Applied Chemical Engineering (2024) Volume 7 Issue 2
doi: 10.59429/ace.v7i2.1860

REVIEW ARTICLE

Recent developments in catalytic and antimicrobial applications of benzimidazole Schiff base: A review

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ABSTRACT

An amino acid and a carbonyl molecule are combined to generate Schiff bases complexes, which are useful compounds. Catalytic activity is high in many metals Schiff base complexes, especially chiral ones. Examples of processes include epoxidation, aldol condensation, hydroxylation, and oxidation. In several activities and in the presence of moisture, complexes display considerable catalytic activity. They have antibacterial, antifungal, antiviral, antimalarial, anticancer, and anti-HIV properties, among other biological activities. Research into these compounds' coordination behavior has exploded because of specific metals on them, their biological activity and their intrinsic chemical interest as multidentate ligands. This article provides an overview of the numerous syntheses and uses for Schiff bases and their metal complexes.

Keywords: schiff base; benzimidazole; antibacterial activity; antifungal activity; antitumor and anticancer activity; antiviral activity

1. Introduction

The reaction between amino and carbonyl compounds is used generally to obtain Schiff bases. They are represented by general formula $R_1R_2C = NR'$ where R' may be any aryl or alkyl group except hydrogen. Schiff bases processed by coordination of ligand to with metal through azomethine nitrogen. This class is very important because these complexes are used in many industries like food, dye, analytical chemistry, fungicides, agrochemical, catalysis, and biological applications[1]. The nitrogen containing ligands have always very promising in biological activity for example triazole[2]. Among a variety of Schiff base, azomethine ligands derived from benzimidazole are of special interest particularly as anticancer agents, antifungal agents, diuretic activities, and antibacterial agents. Biological activities of such compounds are because of carbon-nitrogen linkage in the derivatives of azomethine. Researchers have shown great interest and many azomethine have been reported which have remarkable activity[3] In naturally occurring benzimidazole, *N*-ribosyl dimethyl benzimidazole is very important which is found in core of vitamin B_{12}[4,5]. The role of vitamin B_{12} is very important in amino acid and fatty acid metabolism, and it also works as a cofactor in DNA synthesis for methyl malonyl coenzyme A mutase and methionine synthetase. This vitamin is not produced by plants but by bacteria[6].

Benzimidazole nucleus is bioactive heterocyclic compounds, and its derivatives are found effective in pharmacodynamic and pharmacokinetic uses of various kinds[7]. Anthelmintic medicines such as albendazole, mebendazole, and thiabendazole are commonly used[8]. 2-thioalkyl and thioaryl substituted benzimidazole, as well as 5,6-dinitrobenzimidazole, were used to make benzimidazole

ARTICLE INFO

Received: 7 August 2023

Accepted: 20 October 2023

Available online: 8 March 2024

derivatives for nosocomial strains of Stenotrophomonas maltophilia[9].

2-methyl benzimidazoles were the result of the condensation of acetic anhydride and $C_6H_4(NH_2)_2$(OPD) along and HCL and mono- or di-acetyl-o-diamines with boiling dilute hydro-chloric acid. These condensation reactions of OPD with compounds containing -COOH group were also used for synthesis of 2-substituted benzimidazoles[10].The attachment of α-amino acids into the benzimidazole moiety was found to be effective in enhancing the bioactivity of benzimidazole nucleus[11].

Cescon and Day effectively synthesized-amino-(2-benzimidazolyl)-butyric acid using glutamic acid with OPD[12]. By simply heating at a certain temperature higher than the liquid's melting point reactant materials, the monoacyl derivative of o-phenylenediamine can be easily transformed into the equivalent benzimidazole. When monoacyl derivatives are readily available, this is a particularly successful approach for preparing benzimidazoles. To prevent oxidation, the monoacyl derivative of diamine can be enhanced by heating in the nitrogen atmosphere[13]. O-phenylenediamine diacyl derivatives must be transformed at higher temperatures[14]. Synthetic Novel azetidine-2-one was tested against *E. coli, C. albicans, B. subtilis, Aspergillus niger* and *Aspergillus flavus* with gram-positive bacteria showing more effective antibacterial action. The molecule's high lipophilicity is a crucial characteristic in developing antibacterial actions. 2-Substituted 1-[(5-Substituted-Alkyl/Aryl)-1,3,4-Oxadiazole-2yl] Benzimidazole Derivatives using a nucleophilic substitution method were produced and evaluated for antibacterial activity against Gram positive and Gram-negative microorganisms[15,16].

one pot synthesis of benzimidazole and its derivatives were reported earlier via reaction of *o*-phenylenediamine and various aldehydes. The method used in the synthesis is very short time consuming and give high yield. In another study Zn was used to catalyze the reaction[17–19].

By treating certain 2-chloro- or 2-chloromethyl-1H-benzimidazoles with $C_6H_5NH_2$ derivatives, a seriesof 2-(anilino or 2,6-dichloroanilino)-1,5(6)-disubstituted 1H-benzimidazoles have been produced (1-13 compounds). The antifungal and antibacterial properties of the compounds were investigated in vitro. The compounds shown in **Figure 1** were the most active chemicals[20].

