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REVIEW ARTICLE

Comprehensive Analysis on Compounds Derived from Schiff's Bases

Navya Sri Devarapalli [1*], Sindhu Sree Cholla [1], Vani Hymavathi Dayana [1], Ratna Deepika Pasumarthi [1],Kavya Sri Padala [1], Chudamani Nagasravani Parasa [1],Antro Jennie Xavier [2], Bhaskara Raju Vatchavai [3]

[1] *Student, B.Pharm, Sri Vasavi Institute of Pharmaceutical Sciences, Tadepalligudem, Andhra Pradesh, India*
[2] *Professor, Pharmaceutical chemistry, Sri Vasavi Institute of Pharmaceutical Sciences, Tadepalligudem, Andhra Pradesh, India*
[3] *Professor and Principal, Sri Vasavi Institute of Pharmaceutical Sciences, Tadepalligudem, Andhra Pradesh, India*

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Abstract: Schiff bases, synthesized through the condensation of primary amines with carbonyl compounds, constitute a versatile class of compounds with broad applications. Their adaptable chemical structure enables the integration of diverse functional groups, leading to a spectrum of properties and utilities. Exhibiting significant characteristics in coordination chemistry, materials science, and organic synthesis, Schiff bases play a pivotal role in modern chemistry and technology. This article offers an encompassing overview of Schiff base synthesis, properties, and applications, emphasizing their pivotal role in contemporary chemistry and technology. Additionally, this review provides insights into recent advancements in Schiff base chemistry, including novel synthetic methodologies, their utility as ligands in metal complex catalysis, and their application in drug discovery and biomedical research. Overall, Schiff bases remain a dynamic field of research and innovation, offering promising prospects for the development of novel functional materials and compounds.

Keywords: Schiff bases; Imines; Azomethine; Hydrazones; Chitosan.

1. Introduction

Since their discovery by a German scientist in 1864, Schiff bases have emerged as condensation products of primary amines with carbonyl compounds, constituting a significant and versatile family of chemical compounds. Widely employed across various disciplines, including analytical, inorganic, and biological chemistry, Schiff bases derived from diverse heterocyclic compounds manifest an extensive array of biological actions. [1-4] These encompass analgesic, anti-inflammatory, anti-platelet, antioxidant, antiproliferative, antipyretic, cardio protective, antidepressant, antihypertensive, herbicidal, antiglycation, and cytotoxic properties, as well as antibacterial, antifungal, anti-mycobacterial, anti-anthrax, antiviral, anticancer, anti-protozoal, anti-parasitic, and anticonvulsant activities. [5-9]

Current research endeavors predominantly focus on synthesizing, characterizing, and elucidating the structure-activity relationships of Schiff bases. The nitrogen atom present in the azomethine (-NHN=PH-) or imine (-N=CH-) groups of these compounds garners particular attention due to its distinctive chemical and biological properties. Ashraf et al. demonstrated that the presence of a single pair of electrons in the sp2 hybridized orbital of the azomethine group's nitrogen profoundly influences its chemical and biological behavior. Schiff's seminal work in the 19th century marked the inception of imine production, catalyzing subsequent advancements in synthetic methodologies. [10-14] Various techniques have since been developed for synthesizing imines, with the traditional approach, as described by Schiff, involving the condensation of an amine and a carbonyl molecule through azeotropic distillation. [15, 16]

The synthesis of Schiff bases entails the electrophilic attack of the carbonyl carbon of aldehydes or ketones by the amine nitrogen from a primary amine, resulting in the formation of a carbinolamine (shown in Figure 1). Subsequent deprotonation of the carbinolamine's nitrogen facilitates the displacement of oxygen by the electrons from the N-H bond, yielding a compound characterized by an N-substituted imine and the expulsion of a water molecule. This N-substituted imine, also known as a Schiff base, exemplifies the versatility and significance of these compounds in contemporary chemistry and technology [17, 18]

