THESES OF DOCTORAL (PH.D.) DISSERTATION

Solution chemical and structural comparison of half-sandwich rhodium and ruthenium complexes and their interaction with biomolecules

János Péter Mészáros

SUPERVISOR:
Dr. Éva Anna Enyedy
associate professor, D.Sc. of Hungarian Academy of Sciences

UNIVERSITY OF SZEGED
Faculty of Natural Sciences and Informatics
Department of Inorganic and Analytical Chemistry
Chemistry Doctoral School

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I. Introduction, aims and objectives

Cisplatin and its two clinically approved derivatives (carboplatin, oxaliplatin) are frequently used against cancer. However, their strong anticancer activity is associated with severe side-effects. Moreover, cisplatin resistance can occur, which can be responsible for the cross-resistance of other compounds. Based on these facts, the development of novel metal complexes is an important field of drug research and the basic goal is to find more selective compounds, which are effective on resistant cells as well. In the literature, a plethora of Ru(III/II), Os(II), Ir(III) and Rh(III) complexes was reported with significant anticancer effect. In parallel, characterization of physico-chemical properties and solution equilibrium is also important, since knowing the dominant species under physiological circumstances may help to understand the mechanism of action. These properties and equilibrium constants may contribute to the interpretation of results of (pre)clinical studies as well.

Among the ruthenium containing compounds, NAMI-A (imidazolium-*trans*-[Ru(III)Cl_4(imidazole)(DMSO)]), BOLD-100 (sodium-*trans*-[Ru(III)Cl_4(indazole)$_2$]) and TLD1433 ([Ru(II)(4,4′–dimethyl–2,2′–bipyridine)$_2$–(2–(2′,2″:5″,2‴–terthiophene)–imidazo[4,5–f][1,10]phenanthroline)]Cl_2) entered to clinical phase I/II studies. The mechanism of action of these complexes is different. NAMI-A has antimetastatic effect, without entering to the cytosol. In contrast, BOLD-100 enters to the cell and exerts its cytotoxic effect there. TLD1433 is an agent for photodynamic therapy. The half-sandwich Ru complexes contain a Ru(II) metal centre. Generally, the coordination sphere is completed by a bidentate ligand, a monodentate leaving group and an η^5/η^6-arene ligand. Changing one of the ligands or the metal ion (Ru(II), Os(II), Rh(III), Ir(III)) modifies the solution chemical behaviour and may improve the anticancer effect. With optimal leaving groups the selectivity may be increased using the differences of healthy and cancerous tissues and cells, *e.g.* reductive environment, acidic pH.

Our goals:

- Synthesis of half-sandwich Ru(II) and Rh(III) complexes in solid form. These complexes consist of a bidentate, a monodentate and an η^5/η^6-bound ligand around the metal centre. Characterization with spectroscopic techniques and synthesis of single crystals suitable for single-crystal X-ray crystallographic measurements. The organometallic fragments in the designed compounds are Rh(η^5-C_5Me_5), Ru(η^6-*p*-cymene) and Ru(η^6-toluene) (abbreviated as Rh(C_5Me_5), Ru(Cym) and Ru(Tol), respectively); the bidentate ligands are small molecules with (O,O), (N,O) and (N,N) donor atoms; the monodentate ligands are chloride ion (**Figure 1**) or a monodentate nitrogen-donor small molecule (**Figure 2**).