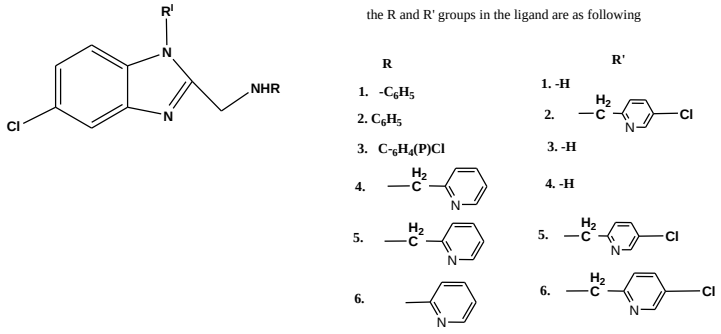

Figure 1. Benzimidazoles derived from aniline and its derivatives.

The benzimidazole Schiff base complexes were reported very efficient for catalyzing many major reactions like Suzuki-Miyaura reaction. Pt Complex were used for better catalyzing ability, but Pt is costly. Thus, transition metal Schiff base complexes have been created for effective and low-cost catalysis, with Cu complexes being the most common[21].Benzimidazole Schiff bases are important in industrial production also. The product of reaction of ketenes and imines work as a useful precursor for catalyzing the industrial production of many enzymes' inhibitor, drugs, and antibiotics[22].

Because of their catalytic activity, Ni Schiff base complexes have been widely explored. These complexes are used as catalyst for cross-coupling, asymmetric transformation, etc.[23].

The ability of polyaza macrocyclic Schiff bases to generate stable compounds with a variety of transition metals has piqued researchers' curiosity. It has been found that these complexes can be applied as

inorganic and organic receptors, homogenous catalyst antimicrobial agents and DNA, RNA interacting agents[24–26]. The derivative of ß-pyrrole called Benzoporphyrin has vast application due to its 18 π-electron system and conjugation[27]. Due to variety in the coordination environment, redox and spectral properties, transition metal complexes produce deep area of interest for research and design species suitable to bind and cleave DNA[28–34]. Benzimidazole is an important Schiff base which includes benzene having imidazole unit fused with it. The derivatives of benzimidazole are studied and synthesized because of their wide applications in medicinal field especially as antibacterial agents of enhanced properties[35–40].

Benzimidazole derivatives have also been used as enzyme inhibition for the disease or disorder originate due to problem in enzyme secretion. For example, diabetes is one of the major health issues and the third of biggest cause of death. Another problem is obesity i.e., the problem of excessive fat gaining. This arises due to heavy food and low energy consumption[41,42].Some other types of Schiff base complex were also examined for their catalytic and antimicrobial activities. Like surfactant-based Schiff bases have exhibited very excellent antibacterial, antifungal, catalytic activities[43–45]. The Azomethine-based pyridine nuclei demonstrated an aptitude for suppressing sulfate reducing bacteria[46].

2. Catalytic application

Many reactions of pharmaceutical or industrial use etc. have been catalyzed by Schiff base complexes. Initially the truncated octahedral platinum etc. are used for catalysis. The division of Most homogeneous catalysts are difficult to make, and there is also the issue of preventing active species from leaching into solution. Copper was utilised to generate a novel benzimidazolyl SBs ligand called 2-benzimidazolyl ethylimino methyl naphthalen-2-ol due to its efficient catalysis under moderate conditions[47].In our body system, there are many types of enzymes, and each have its own work to perform. Phenoxazinone synthase and enzymes which contain Cu metal and it catalyze the oxidation of different amino phenols to Phenoxazinone. For the mimicking of this enzyme, bis-benzimidazole diamide iron (III) complexes has been reported. The ability of this complex to catalyze because of having a pendant arm of benzimidazole[48].

Ligand N-methyl benzo-imidazol-2-yl ethylimino methyl naphanal-2-ol is synthesized with Cu to catalyze the oxidation of 1, 10-phenanthroline to phendione which is an important reaction due to its abilities of binding proteins, DNA interaction, redox properties, etc.[49].The benzimidazolyl 2-[2-(1H-benzo[d]-imidazol-2-yl) ethylimino) methyl] phenol Copper (II) complex was produced and used to convert dopamine to aminochrome[50].An N-substituted benzimidazolyl Schiff base ligand catalyses the oxidation of 1-phenyl propyne to give acetylenic aldehyde or diketonic product in the presence of tert-Butyl hydroperoxide. The importance of this reaction is that dicarbonyl derivatives are used to synthesize the biological active compounds like imidazole, quinoxalines, etc.[51].Nickel compound with the Benzimidazole SBs ligand [2-[2-(1Hbenzo[d]imidazole-2-yl) ethylimino] while in the presence of tert-butyl hydroperoxide, phenol is utilized as a result homogeneous catalyst to oxidize substituted benzyl amines. The geometry of this complex is suggested to be distorted octahedral. The mechanism purposed for the oxidation is shown in **Figure 2**[52].

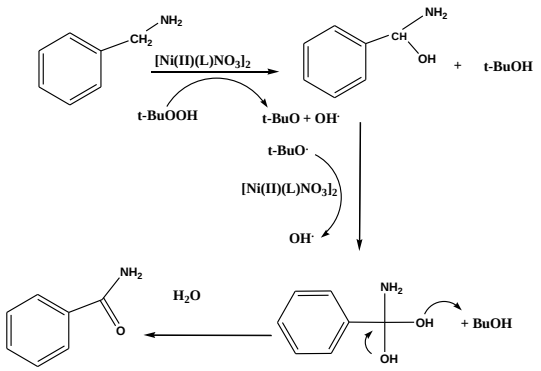

Figure 2. Mechanism of oxidation of substituted benzyl amines by benzimidazoles.

