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Review Paper

Pharmacological Insights into Amino Acid-Based Schiff bases: Trends and Therapeutic Prospects

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ABSTRACT

Schiff bases produced from amino acids have seen a remarkable development in medicinal chemistry because of their broad range of biological activities, ease of synthesis, and structural variety. These exhibit structural and electrical characteristics that allow for their use in a variety of research domains, particularly related with pharmaceutical and medicinal chemistry. Amino acid moieties are added to the Schiff base structure to provide special pharmacological characteristics in addition to improving biocompatibility. This review emphasizes the significance of amino acid based schiff bases and provides an overview of their therapeutic activities as reported in the most recent research. Furthermore, these schiff bases often form metal complexes with improved biological activity, solubility and stability, as compared to their free ligands when coordinated with various metal ions. With an emphasis on their antibacterial, antiviral, anticancer, antioxidant, antifungal, antidiabetic, and antiinflammatory qualities, this review emphasizes the biological assessment of schiff bases based on amino acids and their metal complexes. Due to their customizable nature, metal-binding properties, and advantageous pharmacokinetics, they are excellent prospects for additional research as multi-target therapeutic agents. To stimulate further research in this exciting field, this comprehensive review provides insightful information about the medicinal potential of amino acid-based schiff bases

INTRODUCTION

Amino acid schiff bases (SBs) are of major interest in the area of pharmaceutical chemistry due to their unique structural features and varied pharmacological properties¹. Amino acid-SBs are

prepared by a condensation reaction of amino acids with carbonyl compounds (aldehydes or ketones) to give a characteristic imine or azomethine ($-C=N-$) bond^{2,3}. This synthetic route simplifies the preparation of a wide range of derivatives and allows for systematic

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modifications to tune their biological activities⁴. Amino acid SBs have been an important scaffold in the design of novel therapeutic agents over the years due to the simplicity of their synthesis and the ease with which their molecular framework can be modified^{5,6}. The broad spectrum of bioactivities reported in literature confirms the pharmacological potential of these SBs. These compounds have been shown by several studies to have good anti-inflammatory, antimicrobial, antioxidant, antidiabetic and anticancer properties^{1,4,5,7-38}. Their ability to interact with several biological targets such as enzymes and receptors, supports their therapeutic potential in counteracting several pathological conditions³⁹. The antimicrobial efficacy of some SB derivatives has been ascribed to the growth disruption of bacteria⁴⁰ or to the inhibition of key metabolic enzymes⁴¹. Their radical scavenging ability is related to their antioxidant activity³⁵. In addition, extensive laboratory and animal studies have confirmed the anticancer efficacy of these compounds, demonstrating their ability to control cell growth and apoptosis. Such multi-layered bioactivity profiles not only exemplify their potential as pharmacological agents, but also provide a strong platform for further research on their mechanism of action⁴². In this review, we extensively discussed the different pharmacological effects of amino acid SBs. The objective of this paper is to synthesize the results of different studies to give a comprehensive and detailed account of their potential applications in therapeutics. In addition, the review also emphasizes critical obstacles and limitations encountered in the present research such as inconsistencies in the experimental methodologies and gaps in the toxicological data, thus identifying the scope for future investigations.

Important advantages of amino acid based Schiff bases:

The structural features of Schiff bases prepared from amino acids considerably improve their pharmacokinetics and pharmacological activity, as compared to Schiff bases prepared from simple amines and aldehydes or ketones.

Pharmacokinetic advantages

Amino acid schiff bases usually have better solubility in physiological conditions, leading to better bioavailability. The structural complexity can also help them to avoid rapid degradation and improve their pharmacokinetic profiles⁴³.

Antioxidant and Enzymatic Modulation

Amino acid Schiff bases exhibit antioxidant and enzyme interactions, leading to modulation of enzyme activity (inhibition or activation) that can be exploited for therapeutic purposes, depending on the desired pharmacological effects⁴⁴.

Targeting specific through structural complexity

Amino acid residues incorporated in schiff bases bring chirality and hydrophobicity which enhance drug target interactions. These properties have led to studies on amino acid conjugated schiff bases which showed better binding affinity and biological activity¹⁴.