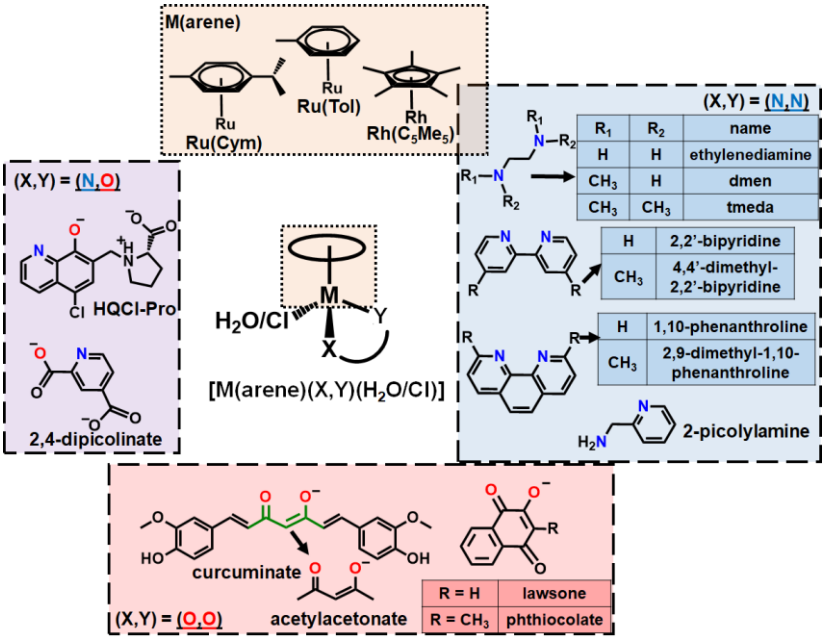

Figure 1: Chemical structures and names of organometallic fragments and bidentate ligands of the studied complexes. HQCl-Pro = (S)–5–chloro–7–((prolin–1–yl)methyl)–8–hydroxiquinoline; dmen = *N,N'*–dimethylethylenediamine; tmeda = *N,N,N',N'*–tetramethylethylenediamine.

- My major goal is to investigate the solution equilibria of complexes shown in **Figure 1** in aqueous phase:

  Determination of the proton dissociation constants of ligands, the stability constants of metal complexes, and equilibrium constants for the deprotonation and substitution processes (substitution with halide ions or with monodentate N-donor ligands) of the coordinated water molecule. Methods: **pH-potentiometry**, **ultraviolet-visible (UV-vis) spectrophotometry** and **^{1}H nuclear magnetic spectroscopy (NMR) spectroscopy**.

- Description of the interaction between half-sandwich organometallic complexes and their interaction with biomolecules (human serum albumin (HSA) and DNA). Comparison of binding preference based on the interaction with binding site model small molecules (1-methylimidazole and guanosine (**Figure 2**)). Methods: **ultrafiltration**, **spectrofluorometric** and **spectrophotometric** techniques.

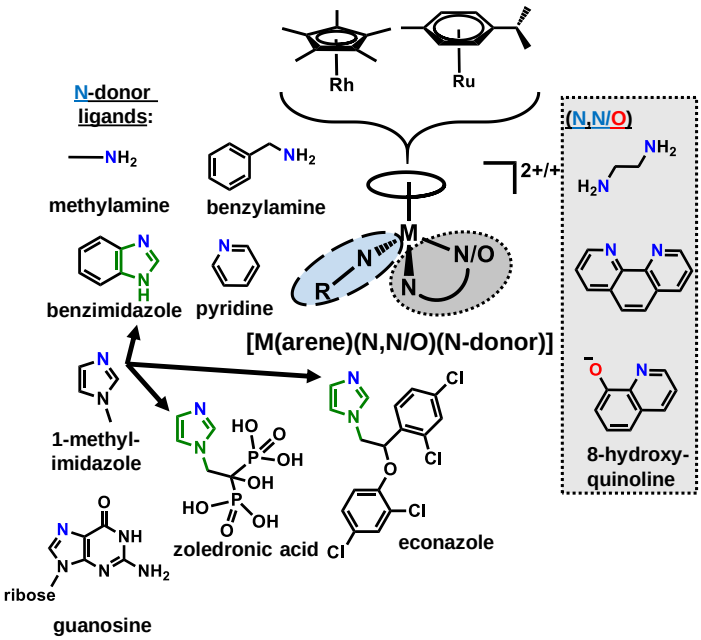

Figure 2: Chemical structures and names of the monodentate and bidentate ligands and organometallic fragments of the studied complexes.

