Original Article

A Review Of Biological Applications Of Isoniazid Derived Schiff Base Complexes

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Abstract

The condensation of an amino compound with carbonyl compounds synthesizes the Schiff bases and their complexes are reported for their wide range of biological activities. These complexes have special attention on activities such as antifungal, antibacterial, antiviral, antitumor and anticancer properties. In the recent years, these complexes have gained good attention because of their unique biological properties. The biological applications of these complexes are reported in the large extent in the recent years. Development of a new chemotherapeutic Schiff bases and their metal complexes is now attracting the attention of medicinal chemists. In this review, a small attempt to show some examples for the biological applications of the Schiff base complexes.

Key Words: Schiff base complexes, Antifungal and antibacterial properties, Antiviral activities and Anti cancer activities.

Introduction

In 1864, Hugo Schiff undergone the condensation process between primary amines and carbonyl compounds, he synthesized the product called as Schiff Bases. Due to the conjugated system, Schiff bases of aromatic aldehydes show more stability than with the aliphatic varieties which are readily polymerized and unstable in nature. The polynuclear complexes are formed by the binding of metal centres in unsaturated coordination compounds with some additional linkers. The presence of imine group (-RC=N-) in the Schiff base compounds have interestingly shown many applications like designing molecular ferromagnets, in catalysis, in biological modeling applications, as liquid crystals, as heterogeneous catalysts and also in self assembling cluster complexes.

The developments of coordination chemistry have attention in the formation of Schiff bases with variety of coordination linkages. The bidentate modes of Schiff bases display varying degrees of flexibility and hence adopt different coordination modes. Among the co ordination compounds, the cobalt Schiff base complexes are important because of their involvement in vitamin B12 models and oxygen carrier properties, but also due to their interesting magnetic and spectroscopic as well as diverse metal ligand interactions. The O- or N- donors in heterocyclic Schiff base ligands and their metal complexes are shown interesting properties.

The presence of hetero atoms like oxygen, nitrogen and sulfur donors in transition metal complexes shows carcinostatic, antitumour, antiviral, antifungal and antibacterial activities.

The complex biological properties of these systems are studied from the structural chemistry of Schiff base ligands and their complexes. The presence of the characteristic azomethie (-N=CH-) group, shows biological activities of complexes of heterocyclic Schiff base ligands.

Sp2 hybridized nitrogen atom of the azomethine linkage shows biological activities due to the presence of lone pair on nitrogen atom. These Schiff base complexes have great attention due to their active part in metalloenzymes and as

biomimetic model compounds. They are very often found inside the natural proteins and enzymes. The presence of N atom has an important role in the coordination of metals as the active site of numerous metallobiomolecules.

The intermolecular forces of strong hydrogen bonds played a very important role in crystal. Even solvent molecules and counter ions are efficiently binded by hydrogen bonds, which contributes the shape and supramolecular assembly of the compound. These interactions are very helpful to stabilize the crystal lattice and therefore of fundamental significance of hydrogen-bonded organic and metal-organic supramolecular structures. Recently, the water content in self-assembly processes has been found to remarkably inf;uence the structural topologies of compounds. Isoniazid, is a therapeutic agent with established clinical application. Compounds of similar backbone have shown antibacterial, antifungal and anti-onchoceral activities.

The metal complexes are used as therapeutic agents and as drugs for the treatment of several human diseases, due to the developments in inorganic chemistry. Because of their potential applications in pharmaceuticals, antibacterial, antifungal, anticancer and anti-inflammatory actions, synthesis of Schiff base metal complexes, particularly those of transition metal ions, with different molecular topologies and sets of donor atoms is becoming an emerging area of research.

Biological Importance of Schiff base complexes

The field of bio-inorganic chemistry increases the interest in Schiff base complexes, and made it biologically important.

Antifungal and Antibacterial Properties

Some of the Schiff base complexes with copper metal have been efficiently studied for their antifungal and antibacterial activities. Their antifungal activities have been assessed against the three phytopathogenic fugi, A.solani, F.equisetti and M.phaseolina. Then their antibacterial activities have also been studied against the two pathogenic bacteria, E.coli and S.aureus. M.E.Hossain et al. reported his study that copper(II) complexes are generally less fungitoxic towards A.solani, F.equisetti and M.phaseolina than either the free ligands or the commercially available antifungal agent nystatin. The copper(II) complexes of benzoylpyridine Schiff base ligands are found to be more active towards the organism F.equisetti. The study shows that the given complexes are active against the organism S.aureus but the presence of E.coli remains stable.

A series of 2-acetylpyridine thiosemicarbazone derivatives were found to have significant antimalarial activities due to the presence of 2-pyridylalkylidene moiety and a thiocarbonyl group. The presence of bulky groups at position N of the thiosemicarbazone moiety increased antimalarial activity. The more number of studies revealed the active nature of thiosemicarbazide ligands are very high when they are associated with a metal ion.

