ABSTRACT

A wide development in the field of multidrug resistance in antimicrobial activity which enhance the search for development of new medicinal drugs with high potential. Schiff base heterocyclic metal complex with imine moiety, act as important antimicrobial agents due to their versatile properties such as chelation, adaptability of fine structure for a specific biological action, and chemotherapeutic drugs. Schiff base compounds derived from various heterocyclic platforms have been competently reviewed.

Keywords: Ligand, Antimicrobial, Antifungal, Anticancer, Metal complex.

INTRODUCTION

Schiff base metal complex, the name you heard about more than 5 decades were considered as a splendid topic in the field of research. The use of Schiff base metal complex and their progress in medical research as a fine powder of drug occupied an optimistic role in the field of pharmaceutical research. In this review article, we are discussing the on-going aspects of biological activities of metal complex such as antitumor, antifungal, antimarial, antibacterial, antiproliferative, anti-inflammatory, and antipyretic. Apart from the biological activities of the metal complex it also shows excellent catalytic activity due to the thermal and moisture stabilities. Heterocyclic compounds possess impressive biological activity due to the strong aromaticity of the ring containing heteroatoms such as O, S, and N. Antimicrobial resistance metamorphoses a global concern in the field of advanced multidrug research. Heterocyclic compounds used in the implementation of metal complexes as drugs to serve as remarkable medicine in the drug discovery. The pharmacological properties of heterocyclic compounds have promoted to a different level in the field of Schiff base metal complex.

The data collected from the various journals were indexed by Scopus, Pubmed, Google scholar, etc., during the past 10 years. There are more numbers of journals, but we considered that pertinent studies which have a sporting idea of the research. This review is summarized to know about the existing aspect of microbial activities of the Schiff base metal complex [1-15].

APPLICATIONS OF HETEROCYCLIC COMPOUNDS AS ANTIMICROBIAL AGENT

Heterocyclic Schiff base ligands were derived by the condensation of 3-hydroxy-methoxy benzaldehyde (iso vanillin) with furan-2-carboxylic acid hydrazide and thiophene-2-carboxylic acid hydrazide. Metal complexes such as Co (II) and Cd (II) prepared with corresponding ligands. Spectroscopic methods such as Fourier transform infrared (FTIR), UV-Vis, 1H and 13C, and magnetic measurements proved that the metal complex geometry is tetrahedral. Gram-positive bacteria and Gram-negative bacteria against metal complex and ligands proved ligands have high microbial activity [16].
Pyrrole ring fused heterocyclic ligands were derived from indole-3-carboxyaldehyde and glycylglycine (glygly). They were characterized by electronic spectra, nuclear magnetic resonance (NMR) studies, and magnetic measurements. The metal complexes are 1:1 electrolytes proved by the conductance measurement. Coordination of the metal complexes is through azomethine nitrogen, peptide nitrogen, and carboxylate oxygen atoms. The studies about the magnetic measurements revealed that the weak ferromagnetic behaviors of Co (II) and Cu (II) show paramagnetic behavior. Metal complexes coordination through water molecule can be identified by IR and thermal studies. Thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC) analysis show the process of decomposition steps. The metal complex crystalline structures were derived from the X-ray diffraction (XRD) studies. The ligand and its complexes were screened by the antimicrobial activity of Kirby–Bayer disc diffusion [18].

A new substituted heterocyclic moiety of Schiff base ligands was prepared by the condensation of salicylaldehyde with 2-amino-4-phenyl-5 methyl thiazole and their metal complexes using the transition metal such as Co(II), Cu(II), Ni(II), and Zn(II). All the spectroscopic studies such as FTIR, NMR, and conductance were studied for the ligands and the metal complexes. Their compounds were screened against the anticancer activity of human tumor cell MCF-7 cell, liver cancer Hep G2, lung carcinoma A549, and colorectal cancer HCT116 in comparison with the activity of doxorubicin as a reference drug and the metal complex of Zn(II) complex showed potent inhibition [19].

The newly formed lanthanide Schiff base complex is prepared by the condensation of 2,6, diamino pyridine and anthracene -9-carbaldehyde and they complex with lanthanide ions such as Praseodymium (Pr), Erbium (Er), and Ytterbium (Yb). FTIR data show the coordination through two Azo methane-nitrogen and the ligand act as a bidentate ligand. The metal complexes were screened against human breast cancer MCF-7 and cervical anticancer cell line which shows high resistance [20].

The in vitro cytotoxicity and DNA cleavage of Schiff based ligand 3-((4-phenylthiazol-2-ylimino) methyl)-2- hydroxybenzoic acid were synthesized and react with transition metal complexes such as Cu(II), Co(II), Ni(II), Cd(II), and Zn(II). For these complexes, elemental analysis, TG/DTA, FTIR, H-NMR, and UV-vis studies were characterized, and the data give an idea about the geometry and coordination through bidentate O-O donor. Moreover, Cu (II), Co (II), and Zn (II) show an enhanced DNA cleavage activity [22].

