

# SCIENTIFIC OPINION

by

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**Member of a scientific jury based on order № P- P-109-545/05.12.2023 of the Rector of Varna Medical University and appointed for preparation of a scientific opinion according to the protocol of the first meeting held on 19.12.2023.**

REGARDING: Public defense of a dissertation work for the acquisition of an educational and scientific degree "Doctor" in the field of higher education 7. Health care and sports, 7.3. Pharmacy and PhD Program "Pharmaceutical Chemistry" of Tanya Nedelcheva Dimova with thesis topic: "NEW AROMATIC IODINE DERIVATIVES - SYNTHESIS, STRUCTURE, PROPERTIES". The scientific supervisors of the dissertation are: Associate Professor Svetlana Fotkova Georgieva, Ph.D. and Associate Professor Iliyan Nikolov Kolev, Ph.D.

## **Literature review, purpose, tasks and used materials and methods**

The literary review is presented in 25 pages. The content of the latter is structured in a way that fully reflects what is indicated in the following thematic points. The doctoral student presents detailed information on the chemistry and methods of synthesis of iodo- and bromoaromatic compounds. The application of organoiodine compounds in medicine is also presented, incl. and their use in imaging diagnostics. The presented information on the synthesis of 2,6-diiodosubstituted aromatic acids, as well as the presented regarding the creation of tissue-imitating and diagnostic materials, is also correctly systematized.

The main dissertation goal is also clearly formulated. The five work tasks are adequately set.

All materials and methods used by the doctoral student are described in detail.

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## Results, conclusions and contributions

In 39 pages, she reflects the most essential information she received regarding her dissertation - "Results and Discussion".

In the indicated section, information is present both on the synthesis of new homo- and heterohalo-substituted aromatic compounds (2-(2-iodo-3,4,5-trimethoxyphenyl)acetic acid (ITMPhAA) and 2-bromo-6-iodo-3,4,5-trimethoxybenzoic acid (BrITMBA)) and for their crystallization. In this regard, the PhD student successfully established the crystal structures of 2,6-diiodo-3,4,5-trimethoxybenzoic acid (DITMBA) and its toluene solvatomorph, as well as those of 2,6-dibromo- (DBrTMBA) and 2-bromo-3,4,5-trimethoxybenzoic acid (BrTMBA).

With diiodo-substituted eudesmic acid, she conducted additional, *in vitro*, studies, with which she established the absence of cyto- and photoinduced toxicity from the acid in question. The potential of the water-soluble sodium salt of the same acid in the construction of real physical phantoms intended for contrast-enhanced mammography was also evaluated.

The doctoral student proved, instrumentally, the activity of the iodination I<sub>2</sub>/AgNO<sub>3</sub> agent in the conversion of three different aromatic compounds/reactants - 3,4,5-trimethoxybenzaldehyde, 3,4,5-trimethoxybenzoic acid and 2-(3,4,5-trimethoxyphenyl)acetic acid. Furthermore, it achieves the synthesis of BrTMBA and DBrTMBA in a new, environmentally friendly way.

The PhD student correctly presents all the results obtained by her. She correctly reflected all conclusions and contributions.

I believe that her personal contribution, in the development of the dissertation, the presentation and interpretation of the results and the shaping of the scientific publications, is also essential.

### Scientific and publication activity

The doctoral student used the obtained data for the preparation of two scientific publications in refereed and indexed scientific journals, as well as in two non-refereed publications with scientific review, which covered the requirements for acquiring the PhD:

- Iliyan Kolev, Tanya Dimova, Ivan Iliev, Marin Rogozherov, Michael Bodensteiner, Further findings concerning 2,6-diiodo-3,4,5-trimethoxybenzoic acid (Part II), *Journal of Molecular Structure*, Volume 1294, Part 1, (2023), 136388, ISSN 0022-2860, <https://doi.org/10.1016/j.molstruc.2023.136388>

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- F. Meurer, T. Dimova, M. Bodensteiner, I. Kolev, 2,6-Dibromo-3,4,5-trimethoxybenzoic acid, (2023), Acta Cryst. 79, ISSN 2056-9890, DOI: 10.1107/S2056989023007831
- Tanya Dimova, Nadya Hadzhieva, Nadezda Nefedova, Iliyan Kolev, Strategies in the synthesis of orto-diiodine-substituted aromatic acids, Industrial Technologies, Vol. 8 (1) 2021, pp. 81-86
- Iliyan Kolev, Tanya Dimova, On the iodination of eudesminic acid with  $\text{INO}_3$  in an aqueous-methanolic medium, Scripta Scientifica Pharmaceutica, 2023, ISSN 0582-3250.

### Critical remarks, recommendations

In the dissertation work and its accompanying abstract, technical and spelling errors are noticed, sporadically. Remarks can also be made regarding the prepared short dissertation content (page 2). The title does not fully cover the content of the manuscript. It should also reflect the presence of bromo-substituted compounds. However, these remarks are not critical; do not detract from the scientific value of the submitted manuscript.

### Conclusion

Provided to me by Tanya Nedelcheva Dimova's dissertation I appreciate as a serious development in the field of pharmaceutical science. The candidate has also completed a number of other mandatory tasks during the period of her studies in her doctoral program. She also expediently solved all the scientific cases and tasks set for her. I perceive all this as proof of the excellent scientific and educational preparation of the doctoral student and the competence she has acquired. This gives me the reason to present my POSITIVE ASSESSMENT and to confidently propose to the honorable scientific jury to award the educational and scientific degree "Doctor" to Tanya Nedelcheva Dimova in the field of higher education "7. Health care and sports", professional direction "7.3. Pharmacy", doctoral program in "Pharmaceutical Chemistry".

Заличено на основание чл. 5,  
§1, б. „В“ от Регламент (ЕС)  
2016/679

31.01.2024

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/Prof. Kaloyan Georgiev, PhD, DSc/

