REVIEW

by prof. Alexander Borisov Zlatkov, Ph.D., DSc,
professor at the Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Medical University - Sofia, designated as a member of the scientific jury on the basis of art. 4, paras 1 and 2, ZRASRB, Decision of the Faculty Council of the Faculty of "Pharmacy" at the MU - Varna and Rector's order No. R-109-545/05.12.2023.

Regarding: dissertation for fulfillment of the requirements for obtaining a doctoral degree in the Higher Education District *7. Health care and sports*, professional direction: *7.3. Pharmacy* and Doctoral Program: *Pharmaceutical Chemistry*

Topic: "New aromatic iodine derivatives - synthesis, structure, properties"

Author: Chief assistant mag.-pharm. Tanya Nedelcheva Dimova, full-time doctoral student in the "Pharmaceutical Chemistry" doctoral program, enrolled by order No. R-109-385/08.10.2020 at the Department of Pharmaceutical Chemistry at the Faculty of Pharmacy, MU - Varna.

Scientific supervisors: Assoc. Prof. Iliyan Kolev, Ph.D
Assoc. Prof. Svetlana Georgieva, Ph.D.

I. General presentation of the procedure and the PhD student

The presented set of materials on paper and electronic media is in accordance with Art. 69 of the Regulations for the Development of the Academic Staff at the MU – Varna dated 21.11.2022 and includes the following documents:

- ✓ Application to the Rector for the disclosure of a protection procedure;
- ✓ Autobiography signed by the doctoral student;
- ✓ Copy of a diploma for a completed higher education educational-qualification degree "Master" with its annex;
- ✓ Enrollment order;
- ✓ Minutes of an examination for the doctoral minimum;
- ✓ Minutes from the SC with a positive decision on the readiness for protection;
- ✓ Deduction order with right of defense;
- ✓ Declaration of originality;
- ✓ List of publications related to the topic of the dissertation with the doctoral student's signature;
- ✓ Copy of the publications related to the topic of the dissertation work
- ✓ Declaration of authenticity of the presented documents
- ✓ Declaration for registration of profiles in scientific databases

✓ Certificate of specialization in drug technology with biopharmacy.

The PhD student has submitted 4 (four) scientific publications, of which 2 (two) in journals in refereed and indexed in world-renowned databases of scientific information and 2 (two) in peer-reviewed journals and not referenced in world-renowned databases of scientific information, all related to the topic of the developed dissertation work. One of the supervisors is not involved in the publications.

I have no notes or comments on the documents.

Tanya Nedelcheva Dimova was born on March 25, 1982. In 2006, she obtained a higher education with a bachelor's degree and professional qualification "Biologist" at Sofia University, Faculty of Biology, specialty "Biology". Miss Dimova continued her education and in 2010 obtained the higher education educational-qualification degree "Master of Pharmacy" at the Faculty of Pharmacy, MU - Sofia and, in parallel, the educational-qualification degree "Bachelor", specialty "Organic Chemical Technologies", professional qualification "Engineer - Chemist" at the University of Chemical Technology and Metallurgy - Sofia , Faculty of Chemical Technology. Apparently stimulated by her successes in 2019, she acquired the "Doctor" degree in a scientific specialty 5.10. Chemical technologies (Technology of composite materials), and in 2020 - a specialty in Drug Technology with Biopharmacy at MU-Varna. In the same year, she was enrolled as a doctoral student in the "Pharmaceutical Chemistry" doctoral program at the Department of Pharmaceutical Chemistry at the Faculty of Pharmacy, MU - Varna. The professional realization of mag.-pharm. Tanya Dimova is fully associated with MU-Varna as an assistant during the period 2011-2019, and from 2019 to now as a chief assistant. The scientific and professional path so far presents ch. assistant Dimova as an ambitious and purposeful young person with a strong affinity for science and education.

By Order No. R-109-385/08.10.2020, she was enrolled as a full-time doctoral student in the field of Higher Education "7. Health care and sports", professional direction: "7.3. Pharmacy", doctoral program: "Pharmaceutical Chemistry" with scientific supervisors assoc. prof. Iliyan Kolev, Ph.D. and assoc. prof. Svetlana Georgieva, Ph.D. at the Department of Pharmaceutical Chemistry of the Faculty of "Pharmacy" at MU-Varna. By Order No. R-109-545/05.12.2023, she was dismissed with the right of defense for up to one year.

II. Brief description of the structure of the dissertation

The presented dissertation is written on 102 pages, of which 1 page introduction, 25 pages literature review, 1 page of purpose and tasks, 13 pages experimental part, 38 pages results and discussion, 1 page conclusions, 1 page contributions, 4 pages literature. The work includes 10 tables, 29 figures and 75 diagrams.

III. Relevance and dissertationability of the development

As is well known, iodine is an essential element involved in and ensures the functioning of the thyroid gland and a considerable number of metabolic reactions. In addition, it has a disinfecting and antiseptic effect, which is why it is widely used in medical practice. Its radioactive isotopes are used as radiopharmaceutical products for the treatment and diagnosis of a number of neoplastic diseases. One of the typical applications of organic iodine derivatives is their use as radiopaque agents. In this regard, the topic of the dissertation work developed by the doctoral student T. Dimova is relevant and dissertable, given the need to expand the number and spectrum of activities of aromatic iodine derivatives.