* Corresponding author: Navya Sri Devarapalli

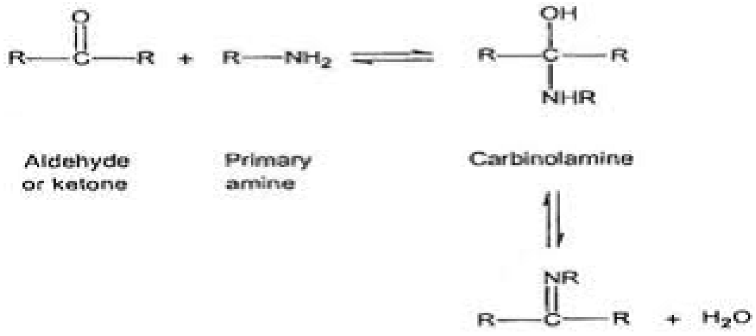
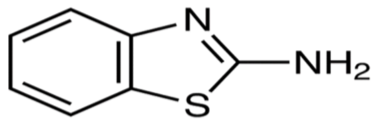


Figure 1. Synthesis of Schiff base

2. Synthesis of some Schiff bases

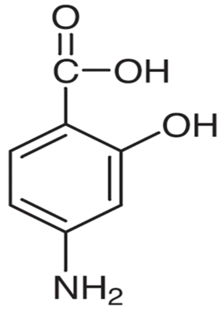
2.1. Synthesis of 2-amino-benzthiazole Schiff bases

To synthesize 2-amino-benzthiazole Schiff bases, 2 grams of 2-amino-benzthiazole were dissolved in 25 milliliters of ethanol, and the appropriate aldehyde was added. The mixture was refluxed for two hours, following which the resulting mixture was filtered [19, 20]. The solid product underwent refinement through recrystallization from ethanol, followed by rinsing with ethanol and drying to yield the desired compound. [21]



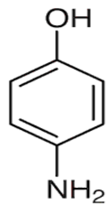
2.2. Synthesis of 4-amino-salicylic acid Schiff Bases

For the synthesis of 4-amino-salicylic acid Schiff bases, 2 grams of 4-amino-salicylic acid were dissolved in 25 milliliters of ethanol, along with the corresponding aldehyde. The resulting mixture underwent reflux for two hours, after which the solid product was separated via filtration. Purification was achieved through recrystallization from ethanol, followed by rinsing with ethanol and drying, yielding the desired compound. [22]



2.3. Synthesis of 4-aminophenol Schiff Bases

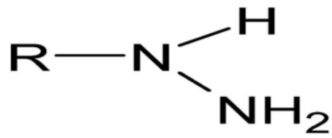
The synthesis of 4-aminophenol Schiff bases involved combining two grams of 4-aminophenol with the appropriate aldehyde in 25 milliliters of ethanol. Following two hours of reflux, the resultant mixture underwent filtration. The solid product was then refined through recrystallization from ethanol, rinsed with ethanol, and dried, resulting in the desired compound. [22-25]



3. Compounds of Schiff bases

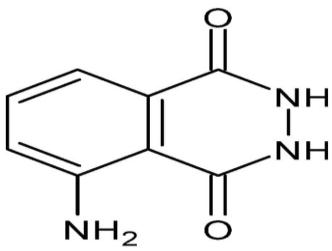
3.1. Hydrazides

Hydrazides, existing in their iminol tautomeric form, represent a specific subgroup within the broader category of Schiff bases. These compounds belong to the class of monosubstituted hydrazine derivatives, characterized by the presence of a -NH-NH- nitrogen bridge along with a carbonyl or sulfonyl group directly attached to one of the nitrogen atoms, as depicted by the terminally occurring hydrazide moiety: R-NH-NH_2. The biological activity exhibited by hydrazides underscores their functional association with Schiff bases. Notably, hydrazides possess well-documented biocidal properties, including bactericidal activity. In combating Mycobacterium tuberculosis infections, hydrazides have been extensively studied since the 1950s, often compared to the efficacy of isoniazid, the first compound evaluated for such antimicrobial qualities. Additionally, hydrazides demonstrate virucidal, fungicidal, and protozoicidal activities [26-29].



