EASTERN UNIVERSITY SRI LANKA (EUSL)
DEPARTMENT OF CHEMISTRY
Chenkalady, Sri Lanka
TEL: +94 652240755, Fax: +94 652240758

17.01.2024

CERTIFICATE

This is to certify that Dr. Nithya Mohan, Assistant Professor, Basic Science and Humanities department, SCMS School of Engineering and Technology is collaborated with the project "Comprehensive EPR investigation of copper(II) chelates based on thiosemicarbazones and salen Schiff bases" by Dr. M Sithambaresan, Professor, Department of Chemistry, Eastern University, Sri Lanka from 01/04/2023.

Dr.M. Sithambaresan
Professor in Chemistry
Department of Chemistry
Eastern University, Sri Lanka

.....

Dr. M. Sithambaresan *B.Sc. Special (Hons) (Jaffna), M.Phill. (Peradeniya), Ph.D (CUSAT, Kerala)*
Professor in Chemistry
Faculty of Science
Eastern University, Sri Lanka
Chenkalady
Sri Lanka
Email: sithambaresanm@esn.ac.lk

Report of the collaborative work with Dr. M Sithambaresan, Professor, Department of Chemistry, Eastern University, Sri Lanka

We have collaborated with Dr. M Sithambaresan, Professor, Department of Chemistry, Eastern University, Sri Lanka for a research work entitled 'Comprehensive EPR investigation of copper(II) chelates based on thiosemicarbazones and Schiff bases' The work mainly focuses on the synthesis, characterization of different novel copper complexes and their application studies. One of the important characterization techniques for the copper complexes are EPR studies and their simulation to get exact structure. The EPR studies and the simulation part were done at Estern University, Sri lanka. The research work has been communicated to Journal of Molecular structure (Elsevier) and the paper is currently under review.

Head of The Department

Dr. Nuja M Unnikrishnan

Journal of Molecular Structure 1319 (2025) 139463

Contents lists available at ScienceDirect

Journal of Molecular Structure

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

Multi-faceted investigation of copper(II) chelates based on ONS donor thiosemicarbazone: Crystal structures, spectral aspects, DNA binding, cytotoxicity and computational studies

Jinsa Mary Jacob [a,b], Nithya Mohan [c,*], Sreejith S . S . [d], M. Sithambaresan [e], E. Manoj [a,*], M.R. Prathapachandra Kurup [a,*]

[a] Department of Applied Chemistry, Cochin University of Science and Technology, Kochi, 682022, India
[b] Department of Chemistry, Bharata Mata College (Autonomous), Thrikkakara, Kerala, 682021, India
[c] Department of Basic Science and Humanities, SCMS School of Engineering & Technology, Karukutty, Kerala, 683576, India
[d] Department of Chemical Oceanography, Cochin University of Science & Technology, Kochi, 682016, India
[e] Department of Chemistry, Faculty of Science, Eastern University, Chenkalady, Sri Lanka

ARTICLE INFO

Keywords:
Thiosemicarbazone
Copper(II) chelate
Single crystal XRD
DNA binding
FMO analysis
Hirshfeld analysis
Molecular docking
Cytotoxicity

ABSTRACT

This investigation unveils the synthesis and characterization of a binuclear copper(II) chelate [(Cubmpt)$_2$] (**1**) and four heteroleptic copper(II) chelates [Cu(bmpt)(hb^1)] (**2**), [Cu(bmpt)(hb^2)] (**3**), [Cu(bmpt)(hb^3)] (**4**) and [Cu(bmpt)(hb^4)] (**5**) based on an ONS donor thiosemicarbazone ligand, 5-bromo-3-methoxysalicylaldehyde-N^4-phenylthiosemicarbazone (H_2bmpt) and the heterocyclic bases 1,10-phenanthroline (hb^1), 2,2′-bipyridine (hb^2), 4,4′-dimethylbipyridine (hb^3), 5,5′-dimethylbipyridine (hb^4) as ancillary ligands. The crystal architectures of chelates **3** and **5** are ascertained using single crystal X-ray diffraction method and it is observed that they occupy triclinic $P\bar{1}$ and monoclinic $P2_1/c$ crystal lattice systems correspondingly. Copper(II) ion exhibits an asymmetric square pyramidal arrangement in both complexes. The DNA binding studies suggest a groove binding mechanism, with complex **4** exhibiting the highest binding value. The experimental findings on DNA binding are strongly validated by complementary *in-silico* investigations employing molecular docking analyses. The FMO analysis of the compounds indicates that the dimeric complex **1** possesses the highest chemical reactivity and polarizability. Hirshfeld surface analysis shed light on noncovalent interactions among complexes (**3a** and **5**) and the results corroborate the crystal structure studies. The *in vitro* cytotoxicity studies involving Dalton Lymphoma Ascites (DLA) cell lines revealed that complex **5** exhibited the highest cytotoxicity.

1. Introduction

The transition metal complexes are playing an increasingly important role as antiproliferative agents [1] due to the toxicity of cisplatin and its derivatives to healthy cells. Also, many cancer types develop resistance to cisplatin after repeated treatment, diminishing its efficacy. This has driven research into alternative metal-based complexes which can overcome these limitations. Thiosemicarbazones being multidentate chelating ligands can effectively attach to a diverse range of transition metals. By modifying the ligand and the donor atoms, the pharmacological characteristics of metal chelates can be finely tuned.

Thiosemicarbazones exhibit versatility as they are synthesized through the condensation reaction involving thiosemicarbazides with aldehydes/ketones in acidic conditions and are capable of displaying a diverse array of biological activities [2–4]. The varied chelating behavior of thiosemicarbazones [5,6], due to potential donor atoms within their structural framework, captivates coordination scientists. Thiosemicarbazones are promising anticancer agents, and their mode of activity is connected to their ability to chelate with metals. Copper is a transition metal that assumes a crucial function in several biological processes because of its capacity to engage in redox reactions. Cu(II) complexes of thiosemicarbazones show improved biological activity in comparison to thiosemicarbazones alone, thus serving as potent cytotoxic agents [7,8] and inhibitors of DNA synthesis [9]. These copper complexes have antitumor activity by effectively inhibiting DNA topoisomerase-II, an enzyme crucial for DNA topology regulation [10].

* Corresponding authors.
E-mail addresses: nithyamohan@scmsgroup.org (N. Mohan), manoje@cusat.ac.in (E. Manoj), mrp@cusat.ac.in (M.R.P. Kurup).

https://doi.org/10.1016/j.molstruc.2024.139463
Received 16 January 2024; Received in revised form 21 July 2024; Accepted 24 July 2024
Available online 25 July 2024