Journal of Molecular Structure 1241 (2021) 130645

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: www.elsevier.com/locate/molstr

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

Atittaya Meenongwa[a,b], Rosa F. Brissos[c,d], Chaiyaporn Soikum[e], Prapansak Chaveerach[e], Yanee Trongpanich[f], Unchulee Chaveerach[b,*]

[a] Health Science and Aesthetic Program, Department of Science, Faculty of Science and Technology, Rajamangala University of Technology Krungthep, Bangkok 10120, Thailand
[b] Materials Chemistry Research Center, Department of Chemistry and Center of Excellence for Innovation in Chemistry, Faculty of Science, Khon Kaen University, Khon Kaen 40002, Thailand
[c] Departament de Química Inorgánica, Universitat de Barcelona, Martí I Franqués 1-11, 08028 Barcelona, Spain
[d] Department of Immunology, Weizmann Institute of Science, Rehovot 7610001, Israel
[e] Department of Veterinary Public Health, Faculty of Veterinary Medicine, Khon Kaen University, Khon Kaen 40002, Thailand
[f] Department of Biochemistry, Faculty of Science, Khon Kaen University, Khon Kaen 40002, Thailand

ARTICLE INFO

Article history:
Received 26 January 2021
Revised 2 May 2021
Accepted 4 May 2021
Available online 13 May 2021

Keywords:
Copper(II)
Amidino−*O*−methylurea
Enrofloxacin
DNA interactions
Antibacterial
Anticancer

ABSTRACT

Two new copper(II) chloride complexes from guanidine derivatives containing a deprotonated enrofloxacin (erx^-) as the second ligand, $[CuL^1(erx)]Cl$ (**1**) and $[CuL^2(erx)]Cl$ (**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 $[Cu(L^1-H^+)(erx)]\cdot 2MeOH$ 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, $[CuL^1Cl_2]_2$ (for **1**) and $[CuL^2Cl_2]_2$ (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^-.

1. Introduction

Since the anticancer drug cisplatin, $[Pt(NH_3)_2Cl_2]$, 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

* Corresponding author.
E-mail address: sunchul@kku.ac.th (U. Chaveerach).

https://doi.org/10.1016/j.molstruc.2021.130645
0022-2860/