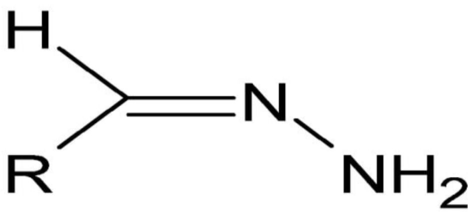
3.2. Dihydrazides

Dihydrazides, akin to hydrazide-hydrazones, encompass a diverse range of compounds wherein alkyl or aryl fragments are connected by a diamide bridge. These structures exhibit symmetrical arrangements, with nomenclature dictated by the presence of a carbonyl group at the outset, resulting in monosubstituted hydrazide configurations. Dihydrazides have found utility as antibacterial, antifungal, and antiparasitic agents, with specific studies indicating the pivotal role of the hydrazide moiety in their biological activity. The presence of an amide-analogous –C (=O)-NH-NH- group facilitates amide-iminol tautomerism, broadening their potential applications to include catalytic roles in enantioselective reactions [30-34]



3.3. Hydrazones

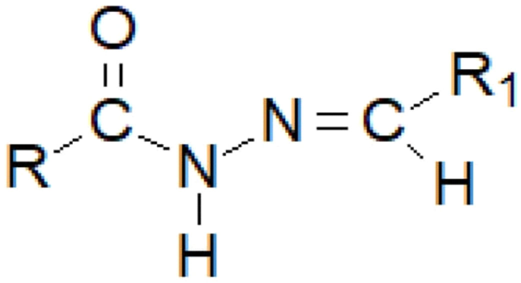
Hydrazones, formed through the reaction between suitable hydrazides and aldehydes, represent another subgroup of hydrazides characterized by the presence of an imine linkage. These compounds are widely employed in various applications, including agriculture as pesticides, insecticides, nematicides, rodenticides, and plant growth regulators. [35-38] Sulfonyl hydrazones, a specific subset of hydrazones, exhibit diverse pharmacological activities, serving as antidepressants, analgesics, anti-inflammatory, anti-cancer, antifungal, and antibacterial agents. Notably, they are potent inhibitors of tyrosine phosphatase B (PtpB) of M. tuberculosis bacterium and are explored for their antibacterial properties in conjunction with sulphonamides [39]



3.4. Hydrazide-Hydrazones

Hydrazide-hydrazones represent a versatile class of hybrid molecules capable of joining diametrically distinct alkyl or aryl fragments via an unsymmetrical amide-imine bridge. The nomenclature of these compounds is contingent upon the interpretation of the order of atoms within the moiety, with variations arising based on the initial identification of either the carbonyl group or the imine link.

These compounds are synthesized with the aim of developing effective antibacterial and antifungal agents, especially crucial in the face of escalating antibiotic resistance [40, 41]

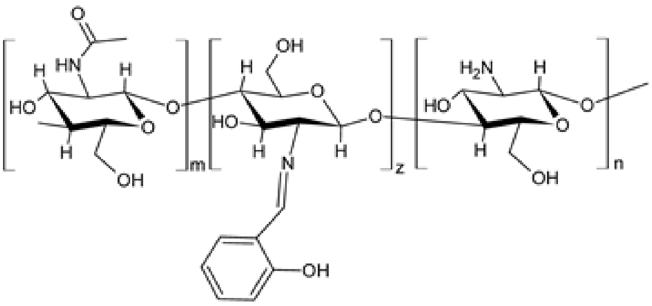


4. Compounds synthesized from Schiff bases

Compounds synthesized from Schiff bases encompass a diverse array of substances with notable therapeutic potential across various medical conditions

