

**Thesis Entitled**

**Ternary Complexes of Some Transition Metals with  
Curcumin and Some Nitrogen Containing Compounds:  
Synthesis, Characterization and Biological Studies**

**Presented**

**By**

**HUDA MAHDI YOUNIS**

**A Thesis Submitted**

To

Faculty of Science

In Partial Fulfillment of the Requirements for

The Degree of Master of Science

(Inorganic Chemistry)

Chemistry Department

Faculty of Science

Ain Shams University

**(2013)**

## APPROVAL SHEET FOR SUBMISSION

### Title of M.Sc. Thesis

**Ternary Complexes of Some Transition Metals with  
Curcumin and Some Nitrogen Containing Compounds:  
Synthesis, Characterization and Biological Studies**

Name of the candidate

**HUDA MAHDI YOUNIS**

The thesis has been approved for submission by the supervisors:

**Prof. Dr. Mostafa M. H. Khalil** .....

Professor of Inorganic Chemistry  
Faculty of Science  
Ain Shams University

**Dr. Eman Hamed Ismaeil** .....

Associate Professor of Inorganic Chemistry  
Faculty of Science  
Ain Shams University

**Dr. Dina Yehya Sabry** .....

Lecturer of Inorganic Chemistry  
Faculty of Science  
Ain Shams University

**Prof. Dr. Hesham A. Madian**

Chairman of Chemistry  
Department  
Faculty of Science  
Ain Shams University

---

## Statement

---

This thesis is submitted in partial fulfillment of the M.Sc Degree, Faculty of Science, Ain Shams University

In addition to the work carried out in this thesis the candidate, **Huda Mahdi Younis**, has attended postgraduate studies in the following topics and passed successfully in the final examination in the academic year 2009-2010:

- 621      Coordination Chemistry
- 622      Radiochemistry and Separation Techniques
- 623      Electrochemistry and Electrochemical Analysis
- 624      Group Theory and Computer Programming
- 625      Spectroscopic Methods for Structural and Analytical Chemistry
- TOEFL

**Prof. Dr. Hesham A. Madian**  
Chairman of Chemistry Department  
Faculty of Science  
Ain Shams University

## ABSTRACT

**Student Name:** Huda Mahdi Younis

**Title of the Thesis:** Ternary Complexes Of Some Transition Metals With Curcumin And Some Nitrogen Containing Compounds: Synthesis, Characterization And Biological Studies

**Degree:** M. Sc. (Inorganic Chemistry)

The present study interested in synthesis and characterization of ternary complexes of some transition metals (Ni(II), Co(II), Cu(II), and Zn(II)) with curcumin in presence of secondary ligand such as 1,10-phenanthroline (phen), 2,2'-bipyridine (bpy) and 8-hydroxyquinoline (HQ).

The new series of mixed-ligand metal complexes of Ni(II), Co(II), Cu(II), and Zn(II) with curcumin using phen, bpy and HQ as secondary ligands were characterized and their structures were confirmed by elemental analysis, molar conductivity, FTIR, Uv-Vis, and  $^1\text{H}$ -NMR spectroscopy and magnetic moments as well as thermal analysis. The resulted ternary complexes were tested for the biological activity against some bacteria and fungi and anti-cancer activity towards the liver line cells.

**Keywords:** curcumin, ternary complexes, 1,10-phenanthroline, 8-hydroxyquinoline, FT-IR and anticancer

## ACKNOWLEDGMENT

*Words are not enough to describe my deep thanks to **Prof. Dr. Mostafa M. H. Khalil**, Professor of inorganic chemistry, Faculty of Science, Ain Shams University, for suggesting the program of this work, his guidance and supervision in the course of the work, and for his stimulating criticisms and help in the preparation of the thesis.*

*I would like to express my deep thanks and gratitude to **Dr. Eman Hamed**, Associate Professor of Inorganic Chemistry, Faculty of Science, Ain Shams University for her invaluable help and support throughout the course of this work.*

*Also, I owe a well-deserved debt of deep gratitude to **Dr. Dina Yehia Sabry**, lecturer of Inorganic Chemistry, Faculty of Science, Ain Shams University for her valuable advice and help throughout the progress of this work.*

