UNIVERSITI TEKNOLOGI MARA

HYDROXAMIC ACID SERIES AND THEIR METAL COMPLEXES: SYNTHESIS, CHARACTERIZATION, CYTOTOXICITY AND NEUROTOXICITY STUDY

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AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work, unless otherwise indicated or acknowledged as referenced work. This topic has not been submitted to any other academic institution or non-academic institution for any other degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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ABSTRACT

The synthesis and characterization of a series of hydroxamic acid namely benzohydroxamic acid (BHA), salicylhydroxamic acid (SHA) and their complexes with Cu(II), Co(II), V(IV), Zn(II), Fe(II), Ni(II) and Cr(III) are described herein. The characterization of the synthesized ligands and complexes were carried out by means of elemental analysis (C,H,N), ^{1}H and ^{13}C NMR and IR spectroscopy, conductivity, magnetic susceptibility and melting point. Through IR and NMR studies, the synthesized ligands were shown to possess the carbonyl (CO) and hydroxylamine (NH_2-OH) groups, characteristics of hydroxamic acid. It was found that the dominant coordination mode in metal-hydroxamic acid complexes was the *O,O'*-bidentate chelates in which the ligands were singly deprotonated (hydroxamato). The coordination through the carbonyl oxygen atom and the deprotonated hydroxy group showed a very stable five-membered chelate was formed. Moreover, depending on pH, two *(O,O)* bonding modes of the ligands are accessible to a series of metal ions like Cu(II), Cr(III), Zn(II), Fe(II) and VO(IV) where in this case, the synthesis took place in acidic environment which making the *O,O*-bonding modes were more favorable. The non-conductivity of the complexes as DMSO solutions indicated the absence of counter ions. The diamagnetic nature of the Ni(II) complex indicated that it has a square planar geometry whereas the paramagnetic Co(II) complex with magnetic moment of 4.04 B.M. indicated either high spin octahedral or tetrahedral geometry. Results of magnetic susceptibility studies of other complexes were also discussed herein in relation to their possible geometries. Cytotoxicity assay with fetal liver cells (WRL68) revealed the toxicity of the ligand 2,6-pyha with IC_{50} at 23 μM. Other ligands were founds to be non-toxic. Ni(II), Zn(II) and Cr(III) complexes of SHA were found to be non-toxic to the cells whereas V(IV), Cu(II) and Co(II) complexes revealed IC_{50} values at 25 μM, 15 μM and 60 μM, respectively. Complex $VO(BHA)_2$ was found to be toxic to cells with IC_{50} value 10 μM. Neurotoxicity testing on treated SHSY-5Y neuroblastoma cells showed that all ligands were found to be non-toxic to neuron cells at the concentration range of 1 nM to 1 mM. The complexes generally showed slightly increased neurotoxicity especially at higher concentration.

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CHAPTER THREE: METHODOLOGY