Transition Metal Chemistry (2021) 46:65–71
https://doi.org/10.1007/s11243-020-00422-8

Synthesis, characterization, cytotoxicity, and molecular docking studies of ampyrone-based transition metal complexes

Mohammad Azam[1] · Saikh Mohammad Wabaidur[1,6] · Mahboob Alam[2] · Zahid Khan[3] · Ibrahim O. Alanazi[4] · Saud I. Al-Resayes[1] · Il Soo Moon[5] · Rajendra[6]

Received: 3 June 2020 / Accepted: 20 August 2020 / Published online: 27 September 2020

Abstract

A novel series of mononuclear transition metal complexes, [Cu(L)Cl] **1**, [Zn(L)Cl] **2**, [Pd(L)Cl] **3**, [Cd(L)I] **4**, [Pt(L)Cl] **5**, and [Hg(L)Cl] **6**, was constructed from a pyrazole-derived Schiff ligand, **HL**, and characterized by physicochemical and spectroscopic methods. Fourier-transform infrared (FT-IR) spectral data showed the studied ligand to be tridentate and coordinated to the metal ions via ONO donor atoms, whereas powder X-ray diffraction (PXRD) analysis revealed the crystalline nature of all the complexes. The in vitro cytotoxicity of the studied ligand and its complexes were tested by the 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2*H*-tetrazolium (MTS) assay against the human colorectal cancer cell lines HCT116 and HT29. The results suggested that the HCT116 cell line is highly sensitive to complex **1** with a half-maximal inhibitory concentration (IC_{50}) of 45.6 µM, while both cell lines tolerated complexes **2** and **4** better in comparison with **HL**. In addition, complex **1** with significant anticancer activity was analyzed by molecular docking studies to explore its binding efficacy to the cyclin-dependent kinase 2 active site.

Introduction

Cisplatin, a revolutionary drug in anticancer research, has been successfully applied in the treatment of various tumors, particularly ovarian, testicular, and neck cancers [1–3]. However, the use of cisplatin is limited because of its association with several side effects including nausea, hair loss, kidney toxicity, and nerve damage [4, 5]. These disadvantages linked to the use of cisplatin have motivated researchers to develop potential transition metal-based anticancer drugs with reduced side effects and wide-spectrum action against curable cancers [6–8]. Schiff bases, which are versatile organic blockers, are considered to be the most "privileged ligands" and have been widely used due to their preparative accessibility, structural diversity, and solubility in most common organic solvents [9, 10]. Furthermore, Schiff base ligands coordinate to various metal ions due to their strong chelating properties and stabilize them in various oxidation states [11]. Over the past several years, the coordination chemistry of transition metal Schiff base complexes with heterocyclic compounds containing N, O, and S atoms has attracted extensive research interest because of their various medicinal properties, viz. in diabetes and cancer, as

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s11243-020-00422-8) contains supplementary material, which is available to authorized users.

✉ Mohammad Azam
azam_res@yahoo.com

✉ Mahboob Alam
mahboobchem@gmail.com

✉ Rajendra
krajendra@banasthali.in

[1] Department of Chemistry, College of Science, King Saud University, P. O. Box 2455, Riyadh 11451, Kingdom of Saudi Arabia

[2] Division of Chemistry and Biotechnology, Dongguk University, 123 Dongdae-ro, Gyeongju, Republic of Korea

[3] Genome Research Chair, Department of Biochemistry, College of Science, King Saud University, Riyadh, Kingdom of Saudi Arabia

[4] The National Center of Biotechnology, King Abdulaziz City for Science and Technology, P. O. Box 6086, Riyadh, Kingdom of Saudi Arabia

[5] Department of Anatomy, College of Medicine, Dongguk University, Gyeongju 38066, Republic of Korea

[6] Department of Chemistry, Banasthali Vidyapith, Banasthali, Rajasthan 304022, India