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ORIGINAL ARTICLE

Synthesis, physico-chemical investigations and biological screening of metal (II) complexes with Schiff base derived from naphthofuran-2-carbohydrazide and citral

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DNA cleavage

Abstract A series of Co(II), Ni(II), Cu(II), Cd(II), Zn(II) and Hg(II) complexes of the type $CuLCl_2.\ 2H_2O$ and ML_2Cl_2 [M = Co(II), Ni(II), Cd(II), Zn(II) and Hg(II)], respectively, where L = Schiff's base derived from condensation of citral and naphthofuran-2-carbohydrazide have been synthesized. The proposed structures of the obtained complexes have been established from elemental analyses, IR, Electronic, Mass, ^{1}H NMR, ESR spectral data, magnetic and thermal studies. From the above spectral studies it is concluded that the ligand acts as a bidentate coordinating through azomethine nitrogen and amide oxygen. The measured low molar conductance values in DMF indicate that the complexes are non-electrolytic in nature. The electron transfer mechanism of the Cu(II) complex is investigated by the aid of cyclic voltammetry. The free ligand and its metal complexes have been screened for their antioxidant activity by the DPPH method and *in vitro* antibacterial (*Escherichia coli, Staphylococcus aureus, Bacillus subtilis* and *Pseudomonas aeruginosa*) and antifungal (*Aspergillus niger, Aspergillus flavus, Cladosporium oxysporum* and *Candida albicans*) activities by the minimum inhibitory concentration (MIC) method. The DNA cleavage studies of all the complexes were studied by agarose gel electrophoresis method. The results indicate that the biological activity increases on complexation.

1. Introduction

Naphthofuran nuclei are key structural moieties found in a large number of biologically important natural products. Many of the natural naphthofurans, such as (±)-laevigatin, (+)-heritol and balsaminone A possess interesting pharmacological and cytotoxic properties (Cumhur kirilmis et al., 2009). A large number of naphthofuran derivatives possess various biological activities like anthelmentic, anticonvulsant and antipyretic (Basavaraj Padmashali et al., 2005). They also act as florescent dyes and probes as well as photosensitizers.

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Naphthofurans when condensed with various heterocycles exhibit a wide spectrum of activities (Kumaraswamy and Vaidya, 2005; Kumaraswamy et al., 2008; Nagendra Prasad et al., 2010). Many heterocycles and metal containing compounds (Bukhari et al., 2008) have exhibited various antioxidant activities, more importantly naphthofuran derivatives have been proven to be potent antioxidant agents (Basavaraj Padmashali and Vaidya, 2002). Citral is an acyclic monoterpene and an important constituent of lemon grass oil.

Although a large number of Schiff base ligands have been investigated, similar studies on coordinated ligands are relatively scarce. Schiff base ligands are extensively important and studied widely because they can readily form stable complexes with most of the metal ions (Yu et al., 2005; Lin and Feng, 2005). In addition they possess interesting antibacterial, antifungal and antitumor activities (El-Gammal, 2010; Chohan et al., 2005). Metal ions when bonded to biologically active molecules may modify and enhance their activity (Al-Shaalan, 2007). Schiff base complexes involving oxygen and nitrogen donor ligands are well known (Abdallah et al., 2010) and have excited great interest among chemists due to their applications in catalysis and their relevance to bioinorganic systems (Raman and Sobha, 2010). During the last decades there has been curiosity owing to the interaction of small molecules with DNA (Tan et al., 2008). The reaction of metal complexes with DNA has been extensively studied in relation to the progress of development of new reagents in the field of medicine and biotechnology.

In this communication, we describe the chelation behavior of Schiff base derived from the condensation of naphthofuran-2-carbohydrazide and citral. Further the metal complexes were obtained employing different metal ions like Co(II), Ni(II), Cu(II), Cd(II), Zn(II) and Hg(II) in order to obtain more potent biologically active compounds and to know the geometry of the compounds. All the synthesized compounds were studied by analytical, thermal and various spectral techniques. Biocidal activity was carried out for all the compounds.

