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**PROJECT ACHIEVEMENT (Prestasi Projek)**

ACHIEVEMENT PERCENTAGE			
Project progress according to milestones achieved up to this period	0 - 50%	51 - 75%	76 - 100%
Percentage (please state #%)			√
RESEARCH OUTPUT			
Number of articles/ manuscripts/ books (Please attach the First Page of Publication)	Indexed Journal	Non-Indexed Journal	
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Conference Proceeding (Please attach the First Page of Publication)	International	National	
Intellectual Property (Please specify)			

**E PROBLEMS / CONSTRAINTS IF ANY (Masalah/ Kekangan sekiranya ada)**

NIL

**F RECOMMENDATION (Cadangan Penambahbaikan)**

NIL

**G RESEARCH ABSTRACT – Not More Than 200 Words (Abstrak Penyelidikan – Tidak Melebihi 200 patah perkataan)**

Six ternary copper(II) complexes of amino acids and polypyridyl ligands, Cu-Thr-Byp, Cu-Phe-dmByp, Cu-Val-Byp, Cu-Thr-Phen, Cu-Phe-Phen and Cu-Val-Phen, have been synthesized and characterized by CHN elemental analysis, AAS, FT-IR and UV-Vis spectroscopic. The preparation of the complexes is easy and the complexes are stable at room temperature. All the complexes are structurally characterized by X-ray crystallography. Each complex shows coordination geometry of square-pyramidal (4+1) with slight distortion. The copper(II) ion is five-coordinated by N and O atoms from the amino acids and two N atoms of polypyridyl ligands occupied the four corners of the basal plane while the apical position is occupied by a water molecule or Cl atom.

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## Zn(II)ferrocenylthiosemicarbazones: DNA Binding and Nuclease Activity

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A series of Zn(II) ferrocenylthiosemicarbazones complexes derived from thiosemicarbazide and 4-methyl-, 4-ethyl-, and 4-phenyl-5-thiosemicarbazide were evaluated for their DNA binding propensity and chemical nuclease activity. The equilibrium binding constants,  $K_b$ , of the complexes for binding with calf thymus DNA (CT DNA) were in the range of  $0.68 \times 10^3$  to  $2.8 \times 10^4 \text{ M}^{-1}$ . The complexes do not intercalate into the nucleobases of CT DNA, as evident from viscosity measurements. They exhibit efficient nuclease activity in the absence of an activating agent and cleave supercoiled DNA into nicked and linear circular forms of DNA at very low concentrations.

**Keywords** crystal structure, DNA binding, ferrocene, nuclease activity, Zn(II) complex

### INTRODUCTION

An important criteria for the development of metallodrugs as chemotherapeutic agents are the ability of the metallodrug to bring about DNA cleavage.<sup>[1]</sup> In general, anticancer agents that are approved for clinical use are molecules which damage DNA, block DNA synthesis indirectly through the inhibition of nucleic acid precursor biosynthesis, or disrupt the hormonal stimulation of cell growth.<sup>[2]</sup> The cleavage of DNA can be achieved by targeting its basic constituents such as base and/or sugar by an oxidative pathway or by the hydrolysis of phosphoester linkages.<sup>[3]</sup> Transition-metal complexes, which are characterized by high stability, structural versatility, and unique spectroscopic and redox properties, are exploited in many of these efforts.

They are capable of binding to DNA by a multitude of interactions and cleaving DNA by virtue of their intrinsic chemical, electrochemical, and photochemical reactivities.<sup>[4–7]</sup> Redox active complexes are known to be useful for the oxidative cleavage of DNA involving nucleobase oxidation and/or the degradation of sugar by the abstraction of deoxyribose hydrogen atom(s) while complexes containing strong Lewis acids are suitable for the hydrolytic cleavage of DNA.<sup>[8]</sup> The oxidative method of cleaving DNA has the disadvantage of affecting biomolecules indiscriminately,<sup>[9]</sup> which is undesirable in treating diseases and studying the interactions of DNA with other molecules. For example, both carbon-centered and hydroxyl radicals are known to modify histone proteins, causing either protein-DNA crosslinking<sup>[10–12]</sup> or the dissociation of protein-DNA assemblies<sup>[13]</sup> in addition to cleaving DNA. Furthermore, oxidative damage results in DNA strand termini which prevent subsequent enzymatic manipulation.<sup>[14]</sup> The hydrolytic cleavage of DNA in particular is challenging because the phosphoester linkages have remarkable stabilities and are extraordinarily resistant to hydrolysis under uncatalyzed physiological conditions.<sup>[15]</sup> Among the various metal ions that have been studied and are undergoing studies with nucleic acids and nucleobases, Zn(II) is regarded as one of the best suited metal ion for the development of artificial metallonucleases. This is because Zn(II) is a strong Lewis acid and exchange ligands very rapidly, it is of low toxicity and it is not redox active, catalyzing only the hydrolytic cleavage of DNA.<sup>[16,17]</sup> The selection of ligands in preparing Zn(II) complex is very important as it should favor metal center-DNA interaction while maintaining the stability of the complex. Ferrocene is suitable to be coupled with Zn(II) because it has excellent stability in biological media and is composed of Fe(II), the only redox active metal ion found in hydrolytic enzymes.<sup>[16]</sup> Recent studies show that ferrocene moiety plays a significant role in the nuclease activity of Cu(II) complexes.<sup>[18–20]</sup> Here in this study, we investigate the DNA binding and nuclease activity of zinc complexes made with ferrocenylthiosemicarbazone ligands (Scheme 1).

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