Benzene fused ring system has been used in the condensation of Schiff based complexes which gives new complexes with Amoxicillin trihydrate and nicotin aldehyde. Their metal complexes were characterized under spectrochemical techniques such as UV-Vis, scanning electron
microscopy (SEM), electron paramagnetic resonance (EPR), FTIR, Mass spectroscopy, melting point, and conductivity measurements. The powder XRD pattern reveals the crystal structure of Cu (II) complex as a triclinic crystal system. Further tetrahedral geometry was recommended for EPR studies. Using two different concentrations the in vitro antibacterial studies were tested, and the data showed that their bacterial activity was high with the parent drug [23].

Recently reported article about the newly synthesized heterocyclic Schiff based compounds which are prepared from chalcone-3-chloro-6-hydroxy-2-methyl phenyl-3-(3,4 dimethoxy phenyl) prop-2-en-1-one with isonicotinic hydrazide in the ethanolic medium. The characterization of these compounds and their results are obtained using the techniques such as UV, Mass, FTIR, and molar conductance IR studies suggest that toward Fe(III) ligand act as a monobasic tridentate ONO donar and ON donar against VO (IV). Some more studies regarding thermal stability and decomposition of the complex are also obtained [24].

Coordination of the metal complexes plays a good role in the field of medical research. A series of tridendate Schiff base ligands are derived from the condensation of 2-hydroxyacetophenone with S-benzyldithio carbazate have been synthesized and characterized by magnetic measurements, IR, Electronic Spectra, and molar conductance, etc. The geometry of the molecule is also correlated with the biological activity. The complexes are screened and found to have high potential microbial character [25].

The antibacterial activity of new Schiff base ligands and their metal complexes were studied by the combination of ethylenediamine and salicylaldehyde. Using different concentration, the antibacterial activity was tested for different types of bacteria such as Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumonia, Bacillus cereus, and Salmonella typhi, and Staphylococcus aureus. Comparing the metal complexes such as Cu, Co, and Ni, Cu showed 9.5, 9.0, and 8.0 mm zone of inhibition against E. coli, S. typhi, and S. aureus, and Co showed the zone of inhibition against E. coli, B. cereus, K. pneumonia, and S. aureus, in the range of 17, 19, and 22.5. Hence, these types of complexes provide useful antibiotic drugs in the research field of medicine [26].

New Schiff base ligand has been prepared using 4-AminoAntipyrine and Thiohene-2-carbaldehyde, and their metal complexes are prepared using the metals Cu(II), Ni(II), and Zn for which the spectroscopic studies were characterized and results give an idea about the structure of the metal complexes. The biological activity of the compound also tested with the ligands and their metal complexes [27].

Heterocyclic compounds containing sulfur and Nitrogen of 2-aminothiazole and 8-hydroxyquinoline are mixed with Benzoinoxime to form the primary and secondary ligands. These ligands react with metal such as Co (II) and Zn (II). The metal complexes are formed in the ratio 1:2:2 with oxime as a primary ligand. The Co (II) metal complexes show distorted the octahedral geometry of mixed ligands and complexes of oxime form a square planar geometry. The mixed ligand of Zn (II) complexes shows distorted octahedral geometry and with oximes shows square planar geometry. The complexes are screened for the antimicrobial activity [28].
New synthesis of Zn(II) complexes using novel heterocyclic compounds have been derived from the ligands $8\cdot\{[(Z)-\{3-(N\text{-}methylamino)propyl\}imino]methyl\}-7$-hydroxy-4-methyl-2H-chromen-2-one, $2\cdot\{[(E)-\{4-(1H\text{-}1,2,4\text{-}triazol1-ylmethyl)phenyl\}imino]methyl\}phenol$, and $\{4S\}\cdot4\cdot\{[(E)-(2$-hydroxybenzylidene)amino]benzyl\}-1,3$-oxazolidin-2-one. Zn(II) complexes were studied by many spectroscopic techniques proposed for the structure to be Octahedral. The in vitro antimicrobial activity was screened against Gram-negative bacteria and Gram-positive bacteria and fungi such as *Candida albicans* and *niger* which showed the enhanced biological activity of Zn(II) complexes [29].

![Substituted Benzofuran derivatives have been synthesized, and their metal complex was characterized by elemental analysis, magnetic moments, and conductance measurements. The elemental analysis confirms the formula ML (Cl) n where L= E-1-Methoxy-N1-[2, 4, 5- trimethoxy benzylidene]benzofuran -2-carboxyhydrazide (L1) or (E)-N1-[2,6 dichlorobenzylidene]-7-methoxy benzofuran-2-carboxyhydrazide L2 of the complex. The complexes were screened for their anti-bacterial activity. Among the metal complexes Co, Cu, and Ni show high activity against all microbes [32].](image1)

![The acetylacetonate Schiff base ligand was obtained from the condensation of 4-(diethyl amino)-2-hydroxy benzaldehyde and 4 nitro benzo hydrazide or 4 methoxy-benzohydrazide. The metal complexes were prepared with Co (II), Mn(II), and Mg(II) metals. FTIR reveals the Schiff base as bidentate chelating ligands through nitrogen of azomethine and phenolic oxygen atoms. The in vitro antimicrobial screening was done against *S. aureus* and *Enterococcus facials* which showed the high potential activity of metal complex [33].](image2)