Different complexes of 2-(α-Hydroxymethyl) benzimidazole with transition metals were reported for their catalytic activities. PS-[Cu(2-(α-Hydroxymethyl) benzimidazole)$_2$] and PS-[VO (2-(α-Hydroxymethyl) benzimidazole)$_2$] catalyze the oxidation of ethyl benzene and styrene. Similarly, PS-[VO (2-(α-Hydroxymethyl) benzimidazole)$_2$] and PS-[MoO_2 (2-(α-Hydroxymethyl) benzimidazole)$_2$] have been synthesized and confirmed for the oxidative bromination of Salicylaldehyde[54]. Sulfonic acid group functionalize benzimidazole derivative BAIL (Bronsted acid ionic liquid) were created and these compounds showed significant catalytic activity for Biginelli reaction which is important for synthesis of dihydropyrimidinones[55].

Suzuki-Miyaura reaction catalyzed by 1-substituted trimethylsilyl benzimidazoles was shown to have high catalytic activity[56].

Benzimidazole ligand has also been used for Heck reaction as an efficient catalyst with palladium[57].

3. As antibacterial agents

Some 2-subsitituted benzimidazole derivatives such as 1-(1H-benzo[d]imidazol-2-yl)-2-methyl propan-1-amine, 1-(1H-benzo[d]imidazol-2-yl) pentane-1,5-diamine have shown very effective antibacterial property against *Staphylococcus aureus, Proteus vulgaris, Streptococcus faecalis, Klebsiella pneumonia, Pseudomonas aeruginosa* and *Escherichia coli*. The commonly used method for the activity is agar well diffusion method[58].

The Schiff base ligands generated by $C_5H_7N_3$, and o-benzoyl benzoic acid metal (**Figure 3**) were shown to be especially efficient *Bacillus subtilis* and *Staphylococcus aureus* are Gram +ve bacteria and Gram −ve bacteria like *Neisseria gonorrhoeae* and *Escherichia coli* gram negative bacteria[59]. The complexes of 2-aminobenzimidazole and salicylaldehyde show good antibacterial activity against *E. coli*[60].

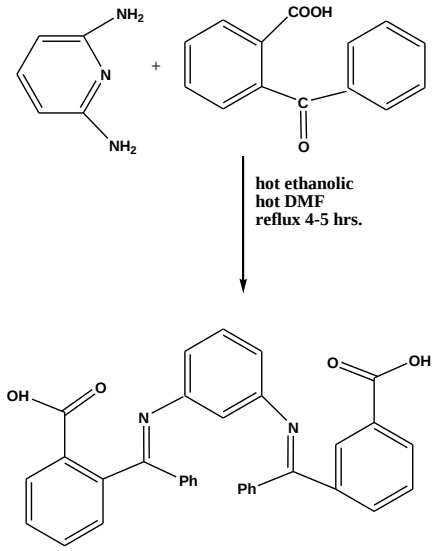

Figure 3. Scheme of synthesis of benzimidazole from pyridine.

As it has been clearly stabilized fact that benzimidazole moiety possess various biological application, new synthesized ligands are constantly reported. In order of this, novel benzimidazolyl tetrahydro protoberberines ligand was synthesized. It was found that the ligand containing 5-fluor benzimidazole moiety possesses highest activity in comparison with standards Norfloxacin, Fluconazole etc. against both antibacterial like *E. coli, B. subtilis, B. proteus,* etc. The enhanced biological activity of benzimidazole is a tribute to the presence of hydroxyl or methoxy group on benzene ring in the berberines structure andcontains isoquinoline backbone.

Using 5(6)-substituted 2-mercapto-benzimidazol-thiols as a precursor, two benzimidazole derivatives were synthesized and tested for antibacterial activity against *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, and other bacteria. Compounds containing phenylpropyl have a high antibacterial activity in the group 1, 3-disubstituted-2-imino-benzimidazoles[61]. Novel ligands were created for antibacterial research against Salmonella typhi, Escherichia coli, *Bacillus subtilis*, and *Bacillus stearothermophilus*. Three types of ligands synthesized were 2-(α-methylsalicylidenehydrazino) benzimidazole (L_1), 2-(α-phenyl salicylidenehydrazino) benzimidazole (L_2), 2-(o-vanillinidenehydrazino) benzimidazole (L_3). Though result explains that free ligand had lesser activity than complexes and the reason is chelation effect[62].2-(o-anisylidene-2'-imino) amino benzimidazole (OAB) and 2-(furfurylidene imino) amino benzimidazole (FIAB) were produced and evaluated for antibacterial activity against Gram positive bacteria B. subtilis and B. stearothermophilus, as well as Gram negative bacteria E. coli and S. typhi. The activity of complexes containing both ligands was excellent[63]. The 1, 2-disubstituted-1H benzimidazole-N alkylated-5-carboxamidine derivatives were found to have extremely high antibacterial action against methicillin-resistant *S. aureus*[64].

Amino organophosphorus Imidazole's derivatives were prepared and the compound having 3-chloro-4-fluorophenyl group exhibited most potency against bacterial strains Staphylococcus aureus and anti-S. cerevisiae[65].

A(E)-2-(4-(1H-benzo[d]imidazol-2-yl)phenylimino)methyl)-4-bromo phenol benzimidazole derivative as well as the related Zn(II), Ni(II), Cu(II), and Pd(II) complexes were made. When all compounds were tested for antibacterial activity, the Ni(II) complex displayed promising results against both Grammpositive and Grammnegative bacterial strains, while the other compounds displayed activity only against kinds of bacteria[66].