*Also, I offer my thanks and appreciations to all of those who supported me in any respect in the Chemistry Department during the completion of this thesis.*

*Last but not Least, my thanks are due to my family, especially my husband, for support and encouragement which gave me the strength to finish this work.*

*Huda Mahdi Younis*

---

---

# CONTENTS

---

---

|                                                     |     |
|-----------------------------------------------------|-----|
| ACKNOWLEDGMENTS                                     | i   |
| ABSTRACT                                            | ii  |
| CONTENTS                                            | iii |
| LIST OF FIGURES                                     | vi  |
| LIST OF TABLES                                      | ix  |
| AIM OF WORK                                         | xi  |
| SUMMARY                                             | 1   |
| CHAPTER 1. INTRODUCTION                             |     |
| 1.1. Introduction                                   | 6   |
| 1.2. Effect of pH                                   | 9   |
| 1.3. Structure of curcumin and mode of coordination | 11  |
| 1.4. Free-radical scavengers                        | 14  |
| 1.5. Binary curcumin complexes                      | 16  |
| 1.6. Mixed ligand complexes                         | 25  |
| 1.6.1. 2,2'-Bipyridine mixed ligand complexes       | 26  |
| 1.6.2. 1,10-phenanthroline mixed ligand complexes   | 29  |
| 1.6.3. Ternary complexes using 8-hydroxyquinoline   | 38  |
| 1.7. Ternary complexes of curcumin                  | 42  |
| CHAPTER 2. MATERIALS AND METHODS                    |     |
| 2.1. Chemicals                                      | 47  |
| 2.2. Analytical instruments                         | 47  |
| 2.2.1. Elemental analysis                           | 47  |
| 2.2.2. FTIR spectra                                 | 48  |
| 2.2.3. Thermogravimetric analysis                   | 34  |
| 2.2.4. Magnetic measurements                        | 49  |
| 2.2.5. UV-Visible spectra                           | 49  |

|                                                                                         |           |
|-----------------------------------------------------------------------------------------|-----------|
| <b>2.2.6. Mass spectra</b>                                                              | <b>49</b> |
| <b>2.2.7. <sup>1</sup>H NMR spectra</b>                                                 | <b>49</b> |
| <b>2.2.8 ESR spectra</b>                                                                | <b>50</b> |
| <b>2.3 Synthesis of the ternary complexes</b>                                           | <b>50</b> |
| <b>2.3.1 Synthesis of the ternary complexes of curcumin with 1,10-phenanthroline</b>    | <b>50</b> |
| <b>2.3.2 Synthesis of the ternary complexes of curcumin with 2,2'-bipyridine</b>        | <b>51</b> |
| <b>2.3.3 Synthesis of the ternary complexes of curcumin with 8-hydroxyquinoline</b>     | <b>51</b> |
| <b>2.4 Antimicrobial studies</b>                                                        | <b>51</b> |
| <b>2.5 In Vitro anticancer screening</b>                                                | <b>52</b> |
| <b>CHAPTER 3. RESULTS AND DISCUSSIONS</b>                                               |           |
| <b>3.1 Introduction</b>                                                                 | <b>53</b> |
| <b>3.1 Metal-curcumin-Phen mixed ligand complexes</b>                                   | <b>55</b> |
| <b>3.1.1 Characterization of the metal-curcumin-Phen mixed ligand complexes</b>         | <b>55</b> |
| <b>3.1.2 <sup>1</sup>H NMR studies</b>                                                  | <b>68</b> |
| <b>3.1.3 Electronic spectra and magnetic moments of ternary M-Cur-Phen complexes</b>    | <b>71</b> |
| <b>3.1.4 Thermal analysis of the [Cu(Cur)(phen)]NO<sub>3</sub> complexes</b>            | <b>74</b> |
| <b>3.1.5 Biological activity</b>                                                        | <b>78</b> |
| <b>3.1.6 Cytotoxicity evaluation of the curcumin-phen mixed complexes</b>               | <b>80</b> |
| <b>3.2 Ternary metal complexes of curcumin with 2,2'-bipyridine as secondary ligand</b> | <b>88</b> |