![Metal complexes derived from 4-aminoantipyrine, vanillin, and O-anisidine were prepared and synthesized. The spectroscopic techniques such as FTIR, NMR, and $^1H$ and $^{13}C$ NMR are analyzed and obtained the following data. Antimicrobial screening test was performed within the metal complexes. The minimum inhibitory concentration values of metal complex exhibit greater antimicrobial activity than free ligand [34].](image3)

![Transition metal complex derived from 2-aminomethylbenzimidazole and 4-chlorobenzaldehyde (1-(1H-benzimidazol)-2H-N-(4- chlorobenzylidene methamine) was synthesized. The spectroscopic methods such as $^1H$ and $^{13}C$ NMR, electron spin resonance (ESR), FTIR, UV-Vis spectra were analyzed](image4)
for all these metal complexes which proposed an octahedral geometry to all metal complexes. The in vitro screening of antimicrobial activity was studied against two Gram-negative and Gram-positive bacteria. All the metal complexes are highly active than the ligand [35].

The synthesis of new benzaldehyde thiosemicarbazone-BTSCH and 3,4 dimethoxy benzaldehyde-DMBA and their metal complex was prepared and screened for antibacterial activity with the five human pathogenic bacteria strains such as \textit{S. aureus}, \textit{Bacillus subtilis}, \textit{K. pneumonia}, \textit{E. coli}, and \textit{Proteus vulgaris}. The concentration ranging between 0.01 and 10 µg/ml has a very good antibacterial activity of the metal complex [36].

New metal chelates of the type M (NQO), were synthesized from metals such as Hg, Cd, Zn, and Pb where NQO-1,2 Naphthoquinone dioxide. The metal chelates were synthesized and characterized by FTIR, electronic Spectra, H and 13C NMR, DSC, and Electron Microscopy with EDAX. Square Planar structure was proposed for these metal chelates, and it is thermally stable up to 350°C. The antimicrobial activity was screened with Gram-positive and Gram-negative bacteria and fungi with cisplatin as chemotherapeutic agent [37].

Walaah. Mohamed and \textit{et al.} synthesized a new series of metal complexes derived from lornoxamic and 1, 10 phenanthroline and characterized by spectroscopic tools such as mass spectra, IR, UV-visible, H and 13C NMR, and ESR. Electrolytic nature was confirmed by the molar conductance. IR studies reveal the coordination of metal ions in a neutral bidentate manner. ESR spectra and electronic spectra assigned octahedral geometry of the ternary complexes. These complexes are screened for their antimicrobial, antitumor activity against cancer cell line. The result revealed complexes have more potent than the parent ligand [38].

Transition metal complexes of Ni (II), Zn (II), Cd (II), and Hg(II) have synthesized from dihydropyrimidine derivative of vanillin and 4-Amino Antipyrine. The complexes are characterized by UV-Vis, H, and 13C NMR, which proposed the complexes have ML2 type. The tetrahedral geometry was suggested by UV-Vis and susceptibility data expects Nickel which shows a square planar complex. The \textit{in vitro} antimicrobial studies were carried on these ligand and metal complexes. The metal complexes show more activity than the ligand [39].

Two metal complexes were synthesized from 2,6 bis (2-Aminophenoxymethyl)pyridine and 2,2’-bipyrindine 6,6’-dicarboxaldehyde in the presence of Hg(II) and Cu(II) perchlorate salts. Both compounds showed cytotoxicity on 2 cell line as a dose-dependent manner. Among the complexes, the one with Hg(II) according to apoptotic morphology and DNA fragmentation exhibits promising potential as an anticancer compounds [40].

Unsymmetrical Schiff base ligands derived from Salicyaldehyde/5-methylsalicylaldehyde and ethylene diamine or diaminomaleonitrile. They were characterized by elemental analysis and spectroscopic methods. ESR spectra showed that Cu (II) complexes show four lines which are a characteristic of square planar geometry. The antimicrobial activity was tested against bacteria such as \textit{S. aureus}, \textit{Bacillus subtilus}, \textit{K. Pneumonia}, and also antifungal activities. The metal complexes generally show more potent than the ligand [41].

Schiff base ligands were derived from imidazole-2-carbaldehyde and glycine-glycine. The ligands react with metals such as Co (II), Cu (II), and Ni (II). Molar conductance indicates the 1:1 electrolytic nature and IR data showed that the ligand is tetradentate with imidazole nitrogen and carboxylate oxygen donor group. The SEM image shows the surface morphology of the complex. Antibacterial and antifungal studies were carried out using bacterial and fungal species which shows high for metal complex [42].

New ONO donor Schiff base ligand derived from the condensation of 5-Methyl, 3-Phenyl -1H-Indole-2-Carboxyhydrazide with 2-hydroxy-1-naphthaldehyde. The spectral analysis of the metal complex was characterized by UV-Vis spectra, ESR, Thermal analysis, power XRD, and conduct metric, and magnetic susceptibility measurements. Co (II), Cu (II), and Ni (II) complexes have octahedral geometry and 1:2 stoichiometric ratio of the type M (L). The antimicrobial activity was screened for metal complexes and found that it possesses high potential activity [43].

A series of novel Schiff base derivatives with different substituent were screened for antibacterial activity against \textit{S. aureus}. Synthesized compounds showed a significant antibacterial activity [44].