Co(II) metal complex of Benzimidazole synthesized from 5-chlorosalycyaldehyde with aminophenol and derivatives of *o*-phenylenediamine was checked for antibacterial activities and found more active than the ligand[67]. Ni(II), Co(II), Cu(II), Mn(II), and Zn(II) VO(IV) metal complexes with Schiff bases made from 2-(2-amino-phenyl)1-H-Benzimidazol (2-[(Z)-(2-(1H-benzimidazole-2yl)phenyl]iminomethyl]) and3-Ethoxy Salicylaldehyde andwere produced using synthesis. Two grammnegative bacteria, E. Coli and Pseudomonas fluorescens, as well as two grammpositive bacteria, Bacillus subitilis and Staphylococcus aureus, were used to test the ligand's and its metal complexes' antimicrobial properties. According to the activity data, metal complexes are more effective than free ligands[68].

4. As antifungal agents

Because of the ineffectiveness or resistance of fungal pathogens, patients have died because of fungal infections. The newly synthesized benzimidazole derivative ligand (S)-2-(1-aminoisobutyl)-1-(3-chlorobenzyl) benzimidazole was found to have potent antifungal action against Candida glabrata and *C. krusei*. These species have showed the greatest resistance to antifungal medicines currently available[69]. Synthesis of compound is shown in **Figure 4**.

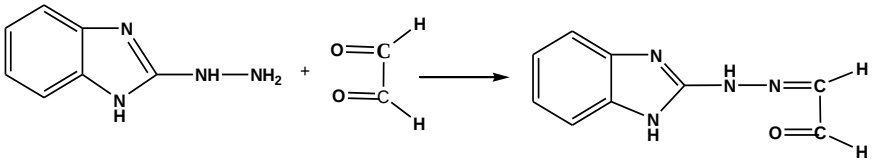

Figure 4. Synthesis of benzimidazole derivative ligand (S)-2-(1-aminoisobutyl)-1-(3-chlorobenzyl) benzimidazole.

The benzimidazole ligands 2-(benzimidazolyl–2-amino) imino-1, 2-dimethyl ethanone, 2-(benzimidazolyl-2-amino) imino-1, 2-diphenyl ethanone, and 2-(benzimidazolyl-2-amino) imino-1, 2-diphenyl ethanone (By using the Potato dextrose agar diffusion method, these complexes show efficacy against two fungus strains, *A. niger* and *A. flavus*[70]. Antifungal activity has been reported against *Candia albicans* and *Aspergillus niger* by Schiff base ligand prepared by 2-aminobenzimidazole condensation with salicylaldehyde[71].

The fungicidal activity of 2-(o-anisylidene-2'-imino) amino benzimidazole (AIAB) and 2-(furfurylidene imino) amino benzimidazole (FIAB) ligands against *A.niger* and *A.flavus* was found to be very good. The activity is explained due the presence of C=N. Also, the ligands make the metal ion less polarwhich facilitates the penetration of microorganism membrane[63].

Benzimidazole Schiff bases were prepared by condensation of Oct-2-ynoic acid and substituted amines. Antifungal activity was found against *Aspergillus carbonarius, Aspergillus flavus*, *Aspergillus fumigatus, Aspergillus niger, Aspergillus parasiticus, Fusarium proliferatum*, and *Fusarium verticillioides* using these chemicals. The ligand bearing carboxyl and sulphonyl group [exhibited more fungicidal activity[72].

When tested against *Colletotrichum gloeosporioides, Alternaria solani, and Fusarium solani*, 2-chloromethyl-1H-benzimidazole derivatives exhibited excellent efficacy. The most active compound was bearing oxo phenyl group as side chain attached to benzimidazole moiety[73].Alkylated mono-, bis- and tris-Benzimidazole derivatives were formed and reported that bis benzimidazole were very active for fungicidal activities against yeast and *filamentous fungi*. The compound bearing alkyne group has most potency[74].

Pyridine based macrocyclic Schiff base were synthesized and studied for antifungal activities and found to be very potent against several fungi species like *C. albicans* with a standard Gentamycin[75,76].

The Schiff bases produced by the condensation of 2-amino-5-cWoro benzimidazole and 2-aminobenzimidazole with 1-(1-phenyl-3-p-chlorophenyl) pyrazolylcarboxaldehyde reacted with hydrated acetates of Co(II), Ni(II), Cu(II), and Zn(II). These complexes' antifungal behaviour has also been investigated in relation to the fungi that harm crops, H. oryzae and R. solani[77]. Complexes were created with general formula [MX2(HL)(H2O)].yH2O, where X = Cl, $(SO_4)_2$ and M = Mn(II), Co(II), Ni(II), Cu(II), Zn(II), and Cr(III).The synthesised complexes' fungicidal activity was assessed against three soil-borne fungi, as well as that of the free ligand. Data obtained indicated that the synthesised complexes had greater biological activity than the original Schiff base ligand. The new formulation's fungicidal activity was assessed and contrasted with that of the industry-standard fungicide Pencycuron (Monceren 25% WP). Under laboratory circumstances, the novel formulation often had stronger fungicidal action than the traditional fungicide[78].Three ferrocene-containing benzimidazole derivatives—2-[(ferrocen-1-yl)-5-x-6-y-1H-benzimidazole (x=methyl, y=H; BZ(1); (x = methyl, y = methyl; BZ(2); x = chloro, y = nitro; BZ(3)—and their CoCl2 complexeswere produced and characterised. The Co(II) combination of BZ(2) (**Figure 5**) had the strongest antifungal activity against C. parapsilosis, with a MIC value of 19.5 mu g/mL[79].