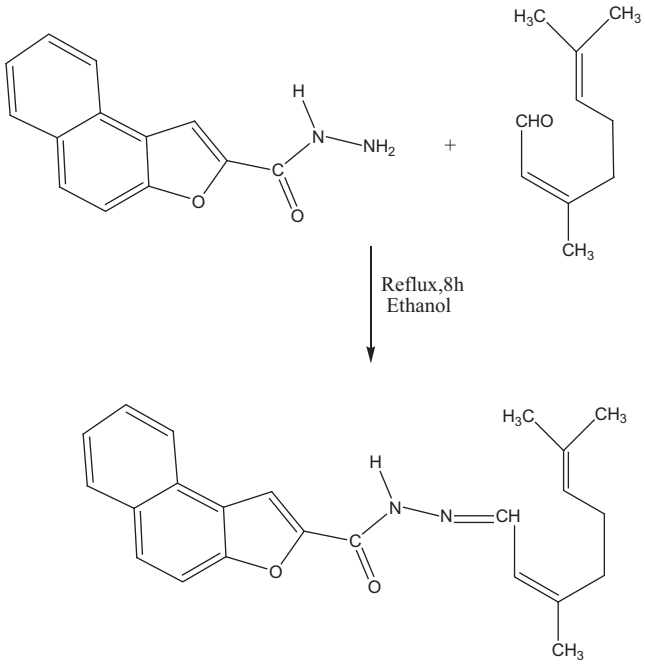
2. Experimental

All chemicals and reagents were of reagent grade and are used without further purification. Melting points of the compounds are determined in open capillaries and are uncorrected. The metal salts were used as their chlorides. Naphthofuran-2-carbohydrazide was prepared as reported (Kawas et al., 1962). The metal and chloride contents were determined as described in the literature (Vogel, 1968).

2.1. Synthesis of Schiff's base ligand

The synthesis of Schiff base is schematically represented in Scheme 1. A mixture of naphthofuran-2-carbohydrazide (0.01 mol, 2.26 g) and citral (0.01 mol, 1.71 mL) in 20 mL hot ethanol was boiled under reflux for 8 h on a water bath during which a pale yellowish solid separated. It was filtered, dried and recrystallized from hot ethanol. The purity of Schiff's base was checked by TLC.

$M.F = C_{23}H_{25}O_2N_2$, Mol.wt = 361, m.p = 110°C, Yield = 75%



Scheme 1 Synthesis of Schiff's base ligand.

2.1.1. General method for the synthesis of Co(II), Ni(II), Cu(II), Cd(II), Zn(II) and Hg(II) complexes

An ethanolic solution (30 mL) of Schiff base and metal salts in the ratio 1:1 for Cu(II) complex and 2:1 for Co(II), Ni(II), Cd(II), Zn(II) and Hg(II) complexes was refluxed with an ethanolic solution (10 mL) of metal salts on water bath for about 3 h. Then, to the reaction mixture an aqueous alcoholic solution of sodium acetate was added to adjust the pH to 6.0–7.0. The precipitated complexes were further refluxed for about an hour. Later they were filtered off, washed thoroughly with water and little warm ethanol to remove any traces of unreacted starting materials and finally dried in a vacuum desiccator over fused $CaCl_2$. (Yield: 50–55%).

2.2. Analysis and physical measurements

Elemental analyses (C, H and N) were performed on Perkin Elmer 240C model elemental analyzer at the Central Drug Research Institute (CDRI), Lucknow. The IR spectra of all the compounds were recorded on a Perkin Elmer 783 FT-IR spectrophotometer in the 4000–350 cm^{-1} region in KBr pellets. The ^1H NMR spectra were recorded in DMSO-d_6 on a BRUKER 400 MHz spectrophotometer using TMS as an internal reference. The electronic spectra of the Co(II), Ni(II) and Cu(II) complexes were recorded on an ELICO SL-164 double beam UV–Visible spectrophotometer in the range of 200–1100 nm in DMF (10^{-3} M) solution. At room temperature the ESR spectrum of the Cu(II) complex in the polycrystalline state was recorded on a Varian-E-4X band EPR spectrophotometer using TCNE as the 'g' marker (g = 2.00277). The LC-MS was recorded on a TOF MS ES + mass spectrophotometer. The DART-MS was recorded on a JEOL-Accu TOF JMS-T100LC mass spectrometer having a DART source.

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