In vitro cytotoxic activity of a novel Schiff base ligand derived from 2-hydroxy-1-naphthaldehyde and its mononuclear metal complexes

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ABSTRACT

Mononuclear Cu(II), Ni(II) and V(IV) complexes of a bidentate Schiff base ligand derived from 2-hydroxy-1-naphthaldehyde and 2-methoxyethylamine were synthesized and determined by spectroscopic methods. The crystal structures of HL ligand and Cu(II) complex was determined using single crystal X-ray diffraction method. HL Schiff base behaves as a bidentate ligand and coordinates to the metal ions via the nitrogen and oxygen. The obtained data revealed that the Cu(II) center in the complex (1) is coordinated by oxygens and nitrogens of two ligands in a regular square-planar fashion. The electrochemical behavior of the complexes was studied using cyclic voltammetry. The inhibitory activity of ligand and all the obtained complexes were tested in vitro against MKN-45 cancer cell line. It was found that among synthesized complexes, Ni(II) Schiff base complex namely (2), showed strong inhibitory activity against cancer cells, with IC50 = 6.854 ± 0.445 μg/mL.

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1. Introduction

Medicinal chemistry against disease was based on natural products and organic compounds, but nowadays, a developing interest in the synthesis of metal complexes as anticancer drugs have been uncovered to design and describe complexes as models for biological systems. Metal ions such as platinum, palladium, vanadium, copper, cobalt and nickel, with important biological activity, have been investigated and regarded as the most promising anticarcinogens [1–7]. Metal Schiff base complexes, which are known as drugs in cancer chemotherapy, could inhibit in vitro tumor cell growth and can affect the function of proteins, target nucleic acids, catalyze the formation of ROSs and are able to bind and cleave DNA which leads to cell cycle arrest and apoptosis [8–13]. Today, usage of metal-based anticancer drugs is one of the advanced and attractive areas of pharmaceutical research and many attempts are being made to replace antitumor drugs with better alternatives and numerous metal complexes have been synthesized and studied for their anticancer activities [13–16]. Schiff bases derived from hydroxy aldehydes, with O and N-donor atoms, can coordinate to central metal ions and form complexes and have a great interest due to their different applications in various areas [9,17–20]. This type of complexes, show strong intercalation with DNA and good biological activity and have received special attention. Several complexes containing N, O-donor Schiff base ligands derived from 2-hydroxy-1-naphthaldehyde, exhibited good selectivity against tumor cells and resulting in proliferation stoppage and apoptosis induction in cancer cells [21–25]. In addition to the effect of ligand, the selection of metal ion is a significant factor in the design of metal based chemotherapeutic agents. We have focused part of our research program on the synthesis and study of N, O-donor Schiff base ligands and coordination complexes with amines containing methoxy group and the effects of their structure on biological activity [26,27]. Based on these earlier findings of copper and nickel complexes, it seemed interesting to investigate the structural role of Schiff base ligands on the antitumor activity of complexes. The newly synthesized compounds were analyzed for their antitumor activity against gastric cancer cell line (MKN-45) by MTT assay. (see Scheme 1)

2. Experimental

2.1. Materials and characterization

All the starting chemicals and solvents used such as 2-hydroxy...