Improved stability and binding potential

Amino acid-derived schiff bases often display better stability due to the coordination capabilities of additional functional groups, such as -COOH and -NH₂, leading to enhanced metal complexation and biological activity. These features facilitate better binding to biological targets, as observed in studies evaluating metal complexes of amino acid schiff bases⁴⁵.



Enhanced antimicrobial activity

Amino acid based schiff bases display significant antibacterial and antifungal activities. This enhancement is often attributed to their ability to act as tridentate ligands and form stable complexes with transition metals, which are more biologically active than the parent ligands²².

Pharmacological activities:

Antibacterial activity

The bactericidal qualities of several Schiff bases made from amino acids and their metal complexes have been reported in numerous studies. In a study done by Sakiyan *et al* (2004) amino acid SBs and manganese (III) complexes were created by reacting 2-hydroxy-1-naphthaldehyde with glycine, L-alanine, L-phenylalanine, L-histidine, and L-tryptophan. The antibacterial activity of these complexes was evaluated *in vitro* against *E. coli*, *S. aureus* and *B. polymyxa* bacteria. It was observed that generally SBs were either more or equally active than the complexes. However, when compared to

the corresponding Schiff bases, the manganese (III) complexes of the SBs synthesized from glycine and L-phenylalanine exhibited more activity against *S. aureus*. Additionally, it is discovered that the compound's antibacterial activity is decreased as the size of the amino acid residue is increased⁷.

Another study done on amino acid SBs made from cinnamon aldehyde and amino acids by Wang *et al* (2016) exhibited their antibacterial effectiveness against *S. aureus* and *E. coli*. Potassium 3-(4-hydroxyphenyl)-2-(((1Z,2E)-3-phenylallylidene)amino)propanoate and potassium 2-(((1Z,2E)-3-(4-chlorophenyl)allylidene)amino)propanoate demonstrated excellent antibacterial activity against both bacteria. Overall, the inhibition zone

diameters of ciprofloxacin, which was used as a control in this experiment along with cinnamon aldehyde, were larger than those of the majority of new compounds⁹. Pervaiz *et al* (2019) conducted a recent investigation on amino acid SBs through the interaction of leucine and salicylaldehyde in a basic medium. As a ligand, the Schiff base reacted with the metals Cd, Mn, Cu, and Co to create stable complexes. Every chemical, including complexes and ligands, was evaluated against various bacterial species. The Cobalt complex exhibited the highest activity against *B. subtilis* at 11.47 ± 0.8 . The outcomes were contrasted with those of the common medication Rifampicin, which exhibited the highest activity at 20 ± 0.2 ¹⁵.

Salihovic *et al* (2021), synthesized two new SBs from L-cysteine and substituted benzaldehydes: the first derivative, [2-((2-chlorobenzylidene) amino)-3-mercaptopropanoic acid], and second derivative [3-mercapto-2-((2-methoxybenzylidene) amino) propanoic acid]. These compounds were tested against several gram-positive and gram-negative bacteria. The study demonstrated the MIC values of 1.284 mM and 2.616 mM respectively for the two derivatives. The first derivative showed better activity, maybe because of the existence of chlorine, leading to increased lipophilicity and activity²¹.

A very unique water-soluble copper (II) complex made from newly synthesized Schiff base amino acid ligands was described by Saikumari N (2021). Alanine and salicylaldehyde were condensed to create schiff base. The antibacterial activity of these synthesized SBs was evaluated (well diffusion method) against a variety of microbes, including *Bacillus subtilis* and *Escherichia coli*. At varying dosages, synthesized complexes demonstrated antibacterial activity with inhibition zones between 10 and 16 mm and inhibition percentages between 11.22 and 17.77% against harmful microorganisms²².