Synthesis and biological activity of transition metal complexes containing a tetradentate N2O2 donor type Schiff base derived from the condensation of 4-aminooxime (1-phenyl-2,3-dimethyl 4-aminopyrazole5-one) with benzyl which forms stable complexes with transition metal ions such as Cu(II), Ni(II), Co(II), Mn(II), Zn(II), and VO(IV) were reported [45]. Screening results indicated that the complexes show higher antimicrobial activity than the free ligand. Such increased activity of the metal chelates can be explained on the basis of Overton’s concept [46] and the ‘Tweedy’s chelation theory’ [47].

The synthesized and screened for their antimicrobial Schiff base and its 3d transition metal complexes (7) of Mn(II), Fe(III), and VO (IV) derived from Ethyl 4-methyl-2-oxo-6 phenylhexahydropyridine5- carbonate and 4-aminooximantipyrine suggesting the possible use of the complexes as antibiotics [48].

The complexes of different Schiff bases (5- methyl 2-hydroxy acetophenone morpholine-Nthiohydrozone, 5-chloro2hydroxy acetophenemonemorpholine-N-thiobicydrazone and 5-methyl 2-hydroxy acetophenone antipyrine) with Mn (III) and Mn (II) have been synthesized [49].

Five new novel metal complex derivatives of 2N-salicylidene-5-(p-nitro phenyl)-1,3,4-thiadiazole, HL with the metal ions VO(II), Co(II), Rh(II), Pd(II), and Au(III) have been successfully prepared in an alcoholic medium. The complexes obtained are characterized quantitatively and qualitatively using micro elemental analysis, FTIR spectroscopy, UV-Vis spectroscopy, mass spectroscopy, H and 13C NMR, magnetic susceptibility, and conductivity measurements. From the spectral study, all the complexes obtained as the monomeric structure and the metal center moieties are four-coordinated with square planar geometry except VO (II) and Co complexes which exist as a square pyramidal and tetrahedral geometry, respectively. The preliminary \textit{in vitro} antibacterial screening activity revealed that complexes showed moderate activity against tested bacterial strains and slightly higher compared to the ligand, HL [50]. Coordination of biomolecules to the metal ions significantly alters the effectiveness of the biomolecules. In view of the antimicrobial activity, a series of nickel, copper, and zinc complexes of tridentate Schiff base derived from the condensation reaction of S-benzylidithiocarbamate with 2-hydroxycetophenone have been synthesized and found to be potential antimicrobial agents. An attempt is also made to correlate the biological activities with the geometry of the complexes. The complexes have been characterized by molar conductance, magnetic susceptibility, IR, and electronic spectroscopic techniques [27]. Novel Schiff base ligand derived from 2-hydroxybenzophenone with S-benzylidithiocarbamate and its metal complexes with Ni(II), Cu (II), Zn (II), and Cd (II) have been synthesized and evaluated for their antibacterial activities by disc diffusion method.
and antifungal activities by PDA medium. The complexes have been characterized by conductance, magnetic, IR, and electronic spectroscopic techniques [51]. Transition metal complexes with Schiff bases derived from 2-formylnitro, salicylaldehyde, and N-aminomethylhydrazine. The Schiff base ligands and their metal complexes were also screened for antimicrobial activities against Bacillus cereus, E. coli, P. aeruginosa, S. aureus, and C. albicans. The results indicated that the ligands do not have any activity, where as their complexes showed more activity against the same organisms under identical experimental conditions [57]. Nickel II metal complexes from benzaldehyde and thiocarbohydrazide were synthesized and characterized by IR spectral analysis, conductance measurement, UV-visible spectral studies, and elemental analysis. The melting point of the Schiff base determined is 120°C. The decomposition temperature of the nickel (II) complex is 155°C, while the molar conductance value is 10.7 ohm-1 cm2 mol-1. Antimicrobial screening of the compounds was carried out in vitro against E. coli, S. typhi (Gram-negative), and S. aureus, and Streptococcus spp. (Gram-positive). The bioassay reveals a considerable activity of the Schiff base complex against the bacterial isolates [58]. The synthesis of a series of some novel Schiff base complexes of Cu(II), Ni(II), Co(II), and Zn(II) with a tetradentate Schiff base has been achieved by the reaction of malonic hydrazide with dehydroacetic acid in ethanol under refluxing condition. All the synthesized metal complexes and ligand were characterized on the basis of elemental analysis, UV-Visible, H and 13C NMR, IR spectroscopy, and mass spectrometry. The IR spectral data suggest that amine and enolic O atom are involved in coordination with metal ions, and the ligand behaves as a tetradentate ligand with two N-donor atoms. The UV–Visible spectra of the complexes show a characteristic absorption band in the range of 220-280 nm, characteristic of square-planar geometry, with nuclear hyperfine spin 3/2. The in vitro antimicrobial activity of the investigated compounds was tested against human pathogenic bacteria such as S. aureus, Bacillus subtilis, K. pneumoniae, P. aeruginosa, and E. coli. The antifungal activity was tested against C. albicans. In general, the metal complexes have higher antimicrobial activity than the free ligands [42]. Metal complexes of (E)-N-(4-(thiophen-2-ylmethylene) amino) phenylsulfonyl) acetamide (S. TH) Schiff bases derived from malonamide (N-[4-(aminomethyl) sulfonyl]I acetamide) and 2-thiopheneacarboxaldehyde were synthesized and characterized. Spectroscopic studies suggested that most of the
