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FULL PAPER

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Novel heteronuclear Pt (II)-L-Zn (II) complexes: synthesis, interactions with biomolecules, cytotoxic properties. Two metals give promising antitumor activity?

Tanja V. Soldatović[1] | **Enisa Selimović**[1] | **Nevena Milivojević**[2,3] | **Milena Jovanović**[3] | **Biljana Šmit**[2]

[1]State University of Novi Pazar, Department of Chemical-Technological Sciences, Vuka Karadžića bb, Novi Pazar, 36300, Serbia

[2]University of Kragujevac, Institute of Information Technologies, Department of Science, Jovana Cvijića bb, Kragujevac, 34000, Serbia

[3]University of Kragujevac, Faculty of Science, Department for Biology and Ecology, Radoja Domanovića 12, Kragujevac, 34000, Serbia

Correspondence
Tanja V. Soldatović, Department of Chemical-Technological Sciences, State University of Novi Pazar, Vuka Karadžića bb, 36300. Novi Pazar, Serbia.
Email: tsoldatovic@np.ac.rs

The novel heteronuclear complexes [{*cis*-PtCl (NH_3)(μ-pyrazine)ZnCl (terpy)}](ClO_4)$_2$ (Pt-L1-Zn) and [{*cis*-PtCl (NH_3)(μ-4,4′-bipyridyl)ZnCl (terpy)}](ClO_4)$_2$ (Pt-L2-Zn) (where terpy = 2,2′:6′,2″-terpyridine, L1 = pyrazine, L2 = 4,4′-bipyridyl) were synthesized and characterized. The pK_a values were determined, and based on them it was established that the π-acceptor ability of the pyrazine bridging ligand is more affective on lower pK_a values. The kinetic measurements of the substitution reactions with biologically relevant ligands, such as guanosine-5′-monophosphate (5′-GMP), inosine-5′-monophosphate (5′-IMP) and glutathione (GSH), were studied at pH 7.4. The reactions were followed under *pseudo*-first-order conditions by UV–Vis spectrophotometry. The order of reactivity of the investigated biomolecules for the first reaction is 5′-GMP > 5′-IMP > GSH, while for the second is 5′-IMP > GSH. Pt-L1-Zn complex is more reactive than Pt-L2-Zn. The cytotoxic activity of heteronuclear Pt-L1-Zn and Pt-L2-Zn complexes was determined on human colorectal cancer cell line (HCT-116) and human breast cancer cell line (MDA-MB-231). Both complexes significantly reduced cell viability on tested cell lines and exerted significant cytotoxic effects, with better effect on HCT-116 cells than cisplatin, especially after 72 hr (IC_{50} < 0.52 μM). The Pt-L2-Zn complex showed higher activity against human breast cancer cells (MDA-MB-231) than cisplatin after 72 hr. The higher reactivity toward DNA constituent and significant cytotoxic activity may be attributed to the different geometry, Lewis acidity of different metal centers, as well as, to choice of bridging ligands.

KEYWORDS

biomolecules, cytotoxic activity, heteronuclear complexes, structure-reactivity correlation, zinc (II) and platinum (II)

1 | INTRODUCTION

The first metal-based antitumor drug cisplatin or *cis*-diamminedichloridoplatinum (II), *cis*-[$PtCl_2(NH_3)_2$], is widely used for treatment of different type of cancers. The effectiveness is limited by toxicity during treatment. Resistance, nephrotoxicity, ototoxicity, neurotoxicity, cardiotoxicity, vomiting are just one part of negative side effects.[1] The mechanism of antitumor action of cisplatin is extensively investigated, and it is generally accepted that the antitumor activity depends on interactions between the metal complex and DNA, mostly N7 atoms

