



Faculty of Education
Chemistry Department

**Synthesis and Characterization of New
Solid Complexes of Hydrazone
Derivatives: Nano-particle Studies and
Different Potential Applications**

Thesis Submitted

By

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Synthesis and Characterization of New Solid Complexes of Hydrazone Derivatives: Nano-particle Studies and Different Potential Applications

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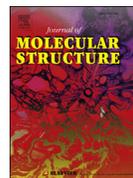
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Synthesis, characterization, and antioxidant/cytotoxic activity of new chromone Schiff base nano-complexes of Zn(II), Cu(II), Ni(II) and Co(II)



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ABSTRACT

A chromone Schiff base complexes of Zn(II) (1), Cu(II) (2), Ni(II) (3) and Co(II) (4) were successfully prepared in nano domain with crystalline or amorphous structures. The spectroscopic data revealed that the Schiff base ligand behaves as a monoanionic tridentate ligand. The metal complexes exhibited octahedral geometry. Transmission electron microscope (TEM) analysis showed that Cu(II) complex have aggregated nanospheres morphology. The obtained nano-complexes were tested as antioxidant and antitumor agents. The H₂L and its Cu(II) complex (2) were found to be more potent antioxidant (IC₅₀(H₂L) = 0.93 μM; IC₅₀(Cu(II) complex) = 1.1 μM than standard ascorbic acid (IC₅₀ = 2.1 μM) as evaluated by DPPH• method. The H₂L and its complexes (1–4) were tested for their *in vitro* cytotoxicity against Ehrlich Ascites Carcinoma cell line (EAC). The Cu(II) nano-complex (2) effectively inhibited EAC growth with IC₅₀ value of 47 μM in comparison with its parent compound and other prepared complexes. The high antioxidant activity and antitumor activity of Cu(II) nano-complex (2) were attributed to their chemical structure, Cu(II) reducing capacity, and nanosize property. The toxicity test on mice showed that Zn(II) (1) and Cu(II) (2) nano-complex have lower toxicity than the standard *cis*-platin.

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1. Introduction

Cancer diseases are the second most frequent cause of death in the world. The discovery of antitumor activity of cisplatin aroused searching for other complexes with high cytotoxic and low toxicity properties against cancer [1]. The activity of transition metals complexes has started the development of metal-based drugs with promising pharmacological application [2].

Schiff bases of 3-formyl chromone and its complexes also have a variety of applications in biological and physiological activities including antimycobacterial, antifungal, anticonvulsant, antimicrobial, antiallergenic, antiviral, antitubulin, antihypertensive, anticancer, and mushroom tyrosinase inhibition activities [3,4].

The practical biomedical applications of the transition metal complexes require preparation of these complexes in nanoscale. Production of transition metal complexes in nano domain creates new materials with unique physical, chemical, and biological

properties. Till now, the majority of reports about the transition metal complexes with chromone-based ligands and their biomedical applications are in bulk scale. The reports about nano-scale transition metal complexes with chromone-based ligands are limited.

Thus, we are concerned, in this paper, with the synthesis and characterizations of new hydrazone ligand (11E)-2-hydroxy-N'-(((4-oxo-4H-chromen-3-yl)methylene)benzohydrazide) and its metal complexes in nano domain for antioxidant and antitumor applications. Also, the toxicity of the high active nano-complexes were included an investigated.

2. Experimental

2.1. Materials

The starting materials used in these studies were analytical grade. They included methyl salicylate (Chemical Laboratory) and hydrazine hydrate (Panreac Quimica). Metal salts, phosphorous oxychloride, o-hydroxyacetophenone, 2,2'-Diphenyl-1-pikrylhydrazyl (DPPH), and ascorbic acid from BDH, Analar, or Merck

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ABSTRACT

New transition and lanthanide metal binary nano-complexes as well as dispersed into silica matrix were prepared in nano domain with crystalline or amorphous structures for biomedical applications. Also, the mixed ligand nano-complexes were prepared by using potassium thiocyanate (KSCN), 8-hydroxyquinoline (8-HOQu), 2,2'-bipyridyl (Bpy) and 1,10-phenanthroline (Phen) as secondary ligands. The antimicrobial and antioxidant activities for H_2L^1 Ligand and its binary nano-complexes were investigated. The H_2L^1 and its nano-complexes (**1-32**) were tested for their *in vitro* cytotoxicity against Ehrlich Ascites Carcinoma cell line (EAC). Sm(III) complex-silica xerogel nanohybrid have highest antitumor activity. The Sm(III) complex drug storage/release process was investigated by absorption spectra. The toxicity test on mice showed that Binary Cu(II), Zn(II) and Sm(III) nano-complexes as well as Sm(III) complex-silica xerogel nanohybrid have lower toxicity than standard *cisplatin*. Therapeutic effect of Sm(III) nano-complex dispersed in silica xerogel on tumor of colon (*in vivo*) was studied as antitumor drug on mice.

Two novel nano-complexes $[(\text{Cu})_2(\text{L}^1)(\text{NO}_3)_2(\text{OH}_2)]$ (uncapped CuH) (**33**) and $[\text{Cu}(\text{HL}^1)(\text{OH}_2)_2(\text{NO}_3)]$ (capped CuCTH) (**34**) were synthesized by new environmentally friendly hydrothermal method at 200°C for 48 hrs in absence and presence of surfactant (CTAB), respectively.) The cytotoxicity of these nano-complexes were tested against Ehrlich Ascites Carcinoma cell line (E.A.C.). Different molar ratio of capped CuCTH (**34**) and Zn(II) (**1**) nano-complexes were tested for their *in vitro* cytotoxicity and *in vivo* toxicity. M^{D} molecular modeling study was performed to gain better insight on the molecular structures of ligand and its nano-complexes.

New Series of metal nano-complexes of Zn(II), Cu(II), Ni(II) and Co(II) with Schiff base ligand H_2L^2 , (E)-2-hydroxy-N'-((thiophen-2-yl)methylene)benzohydrazide were prepared. The antimicrobial activity for complexes was investigated. AT B3LYP/6-311G (d,p) level, Density Functional Theory (DFT) calculations of were carried out to investigate the optimized structure of both, the ligand and complexes. Besides, dipole moment, and structure activity relationship were performed and discussed. DFT calculations confirm the practical antimicrobial results

The Prepared complexes were identified by elemental, thermal, FT-IR, UV-Vis, ¹H-NMR, TEM and XRD analysis, as well as molar conductivity and magnetic moment measurements.