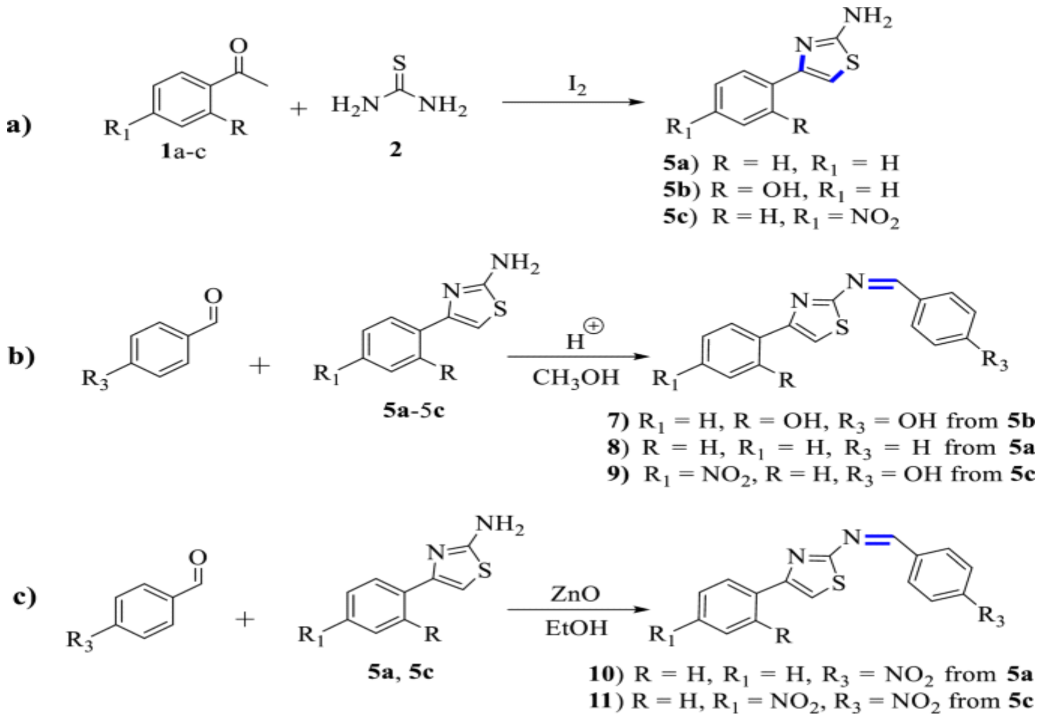
4.1. Chitosan based Schiff bases

Chitosan, a naturally occurring biopolymer, undergoes chemical modification via imine functionalization to yield chitosan-based Schiff bases (CBSs). These compounds exhibit promising antibacterial and antifungal properties. Notably, recent studies have highlighted their efficacy in removing Cr(VI) from wastewater. Structural variations, such as the insertion of alkyl and/or aryl groups, enhance the hydrophobicity of these derivatives, thereby augmenting their antimicrobial activity [42].