II. Synthesis of metal complexes and experimental methods

Ligands and precursor half-sandwich dimers required for complexes are the products of Sigma Aldrich and were used without further purification. The $[Ru(Tol)Cl_2]_2$ precursor was synthesized earlier in our group, and the synthesis of the *L*-proline-8-hydroxyquinoline hybrid molecule HQCl-Pro was done in the laboratory of Dr. István Szatmári. Complex preparation was performed via mixing the solutions of the given dimeric precursor and the given ligand, using methanol or water as solvent. Stirring at room temperature was followed by precipitation, filtration and washing of the complexes. Slow crystallization resulted in single-crystals found to be adequate for single-crystal **X-ray diffraction** measurement. Characterization of the solid compounds was performed by high performance electrospray ionization mass spectrometry **(HR-ESI-MS)**, **^{1}H and ^{13}C NMR** spectroscopic methods.

Stock solutions were prepared on a weight-in-volume basis. Exact concentrations and equilibrium constants (proton dissociation and cation hydrolysis) of organometallic cation and ligand stock solutions were determined using **pH potentiometric titrations**

(0.20 M (KCl or KNO_3) or 0.10 M (KCl) ionic strength). pH values were measured with a combined glass electrode, and a computer-controlled Metrohm 665 Dosimat automatic burette was used for KOH solution dosage reaching chemical equilibrium in each points. Calculations were performed with HYPERQUAD software.

UV-vis spectrophotometry is suitable to follow various types of reactions, since most of the ligands have chromophoric group(s) resulting in ligand bands usually in the UV region. Charge transfer (CT) bands of the metal complexes are found in the UV-visible region. The CT band is sensitive for the substitution reactions of the coordinated water molecule and for the arene ligand dissociation, and both bands are sensitive for complex formation with bidentate ligands and for competition reactions. Stability constants were determined based on the spectra recorded by an Agilent Cary 8454 diode array spectrophotometer using the PSEQUAD software.

The half-sandwich Ru(II) and Rh(III) complexes are diamagnetic and can be measured by different **NMR spectroscopic** methods. It is a useful technique to follow slow complex formation and ligand competition reactions. It supports the results determined by other methods to describe solution speciation and to determine stability constants. For the characterization of the synthesized compounds ^{1}H (and ^{13}C) NMR spectra are essential, since peaks belonging to the unreacted reactants are clearly visible in the spectra. The samples prepared in aqueous solution were measured with 10% (v/v) D_2O/H_2O, while non-polar deuterated solvents (*e.g.* methanol-d_4, DMSO-d_6) were used for the characterization of synthesized products. The measurements were performed on a 500 MHz Bruker Avance III HD Ascend 500 Plus instrument.

Interaction with high mass biomacromolecules was studied by **ultrafiltration**. After the given incubation time (based on previous experiments) the samples were filtered through a Millipore Amicon Ultra-0.5 membrane filter, through which only molecules with less than 10 kDa molar weight can pass. Concentrations in the filtrate were measured by UV-vis spectrophotometry. For additional information, **spectro-fluorometry** was applied. In HSA the Trp214 amino acid can be selectively excited and the binding of complex nearby causes a decrease in its emission (quenching). For DNA binding fluorometric studies, ethidium bromide as fluorescent probe was used. The fluorometric intensity decreases upon addition of the complex, indicating the liberation of ethidium bromide. The measurements were performed on a Hitachi F4500 instrument.

Additional techniques were performed by our partners: **HR-ESI-MS** (Dr. Zoltán Kele), **single crystal X-ray crystallography** (Dr. Nóra V. May, Alexander Roller), ***in vitro* cytotoxicity on cancer cells** (Dr. Michael A. Jakupec, Dr. Gabriella Spengler, Dr. Gergely Szakács), **antibacterial activity** (Dr. Gabriella Spengler) and metal accumulation studies by **total reflection X-ray fluorescence spectrometry** (TXRF, Dr. Norbert Szoboszlai).

III. New scientific results

T1. Compared with the earlier investigated complexes of hydroxypyr(idin)one ligands, the half-sandwich Ru(Cym), Ru(Tol) and Rh(C_5Me_5) complexes of (O,O) donor ligands of natural origin, 2-hydroxynaphthoquinones (lawsone and phthiocol) and the β-diketone curcumin have lower stability in aqueous solutions. It was concluded that in case of these ligands, the metal complexes in their original forms can not be responsible for the anticancer activity, since at pH 7.4 the complexes dissociated in the presence of cell medium components.

