International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: 6.614
Available Online at www.journalijcar.org
Volume 11; Issue 01 (C); xxx 2022; Page No.xx-xx
DOI: http://dx.doi.org/10.24327/ijcar.2022.xx.xx

Review Article

MEDICINAL PROPERTIES OF SCHIFF BASES AND METAL COMPLEXES: A REVIEW

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A R T I C L E I N F O

Article History:
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Key words:
Schiff bases, Metal Coplexes, Multifunctions, Bioactivities.

A B S T R A C T

Metal complexes play an essential role in chemical and medicalsciences for their importance and variety of actions. Schiff bases were multifunctional pharmacophores able to form chelating complexes with several metals in different oxidation states. Complexes with Schiff bases are widely described in the literature for their multiple actions and numerous advantages, such as low cost and easy synthesis. They show multifunctional bio-activities, such as antimicrobial, antioxidant, antimalarial, anti-inflammatory and antitumor, anticancer, DNA binding etc. Schiff bases may also form complexes with many Inner-transition elements acting as catalysts (e.g., in various synthetic processes) and antitumor agents. This review offers to extends preparation and the uses of Schiff bases as antitumorals, highlighting the importance, in the field of the anticancer agents, of these tools as ligands of metal complexes.

INTRODUCTION

Schiff bases ($R_1R_2C=NR_3$) are interesting organic compounds containing an azomethine (-CH=N-) or an imine (-C=N-) group generally formed by the condensation of active carbonyl groups and amino compounds, in which the nitrogen atom is bonded to an aryl or alkyl group. These compounds form highly stable complexes with transition metal ions and Inner transition metal ions. Metal complexes in which the metal is coordinated to different ligands, able to stabilize the metal and modify its chemical and medicinal properties, have gained considerable importance in Pharmaceutical chemistry as antibacterial agents [1-5], antifungal agents [6-10], antimicrobial agents [11-15], antioxidant activity [16-20], anticancer [21-25], DNA binding agents [26-30]. Complexes containing the transition metals copper, zinc, cadmium, platinum, palladium, gold and silver have attracted much attention due to their various biological activities.

Antibacterial

(Shoaib, 2013) were synthesized many metal complexes of Cu(II), Co(II), Ni(II), Mn(II), Zn(II) are tested for antibacterial activity versus Staphylococcus aureus strain were screened. Both ligands exhibited a potent effect, although the Mn complex of HL1 and the Ni complex of HL2 exhibited high efficacy against the reference medication [1]. (Gulcan, 2011) synthesized many metal complexes of Cu(II), Ni(II), Co(II), Pd(II) and Pt(II) and all shows Antibacterial property towards Staphylococcus aureus ATCC 4230 was determined using Ampicillin trihydrate as a comparative medication. All of them inhibits the growth of bacteria but the antibacterial activity of Co(II) and Cu(II)exhibit antibacterial activity that is both efficient and selective against gram-positive and negative bacteria [2].Several metal complexes of Zn(II), Cd(II), and Hg(II) derived by(C & Sekhar, 2018) and evaluated for antibacterial activity towards bacterial bacillus megaterium (Gram-positive) and Klebsiella pneumoniae, respectively (Gram-negative). Researchers can conclude that the complexes are more effective than the ligands alone using this data. Hg complexes of all the chemicals investigated exert a higher action on the bacteria than any of the other compounds[3]. (Abdulghani & Hussain, 2015)were synthesized many metal complexes of Pt(II), Pd(II), Cu(II), Ni(II) and their antibacterial activity were carried out versus E.coli Staphylococcus aureus, Pseudomonas arginosa and Streptococcus pneumonia. All metal complexes show selective activity against one or two bacteria but Pt complex [Pt (Ln)Cl_3](H_2O. 0.5 OH) was active against all contains highest activity against Streptococcuspneumonia and Pseudomonas aeruginosa [4].(Sumrra *et al*., 2020)derived many metal complexes of Co(II), Ni(II), Cu(II) and Zn(II), all were checked for antibacterial activity versus E.coli, Streptococcus farelis, Pseudomonas aeruginosa, Khensiella pneumonia, Staphylococcus aureus and Bacillus subtilis. While all complexes were microcrystalline and all but Zn(II) complexes exhibited a strong color, only the MIC compounds significant antibacterial properties were chosen for MIC investigations[5].