Several L-arginine SBs acylated chitosan derivatives were created in the work by Cui *et al* (2022) to enhance chitosan's antimicrobial activity by incorporating the pyridine ring, furan ring, and L-arginine structure. CRFF (chitosan-L-arginine-furfural), CRCF (chitosan-L-arginine-5-chloro-furfural), and CR3PCA (chitosan-L-arginine-3-pyridinecarboxaldehyde) demonstrated reduction of *Staphylococcus aureus*, nearing 1.00 mg/mL. *Escherichia coli* were more effectively inhibited by CRCF and CR2B3PCA (chitosan-L-arginine-2-bromo-3-pyridinecarboxaldehyde) than by other substances. According to the study, guanidine and the positively charged chitosan may interact with opposite charged cell wall components, causing chemicals to leak in and interfere with the bacteria's regular metabolic processes³⁰.

In 2023, Sasikumar et al. described mixed-ligand complexes composed of metal (II) complexes, heterocyclic bases, and Schiff base ligands. The synthesized complexes had potent antibacterial effect at 20 µL/mL strength. The antibacterial action was largely dependent on the coordination of metal ions with diamine, and the inhibitory activity of these complexes is strongly correlated with metalation. Chelation increased the chemicals' lipophilicity, which allowed them to pass through the cell membrane and destroy DNA⁴⁶. Oxovanadium (iv) complexes of α -amino acid SB were synthesized and structure elucidation was done based on analysing physical properties, elemental evaluation, measurement of conductivity and magnetic moment along with spectroscopic analysis. All the derivatives demonstrated a moderate to excellent antibacterial activity⁴⁷.

Antifungal Activity

Adam and Elsayy (2018) used Nystatin as the standard antifungal reference to assess the antifungal activity of vanadyl (VO²⁺) Schiff base amino acid complexes against *Candida albicans*.

At 20 and 40 µg/mL, the compounds with the largest zones of inhibition and the highest antifungal activity were those with extended aliphatic side chains. The increased activity was ascribed to structural characteristics that improved the hydrophobic contacts between the complexes and the fungal cell membrane, compromising cell integrity and making it easier for the fungal lipid bilayer to break down. Other substances exhibited moderate to weak antifungal activity, highlighting the importance of ligand type and aliphatic chain length in regulating antifungal activity¹¹.

A study done by Barczynska-Felusiak *et al* (2021), demonstrated significant antifungal activity by the zinc (II) complexes, especially against *Candida albicans*. The compound Zn[(acac)(LTrp)(H₂O)], which contains L-tryptophan, proved particularly successful among them. At concentrations below 0.1 mg/mL, it dramatically suppressed *C. albicans* growth, suggesting powerful antifungal activity at low concentrations. Compared to the original Schiff base ligands and the precursor complex Zn[(acac)₂(H₂O)], the zinc–amine acid complexes exhibited noticeably greater antifungal activity may be due to synergistic interaction between the coordinated organic ligand and the zinc ion⁴⁸.

In the study by Borrego-Muñoz *et al* (2023), 48 enamine-type schiff bases originating from L-alanine, L-tyrosine, and L-phenylalanine were produced and assessed for their antifungal activity against *Fusarium oxysporum*. All compounds demonstrated *in vitro* efficacy, exhibiting IC₅₀ values below 40 mM. The size of the substituents on the acetylacetone derivatives and the electronic characteristics of the cyclohexane-3-one moiety were shown to have an impact on the antifungal activity. Atom-based 3D-QSAR models ($R^2 > 0.70$, $Q^2 > 0.60$) identified key structural features associated with enhanced activity, such as the presence of hydrophobic alkyl esters and electron-withdrawing enamine groups. Some of the synthesized compounds significantly reduced



disease severity in cape gooseberry plants while maintaining healthy physiological characteristics, highlighting amino acid-based Schiff bases as promising antifungal agents⁴⁹.