complexes were coordinated in a regular octahedral arrangement where STH ligand and the central metal atom were coordinated through two N amino azomethine groups (−H=N−) and two sulfur atoms of Sthiophene rings in 2L:1 M molar ratio. Complexes have shown a promising activity on screening for the antibacterial characteristics, and antifungal (Aspergillus fumigatus and C. albicans) [60]. A new Schiff base derivative ligand (LI) has been produced by condensation of 2-amino 4,6 dihydroxypyrimidine and P- chlorobenzaldehyde has been reported. The Schiff base was synthesized and distinguished by H, 13C-NMR, (CHN) elemental analysis, UV-visible, mass spectroscopy, and FTIR methods. The metal ions, cobalt(II), nickel(II), and copper(II) complexes were synthesized with the ligand. The complexes were typified by, UV-Visible, FTIR, atomic absorption, molar conductance, magnetic susceptibility, and elemental analysis (CHN) techniques. Octahedral geometry are suggested for the metal complexes based on the results of physicochemical and spectral techniques. The TLC for (LI) ligand and complexes demonstrated single spot for each, signifying their compounds purity. All these compounds were determined aligned with two classes of human pathogenic; bacteria Gram-positive and Gram-negative [61]. The synthesis and characterization of novel transition 3d metal complexes of copper (II), nickel (II), cobalt (II), and chromium (III) involving the Schiff base of melonal were explored to examine their biological activity. Characterization of the complexes was carried out using matrix-assisted laser desorption/ionization-time of flight, gas chromatography/mass spectrometry, TGA, UV-Visible, and IR spectrophotometry. The antimicrobial studies were conducted against six bacterial strains and six fungi. The minimum inhibition concentration observed was compared against the standard antibiotic gentamycin and the antifungal drug amphotericin. The activity studies indicated that cobalt (II) complex exhibited activity better than standard drug amphotericin against Penicillium chrysogenum. Molecular docking study confirms the protein binding and supports the experimental finding. Binucular cobalt (II) and chromium (III) bridging complexes of Schiff base ligand were obtained [62]. Metal complexes of Mnf(II), Fe(II), Co(II), and Cd(II) ions with Schiff base ligand 4- ((pyridin-2-yilino)methyl)phenol derived from condensation of 2-amino pyridine with 4- hydroxybenzaldehyde were prepared. The ligand and complexes were isolated from the reaction in the solid form and characterized by conductivity, magnetic moment, TLC, IR, UV-Visible, thermal analysis, and some physical measurements. During complexation reaction with transition metal ions Schiff base act as a deprotonated tridentate ligand and IR spectra showed that N and O atoms are coordinated to the central metal atom. The observed values confirmed that the complexes have octahedral geometry. The Schiff base and its metal complexes have been found to have moderate to strong antibacterial activity [63]. The transition metals with the Schiff bases, formed by condensation of 2-Hydroxy-1 naphthaldehyde/Saliclyalddehyde and p-Anisidine with Neutral bidentate ligand 4-Hydroxybenzaldehyde/3-Ethoxy-4 hydroxybenzaldehyde (Ethylenealine) and o-Phenyleneediamine have been synthesized and characterized. All prepared compounds were also evaluated for their antibacterial and antifungal activities by the agar well diffusion method. The antibacterial activity was tested against the bacteria B. subtilis (Gram-positive), E. coli (Gram-negative). The antifungal activity was tested against A. niger. The standard Streptomycin has been evaluated with the results obtained for antibacterial and antifungal activities [64]. Schiff base ligand derived from 2-amino 4,6 dihydroxyprpyrimidine and P- chlorobenzaldehyde has been reported and the ligand was treated with Cu, Ni, and Co to obtain the following metal complexes. The ligand and its complexes were screened for their antifungal and antibacterial activity against A. niger, P. chrysogenum, Fusarium monoliforme and Aspergillus flavus and E. coli, S. typhi, S. aureus, and B. subtilis. The result indicated that the complexes exhibited good antifungal and antibacterial activities [65]. The synthesized ligands, along with its metal complexes were screened for their in vitro antibacterial activity against four bacterial pathogens (E. coli, B. subtilis, S. aureus, and Proteus vulgarus). A novel Schiff base metal complexes were synthesized and well characterized by elemental analyses and spectral studies. Physical and analytical data suggest that the Schiff base acts as tridentate ligand toward metal ions through azomethine-N, deprotonated-O of 2-aminophenol, and O-atom of furan moiety. The results of these studies revealed that the free ligand and its metal complexes showed significant antibacterial potency [66]. All the newly synthesized compounds were screened for their antimicrobial activity. For antibacterial activity, we used S. aureus microbial type culture collection (MTCC 96) and Streptococcus pyogenes (MTCC 443) as Gram-positive, E. coli (MTCC 442) and P. aeruginosa (MTCC 443) as Gram-negative strains using ampicillin, chloramphenicol, and ciprofloxacin as a standard antibacterial drug. Antifungal activity was screened for three different fungal spieces C. albicans (MTCC 227), A. niger (MTCC 282), and Aspergillus clavatus (MTCC 1323). Griseofulin and nystatin used as a standard antifungal drug. Majority of the compounds exhibited good antibacterial, antifungal, and antituberculosis activity [67].