---

|                                                                                                                                                                |     |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| 3.2.1 Characterization of the ternary complexes<br>M-curcumin-bipyridine                                                                                       | 88  |
| 3.2.2 Electronic spectra and magnetic moments of<br>ternary M-Cur-bpy complexes                                                                                | 98  |
| 3.2.3 Thermal studies of ternary<br>[M(Cur)(bpy) <sub>2</sub> ] <sub>2</sub> NO <sub>3</sub> complexes                                                         | 98  |
| 3.2.4 Biological Studies of [M(Cur)(bpy) <sub>2</sub> ] <sub>2</sub> NO <sub>3</sub><br>ternary complexes and cytotoxicity of<br>curcumin-based Cu(II) complex | 99  |
| 3.3 Ternary metal complexes of curcumin with 8-<br>Hydroxyquinoline as Secondary ligand                                                                        | 102 |
| 3.3.1 FTIR spectra of the ternary complexes of<br>curcumin with 8-Hydroxyquinoline                                                                             | 102 |
| 3.3.2 Mass spectra of the ternary complexes of<br>curcumin with 8-Hydroxyquinoline                                                                             | 103 |
| 3.3.3 Magnetic moments, ESR and electronic<br>spectra                                                                                                          | 104 |
| 3.3.4 Thermal studies of the ternary complexes<br>of curcumin with 8-hydroxyquinoline as<br>secondary ligand                                                   | 116 |
| 3.3.5 Cytotoxicity of [Cu(Cur)(HQ)] complex<br>against hepatocellular carcinoma (HePG2)                                                                        | 117 |
| REFERENCES                                                                                                                                                     | 119 |

## ARABIC SUMMARAY

---



---



---

## List of Figures

---



---

| Figure                                                                                                                                                                                                                                                | Page |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|
| 1.1. Chemical structures of the three major curcumin polyphenols                                                                                                                                                                                      | 8    |
| 1.2. Structure of curcumin at different pH                                                                                                                                                                                                            | 10   |
| 1.3. Two-dimensional chemical structures of syn-diketo curcumin (a), anti-diketo curcumin (b), and enolic curcumin (c).                                                                                                                               | 12   |
| 1.4. Absorption spectra of curcumin with different concentrations of Hg <sup>2+</sup>                                                                                                                                                                 | 13   |
| 1.5. An ORTEP view of [Cu(phen)(L)](ClO <sub>4</sub> ) (1) and [Cu <sub>2</sub> (phen) <sub>3</sub> (L)(O <sub>2</sub> CMe)] (ClO <sub>4</sub> ) <sub>2</sub> (2) showing thermal ellipsoids of 50% probability along with the atom numbering scheme. | 33   |
| 1.6. Schematic drawings of curcumin (Hcur), complexes 1-3 (having curcumin ligand) and 4-6 (having acac ligand).                                                                                                                                      | 43   |
| 1.7. Schematic drawing of the oxovanadium(IV) complexes 1-4 and the ligands used.                                                                                                                                                                     | 46   |
| 3.1. Keto-enol form of curcumin                                                                                                                                                                                                                       | 54   |
| 3.2. FTIR spectrum of curcumin                                                                                                                                                                                                                        | 57   |
| 3.3. FTIR spectrum of 1,10-phenanthroline                                                                                                                                                                                                             | 58   |
| 3.4. Mass spectrum of [Ni(Cur)(phen)]NO <sub>3</sub> complex                                                                                                                                                                                          | 60   |
| 3.5. Mass spectrum of [Co(Cur)(phen)]NO <sub>3</sub> complex                                                                                                                                                                                          | 61   |
| 3.6. Mass spectrum of [Cu(Cur)(phen)]NO <sub>3</sub> complex                                                                                                                                                                                          | 62   |
| 3.7. Mass spectrum of [Zn(Cur)(phen)]NO <sub>3</sub> complex                                                                                                                                                                                          | 63   |