Antiviral Activity

Amino acid-based schiff bases are significant because of their broad-spectrum pharmacological characteristics, especially in antiviral studies. Zhang *et al* (2016) conducted a noteworthy study that examined the antiviral activity of gossypol-based schiff bases produced with different amino acids against the tobacco mosaic virus (TMV). When compared to gossypol alone, these schiff bases showed noticeably better anti-TMV action in addition to being simpler to synthesize in disodium salt form and having increased water solubility. The presence of carboxyl groups and the type of R-side chain in the amino acid moiety affected both biological activity and the production of reactive oxygen species (ROS), according to a structure–activity relationship (SAR) study. Specifically, it was discovered that there was a stronger correlation between the formation of superoxide anions ($O_2^{\cdot-}$) and hydrogen peroxide (H_2O_2), which was discovered to have a stronger correlation with antiviral effectiveness. Superior activity was demonstrated by compounds like D-serine, D-threonine, and D-asparagine schiff bases, underscoring the function of stereochemistry in regulating bioactivity. Remarkably, D-amino acid-derived schiff bases frequently performed better than their L-isomers, indicating that host-pathogen interactions might favor particular chiral configurations. According to the study, ROS—particularly $O_2^{\cdot-}$ —are important mechanistic markers for assessing potential schiff base candidates because they limit viral replication early on. This study opens the door for the use of schiff bases derived from amino acid in the development of plant-based or medicinal antiviral medicines by highlighting their

twin benefits of strong antiviral activity and advantageous physicochemical characteristics⁵⁰.

Anticancer Activity

The anticancer properties of several schiff bases produced from amino acids and their metal complexes have been extensively studied, particularly against various human cancer cell lines. Three hexacoordinated octahedral nickel (II) complexes were created by Li *et al.* (2020): $[Ni(\text{Trp-sal})(\text{phen})(\text{CH}_3\text{OH})]$, $[Ni(\text{Trp-o-van})(\text{phen})(\text{CH}_3\text{OH})] \cdot 2\text{CH}_3\text{OH}$, and $[Ni(\text{Trp-naph})(\text{phen})(\text{CH}_3\text{OH})]$, where Trp-sal is a schiff base derived from tryptophan and salicylaldehyde, phen = 1, 10-phenanthroline). These three hexacoordinated octahedral nickel (II) complexes were tested against normal human cells (HSF) and four human cancer cell lines (breast cancer MCF-7, gastric cancer SGC-7901, esophageal cancer Eca-109, and hepatocellular carcinoma HepG2) using the MTT assay method. Cisplatin served as a benchmark for comparison. The first two complexes were shown to be non-toxic to four human cancer cell lines with IC₅₀ values greater than 80 μM . SGC-7901 and Eca-109 cells were mildly cytotoxically affected by the third complex and NI (CH_3COO)₂, with IC₅₀ values of 42.70 ± 1.13 , 48.36 ± 4.99 , 41.35 ± 0.87 , and 43.51 ± 1.34 , respectively. However, complexes were moderately cytotoxic to Eca-109 cells, as indicated by their IC₅₀ values of 23.95 ± 2.54 , 18.14 ± 2.39 , and $21.89 \pm 3.19 \mu\text{M}^1$.

In 2021, Noser *et al.* created two new amino acid SB ligands that included heterocyclic groups like quinazolinone and indole. They tested these compounds using an MTT assay to see how well they stopped the growth of cancer cells like MCF-7, MDA-231, and PCL, and how toxic they were to normal cells, specifically the WISH cell line, after 48 hours. It was discovered that both of these substances were strong anticancer prospects²⁴.



Sasikumar *et al* (2023) created a number of new metal complexes using Co (II), Ni (II), Cu (II), and Zn (II). The appropriate metal salts, heterocyclic bases, derivatives of salicylaldehyde, and amino acids containing SB were used to form the complexes. The amino acids containing SB displayed advantageous pharmacological properties following complexation. The researchers tested the toxic effect of these Cu (II) complexes on human skin cells called HDF. They also compared this with cancer cells from the lungs, cervix, and breasts to normal cells. They used the MTT method to evaluate the state of the cells being studied. The A549, HeLa, and MCF-7 cell lines had complex [Cu(L)(phen)] IC₅₀ values of 25.95 ± 1.82 , 26.26 ± 1.06 , and 17.13 ± 0.74 $\mu\text{g/mL}$, respectively. The findings showed that complex [Cu(L)(phen)] was more effective against cancer than complex [Cu(L)(bpy)], and its value was remarkably similar to cisplatin⁴⁶.

