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Schiff Bases in Biomedical Applications: A Review

Abstract

Schiff bases, a prominent class of organic compounds formed via condensation reactions between primary amines and carbonyl compounds, have attracted increasing attention in biomedical research. Their structural flexibility and chemical functionality enable a wide range of biological activities, positioning Schiff bases as promising candidates in antimicrobial strategies, drug delivery systems, diagnostic technologies, and biomaterial design. In recent studies, diverse Schiff base derivatives have demonstrated notable effectiveness against a broad spectrum of microbial strains, highlighting their potential as alternative or complementary agents in addressing antimicrobial resistance.

Beyond their direct biological activity, Schiff bases have been extensively investigated as functional components in advanced and targeted drug delivery systems. Their chemical adaptability supports the development of delivery platforms with controlled release behavior, improved bioavailability, and enhanced therapeutic efficiency. Such systems are particularly valuable in minimizing off-target effects and optimizing drug performance in complex biological environments. In parallel, the distinctive coordination and signaling properties of Schiff bases have facilitated their application in diagnostic and sensing technologies, where they have been employed in the detection and monitoring of biologically relevant species with high sensitivity and selectivity.

This narrative review critically discusses the biomedical applications of Schiff bases, with particular emphasis on their antimicrobial mechanisms, roles in targeted drug delivery, diagnostic sensing capabilities, and contributions to biomaterials for tissue engineering.

Keywords: *schiff bases, antimicrobial activity, drug delivery, diagnostic sensors, biomaterials*

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Introduction

Schiff bases constitute an important family of organic compounds characterized by the presence of an azomethine (–C=N–) functional group, typically obtained through condensation reactions between primary amines and aldehydes or ketones (Savita et al., 2025). Due to their synthetic accessibility, structural diversity, and tunable physicochemical properties, Schiff bases have long been studied in various fields of chemistry. In recent years, their biomedical relevance has become increasingly apparent, particularly in response to emerging challenges such as antimicrobial resistance, targeted therapy requirements, and the demand for advanced diagnostic tools (Alammari et al., 2025).

The biological versatility of Schiff bases arises from their ability to interact with biomolecular targets through hydrogen bonding, coordination interactions, and electronic effects associated with the azomethine linkage (Pankaj et al., 2025). These features have enabled the exploration of Schiff bases across multiple biomedical domains, including antimicrobial agents, drug delivery platforms, diagnostic systems, and biomaterials for tissue engineering (Alshehab et al., 2025). This review focuses on these application areas, providing a structured discussion of mechanisms, advantages, and limitations.

Research

Antimicrobial Properties of Schiff Bases. Among the various biomedical applications of Schiff bases, their antimicrobial activity has been one of the most extensively investigated. Schiff base compounds and their derivatives have demonstrated effectiveness against a broad spectrum of microorganisms, including bacteria and fungi. Several mechanistic pathways have been proposed to explain their antimicrobial behavior (Buldurun et al., 2019). One of the primary mechanisms involves disruption of microbial cell membranes. Schiff bases and their degradation products are capable of compromising membrane integrity, leading to leakage of cellular contents, osmotic imbalance. This membrane-targeting effect plays a crucial role in both antibacterial and antifungal activity.

Another important mechanism is the generation of reactive oxygen species. Certain Schiff base compounds can induce intracellular ROS accumulation, resulting in oxidative stress that damages essential cellular components such as proteins, lipids, and nucleic acids, ultimately leading to microbial cell death (Yan et al., 2024).

Additionally, Schiff bases may interact directly with key cellular constituents. Binding to enzymes, structural proteins, or genetic material can disrupt vital biological processes and inhibit microbial growth. Such interactions further enhance their antimicrobial efficacy and highlight their potential as alternative antimicrobial agents (Morales-Guevara et al., 2025).

Given the global rise in antibiotic resistance, these multifaceted antimicrobial mechanisms make Schiff bases particularly attractive candidates for the development of new bioactive agents. In a broader context, structurally related azomethine-based systems, including hydrazone-derived organic ligands, have also been reported to exhibit notable application prospects owing to their adaptable coordination behavior and functional versatility, further supporting the biomedical relevance of this class of compounds (Huseynova, 2025).

