

# Refining the structures of novel Cu(II) bioactive complexes: XAFS spectroscopy, laboratory techniques and DFT calculations

Paweł Rejmak,<sup>1</sup> Aleksandra Drzewiecka-Antonik,<sup>1</sup> Marcin Klepka,<sup>1</sup> Anna Wolska,<sup>1</sup> Piotr Pietrzyk,<sup>2</sup> Marta Struga<sup>3</sup>

<sup>1</sup>Institute of Physics PAS, Al. Lotników 32/46, Warszawa, Poland <sup>2</sup>Department of Inorganic Chemistry, Faculty of Chemistry, Jagiellonian University, Gronostajowa 2, Kraków 30-387, Poland <sup>3</sup>Department of Biochemistry and Laboratory of Centre for Preclinical Research, Medical University of Warsaw, Banacha 1B, PL-02097 Warsaw, Poland

[rejmak@ifpan.edu.pl](mailto:rejmak@ifpan.edu.pl)

**Introduction** Copper complexes with thiourea based ligands are widely studied for their potential medicinal use as antitumor chemotherapeutics, antimicrobial agents or as radionuclide carriers. Such compounds are frequently difficult to be obtained in the form of monocrystals suitable for X-ray diffraction study, hence the alternative approach to identify their structure is needed. We present structure refinement of three novel Cu(II) –thiourea derivative complexes, obtained by combined means of spectroscopic techniques, notably X-ray absorption fine structure (XAFS) spectroscopy, and the density functional theory (DFT) simulations.

**Methods** The complexes were obtained from the direct synthesis in solution in the non-crystalline form. The preliminary characterization of new compounds have been performed using laboratory spectroscopic techniques: infrared, UV-Vis and electron paramagnetic resonance (EPR). The antimicrobial and cytotoxic activity of studied compounds were evaluated. The XAFS spectra for Cu K-edge were recorded at Elettra synchrotron (Triest, Italy). The experimental part was supplemented with DFT computational study.

**Results and discussion** Three new complexes of Cu(II) with ligands, consisting of thiourea system attached to polycyclic imide and Br substituted phenyl moieties, were obtained from the direct synthesis in the powder form. One of these compounds was found to exhibit high antibacterial activity against *Staphylococcus* strains, even higher than of commercially available ciprofloxacin drug.

Thiourea derivatives used in this work may act as multidentate *S,N,O*-ligands, therefore predicting the structure of new complexes without crystal data was not a trivial task. The chemical composition of studied compounds was established from combustion elemental analysis, followed by laboratory spectroscopic measurements. The infrared spectroscopy excluded the ligand coordination via carbonyl O atoms. UV-Vis and EPR confirmed the presence of (nearly) non-interacting Cu(II) ions in the square planar coordination.

The final structure of complexes were resolved upon feedback between XAFS data and DFT modeling. The model corresponding to both the best match to XAFS data and the lowest energy in DFT calculation is the structure with peculiar coordination pattern, namely Cu(II) ion being a member of 2 four-atoms rings, formed upon the chelation via S and N atoms from two ligand molecules. In two cases XAFS detected the presence of another Cu and S atoms in the second coordination shell, implying the dimerization of basal mononuclear complexes. DFT calculations confirmed the lack of magnetic coupling in such dimers, reconciling EPR and XAFS results.

**Conclusions** The combined means of XAFS spectroscopy and DFT modeling make a powerful tool for structural characterization of coordination compounds in non-crystalline form.