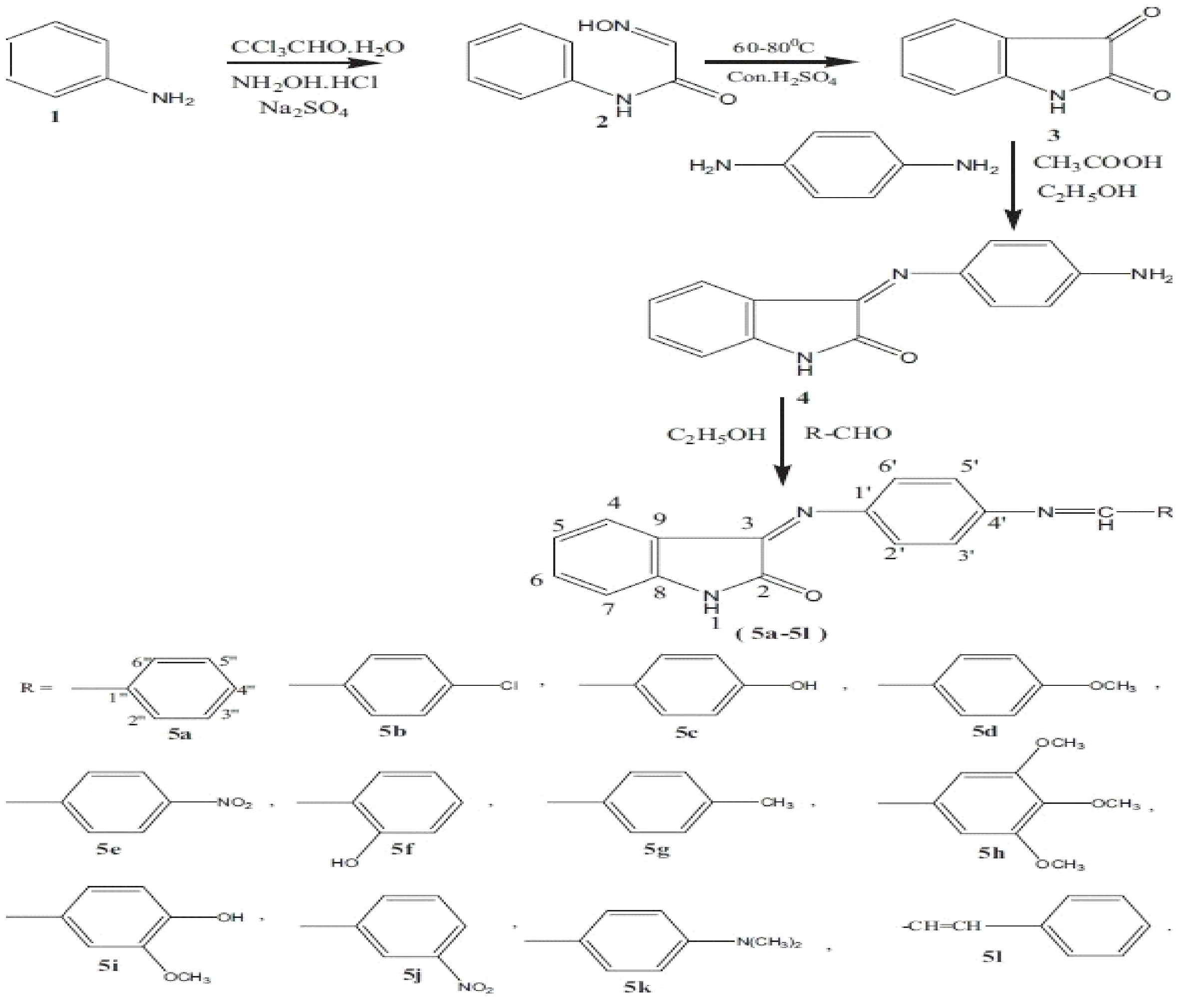
4.2. Thiazolyl and Benzathiazolyl Schiff Bases

Thiazolyl and benzathiazolyl Schiff bases demonstrate analgesic and anti-inflammatory activities, making them potential candidates for addressing conditions such as asthma, rheumatoid arthritis, and psoriasis. While the precise mechanism underlying their antioxidant activities remains under investigation, these compounds are believed to exert their effects through various biochemical pathways. Synthesis methods involve modifications of acetophenone and benzaldehyde derivatives, resulting in thiazole-based Schiff bases with broad therapeutic potential against bacterial, diabetic, cancerous, inflammatory, and viral conditions [43]



