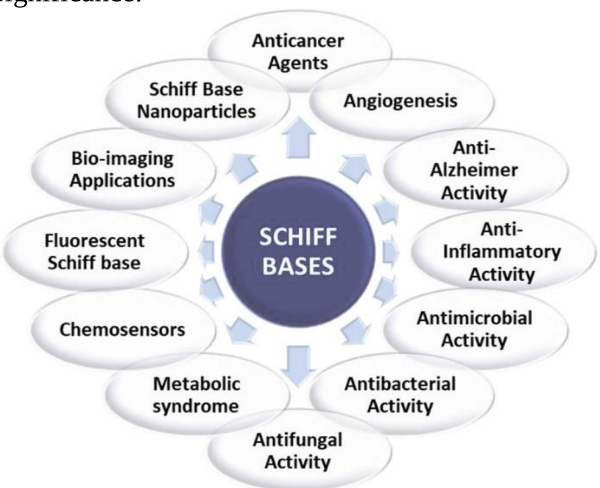


Figure 1: Applications of Schiff Bases

1. Biomedical and Therapeutic Relevance

SBs derived from heterocyclic and aromatic precursors have demonstrated notable pharmacological properties. Their ability to form stable complexes with transition metals enhances their therapeutic potential, making them valuable candidates in drug development. These compounds have shown efficacy in treating bacterial and fungal infections, inflammatory conditions, and even complex diseases such as cancer and HIV [11]. The azomethine linkage contributes to their bioactivity by influencing molecular geometry and electronic distribution, which in turn affects interactions with biological targets. Metal complexes of SBs—especially those involving copper, nickel, and zinc—have exhibited enhanced cytotoxicity against cancer cells, often through mechanisms such as DNA binding, enzyme inhibition, and oxidative stress modulation [12, 13]. Additionally, SB derivatives have shown promise as antimalarial and antipyretic agents, with some compounds advancing into clinical evaluation [14].

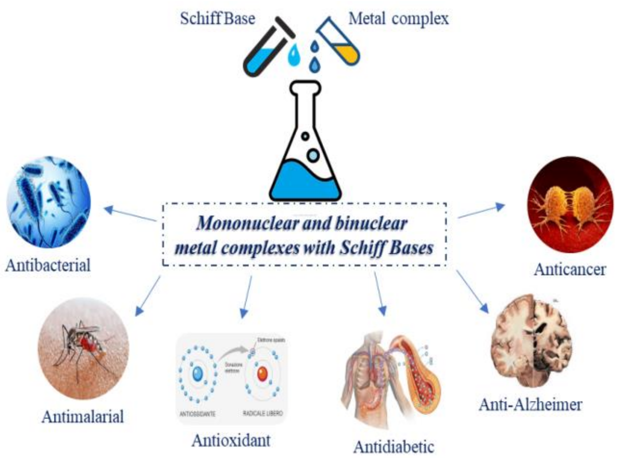
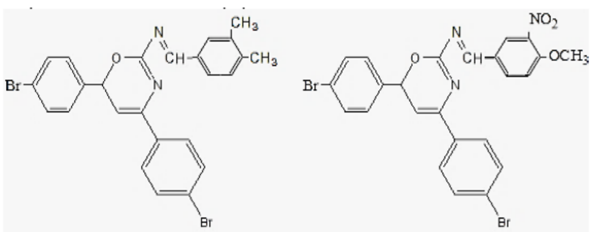
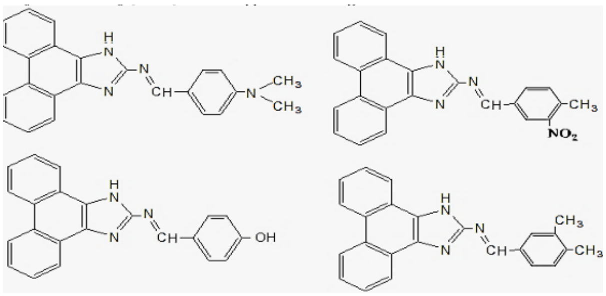


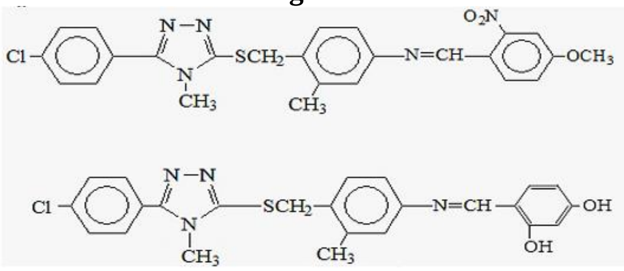
Figure 2: Medicinal application of Schiff Bases



