



## Novel heterometallic Zn(II)-L-Cu(II) complexes: studies of the nucleophilic substitution reactions, antimicrobial, redox and cytotoxic activity

Asija Halilagić<sup>a,b</sup>, Enisa Selimović<sup>a</sup>, Jelena S. Katanić Stanković<sup>c</sup>, Nikola Srećković<sup>b</sup>, Katarina Virijević<sup>c</sup>, Marko N. Živanović<sup>c</sup>, Biljana Šmit<sup>c</sup> and Tanja V. Soldatović<sup>a</sup>

<sup>a</sup>Department of Natural-Mathematical Sciences, State University of Novi Pazar, Novi Pazar, Serbia;

<sup>b</sup>Faculty of Science, Department of Chemistry, University of Kragujevac, Kragujevac, Serbia; <sup>c</sup>Institute for Information Technologies Kragujevac, Department of Science, University of Kragujevac, Kragujevac, Serbia

### ABSTRACT

**New** heterometallic complexes [ $\{\text{ZnCl}(\text{terpy})(\mu\text{-pyrazine})\text{CuCl}(\text{terpy})\}$ ] ( $\text{ClO}_4$ )<sub>2</sub> (**Zn-L1-Cu**) and [ $\{\text{ZnCl}(\text{terpy})(\mu\text{-4,4'}$ -bipyridyl) $\text{CuCl}(\text{terpy})\}$ ] ( $\text{ClO}_4$ )<sub>2</sub> (**Zn-L2-Cu**) (where terpy = 2,2':6',2''-terpyridine, L1 = pyrazine, L2 = 4,4'-bipyridyl) were synthesized. The substitution reactions with biologically important nucleophiles were investigated at pH 7.4 by UV-Vis spectrophotometric method. The obtained results have shown different orders of reactivity of guanosine-5'-monophosphate (5'-GMP), inosine-5'-monophosphate (5'-IMP) and glutathione (GSH) toward heterometallic **Zn(II)-L-Cu(II)** complexes. Spectrophotometric titration of diaqua **Zn-L-Cu** complexes has shown that aqua ligands coordinated to both metal centers can exhibit different  $\text{pK}_a$  values depending on the distance between them. Both synthesized complexes showed moderate antimicrobial activity against most of the tested bacterial and fungal strains. The cytotoxic activity of heteronuclear **Zn-L1-Cu** and **Zn-L2-Cu** complexes was determined on human colorectal cancer (HCT-116) and human healthy lung pleura (MRC-5) cell lines. Both complexes exerted significant cytotoxic effects, especially after 72 h ( $\text{IC}_{50} < 0.01 \mu\text{M}$ ) and significantly reduced cell viability. Complexes induced a significant increase in reactive radical species which consequently induced cell death and thus lower  $\text{IC}_{50}$  values. As the response of the cells to an increased radical level induced by treatment, glutathione level also increased in a time and dose-dependent manner.

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**CONTACT** Tanja V. Soldatović ✉ [tsoldatovic@np.ac.rs](mailto:tsoldatovic@np.ac.rs) Department of Natural-Mathematical Sciences, State University of Novi Pazar, Vuka Karadžića 9, 36300 Novi Pazar, Serbia

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