T1.1 Based on the determined stability constants, we concluded that naphthoquinone complexes have low aqueous stability. At physiological pH, the Ru(II) complexes dissociate completely, while ~15% of the complex $[Rh(C_5Me_5)(phthiocolate)(H_2O)]^+$ remains in the original form (c = 100 μM).

T1.2 We demonstrated that acetylacetone, which is the smallest β-diketone molecule, is an appropriate model for curcumin from the view of solution equilibrium studies and structural studies in solid phase.

T1.3 As a result of the greater hydrolytic tendency of $[Ru(arene)(H_2O)_3]^{2+}$ cations, the $[Ru(arene)(L)(H_2O)]^+$ complexes dissociate in a higher ratio in comparison to the Rh analogues at pH 7.4. Amino acids and proteins are able to liberate acetylacetone from its complexes, and we suggest the same behaviour for the curcumin complexes as well. Our studies revealed that the anticancer activity of curcumin decreased in the presence of Ru(arene), however, remained unchanged combined with $[Rh(C_5Me_5)(H_2O)_3]^{2+}$ cations.

T2. It was confirmed that an extra negative charge on the 2-picolinic acid-type ligand decreases the affinity of half-sandwich Rh(C_5Me_5) and Ru(Cym) complexes for halide ions (Cl^-, Br^-). We established the possibility of the dissociation of arene ligand in the [Ru(arene)(2-picolinate type ligand)$(H_2O)]^+$ complexes, which occurs in the excess of bidentate ligands (*e.g.* 2,4-dipicolinic acid and 1,10-phenanthroline (phen)).

T2.1 Analysis of the time- and pH-dependent UV-vis spectra showed that formation of Ru(arene) complexes is always slower than that of with Rh(C_5Me_5). In all cases, high stability complexes were formed. The stability constant of $[Rh(C_5Me_5)$(2,4-dipicolinate)$(H_2O)]$ complex was determined via ligand competition studies using 2-picolinate and followed by ^1H NMR spectroscopy. In the case of Ru(Cym) complex, arene dissociation occurs instead of the bidentate ligand displacement.

T2.2 In contrast to the halide ion affinity, the additional carboxylate group has no measurable effect on the deprotonation of the coordinated water molecule.

T3. It was showed that the hybridization of 8-hydroxyquinoline with *L*-proline can increase the water solubility of the ligand and its complexes. We confirmed the previously described assumption that the –CH_2–N– substitution in position 7 (in the 8-hydroxyquinoline ligand) increases the cytotoxic activity on the doxorubicin resistant cancer cell lines (Colo320). This is true for the HQCl-Pro ligand and its half-sandwich Rh(C_5Me_5) complex as well. Most probably the lower cytotoxic activity of Ru(Cym) and Ru(Tol) compounds is in connection with the loss of arene ligand occurring in these complexes and less Ru can be detected in the cells after one day incubation than in case of the Rh complex.

T3.1 Based on ^{1}H and ^{13}C NMR spectra, the half-sandwich Ru(Cym) and Rh(C_5Me_5) complexes of HQCl-Pro ligand are present in two isomeric forms in methanol, most probably in solid phase and in water as well. It is due to an intramolecular hydrogen bond between the coordinated phenolate-O^- and the protonated amino group causing two different positions of the proline ring.

T3.2 The stability of the HQCl-Pro half-sandwich complexes is high, however, the dissociation of the arene ligand in Ru(Cym) complexes occurs in excess of the bidentate ligand. The flexible ethylenediamine and the (O,O) donor deferiprone do not cause arene loss, rigid ligands having (N,O) and (N,N) donor set are able to replace it.