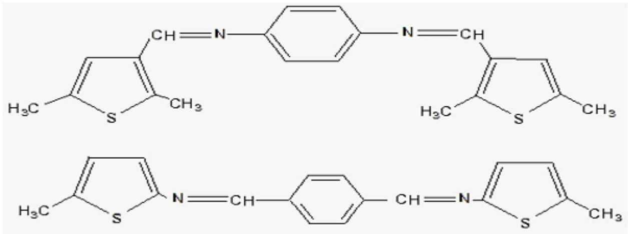
Azomethine Drug as Anticancer



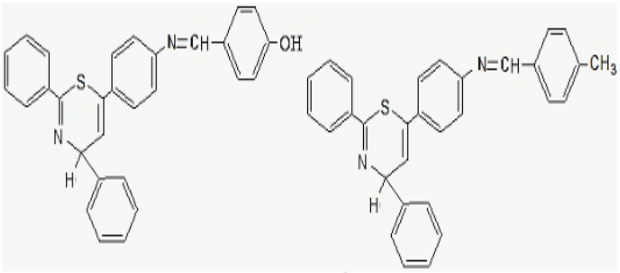
Azomethine Drug as Antibacterial



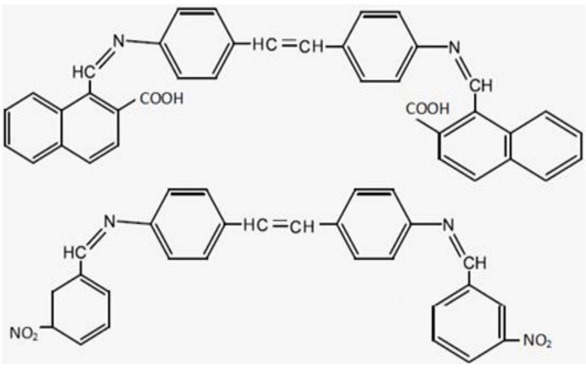
Azomethine Drug as Anticancer of Skin



Azomethine Drug as Antifungal



Azomethine Drug as Antioxidant



Azomethine Drug as Anticancer of Liver

2. Analytical and Sensor-Based Applications

The electron-donating nature of the azomethine nitrogen allows SBs to act as effective chelating agents, making them suitable for analytical applications. Their ability to form colored complexes with metal ions has been utilized in spectrophotometric assays and chromatographic techniques for metal detection and quantification [15]. SBs have also been integrated into optical sensors, where they provide high selectivity and sensitivity for detecting trace elements such as iron, cobalt, and copper [16]. In chromatographic systems, SB-modified stationary phases have improved separation efficiency and selectivity for specific analytes [17]. Their incorporation into solid-phase extraction protocols has enhanced the recovery of trace metals from environmental and biological matrices. Furthermore, their redox-active nature has enabled their use in electrochemical sensors, contributing to signal amplification and improved detection limits [18].

3. Industrial and Catalytic Utility

SBs serve as versatile intermediates in the synthesis of industrially relevant compounds. Their reactivity allows for various transformations, including ring closure, substitution, and rearrangement reactions, leading to the formation of heterocyclic structures, polymers, and specialty chemicals [4]. In the dye industry, azomethine derivatives combined with azo groups produce thermally stable pigments with hues ranging from yellow to brown, ideal for textile and nylon applications [19]. Catalytically, SB-metal complexes have been employed in numerous organic reactions, such as oxidation, reduction, and polymerization. Their tunable electronic properties and ligand flexibility allow for precise control over reaction pathways. Complexes of manganese, cobalt, and vanadium have shown high efficiency in oxidation processes, while copper and nickel complexes have been used in cross-coupling and C–H activation reactions [20]. SBs also function as corrosion inhibitors, forming protective layers on metal surfaces that prevent oxidative degradation. This application is particularly valuable in harsh industrial environments, where corrosion resistance is critical for equipment longevity [21].

4. Coordination Chemistry and Ligand Versatility

The azomethine nitrogen atom acts as a primary donor site in SBs, facilitating coordination with a wide range of metal ions [22]. Depending on the presence of additional donor atoms such as oxygen, sulfur, or nitrogen, these compounds can behave as bidentate, tridentate, tetradentate, or polydentate ligands. This flexibility enables the formation of mono- and polynuclear complexes with diverse geometries and electronic configurations [23]. The spatial arrangement and nature of donor atoms significantly influence the stability and reactivity of the resulting complexes. For example, O,N-bidentate SBs often form square planar or octahedral complexes, while S,N-donor systems may yield tetrahedral structures. These variations allow for the design of complexes tailored for specific catalytic, magnetic, or therapeutic functions [24]. Recent research has explored SB-metal complexes as biomimetic catalysts, replicating the activity of metalloenzymes [25]. Their role in supramolecular chemistry and crystal engineering further highlights their importance in advanced materials science.

Emerging Directions and Future Outlook

The scope of SB chemistry continues to expand, with new derivatives being developed for targeted drug delivery, responsive materials, and photodynamic therapy [6, 26]. Hybrid SBs that incorporate multiple functional groups are being explored for their synergistic effects and enhanced specificity [27]. Their integration into nanostructured materials, such as metal-organic frameworks and dendritic polymers, has opened new avenues for catalysis, sensing, and biomedical imaging [28]. Efforts are also underway to adopt greener synthesis methods for SB derivatives, including solvent-free reactions, microwave-assisted protocols, and the use of bio-based precursors [29]. Computational tools such as molecular docking and quantum chemical modeling are increasingly used to predict biological activity and optimize ligand design, accelerating the discovery of novel therapeutic agents [30].

Conclusion:

SB derivatives and azomethine compounds continue to demonstrate remarkable versatility across scientific disciplines. Their structural tunability and coordination potential make them invaluable in medicinal, analytical, and industrial applications. Metal complexation further enhances their functionality, enabling targeted therapeutic and catalytic roles. Emerging innovations in green synthesis and nanotechnology are expanding their relevance in sustainable and advanced material design. As research progresses, SBs remain central to solving contemporary chemical and biomedical challenges.

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