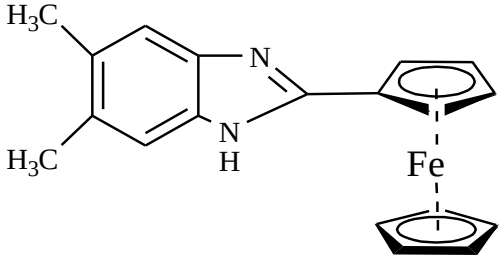

Figure 5. Structure of 2-(ferrocen-1-yl)-5,6-dimethyl-1H-benzimidazole.

5. As antiviral agents

The anti-HIV activity of some new benzimidazoles was check against HIV-1 reverse transcriptase (HIV-1 RT) inhibitory activity. Among all then complexes four complexes 3-(1H-benzo[d]imidazol-1-yl)-N-(2-chloro-4-methylphenyl) propionamide, 3-(1H-benzo[d]imidazol-1-yl)-N-(3-chloro-2-methylphenyl) propionamide, 3-(1H-benzo[d]imidazol-1-yl)-N-(3, 4-dichlorophenyl) propionamide and 3-(1H-benzo[d]imidazol-1-yl)-N-(4-bromophenyl) propionamide have shown higher activity than the standard Though the inhibitory action is lower than the standard employed, -N-(2,4,6-tribromophenyl) propionamide has the highest inhibitory percentage (Efavirenz)[80].2-[(benzotriazol-1/2-yl) methyl] benzimidazole were tested against antiviral activities viruses such as Flaviviruses (Virus of Yellow Fever) and Pesticiruses (Virus of Bovine Viral Diarrhea), as well as HIV-1. At position 1, these derivatives include either linear (dialkylamino) or bulky (quinolizidin-1-yl) alkyl moieties, and compounds with quinolizidin-1-yl have been found to have moderate action against Flaviviruses and Pesticiruses[81].

Benzimidazole derivatives have been tested against Hepatitis *C virus*. It was identified that derivatives synthesized from 4-aminoquinolines and piperazine exhibit antiviral properties. Compound B-5 among the checked compounds is found to exhibit better property against Hepatitis *C virus*[82].Antiviral properties of benzimidazole derivatives are due to the benzimidazole moiety. The triazole substituted Benzimidazole exhibit anti hepatitis *C virus* activity[83]. Benzimidazole derivatives in combination with pyrimidine also showed good anti hepatitis property[84]. Benzyl-2-(2-(1-methyl-1H-pyrrol-2-yl) ethyl)-1H-benzoimidazole, a benzimidazole derivative of pyrrole, on the other hand, demonstrated significant anti-hepatitis B viral action[85]. The activity of 5-acetyl-2-aryl benzimidazole and its derivatives against viral RNA was investigated. the following compound (**Figure 6**) is the most potent of all the compounds[86].

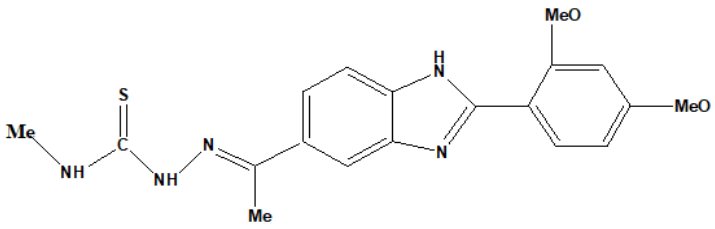

Figure 6. 5-acetyl-2-aryl benzimidazole.

For testing, 2-phenyl benzimidazole was produced and found to be effective against YFV, BVDV, HSV-1, Sb-1, and CVB-2[87]. 4-chloro-2-(6-nitro-1H-benzo[d]imidazol-2-yl) phenol and 4-chloro-2-(6-methyl-1H-benzo[d]imidazol-2-yl) phenol (**Figure 7**) were synthesized and their antifungal as well as antibacterial properties were excellent against *M. luteus, S. aureus*, etc. and *A. flavus*, etc.[88].

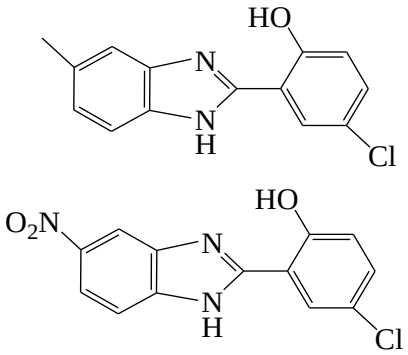

Figure 7. 4-chloro-2-(6-nitro-1H-benzo[d]imidazol-2-yl) phenol and 4-chloro-2-(6-methyl-1H-benzo[d]imidazol-2-yl) phenol.

By examining their ability to reduce HIV-induced cytopathogenicity in MT-4 cells, new Schiff base ligands made from 5-amino-4-phenyl-4H-1,2,4-triazole-3-thiol 1 and substituted benzaldehydes, as well as their metal complexes with Cu(II), Fe(II), Au(III), and Mn(II), were tested for anti-HIV-1 and HIV-2 activity. When tested in cell culture, the substances I and II (**Figure 8**) were shown to be the most effective inhibitors of HIV-1 (EC50 = 12.2 g/mL (SI = 4) and > 2.11 g/mL (SI ≥ 1), respectively), while I (**Figure 8**) demonstrated inhibition of HIV-2 with an EC50 > 10.2 g/mL and SI = 9[89].