---

|      |                                                                                                                                                                                                                                                                               |    |
|------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|
| 3.8. | FTIR spectra of a) $[\text{Ni}(\text{Cur})(\text{phen})_2]\text{NO}_3$ ; b) $[\text{Co}(\text{Cur})(\text{phen})_2]\text{NO}_3$ ; c) $[\text{Cu}(\text{Cur})(\text{phen})_2]\text{NO}_3$ and d) $[\text{Zn}(\text{Cur})(\text{phen})_2]\text{NO}_3$ .                         | 67 |
| 3.9. | $^1\text{H}$ NMR spectrum of (a) curcumin (Jiang et al 2011) and (b) measured in this work                                                                                                                                                                                    | 70 |
| 3.10 | $^1\text{H}$ NMR spectrum of $[\text{Zn}(\text{Cur})(\text{phen})]\text{NO}_3$ complex                                                                                                                                                                                        | 70 |
| 3.11 | Absorption spectra of curcumin and its ternary complexes                                                                                                                                                                                                                      | 72 |
| 3.12 | ESR spectrum of $[\text{Cu}(\text{Cur})(\text{phen})_2]\text{NO}_3$                                                                                                                                                                                                           | 74 |
| 3.13 | TGA curve for decomposition of curcumin                                                                                                                                                                                                                                       | 76 |
| 3.14 | TGA curves of the mixed ligand complexes: a) $[\text{Ni}(\text{Cur})(\text{phen})_2]\text{NO}_3$ ; (b) $[\text{Co}(\text{Cur})(\text{phen})_2]\text{NO}_3$ ; $[\text{Cu}(\text{Cur})(\text{phen})_2]\text{NO}_3$ and d) $[\text{Zn}(\text{Cur})(\text{phen})_2]\text{NO}_3$ . | 77 |
| 3.15 | Cell viability at different curcumin concentrations                                                                                                                                                                                                                           | 82 |
| 3.16 | Cell viability at different $[\text{Ni}(\text{Cur})(\text{phen})]\text{NO}_3$ concentrations                                                                                                                                                                                  | 83 |
| 3.17 | Cell viability at different $[\text{Co}(\text{Cur})(\text{phen})]\text{NO}_3$ concentrations                                                                                                                                                                                  | 84 |
| 3.18 | Cell viability at different $[\text{Cu}(\text{Cur})(\text{phen})]\text{NO}_3$ concentrations                                                                                                                                                                                  | 85 |
| 3.19 | Cell viability at different $[\text{Zn}(\text{Cur})(\text{phen})]\text{NO}_3$ concentrations                                                                                                                                                                                  | 86 |
| 3.20 | Mass spectrum of $[\text{Ni}(\text{Cur})(\text{bpy})_2]\text{NO}_3$ complex                                                                                                                                                                                                   | 91 |

|      |                                                                      |     |
|------|----------------------------------------------------------------------|-----|
| 3.21 | Mass spectrum of [Co(Cur)(bpy) <sub>2</sub> ]NO <sub>3</sub> complex | 92  |
| 3.22 | Mass spectrum of [Cu(Cur)(bpy) <sub>2</sub> ]NO <sub>3</sub> complex | 93  |
| 3.23 | Mass spectrum of [Zn(Cur)(bpy) <sub>2</sub> ]NO <sub>3</sub> complex | 94  |
| 3.24 | FTIR spectra of [M(Cur)(bpy) <sub>2</sub> ]NO <sub>3</sub>           | 95  |
| 3.25 | TGA of [M(Cur)(bpy) <sub>2</sub> ]NO <sub>3</sub> complexes          | 100 |
| 3.26 | FTIR spectrum of [Ni(Cur)(HQ)]NO <sub>3</sub> complex                | 108 |
| 3.27 | FTIR spectrum of [Co(Cur)(HQ)]NO <sub>3</sub> complex                | 109 |
| 3.28 | FTIR spectrum of [Cu(Cur)(HQ)]NO <sub>3</sub> complex                | 110 |
| 3.29 | FTIR spectrum of [Zn(Cur)(HQ)]NO <sub>3</sub> complex                | 111 |
| 3.30 | Mass spectrum of [Ni(Cur)(HQ)] complex                               | 112 |
| 3.31 | Mass spectrum of [Co(Cur)(HQ)] complex                               | 112 |
| 3.32 | Mass spectrum of [Cu(Cur)(HQ)] complex                               | 113 |
| 3.33 | Mass spectrum of [Zn(Cur)(HQ)] complex                               | 113 |
| 3.34 | Uv-Vis spectra of the [M(Cur)(HQ)] complexes in DMF                  | 114 |
| 3.35 | ESR spectrum of the [Cu(Cur)(HQ)] complex                            | 114 |
| 3.36 | <sup>1</sup> H NMR spectrum of [Zn(Cur)(HQ)] complex                 | 115 |
| 3.37 | TGA of [M(cur)(HQ)] complexes                                        | 116 |
| 3.38 | Cell viability percentage at different [Zn(Cur)(HQ)] concentrations  | 118 |