The metal complexes of 2-aminobenzoic acid with its metals, Fe(III), or Co(II) or Ni(II) showed a good antibacterial activity against Escherichia coli, Pseudomonas aeruginosa and Staphylococcus pyogenes. Fe(III), Cu(II), Zn(II) complexes can inhibit the growth of E.coli. These complexes should be used to prevent some common diseases caused by E.coli. The Schiff base complexes Fe(III), Co(II), Cu(II), Z(II) could inhibit the growth of Gram-positive bacterial strains(Staphylococcus pyogenes and P.aeruginosa).

Gaballa et al. showed in his work, as Platinum(II) Schiff base complexes have antibacterial properties against E.coli, Bacillus subtilis, P.aeruginosa, Staphylococcus aureus. Many reports are already related to this work, Platinum(II) complexes are more active antibacterials than the precursor schiff base ligands against one or more micro organisms. The toxicity is more due to the presence of sulphonic OH, OCH_3, S and CH_3CH_2CH groups, which might interact with double membrane. The reports concluded that antibacterial activity of the compounds are due to the difference in cell wall structure of the bacteria.

Some Schiff base metal complexes of 2-Aminomethythiophenyl-4-bromosalicylaldehyde have been reported for their antimicrobial activities.

Nair et al., reported some Schiff base complexes of Co(II), Ni(II), Cu(II) and Zn(II) with indole-3-carboxaldehyde and m-aminobenzoic acid have excellent antibacterial activity by disc diffusion method. The effect of metal ions on the normal cell membrane decides the activity of the metal complexes. Some metals have chelating with ligands which has both polar and non polar properties. Because of this dual nature, the permeability of metal ions to the cells and tissues get increases with different bacteria. He also reported the CU(II) and Co(II) is more antibacterial active than Ni(II) and Zn(II) .

Shaker et al. reported a series Fe(II) Schiff base complexes derived from the condensation of amino acid and sodium 2-hydroxybenzaldehyde-5-sulfonate. These complexes are characterized by different analysis and undergone the antibacterial activities with Bacillus cereus, P.aeruginosa and Micrococcus bacteria. Many literature survey shows that cobalt Schiff base complexes have amazing antibacterial activities. Because of their aqueous stability, availability and simplicity of synthesis are more studied for Co(II) complexes than Co(III) complexes. The stabilization of Co(III) ion due to the presence of some polydentate ligands with N,O and S donor atoms and in aqueous phase Co(III) shows kinetic inertness in water due to the presence of NH_3. The new hybrid amie-imine-oxime ligand of Co(III) complex shows antibacterial activity against Bacillius subtilis but, with Staphylococcus aureus or the Gram negative bacteria Escherichia coli ad Eterbacter fecalis has no activity.

N. K. Chaudhary and P. Mishra sythsised the series of Schiff base metal complexes by the condensation of amoxicillin trihydrate and nicotinaldehyde with Co(II), Ni(II), Cu(II) and Zn(II) as central metal ions. These complexes have greater activity at high concentration against all the bacterial pathogens due to the presence chelation property. The structural components containing additional C=N bond with N,O donor atom coordinate the metal ion and as a result polarity of the complex decreases. Because of this, there will be efficient permeation through the lipid layer of bacterial organism and destroys their activity.

Antiviral Activities

The pharmacological properties like antibacterial, anticonvulsant, anti-HIV, antifungal and antiviral activities are efficiently indentified in Schiff bases and Mannich bases of isatin. In 2007, A Jarrahpour et al. synthesized a series of Schiff bases having the combination of isatin and 5-flouroisatin with cobalt (III) and reported their antiviral activities. In general, Cobalt (III) ion is not stable in aqueous solution. So it is stabilized in presence of chelating N, O donor ligand atmosphere.

Epstein and coworkers synthesized a series of Co (III) complexes with N, O donor ligands are used in the treatment of blindness, known as epithelial herpetic keratitis. Initially, the drug was applied upon a rabbit eye model infected with Herpes Simplex Virus Type1 (HSV – 1) and found to be active inhibitor of HSV – 1 replication in vitro. Some evidences are available for these complexes to prevent virus entry by inhibiting membrane fusion. The complex inhibited plaque formation by vesicular stomatitis virus VSV and VZV (varicella-zoster virus). Later, the activity of CTC-96 against adenivirus in cell culture model and adenovirus kerato conjunctivitis in a rabbit model was reported.