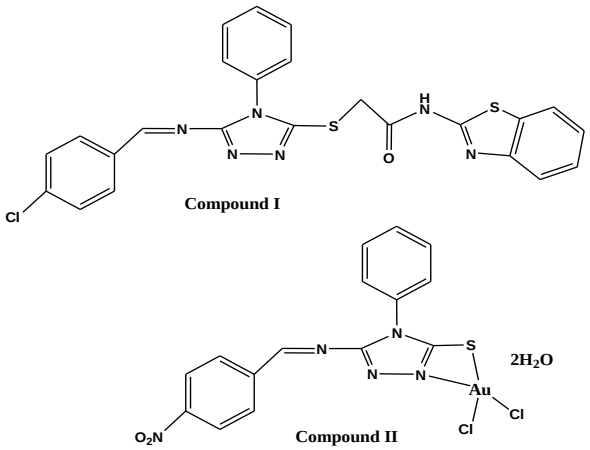

Figure 8. Active compounds against HIV-1 and HIV-2.

6. As anticancer and antitumor agents

Some cyclic benzimidazole synthesized form the condensation of aminobenzimidazole and methoxy substituted benzaldehyde have been reported to show limited anticancer activity against PC3 cells and HeLa cell. Doxorubicin was used for comparison[90]. Cu(II), Zn(II), and Cd(II) SBs compounds originated from 2-acetylpyridine, and l-tryptophan were evaluated for human breast cancer cell (MCF7)[91]. A Schiff base was used to react with malononitrile in 100% ethanol to create the new benzimidazole derivatives (*N*-(3,4,5-trimethoxyphenyl)methylene]-1*H*-benzimidazol-2-amine, (N-(3,4-dimethoxyphenyl) methylene]-*1H*-benzimidazol-2-amineand (N-(4-methoxyphenyl) methylene]-*1H*-benzimidazol-2-amine. The last compound shows average cytotoxicity whereas the activity of other two compounds is limited[92].

The major problem in drug discovery for cancer treatment is the low solubility. To overcome this problem some benzimidazole Schiff base have been synthesized containing amine or oxetane. Compound (5-(4-(methyl (oxetan-3-yl) amino) benzoyl)-1H-benzo[d]imidazol-2-yl) carbamate was discovered. **Figure 9** containing oxetane shows excellent anti-cancer efficacy in the lungs, prostate, and ovary[93].

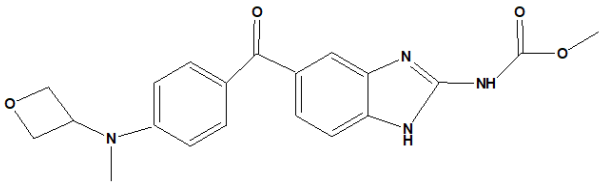

Figure 9. (5-(4-(methyl (oxetan-3-yl) amino) benzoyl)-1H-benzo[d]imidazol-2-yl) carbamate.

The anticancer ability of pyrido [1, 2-a] benzimidazole were enhanced by functionalizing it with specific substitution. Great activity against different cancer cells like melanoma, CNS cancer was shown by the compound 3-Methyl-1-(4-substituted phenylamino) pyrido [1, 2-a] benzimidazole-4-carbonitrile. This

enhancement is attributed to the presence of 3-triflauro methyl group[94]. It is well known that hepatocellular carcinoma is the second among the cancer death and the reason for this is that it is diagnosed mostly at its advanced stage. Methyl 2-(5-fluoro-2-hydroxyphenyl)-1H-benzo[d]imidazole-5-carboxylate was found most active against cancer cells in comparison to the standard used, Cisplatin in the MTT essay[95–97].

Quinazoline is an effective backbone for anticancer activity. Some novel derivatives of benzimidazole and quinazoline were formed by condensation with substituted primary amine and checked against no. of cancer cells like CNS cancer, melanoma cancer, breast cancer, etc. Three of these compounds 1-Allyl-2-methyl-1H-benzimidazol-5-ylamine and 3-Allyl-2-methyl-3H-benzimidazol-5-ylamine, 4-Fluorophenylamine were reported highly potent against these cancer cell lines[98]. A family of 2,5,6-trisubstituted imidazo[2,1−b] [1,3,4]-thiadiazolefor anticancer activity, was produced, including 5-bromo-6-(4-chlorophenyl)-2-cyclopropylimidazo[2,1−b]. [1,3,4] The bromo derivative of the ligand, thiadiazole, was found to be the most effective against leukemic cancer cell lines[99]. In liver, and lung, breast cancer cell lines, the anticancer activity of a new 2-(4-(1H-benzo[d]imidazol-2-yl) phenyl imino) methyl) phenol was demonstrated[100]. The reaction of 4-(1H-benzo[d]mdazl-2-yl)aniline with various aromatic aldehydes using conventional heating and microwave irradiation produced a new series of Schiff bases containing benzimidazole moiety. The in vitro anticancer effects of the newly synthesised ligand 2-(4-(1H-benzo[d]imidazol-2-yl)phenylimino) methyl)phenol and its complexes were evaluated in breast, liver, and lung cancer cell lines. Results indicated that this newly synthesised ligand and its complexes had significantly greater anticancer activity than the widely used medication doxorubicin, notably Zinc Complex[101]. Transition metal ions, such as copper, silver, nickel, iron, and manganese, were used to create metal complexes of 2-methyl-1H-benzimidazole-5-carboxylic acid hydrazide (4a; L1) and its Schiff base 2-methyl-N-(propan-2-ylidene)-1H-benzimidazole-5-carbohydrazide (5a; L2). Both the human breast cancer cell line MCF-7 and the human lung cancer cell line A549 were shown to be cytotoxic (IC50 = 2 μM) to the silver complex. Manganese complex synthesized [Mn(CO)3(bpy)L]X containing CORMs [bpy = 2,2'-bipyridine, X = hexafluorophosphate (PF6), trifluoromethanesulfonate (OTf), L = imidazole, methylimidazole, benzimidazole, N-benzylbenzimidazole, N-(4-chlorobenzyl)benzimidazole] to release CO in human invasive ductal breast (MCF-7) cell line In vitro tests showed that the chemicals had a cytotoxic effect on breast cancer cells and hindered cell proliferation. In vitro tests showed that the chemicals had a cytotoxic effect on breast cancer cells and hindered cell proliferation[102].