T4. Stability constants for the complexes of the diamine and polypyridine-like ligands having (N,N) donor atoms with half-sandwich $[M(arene)(H_2O)_3]^{2+}$ cations was determined revealing significantly high stability. The only exceptions are the ligands with methyl groups close to the coordinating nitrogen atoms, resulting in strained complex structure. Some ligands were more cytotoxic on doxorubicin resistant cells than on sensitive ones, and their Rh(C_5Me_5) complexes showed the same behaviour. In all cases, Ru(Cym) and Ru(Tol) complexes were less cytotoxic and lost this type of selectivity. In these complexes loss of the arene ligand occurred without ligand excess.

T4.1 The ligands phen and 4,4’-dimethyl-2,2’-bipyridine have greater cytotoxic effect on the doxorubicin-resistant MES-SA/Dx5 cells than on the parental MES-SA cells. Their Rh(C_5Me_5) complexes show the same behaviour. We assume that arene ligand dissociation and formation of inert [M(arene)(L)(OH)] mixed hydroxido species in high extent are responsible for the smaller anticancer effect of Ru(arene) compounds.

T5. Under the same conditions, the complex stability at physiological pH (based on pM* values, which is the negative logarithm of the concentration of the non-ligand-bound metal ion) follows the order of:

$(O,O)_{naphthoquinone}$ < $(O,O)_{\beta\text{-diketone}}$ < $(O,O)_{hydroxypyr(idin)one}$ < $(N,O)_{2\text{-picolinate}}$ < $(N,O)_{8\text{-hydroxyquinoline}}$ ≤ (N,N).

pK_a[M(arene)(L)] and log K'(H_2O/Cl^-) equilibrium constants have the order of Ru(Tol) < Ru(Cym) < Rh(C_5Me_5).

T5.1 Reaction rates of complex formation for a given organometallic cation are found in the order: (N,N) < (N,O) < (O,O).

T5.2 We found that the Rh(C_5Me_5) complexes are present in a greater extent at pH 7.4, which is in connection with the lower hydrolytic tendency of the $[Rh(C_5Me_5)(H_2O)_3]^{2+}$ cation. Only the (N,O) donor complexes of Ru(Cym) are more stable compared to their Rh(C_5Me_5) congeners.

T5.3 The greater the pK_a[M(arene)(L)] constant, the higher the chloride ion affinity. This finding can be explained with the strength of the M–O(water) bond. The strongly bound aqua ligand is a bad leaving group and its O–H bonds are more polarized resulting in more acidic protons.

T6. We set two models for the prediction of water-chloride ion exchange constant. The first model is valid for Rh(C_5Me_5) complexes only and based on geometrical parameters of their structures. The other model is extended for Ru(arene) complexes as well.

T6.1 Structural data of 12 Rh(C_5Me_5) complexes were employed in the first model. The equation:

calculated log K'(H_2O/Cl^-) = 27.59 × (Rh–C_5Me_5 centroid distance) – 0.23 × angle(X–Rh–Y) – 0.23 × (torsion angle between CH_3 and C_5Me_5 plane) + 0.46 × [Rh(C_5Me_5)(L)] charge – 28.75.

T6.2 Second model: 17 Rh(C_5Me_5), 9 Ru(Cym) and 6 Ru(Tol) complexes: calculated log K'(H_2O/Cl^-) = – 0.24 × log $\beta[M_2(arene)_2H_{-3}]$ – 0.63 × pK_a[M(arene)(L)] + 4.53.

T7. Half-sandwich Ru(Cym) and Rh(C_5Me_5) complexes were synthesized, which can be activated by the acidic pH of the cancer tissue. With the use of imidazole-like ligands (zoledronic acid and econazole) activation (dissociation of the monodentate ligand) can be achieved, as it was observed in the anticancer and antibacterial effects.

T7.1 The coordination of N-donor monodentate ligands to highly stable ethylenediamine, phen and 8-hydroxyquinoline complexes was studied. Complexes of heterocyclic monodentate ligands were the most stable. The most promising

compounds contained imidazole nitrogen, which show increased level of dissociation in acidic pH.

T7.2 Most of the Ru(Cym) complexes did not form mixed ligand complexes in contrast to $Rh(C_5Me_5)$ complexes.