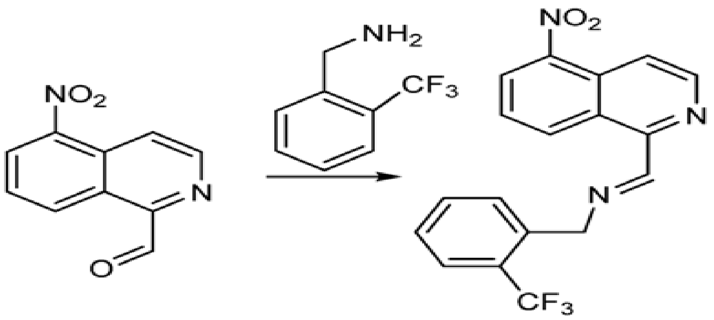
4.3. Iminoisatin Schiff Bases

Derived from isatin, an endogenous substance found abundantly in mammalian bodily fluids and tissues, iminoisatin Schiff bases exhibit diverse biological activities, including anti-inflammatory, anti-HIV, antibacterial, antifungal, and antidepressant properties. Synthetic pathways involve cyclization of isatin followed by reaction with various aromatic aldehydes to form Schiff bases. Notably, these compounds have shown efficacy in blocking the nuclear translocation of KIV-1 and serve as potential inhibitors of virus lysine Schiff base formation [44]



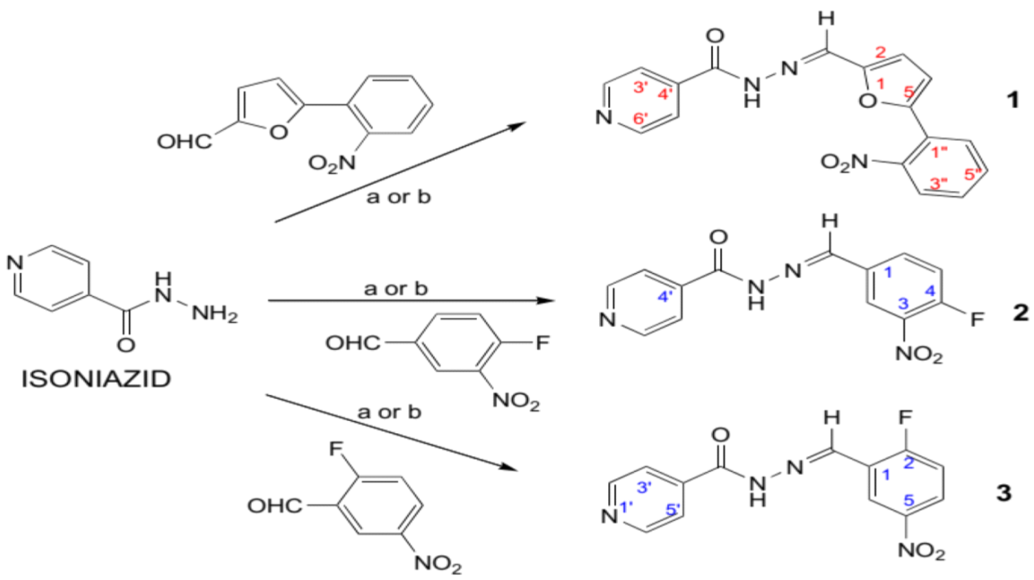
4.4. Schiff Base of Formyl-5-Nitroisoquinoline Methanamine

Schiff bases derived from formyl-5-nitroisoquinoline exhibit promising antimalarial activity against chloroquine-resistant Plasmodium falciparum strains. The imino group of these compounds is implicated in conferring antimalarial action, thus positioning them as potential candidates for combating malaria [45, 46]