In 2024, Kharpan and others made new amino acid SBs, like Potassium (E)-4-((4-(hexadecyloxy)-2-hydroxybenzylidene)amino)butanoate (HL1) and Potassium (E)-6-((4-(hexadecyloxy)-2-hydroxybenzylidene)amino)hexanoate (HL2), as well as their copper (II) and zinc (II) complexes. These were tested on A549 cells in a lab, and their results suggested significant anticancer effects similar to cisplatin³⁶.

Recently, Vanco *et al* (2024) synthesized a new series of potassium isothiocyanato-(N-salicylidene-aminoacidato) cuprates having a general formula of the monomeric unit $\text{K}[\text{Cu}(\text{sal-aa})(\text{NCS})] \cdot x\text{H}_2\text{O}$ ($x=0$ or 2). These complexes are derived from natural amino acids such as glycine, alanine, valine, phenylalanine, and salicylaldehyde. The complexes showed moderate cancer-fighting abilities against some cancer cell lines (MCF-7, A2780, and A2780R), showing IC₅₀ values of 25–35 μM , and comparatively low toxicity to normal fibroblast MRC-5 cells (with IC₅₀ values $> 50 \mu\text{M}$)³².

Zhao *et al.* (2025) created three copper (II) complexes [Cu(o-van-D-Trp)(phen)], [Cu (o-van-D-Trp)(bipy)], and [Cu(naph-D-Trp)(bipy)] using D-tryptophan, vanillin, naphthaldehyde and ligands like phenanthroline and bipyridine. These were tested as possible cancer drugs. When compared with cisplatin, all three complexes were more effective against five thyroid cancer cell lines. The complex [Cu(o-van-D-Trp)(phen)] had very low IC₅₀ values, indicating strong anti-cancer activity against the cell lines tested⁵¹.

Antioxidant activity

Several tests, like DPPH, ABTS, and superoxide scavenging techniques, have been used to assess the antioxidant properties of different Schiff bases generated from amino acids.

In a 2012 study by Al-Garawi and colleagues, two Schiff base compounds were made by combining L-glycine and L-tryptophan with 4-methylbenzaldehyde. These were evaluated for their effects on total acid phosphatase (ACP), prostatic acid phosphatase (PAP), and non-prostatic acid phosphatase (NPA). The baseline activities for ACP, PAP, and NPA were 4.80, 0.30, and 4.50 U/L, respectively. Compound, 2-((4-methylbenzylidene)amino)acetic acid exhibited potent inhibitory effects on ACP and NPA, with maximum inhibition of 72.92% and 77.78% at 5.5×10^{-2} M, respectively. Additionally, it acted as a PAP activator at lower concentrations, increasing activity by 166.67% at 5.5×10^{-5} M. In contrast, compound 3-(1*H*-indol-3-yl)-2-((4-methylbenzylidene)amino)propanoic acid exhibited both inhibitory and activating behavior depending on the concentration; at 5.5×10^{-5} M, it significantly activated ACP and PAP by 125.00% and 1533.33%, respectively, and increased NPA activity by 31.11%. These results suggest that both compounds act in a dose-dependent manner, with 2-((4-methylbenzylidene)amino)acetic acid functioning primarily as an inhibitor and 3-(1*H*-



indol-3-yl)-2-((4-methylbenzylidene)amino)propanoic acid showing a concentration-sensitive dual role, indicating their potential in modulating phosphatase activity through Schiff base chemistry⁴⁴.

In 2022, Verma and others created a group of amino acid SBs linked with quinazolinone and tested their antioxidant property. They used three *in vitro* tests, including DPPH, ABTS, and DMPD methods to evaluate antioxidant activity. A lower IC₅₀ value usually means strong antioxidant ability. Their study showed that the synthesized compounds had strong antioxidant properties, and they were compared with known antioxidants like gallic acid and ascorbic acid. Most of the compounds showed good antioxidant activity. Many synthesized derivatives showed strong ability to remove free radicals, with IC₅₀ values between 6 and 32 µg/mL in the DPPH test. This performance was much better than the standard compounds ascorbic acid (AA) and gallic acid (GA), which had IC₅₀ values of 38 µg/mL each. In the ABTS+ radical scavenging test, different compounds had strong antioxidant effects with IC₅₀ values ranging from 6 to 36 µg/mL, which was better than the commercial standards AA (42 µg/mL) and GA (38 µg/mL). In the DMPD+ radical scavenging test, many compounds also showed strong antioxidant activity, with IC₅₀ values from 6 to 30 µg/mL, which was much better than the standards AA (36 µg/mL) and GA (30 µg/mL) respectively²⁷.

