Determination of the molecular structure of compounds with pharmacological potential using the methodology based on X-ray absorption spectroscopy.

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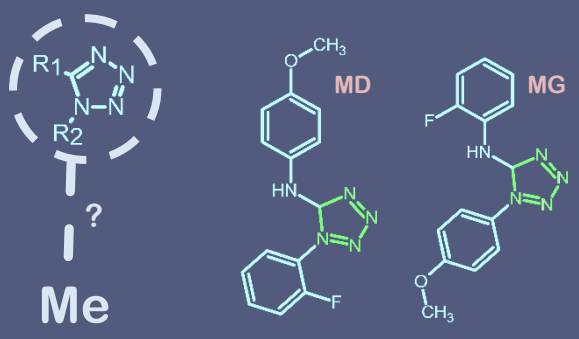
Research goal

Determination of the chemical and molecular structure of non-crystalline, 'metal-organic ligand' coordination compounds with pharmacological potential. In order to reproduce biological examination environment cell culture medium have been used as solvent for complexes preparation.

Motivation

After coordination to metal ions a change in the biological activity used to be observed. Since the potential of pharmacological action depends on the compound's chemical structure, there is an interest in detailed investigation of its molecular structure.



series 1	CuMD, CuMD-20mM, CuMD-10mM
series 2	CuMG, CuMG-20mM, CuMG-10mM
series 3	AgMD, AgMD-20mM, AgMD-10mM
series 4	AgMG, AgMG-20mM, AgMG-10mM

Basic structural characterization

XANES, EXAFS, FTIR, elemental analysis

Initial structural model

EXAFS, DFT, structural DB

Molecular model of coordination polyhedron

DFT, XANES

Complex's molecular model

EXAFS

Research methodology

1st endpoint

Obtaining coordination compounds of Cu (II) and Ag (I) ions with tetrazole derivatives by electrochemical synthesis.

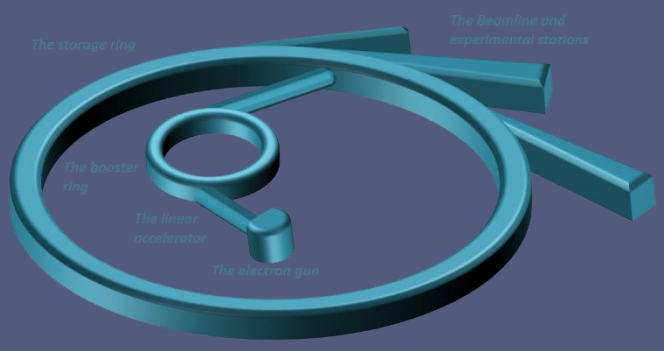
2nd endpoint

Determination of biological (cytotoxic and microbiological) activity of complexes and ligands.

3rd endpoint

Determination of the chemical structure and molecular structure of the complexes using a dedicated methodology based on X-ray absorption spectroscopy

XAFS measurements



Transmission and fluorescence mode, Cu-K Edge (8979 eV), L_3-Ag Edge (3806 eV), Elettra Sincrotrone Trieste (Italy), Synchrotron Light Research Institute (Thailand)

Biological activity

Compounds	Microbiological Activity	Cytotoxic Activity
CuMD complexes	None	Moderate, selective against PC-3 cancer cells
CuMG complexes	Weak	Moderate. Less toxic against normal cells
AgMD complexes	Strong	Moderate in low concentration (< 20 µM)
AgMG complexes	Very strong	Very strong

Microbiological activity - serial dilution method, Cytotoxic activity – MTT test

Summary

Compounds	Coordination polyhedron
Series 1., Series 2.	Tetragonal pyramid with an H_2O molecule at the axial position
AgMD	Pyramidal
AgMG	Pyramidal
AgMD-20mM	Triangle
AgMD-10mM	Triangle
AgMG-20mM	Deformed square
AgMG-10mM	Triangle

Complex's molecular models