7. As antimalarial agents

The ligand made from 2-(2-pyridyl) benzimidazole and its substituted phenacyl halides was evaluated for antibacterial activity and shown to be antimalarial against Plasmodium falciparum[103]. N-substituted-2-(5-nitroheterocyclic-2-yl)-3H-benzo[d] Imidazole-5-carboxamide demonstrated activity when tested against plasmodium species that cause malaria in people[104]. The antimalarial activity of a new class of pyrido [1, 2-a] benzimidazoles was investigated. The compound showed very good potency with IC_{50} value 0.04 3M v 0.1 μM (**Figure 10)**[105].

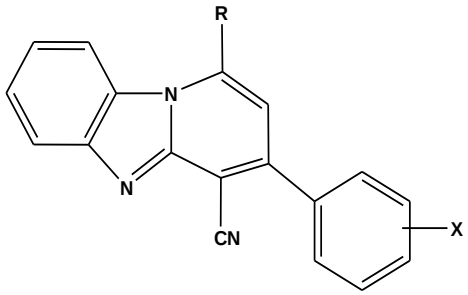

Figure 10. Antimalarial pyrido [1,2-a] benzimidazole.

8. Enzyme inhibitory action

For inhibition of α-glucosidase, benzimidazole derivatives were successfully produced. The enzyme was tested against 2-(1H-benzo (d) imidazole- 2-yl)-2-(4- hydroxyphenyl) ethyl) isoindoline-1, 3-dione and 2-(1H-benzo (d) imidazol-2-yl)-2-phenyl ethyl) isoindoline-1, 3-dione. The chemicals lower blood sugar levels by inhibiting carbohydrate absorption via the digestive tract, according to the mechanism of action[106].The substances N-(p-tolyl) hydrazine carbothioamide (4-bromophenyl) 2-(4-(5,6-dimethyl-1H-benzo[d]imidazol-2-yl) benzoyl) hydrazine carbothioamide, 2-(4-(5, 6-dimethyl- 1H- benzo [d] imidazol-2-yl) benzoyl)-N-(4-nitrophenyl) hydrazine carbothioamide and 2-(5-(6-dimethyl-1H-benzo[d]imidazol-2-yl) benzoyl) N-(p-tolyl) hydrazine carbothioamide, the inhibitory activity of-N-(4-nitrophenyl) hydrazine carbothioamide on the β-glucosidase enzyme has been discovered. More activity is seen in the moiety with an electron withdrawing group[107].

Due to its ability to hydrolyze a variety of hazardous chemicals, glucuronidase is one of the most investigated enzymes. It functions as a glycoside hydrolase. Excessive consumption can result in urinary tract infections, epilepsy, and breast cancer, among other things. By refluxing aryl aldehydes and 3, 5-dichlorobenzene-1, 2-diamine several 4, 6-dichlorobenzimidazole derivatives were produced and reported to inhibit-Glucuronidase more than normal D-Saccharic acid 1, 4 lactones. It was discovered that substances with a hydroxyl group had good inhibitory efficacy, but that substituents like methyl, methoxy, and halide have no effect[108–110].

The glucosidase inhibitory activity of benzimidazole of 4-nitro-o-phenylenediamine o-phenylenediamine and o-phenylenediamine compounds (1–4 in **Table 1**) was investigated with acarbose as positive control.

Table 1. Glucosidase inhibitory activity of different benzimidazoles.

Compound	% Inhibition	IC50 Value(micron)
1. 6,6'-dinitro-1H,1'H-2,2'-bibenzimidazole	100.0 ± 14.0	0.54 ± 0.01
2. 2,2'-(6,6'-dinitro-1H,1'H-2,2'-bibenzimidazole-1,1'-diyl) diacetohydrazide	100.0 ± 2.3	0.44 ± 0.04
3. 2,2'-[(6,6'-dinitro-1H,1'H-2,2'-bibenzimidazole-1,1'-diyl) bis(1-oxoethane-2,1-diyl)] bis (N-phenylhydrazine carbothioamide)	100.0 ± 6.5	1.24 ± 0.05
4. 2,2'-[(5,6'-dinitro-1H,1'H-2,2'-bibenzimidazole-1,1'-diyl) bis(1-oxoethane-2,1-diyl)] bis (N-benzyl hydrazine carbothioamide)	100.0 ± 4.3	0.0.49 ± 0.01
5. Acarbose		

In comparison to acarbose, a standard antidiabetic medicine, the potential of the synthesized chemical 6,6'-dinitro-1H,1'H-2,2'-bibenzimidazole and 2,2'-(1H,1'H-2,2'-Bibenzimidazole-1,1'-diyl) diacetohydrazide was reported to be quite good, with an IC_{50} value of 0.44-0.04 and other values are also described in **Table 1**. The structure of compounds was described as following (**Figure 11**)[111].

Benzimidazole derived from iminoester hydrochlorides and o-phenylenediamines were investigated for their lipase inhibitory action and it was established that these figure complexes have very good activity[112].