A furan ring, a pyridine ring, and the L-arginine structure were added to a series of L-arginine Schiff bases acylated chitosan derivatives in a recent work by Cui *et al* (2022) to increase the antioxidant and antibacterial properties of chitosan. Newly synthesized compounds were shown to scavenge superoxide anion free radicals more quickly than chitosan when their capacity to do so was tested. The results demonstrate the

effectiveness of halogenated compounds in scavenging superoxide anion radicals, with CR2B3PCA, CRCF, CRBF, and CR2C3PCA—equivalent to Vitamin C (VC) at 1.60 mg/mL—being 100.00%, 99.37%, 95.95%, 95.45%, and 95.13%, respectively. Tests of the DPPH free radical's scavenging capacity also revealed that, except for compound CR3PCA, the scavenging rate of other compounds was higher than that of chitosan. Overall, CRCF, CRBF, and CR2PCA had potent scavenging capabilities, and at the concentration of DPPH free radicals, their scavenging capacities were 89.01%, 82.04%, and 80.92%, respectively³⁰.

Anti-inflammatory activity

The ability of various amino acid-derived Schiff bases to reduce inflammation has been studied using lab tests and animal models. These tests include measuring the production of certain proteins and checking how well they block specific biological markers. Naglah *et al* (2016) created a new group of Schiff bases by combining isatin with hydrazides made from nalidixic acid and L-amino acids. To check their anti-inflammatory effects, they looked at how much of two proteins, COX-2 and iNOS, were produced in macrophage cells treated with a substance called LPS. These Schiff bases showed strong ability to stop both COX-2 and iNOS from becoming active, though the effectiveness varied. For COX-2, they inhibited around 56.4% at a dose of 10 µM, but for iNOS, the inhibition was much stronger, reducing expression to between 16.5% and 43.3% at the same dose⁵².

Abood *et al* (2020) used a condensation reaction between 3-phenyl-propenal (cinnamaldehyde) and amino acids (tryptophan or histidine) to create two new Schiff bases. These were utilized to prepare the metal complexes by reacting with copper sulphate. The complexes' inflammatory inhibitory activity was assessed by measuring the paw's



thickness at zero time, which was 3.3 and 3.2 mm for the treatment groups, respectively. The thickness of the paws grew to 3.90 and 3.93 mm after an hour of egg albumin injection. The metal complexes formed from 3-(1H-indol-3-yl)-2-(((E)-3-phenylallylidene amino) propanoic acid 3-(1H-imidazol-4-yl)-2-(((E)-3-phenylallylidene amino) propanoic acid significantly decreased the paw's thickness to 3.56 and 3.80 mm, respectively, after two hours. Because the former complex contained tryptophan rather than histidine, it was more active than the later complex¹⁷.

Verma *et al.* (2022) made and tested a group of Schiff bases that were created by linking amino acids to quinazolinone. These were tested for their ability to reduce inflammation in lab tests. Some of these compounds had strong effects, even better than standard drugs like indomethacin and ibuprofen. The most active ones had IC₅₀ values between 12 and 36 µg/mL, which is better than the standard drugs, which had IC₅₀ values of 36 µg/mL for indomethacin and 40 µg/mL for ibuprofen. The study found that compounds with groups like Cl, NO₂, and F (which takes away electrons) were more effective than those with groups like OH and OCH₃ (which gave electrons). Also, using certain amino acids, like tryptophan and phenylalanine, made the compounds more active than those made with alanine or glycine²⁷.