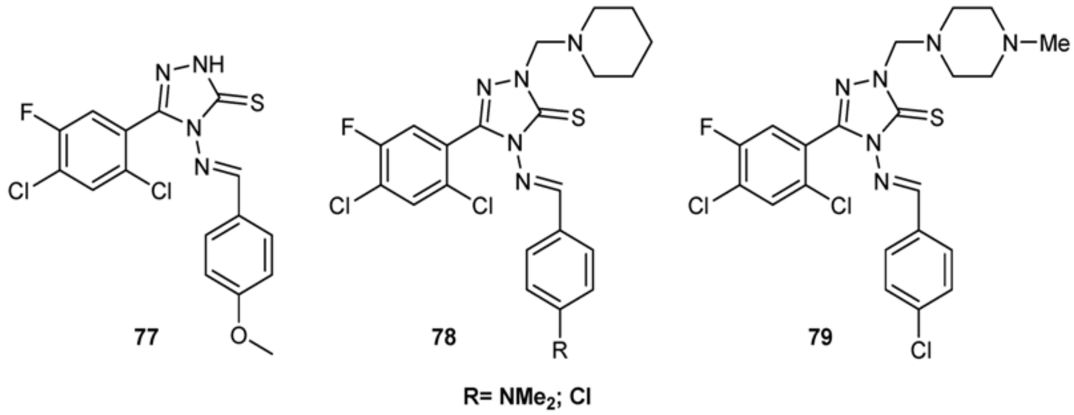
4.5. Schiff Base of Isoniazid

Schiff bases derived from isoniazid demonstrate antimycobacterial activity, inhibiting cell wall synthesis and protein synthesis. Microwave-assisted and conventional synthesis methods are employed to produce these compounds, which show efficacy against various strains of mycobacteria [47]



4.6. Schiff Bases Containing 2,4-Dichloro-5-Fluorophenyl Moieties

Schiff bases incorporating 2,4-dichloro-5-fluorophenyl moieties exhibit potent antibacterial properties, effectively inhibiting the growth of bacterial strains such as Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, and Klebsiella pneumoniae. These compounds hold promise as potential alternatives to conventional antibiotics [48]



5. Therapeutic applications

The therapeutic applications of Schiff bases span a wide spectrum of medical domains, addressing pressing challenges in bacterial, viral, and fungal infections, as well as cancer, inflammation, and various other ailments [49]

5.1. Antimicrobial activity

Given the escalating prevalence of antibiotic-resistant bacteria and systemic fungal infections, the development of novel antibacterial and antifungal medications is imperative. Schiff bases have emerged as promising candidates in this regard, demonstrating efficacy against a range of pathogens [50].

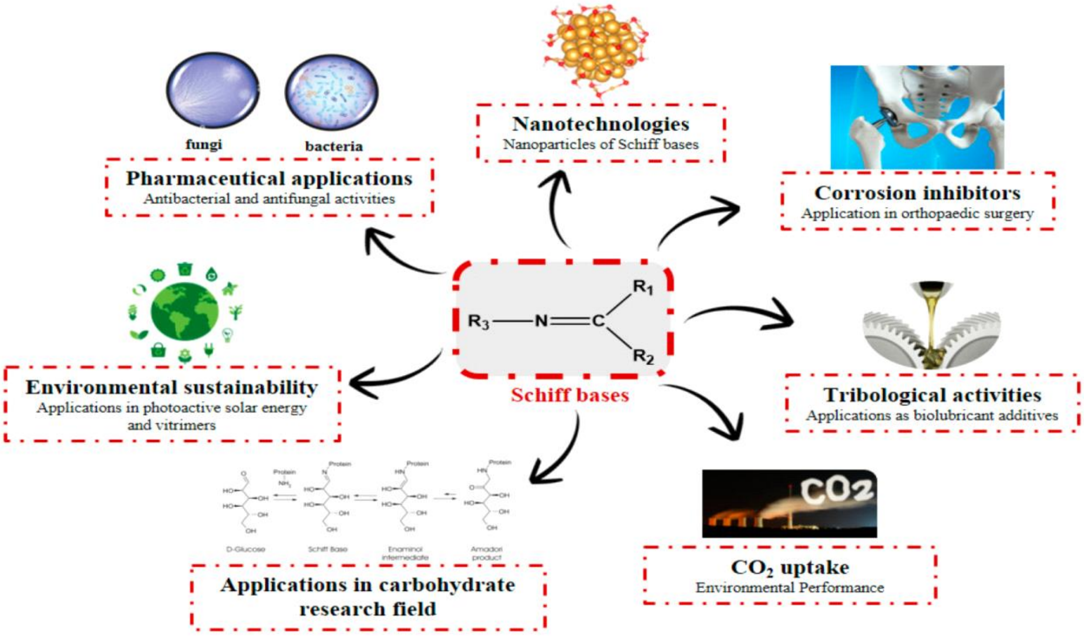


Figure 2. Wide spectrum applications of Schiff bases

5.2. Antiviral activity

Schiff bases exhibit notable antiviral activity, with specific compounds showing effectiveness against viruses such as the mouse hepatitis virus (MHV) and human immunodeficiency virus type 1 (HIV-1). These findings hold significant promise for combating viral infections [51]

