SYNTHESIS, CHARACTERIZATIONS AND BIOLOGICAL PROPERTIES OF SOME HYDRAZONES AND THEIR METAL COMPLEXES

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ABSTRACT

The aim of the project as presented in this thesis concerns on the preparation, characterization and biological evaluation of Schiff bases derived from 3, 5-dihyroxybenzohydrazide and their Cu(II) and Zn(II) complexes. The Schiff bases were synthesized by the condensation of 3, 5-dihyroxybenzohydrazide and hydroxyacetophenone (BzyHAP-H), 5-bromo hydroxyacetophenone (BzyHAP-Br), 5-chloro hydroxyacetophenone (BzyHAP-Cl), salicylaldehyde (BzySAL-H), 5-bromo salicylaldehyde (BzySAL-Br), and 5-chloro salicylaldehyde (BzySAL-Cl). The BzyHAP series ligands were subsequently reacted with the acetate of Zn(II) whereas the BzySAL series ligands were reacted with Cu(II) and Zn(II) acetate in a 1:2 metal to ligand ratio. The chemical structures of the compounds were characterized by means of elemental analyses, , and spectroscopy methods including IR, ^{1}H NMR, ^{13}C NMR, and UV-Vis.The determination of metal content was carried out using atomic absorption spectroscopy. Single X-ray diffraction data collection is carried out for ligand BzySAL-Br. From the structural analysis, the ligand is found to be planar with an r.m.s. deviation for the non-H atoms of 0.16Å. In the crystal structure, the Schiff base molecules and the water molecules are linked together by intermolecular N-H--O and O-H--O hydrogen bonds, leading to layers parallel to the *bc* plane. An intramolecular O-H--N hydrogen bond involving the imine N atom and a hydroxyl substituent is also observed. The synthesized Schiff base and their metal complexes are screened for the *in vitro* cytotoxicity towards prostate cancer cell line (PC-3), colon cancer cell line (HT-29) lung cancer cell line (A549), and normal cell line (WRL-68). All Zn (II) complex Schiff bases show relatively low cytotoxicity against all tested cell line. Complexes labeled as CuBzySAL-H, CuBzySAL-Br, and CuBzySAL-Cl show encouraging value of EC_{50} against colon cancer cell line (HT-29), lung cancer cell line (A549), and normal cell line (WRL-68). On contrary, the cytotoxicity against prostate

cancer cell line (PC-3) is recorded negative. The evaluation of antioxidant reveals that all compounds are moderate DPPH inhibitor compared to the standard vitamin C.

ABSTRAK

Seperti yang dibentangkan di dalam tesis ini, projek yang dijalankan adalah berkenaan penyediaan, pencirian dan penilaian aktiviti biologi bagi bes Schiff yang diterbitkan daripada 3,5-dihidroksibenzohidrazida dan kompleks Cu(II) dan Zn(II)nya. Bes Schiff berkenaan telah disintesis melalui proses kondensasi sebatian 3,5-dihidroksibenzohidrazida dengan hidroksiasetofenon, 5-bromohidroksiasetofenon, 5-klorohidroksiasetofenon, salisilaldehid, 5-bromosalisilaldehid, dan 5-klorosalisilaldehid. Ligan-ligan ini kemudiannya ditindakbalaskan dengan asetat bagi logam Cu(II) dan Zn(II) dalam nisbah 1:2 metal kepada ligan. Struktur kimia sebatian ini kemudiannya dicirikan dengan analisis unsur dan kaedah spektroskopi termasuklah IR, ^{1}H NMR, ^{13}C NMR, and UV-Vis. Penentuan kandungan logam ditentukan dengan kaedah spektroskopi penyerapan atom. Analisis kristalografi dijalankan bagi ligan BzySAL-Br.

Analisis struktural, mendapati bahawa ligan adalah planar dengan nilai sisihan r.m.s. bagi atom bukan hidrogen adalah 0.16Å. Dalam struktur ligan berkenaan, didapati bahawa ianya terhubung dengan molekul air melalui ikatan hidrogen N-H--O dan O-H--O menghasilkan lapisan yang selari dengan satah *bc*. Turut terlibat ialah ikatan hidrogen intramolekul antara atom nitrogen kumpulan imina dan kumpulan penukarganti hidroksi. Kemudiannya, bes Schiff dan kompleks logamnya disaring untuk sitotoksisiti secara *in vitro* terhadap sel kanser prostat (PC-3), sel kanser kolon (HT-29), sel kanser paru-paru (A549), dan sel normal (WRL-68). Kesemua kompleks Zn(II) menunjukkan keisotoksian yang rendah secara relatif terhadap semua sel yang diuji. Kompleks Cu(II) berlabel CuBzySAL-H, CuBzySAL-Br, and CuBzySAL-Cl pula menunjukkan nilai EC_{50} yang menggalakkan terhadap sel kanser kolon (HT-29), sel kanser paru-paru (A549), dan sel normal (WRL-68). Sebaliknya, sitotoksisiti terhadap sel kanser prostat (PC-3) adalah

negatif. Penyaringan terhadap sifat antioksida menunjukkan semua sebatian merupakan perencat DPPH yang sederhana berbanding vitamin C sebagai standard.

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ABBREVIATIONS

%	Percent
π	Pi
λ	Wavelength
δ	Chemical shift
υ	Stretching vibration
Å	Angstrom
^{13}C NMR	Carbon nuclear magnetic resonance
^{1}H NMR	Proton nuclear magnetic resonance
AAS	Atomic absorption spectroscopy
Abs	Absorbance
BHT	Butylated hydroxytoluene
Cu	Copper
DMSO	Dimethyl sulphoxide
DPPH	2,2-diphenyl-1-picrylhydrazyl
EC_{50}	Half maximal effective concentration
EtOH	Ethanol
FRAP	Ferric reducing ability of plasma
IR	Infra-red
M	Mole per litre
m	Multiplet
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
s	singlet
U_{eq}	Equivalent isotropic displacement parameter
UV-Vis	Ultraviolet-visible
Zn	Zinc