(E)-N’-(2, 4-dihydroxybenzylidene)nicotinohydrazide and its Metal Complexes: Synthesis, Characterisation and Antitubercular Activity

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Abstract. Nicotinic acid hydrazide and 2,4-dihydroxybenzaldehyde were condensed at 20 °C to form an acetylhydrazone (H3L1) with ONO coordination pattern. The structure of the acetylhydrazone was elucidated by using CHN analyzer, ESI mass spectrometry, IR, 1H NMR, 13C NMR and 2D NMR such as COSY and HSQC. Thereafter, five novel metal complexes [Mn(II), Fe(II), Pt(II) Zn(II) and Pd(II)] of the hydrazone ligand were synthesized and their structural characterization were achieved by several physicochemical methods namely: elemental analysis, electronic spectra, infrared, EPR, molar conductivity and powder X-ray diffraction studies. An octahedral geometry was suggested for both Pd(II) and Zn(II) complexes while both Mn(II) and Fe(II) complexes conformed with tetrahedral pyramidal. However, Pt(II) complex agreed with tetrahedral geometry. In vitro antitubercular activity study of the ligand and the metal complexes were evaluated against Mycobacterium tuberculosis, H37Rv, by using micro-diluted method. The results obtained revealed that (PdL1) (MIC = 0.56 mg/mL), (ZnL1) (MIC = 0.61 mg/mL), (MnL1) (MIC = 0.71 mg/mL) and (FeL1) (MIC = 0.82 mg/mL), exhibited a significant activity when compared with first line drugs such as isoniazid (INH) (MIC = 0.9 mg/mL). H3L1 exhibited lesser antitubercular activity with MIC value of 1.02 mg/mL. However, the metal complexes displayed higher cytotoxicity but were found to be non-significant different (P > 0.05) to isoniazid drug.

Keywords: hydrazones, metal complexes, electron spin resonance, thermogravimetry, powder X-ray diffraction, antitubercular agents

Introduction

Human tuberculosis (TB) has re-emerged with devastating consequences on global public health and it is currently one of the most widespread infectious diseases. In addition, it is the leading cause of death due to a single infectious agent among human adults in the world (Jenkins et al., 2011). Mycobacterium tuberculosis is one of the most harmful pathogens of mankind, infecting one-third of the global population and claiming two million lives every year (Stewart et al., 2003). Tuberculosis spreads by aerosols from patients with pulmonary disease (Phillip and Graham, 2004). Mycobacterial infection has increased in number worldwide due to a global increase in the number of patients with HIV infection and AIDS disease, increase in number of elderly patients and the emergence of resistant tuberculosis. Tuberculosis arises in two different ways: either from a recent infection with M. tuberculosis or from the reactivation of dormant tubercle bacillus after initial infection. As a consequence, the present level of tuberculosis comprises both individuals with “new” exogenous infections and those with a reactivation of “old” endogenous disease (De Backer et al., 2006). In terms of absolute number of TB cases, 22 countries of the world have the highest TB burden with at least 270 cases per 100,000 populations. Among the top five ranking countries are India, China, Indonesia, South Africa and Nigeria (Harper, 2007; Laughon, 2007). The situation has become more deplorable than it appeared as 0.5 million new cases due to multidrug-resistant (MDR) TB were recorded in 2010 (WHO, 2013). The alarming estimates exposes that 0.22 billion people may acquire TB and 79 million could die due to TB by the year 2030.

Effective TB treatment is difficult, due to the unusual structure and chemical composition of the Mycobacterium cell wall, which makes many antibiotics ineffective and hinders the entry of drugs (Jia et al., 2005). TB disease can be treated by taking several drugs for 6 to 9 months.

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