New urease inhibitors based on 5, 6-dichloro-2-methyl-1H-benzimidazole were developed and examined. The inhibitory activity of all the drugs was higher. The compound 15 [5-(5, 6-Dichloro-2-methyl-1H-benzimidazol-1-yl) methyl)-4-(5, 6-Dichloro-2-methyl-1H-benzimidazol (4-nitrophenyl) The most

effective compound was 2, 4-triazole-3-thione, 2, 4-dihydro-3H-1, which had an IC_{50} of 0.0294 0.0015 M. (reference thiourea). This is explained by the presence of an electron withdrawing group (NO_2) on the phenyl ring[113].

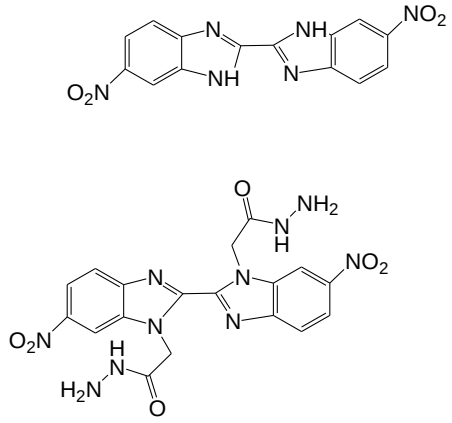

Figure 11. Benzimidazoles having Glucosidase inhibitory activity.

N'-[(2-hydroxyphenyl) methylene], two novel salicylaldimine-based N-heterocyclic hydrazone ligands2-[2-(3-chlorobenzyl)-1H-benzimidazol-1-yl] and 2-[2-(2-phenyl)-1H-benzimidazol-1-yl]acetohydrazone (H2L1)-N'-[(2-(hydroxyimino)-1-ethylpropylidene]. The homo-binuclear nickel(II), copper(II), and zinc(II) complexes of acetohydrazone (H2L2) have been produced. The Cu(II) complex (3b) has the highest activity and the lowest IC50 value (2.50 0.60 M) of all the complexes that showed catalytic activity against the superoxide dismutase enzyme[114]. The Ni(II) and Zn(II) complexes of benzimidazole derived from 4-(1H-benzo[d]imidazol-2-yl) aniline reaction with different aromatic aldehyde have been shown good activity as aurora kinase enzyme inhibitor[101].

9. Conclusion and future prospective

A thorough analysis of the most recent advancements in the catalytic and antibacterial uses of benzimidazole Schiff base compounds has been provided in this review paper's conclusion. We have investigated the synthesis methods, characterisation procedures, and the catalytic and antibacterial characteristics of these fascinating compounds through an extensive literature review. The use of benzimidazole Schiff bases as catalysts in diverse organic transformations has been highlighted in relation to their catalytic uses. The high catalytic activity of these compounds is a result of their distinctive structural characteristics, which also include the presence of the Schiff base moiety and the benzimidazole core. Additionally, the design of catalysts with improved selectivity and reactivity was made possible by the tunability of their structures, allowing for the efficient transformation of a variety of substrates. Benzimidazole Schiff bases have demonstrated considerable antibacterial effects against a variety of diseases in addition to their catalytic capabilities. The development of more effective and targeted antimicrobial drugs has been made easier by these compounds' adaptability to structural alterations. These chemicals' mechanisms of action have also been researched, revealing light on their interactions with microbial cells and their potential as substitute therapies for pathogens that are drug resistant.

Soon, there will be lots of chances to conduct additional research and development in benzimidazole Schiff base chemistry. There is a lot of potential in the design and synthesis of new Schiff base ligands with specialised catalytic characteristics and enhanced antibacterial activity. Additionally, it will result in fascinating discoveries and developments to investigate their possible applications in other disciplines like materials science, bioinorganic chemistry, and drug discovery.

A thorough grasp of the most current developments in the catalytic and antibacterial uses of benzimidazole Schiff base compounds has been given by this review. These compounds represent an intriguing area of study due to the combination of their distinctive structural characteristics, various synthesis techniques, and wide-ranging uses. Benzimidazole Schiff bases are poised to play a significant role in the creation of new catalysts with further research and advancements.

Conflict of interest

There is no conflict of interest.

Abbreviations

No.	Abbreviations	Definitions
1.	*A. flavus*	Aspergillus flavus
2.	*A. niger*	Aspergillus niger
3.	BAIL	Bronsted Acid Ionic Liquid
4.	CNS Cancer	Central Nervous System Cancer
5.	CVB	Coxsackievirus
6.	DMG	*N*,*N*-dimethyl Formamide
7.	EC_{50} value	Effective concentration of a substance to stop microbial growth by 50%
8.	GC%	Gas Chromatography yield
9.	Hela Cells	Henrrietta Lacks Cell line
10.	HSV-1	Herpes simplex Virus
11.	HIV	Human Immunodeficiency Virus
12.	IC_{50} value	Inhibitory Concentration
13.	MCF7	Michigan Cancer Cell Line
14.	Me	Methyl
15.	MeO	Methoxy
16.	*M. Luteus*	Micrococcus luteus
17.	MTT Essay	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl Tetrazolium bromide
18.	PC3 cells	Prostate Cancer Cell line
19.	PS	Polystyrene
20.	*S. aureus*	Staphylococcus aureus
21.	SBs	Schiff bases
22.	SI	Selectivity index
23.	t-BuCOOH	Tertiary butyl alcohol
24.	t-BuO·	Tertiary butoxide radical
25.	YFV	Yellow Fever Virus

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