Antidiabetic Activity

Santha Lakshmi *et al.* (2016) synthesized and structurally characterized two novel Cu(II) complexes derived from Schiff bases of L-valine and coordinated with tetramethylethylenediamine (tmen) to investigate their *in vitro* antidiabetic potential. The Schiff bases, N-(salicylidene)-L-valine and N-(3,5-dichlorosalicylidene)-L-valine, afforded two structurally distinct complexes: one exhibiting a dinuclear architecture featuring syn-anti carboxylate bridging, and the other adopting a distorted square-pyramidal geometry. Their

molecular structures were established using single-crystal X-ray diffraction, FTIR, UV-Vis, circular dichroism (CD), and ESR spectroscopy. The complexes were subsequently evaluated for their inhibitory effects against α -amylase and α -glucosidase, key carbohydrate-metabolizing enzymes associated with the regulation of postprandial blood glucose levels. Both complexes demonstrated appreciable enzyme-inhibitory activity; notably, one complex exhibited greater inhibitory efficacy than the standard drug acarbose, with IC₅₀ values of 389.01 µg/mL against α -amylase and 350.02 µg/mL against α -glucosidase. The schiff base ligand's electron-withdrawing dichloro-substituents were thought to be responsible for the increased activity since they probably facilitated contacts with the active sites of the enzyme. Furthermore, one compound was shown to be especially successful at postponing the passage of glucose across membranes in glucose diffusion studies. These results demonstrate how Schiff base ligands can be tuned with particular substituents to alter biological activity, laying the groundwork for the development of metal-based antidiabetic drugs that use schiff bases produced from amino acids as pharmacophores. Additional *in vivo* research is required to confirm the therapeutic potential¹⁰.

CONCLUSION

Amino acid schiff bases (SBs) occupies a major consideration in the area of pharmaceutical chemistry owing to their special structural features and multiple pharmacological properties. Antioxidant, anti-diabetic, anti-inflammatory, urease inhibitory, antifungal, antibacterial, and anticancer characteristics are just a few of their many pharmaceutical applications. The need to create more potent antimicrobial medications is urgent because of the rising incidence of antimicrobial resistance and the rise in multidrug-resistant bacteria. This review emphasizes the



significance of SBs derived from amino acids and provides an overview of the therapeutic activities of SBs as reported in the most recent research. The ability of SBs to form stable metal complexes further expands their scope, as metal coordination often improves solubility, stability, and biological activity. In the area of antibacterial and antifungal activity, generally both free amino acid-SBs and their particular metal complexes (specific with Cu, Zn, and VO^{2+}) exhibit increased microbial inhibition and membrane penetration, often matching or surpassing the standard drugs. It has been shown that modifications such as halogenation or increase in length of aliphatic chains considerably increase their activity. The Cu(II), Ni(II) and Co(II) metal complexes showed a significant cell killing effect against different cancer cell lines, indicating their promising potential as anticancer agents. Their activity is often associated with ROS generation and damage of mitochondrial membranes. By tweaking the ligand we can create drugs that are target specific. Another important field was the antioxidant activity where several Schiff bases showed IC₅₀ values much lower than commercial standards such as ascorbic and gallic acid. Electron-withdrawing groups and aromatic moieties boosted radical scavenging in multiple assays. The therapeutic potential of these compounds is further increased by their anti-inflammatory and antidiabetic potentials. – Schiff bases with D-amino acids or electron-withdrawing substituents are particularly promising for inhibition of enzyme and glucose diffusion control, indicating their potential in the control of metabolic disorders. Finally, these molecules exhibited strong inhibition of viral replication in antiviral studies, especially through ROS-mediated pathways, and stereoselective activity toward D-isomers. Collectively, these results indicate that amino acid Schiff bases are physiologically relevant as well as being interesting from a chemical perspective.

They can be modified, bind metals and have good pharmacokinetic properties, making them very promising candidates for further studies as multi-target therapeutics. Future studies should focus on in vivo validation, pharmacokinetic profiling and mechanistic elucidation to translate this adaptable scaffold into clinically feasible pharmaceuticals.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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