Schiff Bases in Drug Delivery Systems. Beyond direct biological activity, Schiff bases have also shown significant promise in drug delivery applications. Their chemical adaptability allows them to function as components of systems designed to improve drug solubility, stability, and targeted delivery (Hamad et al., 2025).

One important strategy involves the formation of Schiff base metal complexes. Coordination with transition metals can enhance the physicochemical properties of therapeutic agents, resulting in improved solubility and bioavailability. Such metal–Schiff base complexes often exhibit enhanced pharmacological performance compared to free drug molecules (Ibrahim et al., 2021).

Another notable application is the incorporation of Schiff base linkages into self-healing hydrogels. These systems exploit the dynamic nature of Schiff base bonds, enabling responsiveness to physiological stimuli. Self-healing hydrogels based on Schiff chemistry have been explored for

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controlled drug release, offering sustained therapeutic effects and improved treatment efficiency (Junpeng et al., 2019).

The ability to design stimuli-responsive delivery systems positions Schiff bases as valuable tools in modern drug delivery research (Guilong et al., 2025).

Diagnostic Applications of Schiff Bases. Schiff bases have also found important applications in biomedical diagnostics, particularly in the development of sensing platforms for analyte detection. Their coordination ability and optical properties make them suitable for both electrochemical and optical diagnostic systems (Faridbod et al., 2007).

In electrochemical diagnostics, Schiff bases have been utilized in the construction of ion-selective electrodes (ISEs). These systems enable selective and sensitive detection of metal ions, which is critical in clinical diagnostics and biomedical monitoring as well as environmental analysis (Zhong et al., 2022).

In addition, Schiff base compounds have been widely investigated as fluorescent sensors. Their capacity to exhibit fluorescence modulation upon interaction with specific ions or molecules allows for turn-on or turn-off sensing mechanisms. Such properties are particularly valuable in clinical diagnostics, where rapid and selective detection is essential (Behura et al., 2024).

These diagnostic applications further demonstrate the versatility of Schiff bases in biomedical science.

Schiff Bases as Biomaterials for Tissue Engineering. The role of Schiff bases in biomaterial development has expanded significantly, particularly in the context of tissue engineering and regenerative medicine (Berhanu et al., 2019). Schiff base-derived materials, especially those incorporated into cross-linked or polymeric systems, often exhibit favorable biocompatibility profiles, making them suitable for biomedical use (Klaser et al., 2025).

An important advantage of Schiff base-based biomaterials is their tunability. By modifying chemical structure and cross-linking density, it is possible to design materials with tailored mechanical strength, degradation behavior, and chemical stability. These properties are essential for applications such as wound healing, tissue regeneration, and scaffold design in tissue engineering (Rana et al., 2024).

The adaptability of Schiff base chemistry thus supports the development of functional biomaterials capable of meeting diverse biomedical requirements.

Challenges and Future Perspectives. Despite the promising biomedical potential of Schiff bases, several challenges must be addressed to facilitate broader application. Stability under physiological conditions, long-term biocompatibility, and controlled degradation remain key concerns. Furthermore, systematic evaluation of structure–activity and structure–toxicity relationships is necessary to ensure safe and effective biomedical use.

Future research is expected to focus on rational molecular design, improved understanding of biological interactions, and the integration of Schiff bases into multifunctional biomedical systems. Advances in material science and molecular engineering are likely to further enhance the translational potential of Schiff base-based technologies (Khalifa et al., 2025).

Conclusion

Schiff bases represent a multifunctional and chemically versatile class of compounds with substantial relevance to biomedical applications. Their demonstrated antimicrobial activity, utility in advanced drug delivery systems, effectiveness in diagnostic technologies, and contribution to biomaterial design highlight their importance in contemporary medical research. Continued exploration and refinement of Schiff base chemistry are expected to yield innovative solutions to current biomedical challenges, including antimicrobial resistance and the need for efficient diagnostic and therapeutic platforms.

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