T7.3 In the biological measurements, a small change in the bioactivity data could prove the acidic activation of $[Rh(C_5Me_5)(phen)(1\text{-methylimidazole/pyridine})]^{2+}$ complexes in Colo320 cells. The antibacterial effect of $[Rh(C_5Me_5)(phen)(econazole)]^{2+}$ complex is higher against sensitive and resistant *E. coli* strains at pH 6 than at pH 7.

T8. The coordination of histidine to metal complexes was detected, which is a similar process to the interaction with human serum albumin via histidine nitrogen donors. Based on our results, there are examples where both cytotoxic and non-toxic $Rh(C_5Me_5)$ complexes can bind to DNA with similar extent. Studies with binding site models showed the 1-methylimidazole (protein) preference of $[Rh(C_5Me_5)(2\text{-picolinate})(H_2O)]^+$ type complexes over the guanosine (DNA base).

T8.1 Coordination of histidine causes displacement in the complex of the acetylacetone ligand, while in the case of HQCl-Pro mixed ligand complex forms.

T8.2 Based on our ultrafiltration measurements with $Rh(C_5Me_5)$ compounds, the triaqua cation binds to the DNA in the highest percentage, the 8-hydroxyquinoline complex had the second highest bound amount, followed by the $(N,O)_{2\text{-picolinate}}$ and (N,N) donor complexes.

T8.3 Liberation of intercalated ethidium bromide from DNA was detected by spectrofluorometry after addition of metal complexes. Most probably binding of the metal complex distorts the structure of DNA, which results in the release of ethidium bromide.

IV. Possible applications of the results

In this dissertation the ligands of the introduced complexes are small molecules. However, these are simple models of common types of ligands and their solution equilibrium behaviour may give estimation about the properties of bigger and more effective ligands. Description of the arene ligand dissociation in the Ru(arene) complexes of (N,O) and (N,N) ligands is an important result. The effect of exchange of metal ion centre on different reactions was presented as well. The models capable for the prediction of water-chloride ion exchange constants give the chance to estimate the physico-chemical properties of the complexes, even before the synthesis.

V. Scientific publications

MTMT ID: 10061312

Papers related to the dissertation:

1. **János P. Mészáros***, Veronika F. S. Pape, Gergely Szakács, Gábor Németi, Márk Dénes, Tamás Holczbauer, Nóra V. May, Éva A. Enyedy*
Half-sandwich organometallic Ru and Rh complexes of (N,N) donor compounds: effect of ligand methylation on solution speciation and anticancer activity
DALTON TRANSACTIONS 50 (2021) 8218–8231., IF: 4,174

2. **János P. Mészáros**, Gábor Németi, Jelena M. Poljarevic, Tamás Holczbauer, Nóra V. May, Éva Anna Enyedy*
Effect of the additional carboxyl group in half-sandwich organometallic 2,4-dipicolinate complexes on solution speciation and structure
EUROPEAN JOURNAL OF INORGANIC CHEMISTRY 19 (2021) 1858–1868., IF: 2.529

3. **János P. Mészáros**, Jelena M. Poljarevic, István Szatmári, Oszkár Csuvik, Ferenc Fülöp, Norbert Szoboszlai, Gabriella Spengler, Éva A. Enyedy*
An 8-hydroxyquinoline-proline hybrid with multidrug resistance reversal activity and solution chemistry of its half-sandwich organometallic Ru and Rh complexes
DALTON TRANSACTIONS 49 (2020) 7977–7992., IF: 4.052

4. **János P. Mészáros**, Heiko Geisler, Jelena M. Poljarević, Alexander Roller, Maria S. Legina, Michaela Hejl, Michael A. Jakupec, Bernhard K. Keppler, Wolfgang Kandioller, Éva A. Enyedy*
Naphthoquinones of natural origin: Aqueous chemistry and coordination to half-sandwich organometallic cations
JOURNAL OF ORGANOMETALLIC CHEMISTRY 907 (2020) 121070., IF: 2.066

5. **János P. Mészáros**, Jelena M. Poljarević, G. Tamás Gál, Nóra V. May, Gabriella Spengler, Éva A. Enyedy*
Comparative solution and structural studies of half-sandwich rhodium and ruthenium complexes bearing curcumin and acetylacetone
JOURNAL OF INORGANIC BIOCHEMISTRY 195 (2019) 91–100., IF: 3.063

