Halogenated benzylidene Schiff base Transition metal complexes, potent molecules in the design of antituberculosis agents

C. U. Dueke-Eze
University of Lagos, Akoka, Lagos State, Nigeria

Abstract

Background: The increasing reports of resistance of *Mycobacterium tuberculosis* (*M.TB*) to the classical anti-tuberculosis drugs and co-morbidity of tuberculosis (TB) with HIV infection pose challenges for effective control of TB. Development of new compounds with anti-TB effect to combat the resistance is highly desirable.Objective: Metal complexes represent a major investigational compound. The presence of metal ion in these compounds will make it difficult for the bacteria to develop resistance to as its mode of action will be different from the existing anti-TB agents. The goal of this study is to probe the *in vitro* antituberculosis activity of some halogenated benzylidene Schiff base metal complexes.Materials and methods: The Schiff bases were synthesized by condensation of isonicotinic acid hydrazide (INH) with some halogenated benzaldehydes and then reacted with $CuCl_2.2H_2O$ and $CoCl_2.6H_2O$ to obtain the metal complexes. The compounds were characterized by elemental analysis, infrared (IR), nuclear magnetic resonance (NMR), electronic absorption and molar conductivity. The synthesized compounds were evaluated for their *in-vitro* anti-tuberculosis activity against standard strain (*M.TB* $H_{37}Rv$) using the proportion method and isoniazid (INH) as a reference compound.Results: The Schiff bases reacted as bidentate ligands to yield complexes of 1:1 or 1:2 (M: L) ratio. All the complexes are assigned either octahedral or square planar geometry based on the electronic spectra. The complexes showed enhanced *in-vitro* anti-tuberculosis activity against *mycobacterium tuberculosis* $H_{37}RV$ compared to the free ligands and reference compound (INH). Conclusion: The results demonstrate that compounds with metal ion can display strong anti-TB activity making them suitable for further exploration.

n search of effective bioactive compounds, we have synthesized the new Co(II), Ni(II) and Cu(II) complexes of the Schiff base derived from 8formyl7hydroxy4methylcoumarin and 2hydrazino benzothiazole and characterized by analytical, spectroscopic (IR, NMR, UVvis, Mass), magnetic, powder Xray diffraction data (PXRD) and TGA studies. Elemental analysis suggests the stoichiometry of the synthesized complexes and the solution electronic spectral study revealed the octahedral geometry of the compounds. Thermal analysis shows the presence of water molecule outside the coordination sphere and powderXRD patterns have been studied to test the degree of crystallinity of the complexes and unit cell calculations were made.

All the synthesized compounds were tested against human ovarian cancer cell line (PA1). The synthesized metal complexes exhibited enhanced activity against the tested bacterial (S. aureus and E. Coli) and fungal strains (Candida albicans and Aspergillus fumigatus) as compared to free ligand (LH). The results of the DNAcleavage activity suggest that the ligand and its metal complexes can cleave CTDNA at different degrees. Further, antituberculosis activity was done by using microplate almar blue assay. Among all these synthesized compounds, the Cu(II) complex exhibits good cleaving ability compared to other newlysynthesized metal complexes.

Schiff bases are condensed products of primary amines and carbonyl compounds and are becoming more and more important in current scenarios. Schiff bases are compounds with imine or azomethine functional groups (–C = N–) and have proven to be versatile pharmacophores for the design and development of a variety of bioactive lead compounds. Schiff bases exhibit useful biological activities such as anti-inflammatory, analgesic, antibacterial, anticonvulsant, anti-tuberculosis, anti-cancer, anti-oxidant, repellent, anti-glycemic and antidepressant effects. Schiff bases are also used as catalysts, pigments, dyes, organic synthetic intermediates, polymer stabilizers and corrosion inhibitors. The current review summarizes information on diverse bioactivity and also focuses on a number of recently synthesized Schiff bases as potential bioactivity cores.

Schiff bases have been investigated in relation to a wide range of contexts, including antimicrobial, antiviral and anticancer activity. They have also been considered for the inhibition of amyloid-β aggregation.

Schiff bases are common enzymatic intermediates where an amine, such as the terminal group of a lysine residue, reversibly reacts with an aldehyde or ketone of a cofactor or substrate. The common enzyme cofactor PLP forms a Schiff base with a lysine residue and is transaldiminated to the substrate(s).[10] Similarly, the cofactor retinal forms a Schiff base in rhodopsins, including human rhodopsin (via Lysine 296), which is key in the photoreception mechanism.

Citation C. U. Dueke-Eze; Halogenated benzylidene Schiff base Transition metal complexes, potent molecules in the design of antituberculosis agents, , University of Lagos, Akoka, Lagos State, Nigeria, Petrochemistry *2021*, Webinar, November 22-23, 2021.