

BRIEF REVIEW

by Prof. Vassya Stefanova Bankova, DSc,

Corresponding Member of the Bulgarian Academy of Sciences,
Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences

of the Doctoral Thesis presented for awarding the degree “**Doctor of Sciences**”
in the Field of higher education 4.0. "Natural Sciences", Professional Field 4.2.
"Chemical Sciences", scientific specialty „Organic Chemistry”

Author: Assoc. Prof. Dr. Georgi Milchev Dobrikov,
Institute of Organic Chemistry with Centre of Phytochemistry,
Bulgarian Academy of Sciences (IOCCP-BAS)

Topic: "New Compounds as Perspective Antitubercular and Antiviral Agents”

The materials presented by Assoc. Prof. Dobikov with respect to the procedure for the defense of the dissertation are in accordance with the Regulations for the Development of the Academic Staff of the IOCCP-BAS and meet the criteria of the IOCCP for the acquisition of the scientific degree "Doctor of Sciences". The candidate presents 8 scientific publications on the material included in the dissertation, as well as a list of 303 independent citations, which were not used for the competition for the acquisition of the degree of PhD. According to data from SCOPUS, its h-index is 11 (without self-citations).

Assoc. Prof. Dobikov's dissertation is dedicated to the preparation and study of the activity of new potential drug candidates with anti-tuberculosis action and ones with antiviral action against enteroviruses. Tuberculosis is one of the important socially significant infectious diseases, leading to millions of deaths in the world annual; and chemotherapy of viral diseases, among which poliomyelitis, meningitis, encephalitis, myocarditis and other serious diseases caused by enteroviruses is still far from the achievements in the field of antibacterial agents. This undoubtedly defines the topic of the dissertation as significant and relevant.

The literature review of the dissertation is relatively short, it is written concisely and clearly. Greater attention in it is rightly devoted to antiviral agents, clarifying the complexity of searching for substances with antiviral action. The review shows the excellent and in depth knowledge of the issue, includes 104 literature sources, of which about 30% were published after 2010. The literature data is critically examined, noting the gaps and unresolved issues in the preparation and research of the relevant bioactive substances. On this basis, the aim and tasks of the dissertation are formulated clearly and precisely.

The approach used by the candidate in selecting potentially bioactive series of structures to be synthesized, namely the combination in one molecule of two known pharmacophore groups (with subsequent variations) turns out to be very productive. 109 new compounds in the search for antituberculosis agents and 117 potentially antiviral new compounds were obtained. Two new classes of antituberculosis compounds have been synthesized: with a fenchane and a camphane skeleton.

The obtained numerous new compounds belong to a variety of structural types and in their synthesis the candidate has found the appropriate method and successfully solved the arising difficulties. This indicates an excellent knowledge of synthetic organic chemistry and an ability to apply it creatively. The structures of the obtained substances have been proven by modern spectral methods (MS, NMR, including two-dimensional methods), and in some cases by x-ray structural analysis. An important part of the research is the biological testing of the effect of the obtained compounds, in some cases QSAR studies have been performed. In the antibacterial tests, in addition to tuberculosis, other microorganisms - human pathogens - are used. Of particular interest is one of the representatives of the series of new camphor derivatives with a pyrimidine and an arylidene fragment in the molecule - this substance is not particularly active against tubercular bacteria, but

emerges as a broad-spectrum antibiotic, active against all tested bacteria and fungi at low concentrations. The discovery of the mechanism of action of the well-known antiviral drug, diarylester PI4KB, together with virologists deserves high praise.

A large number of promising bioactive compounds (so-called "hit compounds") have been discovered among the synthesized groups of substances. They are suitable for further drug development in subsequent preclinical phases. The dissertation contains original contributions that can be characterized as new to science and an extension of existing knowledge, as well as contributions with the potential for practical application. An important merit of the work is the indication of promising directions for future research.

I have no critical comments and recommendations for the dissertation, I have only one small remark - it is accepted in Bulgarian to say "karbamid", and somewhere in the work "urea" is used, somewhere else - " karbamid". It is good to use the Bulgarian name everywhere.

I have a question: Since (*S*)-2-amino-1-butanol derivatives are known to be more active, what drew your attention to (*R*)-2-amino-1-butanol derivatives?

The results presented in the dissertation have been published in 8 scientific articles. Of them, 4 are in the first quartile in the respective region (Q1), and 4 – in the second (Q2). The substantial personal contribution of Dr. Dobrikov in the presented publications is undoubted – he is the corresponding author in 5 of the 8 publications. I can also add my personal impressions of Assoc. Prof. Dobikov: I have known him for many years as a competent, inventive researcher with his own profile, and as a good and responsive colleague.

The autoreferate fully reflects the main results achieved in the dissertation.

CONCLUSION

Assoc. Prof. Dobrikov's dissertation contains significant and original scientific contributions in the field of organic chemistry, 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 volume and the undoubted high quality of the scientific contributions reflected in the dissertation, as well as the overall activity of the candidate as an internationally recognized scientist, give me the reason with deep conviction to vote positively for awarding Assoc. Dr. Georgi Dobikov the scientific degree "Doctor of Sciences" and to recommend to the Honorable Members of the Scientific Jury to vote likewise.

21.08.2023

Reviewer:

/prof. Vassya Bankova, DSc/