Antifungal

(Tyagi & Chandra, 2012)synthesised many Schiff bases and their metal complexes of metal Pd(II), Pt(II), Rh(II), Ir(II) and tested their antifungal activity against Aspergilusniger, Aspergilusfumigares, and Fusarium odum. They found that

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dosage plays an important role in raising the degree of inhibition as concentration increases [6]. (Obaid *et al*., 2020)prepared many Schiff base and their metal complexes Cr(III), Mn(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Hg(II) and their antifungal potency versus Candida albicans which the inhibition through metal chelates higher than that with Cd(II) complex and Hg(II) complex with fungal studies[7]. (Mohamed *et al*., n.d.)were prepared many Schiff bases and their metal complexes Fe(II), Co(II), Ni(II), Cu(II), Zn(II), UO_2(II) in furthermore to their antifungal properties, all metal complexes of L1 and Fe(II), Zn(II) , UO_2(II) complexes of HL2 inhibits fungi atsignificant degree of dosage so the parent ligands and standards such compounds are possible antitumour effect studies [8]. (Sumrra *et al*., 2020)were synthesized many Schiff bases and their metal complexes ofCr(III), Co(II), Ni(II), Fe(III), Cu(II), Zn(II) , all were tested for antifungal potency versus Aspergillus flavus and Candida albicans and Ampholericin B. antifugal agent the ligand exhibited no biological activity, whereas all complexes demonstrated action versus Candida albicans fungi. Chelation with various bio-active metals improved the Schiff base's antimicrobial resistance to various microorganisms [9]. Madhavan Sivasankaran *et al*. (Sivasankaran *et al*., n.d.) were synthesized Schiff bases and their metal complexes Co(II), Ni(II), Cu(II), Zn(II) and the antifungal activity versus Candida albicans, Rhizopus niger, Rhizoptonicabataicola. The fungal activity analysis showed that complexes are more microbial toxic than the ligand, based on the lowest inhibitory concentration values of the prepared compounds versus fungi production. Co(II) complex was discovered to be highly active against all microbes. At the same time, Ni(II) and Zn(II)complexes are active [10].

Antimicrobial

Many Schiff bases and their metal complexes of Co(II), Cu(II), Zn(II) and their antimicrobial activity of Schiff base and metal(II) complexes were formed by (Bahron *et al*., 2019)the last sharp rise in inhibitory effects on complexation with the metal(II) ions. The Schiff base and metal complexes outperform the standard drug activity against the fungus C.albicans. The synthesized compounds have a better impact on the suppression of E.coli. Cu(II) complexes have a higher bioactivity than other complexes [11].(Raman *et al*., 2007)were synthesized Schiff bases and their metal complexes of Cu(II), Ni(II), Co(II), Mn(II), Zn(II), VO(IV), Hg(II), Cd(II) and their antimicrobial activity against based on chelation theory, many of the complexes had much antibacterial effects than the free ligand. These complexes also disrupt cell respiration and block protein production, limiting the organisms analyzed [12].(Mounika *et al*., 2010)derived Schiff base and their metal complexes Ni(II), Co(II), Cu(II), Zn(II), and their antimicrobial properties versus different complexes, which varies based on either the barrier properties of the microbes' cells or variations in microbial ribosomes. This outcome indicates that the Cu(II) complex has vigorous activity versus E.coli, while the Co complex has the most excellent inhibition zones against S.aureus[13].(Pervaiz *et al*., 2019)derived Schiff base and their metal complexes Co(II), Mn(II), Cu(II), and Cd(II), and their antimicrobial activity versus the metal complexes exhibits more muscular antimicrobial action than the derived ligand; the maximum activity was 11.47, demonstrated by the cobalt complex against B.subtilis with the reference drug Rifampicin, which shows maximum activity ar 20. The metal complexes had higher antifungal properties than the derived ligand, with the Co complex having the highest activity against A. flavus. In contrast, the standard drug fluconazole has the most significant action at 21.7 [14]. (Fugu *et al*., 2013)were synthesized Schiff base and their metal complexes Mn(II), Co(II), Ni(II), Cu(II), Zn(II) and their antimicrobial activity against Ni(II) complex showed reasonably effect versus E.coli, S.typhi, S.aureus, S.subtilis, Co complex showed very low activities against Pneumoniae, Cu (II) complex exhibited only moderate inhibitory activity against Salmonella typha, klebsiella pneumonia, Streptococuspyogens Bacillus subtilis, Zn(II) complex did not produce any inhibitory zone [15].