CONCLUSION

Schiff base explored versatile antimicrobial activity in the research field. Moreover, metal on complex formation, their in vitro antimicrobial activity has increased more when compared to ligands. This review will create new ideas in the field of medicine which helps the scientist to produce more new drugs which are specific in action. In spite of various syntheses in the drug analysis there is still a need to explore new drugs which are useful for future generation.

AUTHOR'S CONTRIBUTIONS

Corresponding author has reviewed all the research article about antimicrobial activity of Schiff base metal complexes.

CONFLICTS OF INTEREST

Authors declare that they have no conflicts of interest.

REFERENCES

1. Al Mulla A. A review: Biological importance of heterocyclic compounds. Pharm Chem 2017;9:141-7.
2. Bora MA, Bhoi MN, Prapapti NP, Patel HD. Review of synthesis of multispiro heterocyclic compounds from isatin. Int J Rapid Commun Synth Org Chem 2013;43:1057.
3. Sönmez M, Şekerçi M. A new heterocyclic Schiff base and its metal complexes. Synth Reactivity Inorg Metal-Organic Chem 2010;54:489-502.
4. Kajri A, Beas S, Kamboj S, Sharma N, Saini V. Schiff bases: A versatile pharmacophore. J Catalysts 2013;2013:Article ID: 893512, 14.
5. Tobriya SK. Biological applications of Schiff base and its metal complexes-a review. Int J Sci (JISR) 2014;3:1254-6.
6. Tadele KT. Antioxidant activity of Schiff bases and their metal complexes: A recent review. J Pharm Med Res 2017;3:73-7.
7. Parasha RK, Sharma RC, Govind M. Biological activity of some Schiff bases and their metal complexes. Biol Trace Elem Res 1989;23:145-50.
8. Bernadette SC, Brian D, Denise A, Eganat KK, Georgina R. Anticancer and antifungal activity of copper (II) complexes of quinolin-2(1H)-one derived Schiff bases. Inorg Chim Acta 2010;363:4048-58.
9. Singh WM, Dash BC. Synthesis of some new Schiff bases containing thiazole and oxazole nuclei and their fungicidal activity. Pesticides 1985;22:33-7.
10. Shaikh AA, Raghuwanshi MG, Khurshid I, Molvi K, Nazim S. Aspergillus spp in vivo antibactericidal activity of a new pyrimidine Schiff base and its Cu(II), Ni(II), Co(II), Pt(II), and Pd(II) complexes. Turk J Chem 2008;32:487-93.
11. Mehmet G, Mehmet S, Ismet B. Synthesis, characterization, and antimicrobial activity of a new pyrimidine Schiff base and its Cu(II), Ni(II), Co(II), Pt(II), and Pd(II) complexes. Turk J Chem 2012;36:189-200.
12. Pratibha MS, Vatsala P, Uma V. Biologically active Co (II), Ni (II), Cu (II) and Mn(II) complexes of Schiff bases derived from vinyl aniline and heterocyclic aldehydes. Int J Chem Technol Res 2009;1:225-32.
13. Niaz MA, Shaalanand ND, Sahar S. Synthesis, spectroscopic, thermodynamic and biological activity studies of Schiff base and metal complexes derived from 2-[1H-pyrrol-2-ylmino] methyl]-5-phenyl-
1,3,4-oxadiazole. Glob J Sci Front Res B Chem 2015;15:14-8.

15. Asif NK, Ajay P, Sharad T, Jagannath JK, Lokhande MV. Antibacterial activity of 2-[(2-chloro-4-methylbenzylidene) amino] pyridin-4-ol and its some transitional metal ion complexes. IOSR J Appl Chem 2014;7:14-20.

16. Abhishek K, Fernandes J, Pankaj K. Synthesis, antimicrobial and anti-inflammatory studies of some novel Schiff base derivatives. Int J Drug Dev Res 2014;6:165-7.

17. Ahmed RM, Yousof AL, El-Jeboori MJ. Co(I) and Cd(I) complexes derived from heterocyclic Schiff-bases: Synthesis, structural characterization, and biological activity, Hindawi publishing corporation. Sci World J 2013;2013:Article ID: 754868, 6.

18. Nair MS, Arish D, Josephyus RS. Synthesis, characterization, anti fungal, antibacterial and DNA cleavage studies of some heterocyclic Schiff base metal complexes. J Saudi Chem Soc 2012;16:83-8.

19. Josephyus RS, Nair MS. Synthesis, characterization and biological studies of some Co(II), Ni(II) and Cu(I) complexes derived from indole-3-carboxaldehyde and glycyglycine as Schiff base ligand. Arabian J Chem 2013;6:195-204.

20. Abd-Elzaher MM, Labib AA, Mousa HA, Moustafa SA, Ali MM, El-Rashedy AA. Synthesis, anticancer activity and molecular docking study of Schiff base complexes containing thiazole moiety, Beni-Suef university. J Basic Appl Sci 2011;6:85-96.