K.S.Kumar et al. reported a group of Schiff base complexes containing 3-(benzylideneamino)-2-phenylquinazoline-4(3H)-one and their anti viral activity against herpes simplex virus-1(KOS), herpes simplex virus-2(G), Vaccinia virus, Vesicular stomatitis virus, herpes simplex virus-1 TK-KOS ACVr, para influenza-3virus, reovirus-1. Sindbis virus, Coxsackod virus B4, Punta toro virus, feline coronavirus(FIPV) feline herpes virus, respiratory syncytial virus and influenza A H1N1 subtype, influenza A H3N2 subtype, influenza B.

Anti-cancer activities

Cancer is a group of diseases that involves abnormal cell growth with the potential to attack or spend to other parts of the body. Chemotherapy is a drug treatment for both localized and metastasized cancer. The existing drugs have serious side effects, so many researches are going on to overcome these problems. Schiff base linkages present in the organic compounds have well anti cancer properties due to its structures. Not only in organic, but also in inorganic chemistry, are the Schiff base ligands with the metal complexes used as potent drugs or diagnostic agents. Metal complexes can offer unique mechanisms of drug action because of wide range of co-ordination numbers, geometries and kinetic properties, which are not possible with pure organic molecules.

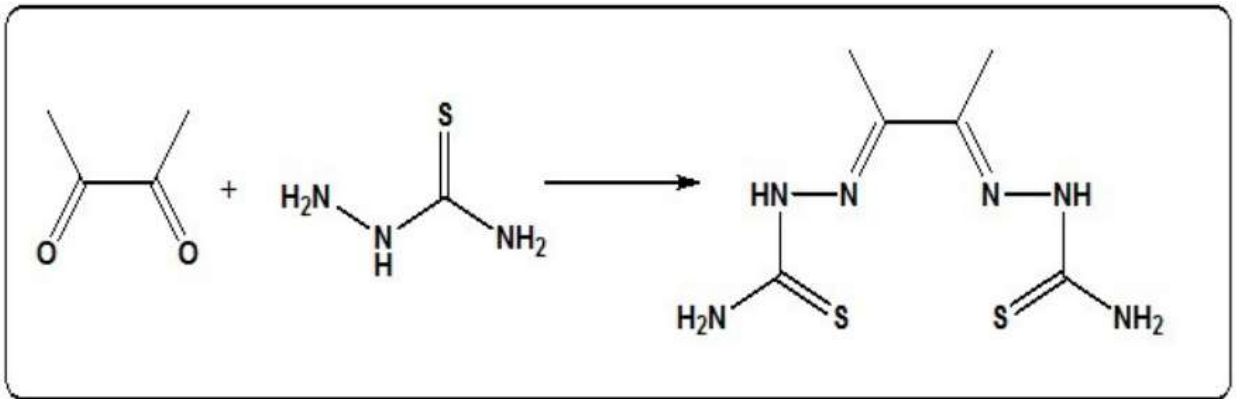
Rosenberg and co-workers invented Cisplatin which is one of the best selling anti-cancer drugs throughout the world. Mokhles M.Abd-Elzaher et.al. reported some metal complexes of the Schiff base of salicylaldehyde with 2-amino-4-phenyl-5-methyl thiazole. The complexes were studied against different human tumor cell lines: breast cancer MCF-7, liver cancer HepG2, lung carcinoma A549 and colorectal cancer HCT 116 in comparison with the activity of doxorubicin as a reference drug.

Another study revealed the activity of Zn II complex which shows the potent inhibition against human TRK in the four cell lines (HepG2, MCF7, A549, HCT116) by the ratio 80, 70, 61 and 64% respectively as compared to the inhibition in the untreated cells 29. A series of metal complexes of Schiff bases derived from vanillin and actoacetanilide with ethylenediamine were tested , its copper complex have higher Inhibitory Concentration (IC50) value around 49µ/ml.

The Schiff base complexes such as Cu(II), Ni(II), Pd(II), and Pt(II) complexes of ortho-naphthaquinone thiosemicarbazone (NQTS) and elucidated their in vitro anti cancer activities against MCF7 human breastcancer cell lines. Ni(II) complex have most potent IC50 value of 2.25 µM.

The following complexes of the Schiff base ligand have a series of Cu2+ -salicylidene-aminoacid Schiff bases – Phen(Bipy) ternary have reported for its good anticancer activities. The synthesized Cu(II) complex have good anti-proliferative activity against PC-3 and LNCaP prostate cancer cell lines.

Mononuclear complexes of Cu(II), Mn(II), Co(II), Ni(II) with bis-schiff base ligand derived from 2,3-butadione and thiosemicarbazide are synthesized and reported for their better anti-cancer activities. The cytotoxicity assay was done against five different kinds of cell lines (HL-60, Spca-1, Tb, MGC, K562). Among these complexes, Cu(II) was found to have better anti-tumor activity.



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