Antioxidant

(Buldurun *et al*., 2020)derived Schiff base and their metal complexes Fe(II), Co(II), and the antioxidant activity against the ligand; both complexes exhibit superior antioxidant and antiradical action, nearly superior to some benchmarks for (2,2'-azinobis-3-ethylbenzothiazoline-6-sulphonic acid) ABTS radicals. Similarly, Fe(II) and Co(II) metal complexes had decent radical scavenging impacts for (1,1'-diphenyl-2-picrylhydrazyl) DPPH radicals [16].(Jafari *et al*., 2017)derived Schiff bases and their metal complexes Co(II), Cu(II), Ni(II), Zn(II), and their antioxidant properties versus the ferric reducing antioxidant power assay (FRAP) was a strategy of broad competency for antioxidant invitro as well as in organisms; the method was based on reduction of Fe(III) to Fe(II), the reducing power of the existing complexes was in satisfactory correlation [17].(Mohamed *et al*., n.d.)were synthesized Schiff base and their metal complex Co(II), Ni(II), Cu(II), Zn(II) and their antioxidant activity against macrocylic Schiff base ligands (W_2O_2) synthesized from condensation of polyamine with 2-Hydroxybenzaldehyde or 2-Hydroxy-3-methoxybenzaldehyde and their Co(II) and Cu(II) complexes have been studied antioxidant activity of Co(II), Cu(II), Ni(II), Zn(II), Fe(II), Ru(II), Pd(II), Cd(II) complexes of Schiff bases of diamine thiocarbohydrazide, sulphanilamide, hydroxyquinoline and benzohydrazide with substituted aldehyde or ketone or piperonal were investigated compounds with nitro and methyl substitutents showed better antioxidant activities than those with 4-hydroxy group leading to inhancement in antioxidant activity through one electron transfer method [18].(Ejidike & Ajibade, 2016)derived Schiff base and their metal complexes Co(II), Cu(II), Ni(II), Zn(II), and their antioxidant action versus Schiff base and DEPH2 and their Co(II), Cu(II), Ni(II), Zn(II) complexes compared to BHT and ascorbic acid. Metal (II) complexes were found to have significant action than unrestricted Schiff bases DEPH2, with the antioxidant activity of the free ligand observed to be 24.20 percent at the lowest concentration, but upon complexation, it raised massively inside the range of 29.80 % - 45.01 % from Zn(DEP) to Cu (DEP) [19].(Obaid *et al*., 2020)derived Schiff base and metal complexes Co(II), Ni(II), and their antioxidant activity even against reduction potential of the DPPH radicals had been deduced from the lowering in its absorbance at 517 nm, which can be influenced by an antioxidant, the total volume of 16 cm^3 in which the mole fraction of each Schiff base s 0.1, 0.4, 0.5, 0.6, 0.8, 0.9 and 1.0, the absorbance of each of these solution mixtures was measured at 620 nm and 700 nm for Co(II) and Ni(II) respectively [20].