---



---

## List of Tables

---



---

| <b>Table</b>                                                                                                                   | <b>Page</b> |
|--------------------------------------------------------------------------------------------------------------------------------|-------------|
| 3.1. Elemental analysis and mass spectrometry of the M-curcumin-phen complexes                                                 | 59          |
| 3.2. Assignments of the important infrared spectral bands ( $\text{cm}^{-1}$ ) for curcumin and their metal complexes          | 66          |
| 3.3. Biological activity of curcumin-phen ternary complexes                                                                    | 79          |
| 3.4. Viability at different curcumin concentrations                                                                            | 82          |
| 3.5 Viability percentage at different <b>[Ni(Cur)(phen)]NO<sub>3</sub></b> concentrations                                      | 83          |
| 3.6 Cell viability percentage at different <b>[Co(Cur)(phen)]NO<sub>3</sub></b> concentrations                                 | 84          |
| 3.7 Cell viability percentage at different <b>[Cu(Cur)(phen)]NO<sub>3</sub></b> concentrations                                 | 85          |
| 3.8 Cell viability percentage at different <b>[Zn(Cur)(phen)]NO<sub>3</sub></b> concentrations                                 | 86          |
| 3.9 Cytotoxicity evaluation of the curcumin-phen mixed ligand complexes                                                        | 87          |
| 3.10 Elemental analysis and mass spectrometry of the M-curcumin-bpy complexes                                                  | 96          |
| 3.11 Assignments of the important infrared spectral bands ( $\text{cm}^{-1}$ ) for curcumin and its ternary complexes with bpy | 97          |
| 3.12 Biological activity of curcumin-bpy ternary complexes                                                                     | 101         |
| 3.13 Elemental analysis and mass spectrometry of the M-curcumin-HQ complexes                                                   | 106         |

3.14 Assignments of the important infrared spectral bands ( $\text{cm}^{-1}$ ) for curcumin and its ternary complexes with 8-hydroxyquinoline 107

---

-

## **AIM OF THE STUDY**

The present work aimed to fulfill the following objectives:

1. Synthesis of ternary complexes of some transition metals with curcumin as primary ligand and some nitrogen containing compounds as secondary ligands.
2. Characterization of the newly synthesized complexes using elemental analysis, FT-IR, mass spectroscopy, Uv-Visible spectra, magnetic susceptibility, thermal analysis.
3. Study of the biological activity of the resulting complexes as antimicrobial and anticancer agent.

## Summary

Curcumin, an extract of turmeric, *Curcuma longa* L., has been used for centuries in a variety of pharmaceutical applications, including as a treatment for arthritis, as an anti-inflammatory agent and as an orally available treatment for diabetes. Curcumin is well absorbed, both in vitro and in vivo, and has an exceedingly low toxicity index. This study interested in synthesis and characterization of ternary complexes of some transition metals (Ni(II), Co(II), Cu(II), and Zn(II)) with curcumin in presence of secondary ligand such as 1,10-phenanthroline (phen), 2,2'-bipyridine (bpy) and 8-hydroxyquinoline (HQ) and study the biological activity and anti-cancer activity towards the liver line cells.

This thesis is divided into three chapters as following:

**Chapter One:** gives a general introduction and literature survey about curcumin and its binary complexes with some transition elements and lanthanides. Ternary complexes using secondary ligands used in the study and ternary complexes of curcumin also surveyed.

**Chapter Two:** deals with the practical methods the ternary complexes and description of the different physicochemical methods of analysis and characterization such as elemental analysis, molar