6. **János P. Mészáros**, Orsolya Dömötör, Carmen M. Hackl, Alexander Roller, Bernhard K. Keppler, Wolfgang Kandioller, Éva A. Enyedy*
Structural and solution equilibrium studies on half-sandwich organorhodium complexes of (N,N) donor bidentate ligands
NEW JOURNAL OF CHEMISTRY 42 (2018) 11174–11184., IF: 3.201

ΣIF=19.085

Papers not related to the dissertation:

1. Éva A. Enyedy*, **János P. Mészáros**, Gabriella Spengler, Muhammad Hanif, Christian G. Hartinger*
Comparative solution studies and cytotoxicity of gallium(III) and iron(III) complexes of 3-hydroxy-2(1H)-pyridinones
POLYHEDRON 172 (2019) 141–147., IF: 2.067

2. Éva A. Enyedy*, **János P. Mészáros**, Orsolya Dömötör, Carmen M. Hackl, Alexander Roller, Bernhard K. Keppler, Wolfgang Kandioller
Comparative solution equilibrium studies on pentamethylcyclopentadienyl rhodium complexes of 2,2'-bipyridine and ethylenediamine and their interaction with human serum albumin
JOURNAL OF INORGANIC BIOCHEMISTRY 152 (2015) 93–103., IF: 3.205

ΣIF=5.272
ΣΣIF=24.357

Oral presentations and posters related to the dissertation:

1. **<u>János P. Mészáros</u>**, Jelena M. Poljarevic, István Szatmári, Oszkár Csuvik, Ferenc Fülöp, Norbert Szoboszlai, Gabriella Spengler, Éva A. Enyedy* (oral pr.)
An 8-hydroxyquinoline-proline hybrid with multidrug resistance reversal activity and solution chemistry of its half-sandwich organometallic Ru and Rh complexes
International Symposium on Metal Complexes, 2021.06.16-18., Białystok, Poland

2. **<u>Mészáros János P</u>.**, Németi Gábor, May Nóra V., Enyedy Éva A. (oral pr.)
The half-sandwich complexes of 2,4-dipicolinate: solution equilibrium and structure
XLIII. Chemistry Lectures, 27-28.10.2020., Szeged, Hungary

3. <u>Orsolya Dömötör</u>, Tamás Pivarcsik, **János P. Mészáros**, Éva A. Enyedy (poster)
Human serum albumin binding of high stability Rh(III)(η^5-C_5Me_5) and Ru(II)(η^6-p-cymene) complexes
1st European NECTAR Conference (COST Meeting), 05-06.03.2020. Belgrade, Serbia

4. **<u>János P. Mészáros</u>**, Wolfgang Kandioller, Alexander Roller, Bernhard K. Keppler, Éva A. Enyedy (poster)
Activation by acidosis: synthesis and solution equilibrium studies of half-sandwich Rh complexes containing monodentate N-donor ligands
9th International Symposium on Bioorganometallic Chemistry, 28.07-01.08.2018., York, United Kingdom

5. Éva A. Enyedy, **János P. Mészáros**, Orsolya Dömötör, Jelena M. Poljarević, Nóra V. May, G. Tamás Gál, István Szatmári, Ferenc Fülöp, Gabriella Spengler (oral pr.)
Solution equilibria of various antitumor half-sandwich organometallic complexes of 8-hydroxyquinolines and 2-picolinates: structure, stability and activity
9th International Symposium on Bioorganometallic Chemistry, 28.07-01.08.2018., York, United Kingdom

6. Orsolya Dömötör, **János P. Mészáros,** Jelena M. Poljarević, Éva A. Enyedy (oral pr.)
Variations on a theme: different ways of albumin binding of half-sandwich organoruthenium and organorhodium complexes
9th International Symposium on Bioorganometallic Chemistry, 28.07-01.08.2018., York, United Kingdom