Anticancer

(Mahmoud *et al*., 2016)derived Schiff bases and their metal complexes Co(II), Cu(II), Ni(II), Zn(II), Cr(III), Mn(II), and Cd(II), as well as their anticancer properties against $[Co(H_2)(H_2O)_2Cl_2]$. The $3H_2O$ complex was the more effective and interactive complex, and it has the potential to be employed as an anticancer agent against breast cancer. The newly derived compounds' greatly improved activity may be due to an azomethine group's presence in the macrocyclic chelate ring, and the complexes' diffusion through the lipid layer of cell membranes was boosted and became more potent [21].(Mahmoud *et al*., 2019)derived the Schiff base ligand, and its metal complexes Cr(II), Fe(II), Cu(II), and Cd(II) had an inhibition fraction greater than 70%. They deduced that Fe(III) and Cd(II) complexes were more effective than the Schiff base ligand, but Cr(III) & Cu(II) complexes were less active than the ligand against the MCF-7 cell line, consequently, the Fe(III) complex with the lowest IC50 value may be shown its magnificent action versus breast cancer cell line compared to other compounds [22]. Schiff bases and their metal complexes were derived by(Bahron *et al*., 2019)Ni(II), Co(II) illustrate anticancer activity, whereas Ni(II) complexes exhibit considerably higher anticancer properties than their variants. The existence of Co(II) complexes implies that the anticancer potency of these compounds is, to some extent, metal reliant. The anticancer activities of Ni(II) and Co(II) complexes are lesser than those of their parent ligand [23].(Ebrahimipour *et al*., 2015)derived Schiff base and metal complexes Cu(II), and the anticancer properties against cell viability deduced utilizing Cu(II) complex higher efficacy compared to the other compounds, the Cu(II) complex has been gotten better after complexation high concentrations could create more adverse side effects, the lowest therapeutic dose creating the desired clinical effect was beneficial, the exact cellular anticancer metabolic pathway of each compound needs to clarify in further studies [24]. (Panchsheela Ashok *et al*., 2020)derived Schiff bases and metal complexes Cu(II), Zn(II), Cd(II), and their anticancer activity was frequently judged in terms of a synergistic effect developed by the central metal ion and the ligands. Because these derived free ligands DMPAQ were observed to be unresponsive against human breast cancer MCF-7 cells, the substantial anticancer action of Cu(II), Zn(II) may be attributed to a common 1,10-phenanthroline ligand moiety or metal. Cu(II), Zn(II) were reported to have potent anticancer activity against MCF-7 cells compared to the reference drug doxorubicin [25].

DNA binding

(Tiwari *et al*., 2011)were derived Schiff bases and their metal complexes Ni(II), Co(II), Cu(II), Zn(II), and their DNA binding. Ni(II) and Co(II) complexes exhibit excellent DNA binding capacity and interaction than Cu, Zn complexes owing to orbital availability in the case of Ni, Co complexes. DNA acted as a ligand, creating binary complexes with H2L as different co-ordinating organisms, and metals responded as the central core [26].(Palanimurugan & Kulandaisamy, 2018)were derived Schiff bases and their metal complexes Cu(II), Co(II), Ni(II), Zn(II), VO(II), and their DNA binding action against to evaluate the binding mode and binding ability of prepared compounds with CT-DNA of [CuL] complex were recorded in the presence and absence of DNA in Tris-HCl buffer (PH 7.2), the intensity of CT-DNA was diversified. In contrast, the metal concentration. The binding propensity was examined by measuring the change in absorbance of the complex as the intensity of CT-DNA enhanced. As the concentration of DNA increased, so did the absorbance of the Cu complex at 255 and 328 nm [27].(Bheemarasetti *et al*., 2018)were derived Schiff base and their metal complexes Co(II), Ni(II), Cu(II), Zn(II), Pd(II), and their DNA binding action against the molecules bind to DNA by interactive because intercalation gives rise to hypochromic in the spectral bands, there was a redshift observed for Co(II), Zn(II), Pd(II) complexes. Pd(II), Ni(II), Co(II), Zn(II), Cu (II) Cu complex has a higher kb value, implying that it has a better binding with DNA [28].(Abdel-Rahman *et al*., 2020)were derived from Schiff bases and their metal complexes Cd(II), Mn(II), Ag(I), and their DNA binding action against the interaction of the complexes with DNA in Tris-HCl buffer (pH=7.2). CT-DNA was thoroughly cleaned by centrifugal dialysis before it could be used, and DNA concentration was determined by monitoring UV absorbance at 260 nm with €260 =6600 mol-1cm2. The stock solution was kept at 40 degrees Celsius and used for around one day [29].(Anupama *et al*., 2012)discovered Schiff bases and their metal complexes Cu(II), Ni(II), Co(II), Zn(II), and VO(II), as well as their DNA binding behaviour against complexes that interact with DNA in hypochromic and bathochromic states due to the stacking interaction between the complexes' aromatic chromophore and the DNA base pairs. The absorption spectra of the complex Co(II)-5-Br-SALAP in the absence and presence of calf thymus DNA revealed that the presence of DNA caused a reduction in peak intensities [30].

CONCLUSION

Based on the above information about the biological and multifunctional applications of Schiff bases and metal complexes it is concluded that they plays a vital role in chemical and medicinal chemistry. We believe that this review helps in finding applications of metal complexes and Schiff bases.

Acknowledgement

The authors are thankful to Coordinator, MGV, Dr Apoorva P. Hiray's continuous support and inspiration in research & also thankful MGV's MSG College, Malegaon, for providing the required Library facilities for this review literature.[1]

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