21. Andiappam KS, Shanmugam A, Deivayanganam E, Karuppasamy P, Kim HS, Vikraman D, et al. In vitro cytotoxicity activity of novel Schiff base ligand-lanthanide complexes. Sci Rep 2018;8:3054.

22. Ikram M, Rehman S, Subhan F, Akhtar MN, Simkrot MO. Synthesis, characterization and thermal degradation and urea inhibitory studies of the new hydrazide based Schiff base ligand 2-(2-hydroxyphenyl)-3-[(E)-(2-hydroxyphenyl) methylidene] amino]-2,3-dihydroquinazolin-4(1H)-one. Open Chem 2017;15:508-19.

23. Karabasanavar S, Alloffi P, Shaikh IN, Kalshetty MB. Synthesis, characterization and antimicrobial activity of some metal complexes derived from thiazole Schiff bases with in vitro cytotoxicity and DNA cleavage studies. Indian J Pharm Educ Res 2017;51:490-501.

24. Chaudhary NK, Mishra P. Metal complexes of a novel Schiff base based on penicillin: Characterization, molecular modeling, and antibacterial activity study. Hindawi. Bioinform Chem Appl J 2017;2017:Article ID: 6922765, 13.

25. Thakare AP, Mandlik PR. Synthesis, spectroscopic and thermal studies of Fe(III) and VO (IV) complexes of heterocyclic Schiff base ligand. Indian J Adv Chem Sci 2017;5:318-25.

26. Naikin D, Alam MA, Hossain MN, Nazimuddin M. Synthesis, characterization and antimicrobial activity of metal complexes of Schiff’s base derived from S-benzylidithiocarbamate with 2-hydroxyacetophenone. Chem J 2013;1:3-9.

27. Sheherayer, ParveenZ, Rahman T, Zeb MMA, Hassan Z, RehmanW. Synthesis and antibacterial activity of Schiff’s base metal complexes. Int J Biosci 2017;10:259-64.

28. Selvi ET, Mahalakshmi S. Synthesis and characterization of heterocyclic Schiff base ligand derived from 4-aminantipyrine and thiophene-2-carbaldehyde, Anti-infective activity of 4-amino antipyrine and benzyl. Synth React Inorg Metal Chem 2002;32:1583-610.

29. Dharmaraj N, Viswananthumurthi P, Natarajan K. Ruthenium (ii) complexes containing bidentate Schiff bases and their antifungal activity. Trans Met Chem 2001;26:105-9.

30. Anjaniyala Y, Rao RP, Benkit K. Preparation, characterization and antimicrobial activity studies on some ternary complexes of Cu (ii) with acetylacetone and various salicylic acids. Synth React Inorg Met Chem 1986;16:257-72.

31. Mohanambal D, Antony SA. Synthesis, characterization and antimicrobial activity of some novel Schiff base 3d transition metal complexes derived from dihydroxypyrimidine and 4-aminopyrimidine. Res J Chem Sci 2014;4:11-17.

32. Nizami G, Gargaud P, Ahmad S. Synthesis, characterization and structural studies of complexes containing different Schiff bases with 2-H- and nii (I) transition metal complexes. Orient J Chem 2013;29:1579-84.

33. Yousif E, Majeed A, Al-mumairs K, Salih N, Salimon J, Abdullah B. Metal complexes of Schiff’s base: Preparation, characterization and antibacterial activity. Arab J Chem 2017;10:1639-44.

34. Naqirin D, Alam MA, Rahman M. Synthesis, characterization and antimicrobial activity of metal complexes of Schiff’s base derived from s-benzyl dithio carbuate with 2-hydroxyacetophenone. Chem J 2013;1:3-9.

35. Naqirin D, Alam MA, Rahman IM, Bani H, Nazimuddin M. Synthesis, characterization and antimicrobial activity of some metal complexes with Schiff base containing o,n and s as the donor atoms. Int J Adv Sci 2013;2:1-8.

36. Kumar G, Kumar D, Singh CP, Kumar A, Rana VB. Synthesis, physical characterization and antimicrobial activity of trivalent metal Schiff base complexes. J Serb Chem Soc 2010;75:629-37.

37. Sikarwar P, Tomar S, Singh AP. Synthesis, spectral characterization and antimicrobial activity of Schiff bases and their mixed ligand metal complexes of co (ii), ni (ii), cu (ii) and zn (ii). Am J Chem Sci 2016;6:119-29.

38. Matar SA, Talib WH, Mustafah MS, Mubarak MS, Al Damen MA. Synthesis, characterization, and antimicrobial activity of Schiff bases derived from benzaldehydes and 3,3′-diaminodipropylamine. Arab J Chem 2015;8:850-7.

39. Kurnari E, Singh SK. Synthesis, characterization and antimicrobial activity of some Schiff base metal chelates. J Chem Pharm Res 2017;9:1804-0.

40. Elzahany EA, Hegad KH, Khalil SK, Youssef KN. Synthesis, characterization and biological activity of some transition metal complexes with Schiff bases derived from 2-formylindole, indole-3-carboxaldehyde and azine). Part II. Natl J Chem 2009;36:760-8.

