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Rewiev report of PhD Thesis by Michał Łomzik entitled:

Synthesis and characterization of hydrid drugs based on ruthenium complexes moiety and biologically active organic compounds

Over the past 25 years, ruthenium complexes have received much attention from researchers due to their interesting chemical and biological properties. Ruthenium complexes are particularly attractive in the cancer therapy field due to their three main properties: **i)** ligand exchange rates, often comparable to those of platinum complexes, which can be tuned by coordinating appropriate ancillary ligands; **ii)** the ability of ruthenium ions to mimic the behavior of iron when binding with certain (main) biological molecules, including serum transferrin and albumin; and **iii)** under physiological conditions, the accessibility of these complexes in several oxidation states (Ru(II), Ru(III), Ru(IV)). Additionally, in biological systems, glutathione, ascorbic acid and single electron transfer proteins are able to reduce Ru(III) to Ru(II). Furthermore, the octahedral structure of the ruthenium(II/III) complexes presents a different mechanism of activity, which creates new opportunities in antitumor therapy.

The reviewed international PhD thesis by Michał Łomzik, supervised by prof. dr. hab. Grażyna Stochel, the Jagiellonian University in Kraków and Dr. Philippe C. Gros, Université de Lorraine was oriented exclusively towards the medical application of ruthenium compounds.

The main goal of the study evaluated in the PhD dissertation was to discuss the synthesis as well as spectroscopic and photophysical characteristics of novel ruthenium(II) polypyridyl complexes containing biologically active molecules as potential theranostic agents. In my opinion, it was the most significant and successfully completed part of the PhD thesis.

It is commonly known that the biological properties of metal complexes are modulated mainly through ligands. Therefore, in the study, I found the use of pyridine-2-carboxyaldehyde semicarbazone and hydantoin derivatives as biologically active moieties fully justified. From among the specific objectives that allowed the PhD student to solve the research problem, the following ones should be mentioned: **i)** the synthesis of four ligands and their complexation with ruthenium ions, **ii)** the determination of photophysical properties of the ruthenium complexes, **iii)** the knowledge of the interaction between ruthenium complexes and human serum albumin. These goals were achieved by the student PhD who applied the experimental methods (NMR (^1H , ^{13}C), UV-Vis, HRMS) and carried out DFT calculations.

From the formal point of view, the evaluated dissertation contains 123 typewritten pages and is arranged into 10 basic chapters, typical of PhD dissertations, based on an experiment, i.e. abbreviations, abstract, contents, introduction, aim and scope of the thesis, methods, results and discussion, summary, synthetic procedures, references.

The Literature part comprises 22 pages presenting the author's information necessary to **i)** explain the need to develop the research area which the doctoral dissertation covers, **ii)** present the scientific achievements in the discussed topic. In the context of the biological studies performed in order to meet the requirements resulting from the main objectives of the dissertation, a special attention should be drawn to the material included in the final part of the theoretical chapter in which the already reported biological activity of semicarbazones and tiosemicarbazones are discussed. A brief description of the research methods is also a valuable part of the dissertation which provides a good starting point for the analysis of the experimental results. To sum up, I would like to emphasize the fact that, in the theoretical part, Michał Łomzik very carefully presents the key issues. He also provides a sound background to the problems addressed directly in the studies, and which have already been covered by his. He does it in a very good language style and considers the latest scientific literature reports (114 references). Additionally, a very careful theoretical preparation to perform his research allowed the author to set the unambiguous research objectives.

The original part of the work presents a wide range of research material that constitutes the basis for discussion, drawing conclusions, and establishing the research potential for more extensive studies in future. The PhD research objectives were achieved by synthesizing four ligands and nine ruthenium complexes, and then, providing an extensive characteristics of photophysically and biologically received calls. It should be pointed out that the initial step of the research required conducting a series of experiments. Therefore, it is noteworthy that Michał Łomzik managed to deal with this difficult task obtaining excellent results. Undeniably, this is due to the large involvement the PhD student presented in the research work. The experimental data are presented in a clear manner, with the use of tables, diagrams, and spectra, which indicates the professional and reliable performance of the experiments. In contrast, the insightful and logical discussion of the results proves the author's high scientific maturity. From among the rich experimental material and a number of analyses presented in this part, the below mentioned points undeniably contribute to the success:

- (1) the synthesis of 4 new bioactive ligands.
- (2) the isolation of nine ruthenium(II) complexes as well as the presentation of their spectroscopic characteristics and physico-chemical properties.
- (3) the ability to combine experimental data resulting from quantum-mechanical calculations and drawing logical conclusions.
- (4) conducting numerous studies to determine the impact of the Ru(II) complexes in their interaction with the human serum albumin.
- (5) the determination of the effect of biologically active ligands on the metal center geometry of the ruthenium complexes.

In conclusion, the objectives of the work have been fully achieved, and the results are positive and scientifically very important. The level of the scientific reports corresponds with the world scientific standards in this field.

Reassuring, in my opinion, the PhD thesis fully meets the criteria set for doctoral dissertations in Article. 13 of the Act of 14.03.2003 (Dz. 2003. Number 65, pos. 595, as amended) regarding the titles and academic degrees. Therefore, I would like to place my positive recommendation to the Faculty of Chemistry of the Jagiellonian University in Kraków concerning Mr. M. Łomzik's admission to further stages of the doctoral degree procedures.

