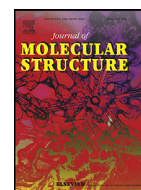




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Enhancement of biological activities of copper(II) complexes containing guanidine derivatives by enrofloxacin



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ABSTRACT

Two new copper(II) chloride complexes from guanidine derivatives containing a deprotonated enrofloxacin (erx^-) as the second ligand, $[\text{CuL}^1(\text{erx})]\text{Cl}$ (**1**) and $[\text{CuL}^2(\text{erx})]\text{Cl}$ (**2**), were synthesized and characterized by elemental analysis and several spectroscopic methods. Crystallographic data of the single crystal of **1** gave a monoclinic with $P2_1/n$ space group of $[\text{Cu}(\text{L}^1-\text{H}^+)(\text{erx})]\cdot 2\text{MeOH}$ with a slightly distorted square-planar CuN_2O_2 geometry. The DNA binding studies of **1** and **2** toward calf thymus (CT) DNA by absorption titration, fluorescence, viscosity measurements and circular dichroism spectroscopy showed non-intercalative binding mode with the K_b values of **1** > **2**. Their cleaving ability toward plasmid pBR322 DNA was investigated by gel electrophoresis and atomic force microscopy (AFM). From these results, an oxidative mechanism is possible to be the main cleaving pathway of **1** and **2**. The antibacterial activity of **1** and **2** was then tested against three human-food poisoning bacteria (*E. coli*, *Salmonella* and *Campylobacter*) by disc diffusion method. Both complexes exhibit inhibitory activity against *E. coli* and *Salmonella* greater than their corresponding starting complexes, $[\text{CuL}^1\text{Cl}_2]_2$ (for **1**) and $[\text{CuL}^2\text{Cl}_2]_2$ (for **2**). Study on the cytotoxicity of **1** and **2** against three human cancer cell lines including oral cavity (KB), breast (MCF-7) and small cell lung (NCI-H187) cell lines was determined using Resazurin Microplate assay (REMA). Results have shown that both complexes display much higher cytotoxicity against MCF-7 than their corresponding starting complexes. The better biological activities of the complexes in this system can be probably ascribed to the presence of erx^- .

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1. Introduction

Since the anticancer drug cisplatin, $[\text{Pt}(\text{NH}_3)_2\text{Cl}_2]$, was discovered in 1969 [1] several transition metal complexes have been extensively prepared to study their cytotoxic activity [2–4]. Researches in this area have shown a great impact on medicine, especially chemotherapy. To increase the biological activity and reduce the side effects, we have previously synthesized metal-based compounds that showed not only anticancer, but also antibacterial activity. In this earlier study, the copper(II) complexes of amidino-O-methylurea and its derivative (Fig. 1.) are reported [5].

Copper is an interesting element and appears as metal center in several complexes. Many copper(II) complexes have been reported to exhibit DNA-binding abilities [6–8]. Basically, the DNA interactions depend on both the types of transition metals and the nature of organic ligands. Hence, copper complexes with the selected organic ligands aiming to improve the biological activity respect to cisplatin have been carefully designed by our groups. Our previously reported copper(II) chloride complex of amidino-O-methylurea and its derivative have shown three interesting biological properties: (i) DNA-binding and cleaving capability, (ii) anticancer activity toward three human cancer cell lines including oral cavity (KB), breast (MCF-7) and small cell lung (NCI-H187) cell lines, as well as (iii) antibacterial activity against three human-food poisoning bacteria (*E. coli*, *Salmonella* and *Campylobacter*) [8,9]. In

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