

REVIEWER STATEMENT

**on a doctoral thesis entitled:
“NEW COMPOUNDS AS PERSPECTIVE ANTITUBERCULAR AND ANTIVIRAL
AGENTS”,**

submitted for the scientific degree „**Doctor of Sciences**“ (DSc)
in Professional field 4.2 „Chemical Sciences” (Organic Chemistry),

Candidate: Assoc.Prof. Georgi Milchev Dobrikov, PhD
Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences

Reviewer: Assoc. Prof. Nikolay Iliev Georgiev, PhD
Department of Organic Synthesis, University of Chemical Technology and Metallurgy

General description of the presented materials

The documents presented by Assoc. Prof. Georgi Dobrikov with respect to the thesis defense procedure are in accordance with the Regulations for the Development of the Academic Staff of the Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences (IOCCP–BAS), and meet the criteria of the Institute for obtaining the degree of “Doctor of Sciences”. Assoc. Prof. Georgi Dobrikov has provided a Doctoral thesis in English, Abstracts in Bulgarian and English, 8 publications not included in the PhD thesis, as well as a list of 303 citations.

Biographical data

Georgi Milchev Dobrikov was graduated in 1998 from the Faculty of Chemistry and Pharmacy at Sofia University “St. Kliment Ohridski”, with a Master degree. He was appointed as a chemist in 1998 and received a Ph.D. degree in 2004 at the Institute of Organic Chemistry with Centre of Phytochemistry at the Bulgarian Academy of Sciences (IOCCP-BAS), where he held the positions of Assistant Professor (2004-2006), Chief Assistant Professor (2007-2016) and Associate Professor (2016). Since 2014, G. Dobrikov he was a participant in 8 scientific projects and was a project leader of 3 of these projects.

Aim of the dissertation

The research and results presented in the dissertation are dedicated in two main directions: the development of new compounds with potential antitubercular and antibacterial activity and development of new diaryl ethers and related compounds with anti-enteroviral activity. The aim of the present thesis was focused to the synthesis of novel compounds, with lowered cytotoxicity and improved pharmacological properties.

The following tasks have been set for the realization of the stated aim:

- Development of new derivatives of (*R*)-2-aminobutan-1-ol as antitubercular agents
- Development of new derivatives of (+)-camphor as antitubercular agents
- Development of new potent analogues of known antiviral agent MDL-860

Review of the dissertation and results

The dissertation is written in English and contains 181 pages, which include 33 figures, 29 schemes, 28 tables and 340 references. The abstract is presented in both Bulgarian and English, on 77 pages and contains the main results and contributions of the dissertation. The dissertation is structured in the following sections: title pages with a table of contents and notes and acknowledgements (3 pages), introduction (16 pages), aim and tasks (1 page), results and discussion (66 pages), experimental (71 pages), references (21 pages), conclusions and contributions (2 pages), appendix with lists of publications, participation in conferences and

projects (4 pages). The presented results are from the research work of the candidate for a 13-year period (2009-2022). After a literature review and analysis of the state of research in the respective fields, the author clearly formulated the aim and tasks of the dissertation. The "Results and discussion" section contains two main chapters: Development of new compounds with potent in vitro antitubercular and antibacterial activity and Development of new diaryl ethers and related compounds with anti-enteroviral activity. In these two chapters the dissertation describes synthesis of more than 300 organic compounds which is really impressive. The antitubercular activity of 6 series of the synthesized new compounds and antiviral activity of 137 new analogues of diarylether MDL-860 were also revealed. The conclusions and scientific contributions are clearly formulated.

Contributions

Contributions of the dissertation are related to the synthesis of new compounds with potential biologically active compounds in two main directions: I) antitubercular agents and II) antiviral agents. The contributions can be summarized in these areas as follows:

- New subclass analogues of classical antitubercular drug ethambutol was synthesized. Some of these analogues demonstrated higher activity and lower cytotoxicity, than ethambutol.
- New class of antitubercular drug-like molecules, bearing fenchane skeleton was synthesized.
- New class of antitubercular drug-like molecules, bearing camphane skeleton was synthesized, showing strong antitubercular and antibacterial activity.
- New drug-like nitrofuranoyl compounds were synthesized and their possible mechanism of strong antitubercular activity was investigated.
- Different new analogues of known diarylether MDL-860 were synthesized. Many of them demonstrated stronger activity toward 6 enteroviruses. Mechanism of action for MDL-860 was revealed.

The results presented in the thesis are published in 8 scientific papers in international research journals from the first two quartile in the respective field (4 in Q1 and 4 in Q2). The number of the noticed citations of the publications included in the dissertation is 24. In 5 of the 8 scientific publications the candidate is on the first placed or corresponding author. The results of the dissertation were reported to 26 scientific forums and were funded by 8 national and international research projects.

Abstract of dissertation

The abstract is in accordance with the dissertation and describes the main results of the research. It also includes a list of publications included in the dissertation, participation in conferences and a list of projects.

Conclusion

The doctoral thesis contains substantial and significant original fundamental and applied scientific contributions, which meet all the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for the implementation of the same Law and the corresponding Regulations of the IOCCP-BAS. The dissertation shows that Assoc. Prof. Georgi Dobrikov has in-depth theoretical knowledge and professional skills in the scientific specialty "Organic Chemistry" by demonstrating qualities and skills for conducting research in the interdisciplinary fields with original and significant scientific contributions.

Based on the above, I give my positive assessment of the research presented by the dissertation of Assoc. Prof. Georgi Dobrikov and with a great pleasure I recommend the Scientific Jury to award him the degree of "Doctor of Science" in the Professional field 4.2. "Chemical Sciences" (Organic Chemistry).

26 Sept. 2023

Sofia

Reviewer:

/Assoc. Prof. N. Georgiev, PhD/