41. Gowenner NR, Jadhav BV, Jadhav KD, Sakare SS, Killeer AA, Sarawadekar RG. Synthesis, characterization and antimicrobial activity of bivalent metal Zn, Cd, Hg, Pb and Ag) chelates of 1, 2-naphthoquinone dioxime. IOSR J Pharm Sci 2012;2:25-33.

42. Mahmoud HW, Mohamed GG, El-Dessouky MM. Synthesis, characterization and in vitro biological activity of mixed transition metal complexes of lornoxicam with 1, 10-phenanthroline. Int J Electrochem Sci 2014;9:145-38.

43. Mangayyarkarasi P, Arulondayu S. DNA cleavage, cytotoxic activities, and antimicrobial studies of some novel Schiff base transition metal complexes derived from 4-aminopyrimine and dihydroxypyrimidine of vanillin. Int J Curr Pharm Res 2016;8:43-7.

44. Ergene E, Sivas H, Benkit K. Biological activities of Cu (II) and Hg (II) complexes of a peptadate Schiff base ligand. Turk J Biol 2010;34:379-387.

45. Rajasekar M, Sreedaran S, Prabhu R, Narayanan V, Jagadeesh R. Synthesis characterization and antimicrobial activities of Ni (ii) and cu (ii) Schiff base complexes. J Coord Chem 2010;63:136-46.

46. Josephyus RS, Nayar MS. Synthesis characterization and antimicrobial activities of transition metal complex with the Schiff base derived from imidazo-2-carbazaldehyde and glycyglycine. J Coord Chem 2008;62:319-327.

47. Gunvanthrao YN, Mathada MB. Metal (ii) complexes of ono donor Schiff base ligand as a new class of bioactive compounds containing indole core: Synthesis and characterization. Int J Pharm Sci 2015;8:197-204.

48. Xia ZL, Yi L, Hua CL, Jun HY, Jun Z, Zhi HP. Inhibitory study of some novel Schiff base derivatives on Staphylococcus aureus by microrcalorometry. Thermochim Acta 2006;440:51-6.

49. Raman N, Kulandaisamy A, Jeyasubramanian K. Synthetic, spectral, redox, and antimicrobial activity of Schiff base transition metal (ii) complexes derived from 4-aminopyrimidine and benzyl. Synth React Inorg Metal Chem 2002;32:1583-610.

50. Dharmaraj N, Viswananthumurthi P, Natarajan K. Ruthenium (ii) complexes containing bidentate Schiff bases and their antifungal activity. Trans Met Chem 2001;26:105-9.

51. Anjaniyala Y, Rao RP, Benkit K. Preparation, characterization and antimicrobial activity studies on some ternary complexes of Cu (ii) with acetylacetone and various salicylic acids. Synth React Inorg Met Chem 1986;16:257-72.
58. Muhammad AS, Shedewo OA, Bayero. Synthesis, characterization and antibacterial properties of nickel (ii) Schiff base complex derived from benzoin and oamino benzoic acid. J Pure App Sci 2015;8:33-6.

59. Saini RP, Kumar V, Gupta AK. Synthesis, characterization, and antibacterial activity of a novel heterocyclic Schiff’s base and its metal complexes of first transition series. Med Chem Res 2014;23:690-8.

60. Abu-Khadra AS, Afify AS, Mohamed A, Farag RS, Hassan Y, Enein A. Preparation, characterization and antimicrobial activity of Schiff base of (e)-n-(4-(diophen-2-ylmethyleneamino) phenylsulfonyl) acetamide metal complexes. Open Bioact Comp J 2018;6:1-10.

61. Waddai FY, Kareem EK, Hussain SA. Synthesis, spectral characterization and antimicrobial activity of some transition metal complexes with new Schiff base ligand (BDABI). Orient J Chem 2018;34:434-43.

62. Sridhar G, Bilal MI, Easwaramoorthy D, Rani SK, Kumar BS, Manoha CS. Synthesis, characterization and antimicrobial activities of copper, nickel, cobalt, chromium complexes derived from (e)-4-fluoro-n-(2,7-dimethylhept-6-enylidene) benzenamine. J Braz Chem Soc 2017;28:756-67.

63. Hossain MS, Zakaria CM, Zahan MK. Synthesis and characterization with antimicrobial activity studies on some transition metal complexes of n, o donor novel Schiff base ligand. J Sci Res 2017;9:209-18.

64. Patel KN, Patel SG, Thakor YJ, Bhatt VD, Srivastava SS, Synthesis, characterization and antimicrobial activity of some transition metal complexes of Schiff base and neutral bidentate ligand. Inorg Chem Indian J 2012;7:16-24.

65. Sakhare DT, Chondhekar TK, Shankarwar SG, Shankarwar AG. Synthesis, characterization of some transition metal complexes of bidentate Schiff base and their antifungal and antimicrobial studies. Ad App Sci Res 2015;6:10-6.

66. Chaudhary NK. In vitro antibacterial studies of some transition metal complexes of Schiff base derived from 2-amino phenol and furan-2-carbaldehyde. Arch App Sci Res 2013;5:227-31.

67. Soni HI, Patel NB. Pyrimidine incorporated Schiff base of isoniazid with their synthesis, characterization and in vitro biological evaluation. Asian J Pharm Clin Res 2017;10:209-14.