5.3. Anticancer and antitumor activity

In the fight against cancer, Schiff bases have demonstrated remarkable potential as anti-cancer agents, inhibiting proliferation and inducing apoptosis in various cancer cell lines. Additionally, their antitumor activity underscores their role in mitigating the progression of malignancies [48-51]

5.4. Anti-proliferative activity

Schiff bases display anti-proliferative effects against cancer cell lines, while their interaction with DNA suggests potential mechanisms of action. These interactions may involve intercalation with DNA molecules, offering insights into their therapeutic efficacy [48-51]

5.5. Antioxidant and anti-inflammatory activity

With their antioxidant properties, Schiff bases contribute to scavenging free radicals and mitigating oxidative stress. Moreover, their anti-inflammatory effects hold promise for alleviating inflammatory conditions and associated symptoms [48-51]

5.6. Anthelmintic and anti-hypertensive activity

Schiff bases exhibit anthelmintic activity against parasitic infections, along with potential antihypertensive effects. These properties highlight their versatility in addressing diverse medical conditions [48-51]

5.7. Antidepressant activity

Schiff bases demonstrate antidepressant effects, offering potential therapeutic options for individuals suffering from depression. The investigation of specific structural modifications further enhances their efficacy and safety profiles [48-51]

6. Conclusion

Schiff bases emerge as remarkably versatile compounds with a diverse range of applications spanning multiple scientific fields. Their distinctive chemical properties and adaptability in structure render them indispensable tools in disciplines ranging from coordination chemistry to materials science. Ongoing research and development in Schiff base chemistry hold the promise of further advancements and novel discoveries, thus enhancing their significance and applicability in contemporary science and technology.

As researchers delve deeper into their synthesis, properties, and applications, Schiff bases remain at the forefront of innovation, presenting exciting avenues for the development of new functional materials, catalytic systems, and therapeutic agents. With their multifaceted nature and potential for customization, Schiff bases continue to ignite curiosity and drive exploration, solidifying their indispensable role within the scientific community

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Author’s short biography

Navyasri Devarapalli

Student at Sri Vasavi institute of pharmaceutical sciences, Tadepalligudem, West Godavari, Andhra pradesh, India.

Sindhusree Cholla

Student at Sri Vasavi institute of pharmaceutical sciences, Tadepalligudem, West Godavari, Andhra pradesh, India.

Dayana Vani hymavathi

Student at Sri Vasavi institute of pharmaceutical sciences, Tadepalligudem, West Godavari, Andhra pradesh, India.

Xavier Antrojennie

Professor, Master of pharmacy in medicinal Chemistry, Sri Vasavi institute of pharmaceutical sciences, West Godavari, Andhra Pradesh, India.

Kavyasri Padala
Student at Sri Vasavi institute of pharmaceutical sciences, Tadepalligudem, West Godavari, Andhra pradesh, India.

Ratna Deepika Pasumarthi
Student at Sri Vasavi institute of pharmaceutical sciences, Tadepalligudem, West Godavari, Andhra pradesh, India.

Parasa ChudamaniNagasravani
Student at Sri Vasavi institute of pharmaceutical sciences, Tadepalligudem, West Godavari, Andhra pradesh, India.

Bhaskara Raju Vatchavai
Master of pharmacy in Pharmaceutical Analysis and PhD, Principal, Sri Vasavi institute of Pharmaceutical sciences, West Godavari, Andhra Pradesh, India.