7. **Mészáros János P.**, Wolfgang Kandioller, Alexander Roller, Bernhard K. Keppler, Enyedy Éva A. (poster)
Potentially anticancer half-sandwich rhodium complexes: acid activated metal complexes
Hungarian Chemical Society Chemist Conference 2019, 24-26.06.2019, Eger, Hungary

8. **János P. Mészáros**, Jelena M. Poljarević, Heiko Geisler, Fanni Veréb, Nóra V. May, Wolfgang Kandioller, Bernhard K. Keppler, Éva A. Enyedy (poster)
A novel 8-hydroxyquinoline derivative with multidrug resistance selectivity and its half-sandwich Ru and Rh complexes
International Symposium on Metal Complexes, 11-14.06.2019., Hajdúszoboszló, Hungary

9. **J. P. Mészáros**, J. M. Poljarević, H. Geisler, F. Veréb, N. V. May, W. Kandioller, B. K. Keppler, É. A. Enyedy (poster)
Comparative solution equilibrium studies on complexes of Ru(η^6-toluene), Ru(η^6-p-cymene) and Rh(η^5-C_5Me_5) formed with (O,O) donor ligands of natural origin
35th International Conference on Solution Chemistry, 26-30.08.2018, Szeged, Hungary

10. M. Mészáros, **J. P. Mészáros**, É. A. Enyedy (poster)
Comparative solution equilibrium studies on complexes of organometallic half-sandwich cations formed with (N,N) donor ligands
35th International Conference on Solution Chemistry, 26-30.08.2018., Szeged, Hungary

11. **Mészáros J.P.**, Enyedy É.A. (oral pr.)
Solution chemistry of potentially anticancer ruthenium- and rhodium complexes
XIVth Conference of the Pro Scientia Golden Medalists, 23-25.08.2018., Budapest, Hungary

12. **János P. Mészáros**, Wolfgang Kandioller, Alexander Roller, Bernhard K. Keppler, Éva A. Enyedy (poster)
Synthesis and solution equilibrium studies of half-sandwich Rh-complexes containing bidentate (N,N) and monodentate N-donor ligands
International Symposium on Metal Complexes, 03-07.06.2018., Florence, Italy

13. Éva A. Enyedy, Jelena M. Poljarevic, Orsolya Dömötör, **János P. Mészáros**, Nóra V. May, István Szatmári, Ferenc Fülöp, Gabriella Spengler (oral pr.)
Comparative solution equilibrium studies on various antitumor half-sandwich organometallic complexes of 2-picolinates and 8-quinolinols
International Symposium on Metal Complexes, 03-07.06.2018., Florence, Italy

14. **Mészáros János P.**, Jelena M. Poljarević, Heiko Geisler, Veréb Fanni, May Nóra V., Wolfgang Kandioller, Bernhard K. Keppler, Enyedy Éva A. (oral pr.)
Solution chemical studies on half-sandwich organometallic complexes formed with (O,O) donor ligands of natural origin
52th Complex Chemical Colloquium, 22-24.05.2018., Balatonvilágos, Hungary

15. Enyedy É.A., Dömötör O., J.M. Poljarevic, **Mészáros J.P.**, May N.V., Gál T.G., Szatmári I., Fülöp F., Spengler G. (oral pr.)
Solution equilibrium studies on the complexes of organometallic half-sandwich complexes of 8-hydroxyquinoline and 2-picolinic acid derivatives
52th Complex Chemical Colloquium, 22-24.05.2018., Balatonvilágos, Hungary

16. **Mészáros J.P.**, Enyedy É.A. (oral pr.)
Solution chemistry and structural characterization of half-sandwich Rh(η^5-C_5Me_5) complexes
XL. Chemistry Lectures, 16-18.10.2017., Szeged, Hungary

17. **J.P. Mészáros**, O. Dömötör, C.M. Hackl., A. Roller, W. Kandioller, B.K. Keppler, É.A. Enyedy (oral pr.)
Half-sandwich rhodium(III) complexes formed with (N,N) ligands: structural characterization and solution chemistry
XXVI. International Conference on Coordination and Bioinorganic Chemistry, 04-09.06.2017., Smolenice, Slovakia