Journal of Molecular Structure 1240 (2021) 130540

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: www.elsevier.com/locate/molstr

Protein binding and cytotoxicity activities of glutamine based metal complexes

Liji John[a], R. Selwin Joseyphus[a,*], Arish Dasan[b], I. Hubert Joe[c], M. Vibin[d]

[a] Department of Chemistry, Mar Ivanios College (Autonomous), (Research Centre: University of Kerala), Nalanchira, Thiruvananthapuram, 695015, Kerala, India
[b] Department of Glass Processing, FunGlass, Alexander Dubček University of Trenčín, Študentská 2, 911 50, Trenčín, Slovakia
[c] Department of Physics, University of Kerala, Karaiavttom, Thiruvananthapuram, 695581, Kerala, India
[d] Department of Biochemistry, St. Albert's College (Autonomous), Ernakulam, 682018, Kerala, India

ARTICLE INFO

Article history:
Received 10 February 2021
Revised 13 April 2021
Accepted 20 April 2021
Available online 4 May 2021

Keywords:
L-glutamine
DFT
EGFR
Antioxidant
Cytotoxicity

ABSTRACT

In the present study, novel metal(II) complexes with an amino acid based bidentate imine ligand (thial-L-gln) derived from thiophene-2-carboxaldehyde (thial) and L-glutamine (L-gln) have been designed theoretically using DFT calculations and successfully synthesized experimentally. Based on the combined (theoretical and experimental) results, tetrahedral/square-planar geometries have been proposed for the complexes. Molecular docking studies indicate greater interactions of [Cu(II)-(thial-L-gln)$_2$] and [Zn(II)-(thial-L-gln)$_2$] with the EGFR evidenced by best binding energy and hydrogen-bonded residues during interactions. The antimicrobial and antioxidant studies revealed that all complexes exhibit significant activities as compared to thial-L-gln. From cell viability assay and morphological studies, it has been confirmed that the [Cu(II)-(thial-L-gln)$_2$] has significant anticancer activity.

1. Introduction

The role of coordination compounds in nature and in biological systems is crucial. Most of the metal ions are essential to maintain human homeostasis and play vital roles in many biological processes by acting as cofactors in the protein's function, thereby stabilizing, regulating, and completing courses of cellular functions [1,2]. Chlorophyll, hemoglobin, and vitamin B12 are some examples of such metal complexes. Inorganic medicinal chemistry appears to be one of the best therapeutic approaches to treat and diagnose diseases [3]. It has been reported that the metal complexes exhibit improved biological properties than free organic compounds due to their varied reactivity pattern, structural diversity, and unique photo and electrochemical properties [4]. Transition metals played a vital role in the development of new metal-based drugs [5]. Therefore, it is crucial to select useful performing chelators with coordinating properties suitable for the proper stabilization of given metalcore. L-Glutamine (L-gln) is involved in many metabolic and biochemical processes and supports rapidly proliferating cells, such as enterocytes and lymphocytes, and acts as N_2 and NH^{4+} carriers kidney and liver. Research has focussed L-amino acids [6], whereas L-gln Schiff base complexes are seldom reported. Continuing our work in this field [7], we report here the synthesis and characterization of Co/Ni/Cu/Zn(II) Schiff base complexes derived from the condensation of thiophene-2-carboxaldehyde (thial) with L-glutamine (L-gln) with unique properties from coordination to biocidal and potent antioxidant, cytotoxicity leads to anticancer activities. In addition to this, theoretical calculations using DFT and molecular docking analysis were performed for the above systems.

2. Experimental and methods

2.1. Materials

The chemicals that were used in the present study were analytical grade and used without any further purification. L-gln, thial, Co/Ni/Cu/Zn(II) chloride salts were purchased from Sigma-Aldrich. The L929 Fibroblast and PA-1 cells for cytotoxicity study were procured from National center for Cell Sciences Pune, India. For cytotoxicity analysis experiments, all chemicals and reagents used were purchased from Sigma-Aldrich, USA. The human ovarian cancer cells-PA1 and L929 (fibroblast) cell lines were procured from National center for Cell Sciences, Pune, India.

* Corresponding author.
E-mail address: selwin.joseyphus@mic.ac.in (R.S. Joseyphus).

https://doi.org/10.1016/j.molstruc.2021.130540
0022-2860/