

Opinion

by Assoc. Prof. Dr. Martin Petrov Tsvetkov, member of the scientific jury, appointed by order ПД 38 - 608/13.11.2023 of the Rector of Sofia University "St. Kliment Ohridski"

on the dissertation of Prof. Dr. Ivayla Nedialkova Pantcheva – Kadreva on the topic “Metal complexes of the carboxylic polyethers monensin and salinomycin: structure, properties & biological activity”, presented for the scientific degree "Doctor of Sciences" in professional field 4.2. Chemical Sciences (Analytical Chemistry)

Prof. Ivayla Pantcheva-Kadreva's dissertation systematizes her research over the past 16 years, which has been published in 27 scientific works (23 scientific articles and 4 chapters of collective monographs). A significant part of Prof. Pantcheva-Kadreva's scientific works have been published in prestigious international scientific journals with a high quartile - 6 in journals with Q1 and 6 with Q2.

The presented dissertation on the topic "Metal complexes of the carboxylic polyethers monensin and salinomycin: structure, properties & biological activity" is written on 155 pages and contains 59 figures, 30 tables, 5 appendices and 188 references.

The introduction, although brief, clearly indicates the main characteristics of the two studied ionophores (monensin and salinomycin), where it is indicated that at the international level the accumulated knowledge about their behavior in the presence of metal ions in an oxidation state higher than one is insufficient (or absent altogether), which limits the understanding of their behavior in living organisms. It is the research of this type of interaction and the subsequent influence on the biological activity of the two antibiotics is the main direction in the presented scientific works of Prof. Pantcheva-Kadreva.

The research presented in the dissertation is in the full sense interdisciplinary, covering areas of experimental inorganic and analytical chemistry (synthesis of complexes with metal ions in the second-fourth oxidation state, combined with extensive physicochemical characterization using a wide range of analytical techniques), theoretical chemistry and biochemistry.

The conducted studies in the solid state show the successful isolation of 39 complexes with the participation of monensin and salinomycin, which are divided by the author into two main groups depending on the method of binding the metal to the ligands - "classical" (32 in number) and "non-classical" (7 in number). The obtaining of single crystals of the complexes with monensin and their crystallographic characterization, I personally consider one of the main contributions to the work of Prof. Ivayla Pantcheva-Kadreva, as this provides a prerequisite for conducting more in-depth theoretical studies, which allows a complete assessment of received materials. Since obtaining single crystals is essentially not a trivial task, the application of other characterization techniques such as FT-IR, NMR, EPR, TEM, FAB/ESI-MS complements or replaces structural characterization where crystallographic information is unavailable. The results obtained for monensin complexes containing more than one metal ion are interesting. Personally, I think this area could be expanded to include more two-, tri-, and four-charged ions, as well as a combination of these. Last but not least, the application of quantum mechanical

calculations and computer modeling of complexes of the type $[\text{CeL}(\text{NO}_3)_2(\text{OH})]$ should be noted.

The application of CD spectroscopy (with its two varieties - UV-CD and VIS/NIR-CD) for the complexes with the participation of monensin is undoubtedly a key point and a serious contribution in the dissertation work. I find the application of the two main varieties of CD spectroscopy extremely elegant in solving problems involving metal ions optically active in different parts of the light spectrum, and in overcoming the shortcomings of the individual varieties. The results of the conducted research combined with quantum chemical calculations allow to outline the main factors determining the behavior and selectivity of the two antibiotics in solutions containing metal ions from group IA and IB.

Last but not least, attention was paid to the biological activity of the obtained materials (antibacterial, antitumor and overall toxicological), which gives completeness to the conducted research. I appreciate the author's self-criticism about the need to carry out more in-depth research in order to gain a complete understanding of their biological activity, but regardless of this, some of the results achieved are optimistic.

I would like to point out that Prof. Ivayla Pantcheva-Kadreva's research is extremely original, both at the national and world level. Attestation for this is that, at this stage, the acquired knowledge about the biological activity of metal complexes of salinomycin and monensin is the result of the work by Bulgarian researchers, one of whom is Prof. Pantcheva-Kadreva.

The documents presented by Prof. Ivayla Pantcheva - Kadreva show that they fully cover, and in some places even significantly exceed, the criteria for obtaining the scientific degree "Doctor of Sciences" in the professional direction 4.2 Chemical sciences. Based on the above, I strongly recommend the respected scientific jury to award **Prof. Dr. Ivayla Nedialkova Pantcheva - Kadreva** the scientific degree "**Doctor of Sciences**".

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Sofia

Assoc. Prof. Dr. Martin Tsvetkov