In this sense, the search for new derivatives with improved pharmacokinetic properties, reduced side effects and potential applicability in imaging diagnostics through targeted preparation of new iodine-containing organic compounds is fully justified.

IV. Critical analysis of the dissertation

The **literary review** (33 pages in total) is based on 148 literary sources in Latin. The literature review shows the doctoral student's good knowledge of the developed problem, it is written concisely and with understanding, but at the same time it is comprehensive and reflects the theoretical aspects of the synthesis and analysis of iodine-containing organic compounds. Due attention is given to the application of iodine and iodine-containing organic compounds and their characteristic pharmacological effects.

The **purpose** of the dissertation work, correctly determined by the literature review, is clearly and accurately stated. For its implementation, 5 specific **tasks** have been identified, formulated precisely and in a logical sequence.

Research methodology

In the section **Experimental part**, the doctoral student has presented a detailed description of the methods used in the present scientific work. The manner of their presentation shows that the dissertation work was developed through appropriately and correctly selected methods, allowing the achievement of the set goal and obtaining an adequate answer to the tasks solved in the dissertation work. Methodically well constructed synthetic, analytical (mainly spectral and crystallographic) experimental methods have been developed and applied.

The methodology does not give rise to doubt and is a prerequisite for obtaining the correct results discussed below.

Characterization and assessment of own research and contributions of the doctoral student

In the **"Results and Discussion"** part, ch. asst. Dimova describes in detail the obtained experimental results and, in parallel, presents their critical discussion.

Emphasis in the synthetic part of the doctoral work is optimization of the preparation of the haloarenes 2-iodo-3,4,5-trimethoxybenzoic acid (ITMBA), 3,4,5-trimethoxybenzoic acid (DITMBA) and 2-iodo-3,4,5- trimethoxy-benzaldehyde (ITMBD), as well as the preparation of two new haloarenes – 2-bromo-6-iodo-3,4,5-trimethoxybenzoic acid (BrITMBA) and 2-(2-iodo-3,4,5-trimethoxyphenyl) acetic acid (ITMPhAA). All compounds are structurally characterized correctly.

The scientific research of the doctoral student also has a practical focus related to the potential application of the sodium salt of 3,4,5-trimethoxybenzoic acid (DITMBA) in imaging diagnostics, showing perspective, given the fact that the indicators of the cited compound are close to those of the one used as referent contrast agent.

The **conclusions** (7 in number) are adequate and correctly reflect the results of the conducted research.

V. Assessment of the PhD student's publications and personal contributions

In connection with the dissertation, 4 (four) scientific publications have been published, of which 2 (two) in journals in refereed and indexed in world-renowned databases with scientific information and 2 (two) in peer-reviewed journals and not referenced in world-renowned databases with scientific information information, all related to the topic of the developed dissertation work, as in one of the publications ch. asst. Dimova is the lead author. There is no evidence that parts of the dissertation have been presented at national and international scientific forums. The doctoral student participated in a scientific project on the topic of the doctoral work at the "Science" Fund, MU-Varna. Based on the critical reading of the presented dissertation and related publications, it is clear that the formulated contributions and the obtained results are the personal work of the doctoral student.

With regard to these scientometric indicators, the doctoral student meets the requirements for awarding the educational and scientific degree "Doctor", laid down in the Rules of the MU -. Varna.

VI. Abstract

The abstract (total volume 59 pages) is made according to the requirements and accurately and sufficiently reflects the content of the dissertation work.

CONCLUSION

The dissertation is written in good scientific language, there are almost no typographical and grammatical errors in the text. In general, the dissertation concerns a topical topic from a theoretical point of view. The set goals and tasks were successfully completed, and the doctoral student mastered and used a number of modern synthetic and analytical methods.

The dissertation contains scientific-theoretical results that represent an original contribution to research on the spectral behavior of iodine-containing aromatic derivatives, as well as scientifically applied contributions. The contribution nature of the dissertation is in accordance with the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), the Rules for the Implementation of the LDASRB and the Rules of the MU - Varna. The presented materials and dissertation results correspond to the specific requirements adopted in connection with the Regulations of the MU - Varna for the application of the LDASRB.

The dissertation shows that the doctoral student chief assistant mag.-pharm. Tanya Nedelcheva Dimova possesses the necessary theoretical knowledge and professional skills and demonstrates qualities and skills for independent conduct of scientific research.

Given the above, I give my **positive assessment** of the conducted research, presented by the above-reviewed dissertation work, abstract, achieved results and contributions, and **I propose to the honorable scientific jury to award the educational and scientific degree "doctor"** to chief assistant mag.-pharm. Tanya Nedelcheva Dimova in a doctoral program in Pharmaceutical Chemistry.

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

Sofia.

01 February 2024

Reviewer:

(prof. Al. Zlatkov, Ph.D., DSc)