OPINION

by Petko Denev, PhD

professor in at the Institute of Organic Chemistry with Centre of Phytochemistry – BAS

on a dissertation for the award of the scientific degree "Doctor of Sciences" (DSc)

in the field of Higher education 4. Natural Sciences, Mathematics and Informatics,

Professional field 4.2 Chemical sciences (Organic chemistry)

Candidate: Assoc. Prof. Dr. Petko Ivanov Bozov

Title: "Clerodane diterpenoids from species of family *Lamiaceae*"

1. General presentation of the procedure and the candidate

By Order № P33-902/11.03.2021 of the Rector of the University of Plovdiv "Paisii Hilendarski" (PU) I was appointed as a member of the scientific jury of a dissertation entitled "Clerodane diterpenoids from species of family *Lamiaceae*" for the award of the scientific degree "Doctor of Sciences" (DSc) in the field of Higher education 4. Natural Sciences, Mathematics and Informatics, Professional field 4.2 Chemical sciences (Organic chemistry). Author of the dissertation is Petko Ivanov Bozov, PhD, who is associate professor at Department "Biochemistry and microbiology", Faculty of Biology, Plovdiv University (PU) "Paisii Hilendarski". The set of materials presented by Assoc. Prof. Petko Bozov, PhD is in accordance with Art. 45 (4) of the Regulations for development of the academic staff of PU. The applicant has applied 27 scientific articles in refereed journals and one article in a conference proceedings.

2. Actuality of the subject

The subject of research in the presented dissertation are clerodane diterpenoids in Bulgarian plant species of the genus *Scutellaria, Teucrium polium* subsp. *vincenti-num* L. (Rouy) D. Wood, *Teucrium scordium* subsp. *scordioides* (Schreb.) Maire et Petitmengin, *Salvia splendens* Ker.-Gawl. and *Salvia nemorosa* L. Research related to the identification of new molecules of plant species is interesting and relevant because it enriches the scientific knowledge of the phytochemical composition of plants and contributes to elucidating the biological effects of these species known from ethnopharmacology and folk medicine. On the other hand, such studies have significant social significance and applied potential, because most modern drugs are based on plant biologically active molecules or their analogues. Diterpenes are characterized by a wide variety of chemical structures,

and interest in their diverse biological activity is great. That is why I find the presented dissertation extremely interesting and topical in scientific terms.

3. Familiarity with the problem

From the content and structure of the literature review, it is evident that the applicant is deeply acquainted with the researched problem. The review presents detailed information on clerodane diterpenoids of the genera *Scutellaria*, *Teucrium polium* and *T. scordium*, as well as isolated polyphenols in species of the genus *Scutellaria*, and considers their classification, nomenclature, biosynthesis and biological activity. The skeletal substructures, the main functional groups, characteristic for the compounds, isolated from the species of the genus *Scutellaria* growing in Bulgaria are described. To develop the dissertation, assoc. prof. Bozov stepped on a very solid foundation of his own research on the topic of the dissertation, as well as those of the Department of Organic Chemistry at PU "Paisii Hilendarski" related to diterpenoids.

4. Research methodology

The methods used are reliable and allow the implementation of the research tasks. The use of a combination of classical phytochemical methods for extraction and purification of plant molecules, modern methods for their identification, and those for determination of biological activity makes an extremely good impression. The ability of assoc. prof. Bozov to use a combination of different spectral methods (infrared spectroscopy, mass spectrometry, proton nuclear magnetic resonance, carbon-13 magnetic nuclear resonance and two-dimensional NMR spectra) to determine the structure and stereochemistry of the studied compounds, as well as to interpret the obtained spectra is impressive.

5. Characteristics and evaluation of the dissertation

The presented dissertation is an in-depth study on the isolation, structure elucidation and biological activity of clerodane diterpenoids of the genus *Scutellaria, Teucrium polium* and *T. Scordium* It is distinguished by significant scientific and applied contributions. The applicant has conducted a detailed phytochemical analysis for the presence of clerodane diterpenoids in 15 Bulgarian plant species of 5 genera of the Lamiaceae family. 48 diterpenoids were isolated and spectrally characterized - one with a labdan skeleton, three with a 19-*nor*-clerodane skeleton and 44 *neo*-clerodane diterpenoids. There are 22 diterpenes with new structures for science: two with a 19-*nor*-clerodane skeleton and twenty with a neo-clerodane skeleton. Another 13 diterpenoids were detected for the first time in the studied species. The literature was enriched with a full set of 1D and 2D NMR spectra of isolated diterpenoids. As a result of the conducted researches, some published structures have been corrected. As an indicator of biological activity, the antifeedant activity of 43 clerodane diterpenoids

against Colorado potato beetle larvae, cytotoxic activity of 12 *neo*-clerodane diterpenoids against two cell lines of human lung carcinoma cells, as well as antimicrobial activity of 22 clerodane diterpens against twenty-one strains of microorganisms were studied.

6. Evaluation of the publications and the personal contribution of the candidate

The dissertation includes 27 scientific publications in refereed journals and one article in a conference proceedings. Eighteen of the referenced publications are with impact factor or impact rank. In most of the articles, assoc. prof. Bozov is either the first author or the author for correspondence, which testifies to his personal contribution to the elaboration of the experimental work on these publications, the analysis and interpretation of the results. There are some inaccuracies in the presentation of the impact factors of the journals. For example, the journal Bulgarian Chemical Communications does not have an impact rank after 2017, but only an impact rank.

7. Summary of the dissertation

The summary of the dissertation is standardly written and well reflects the essence of the dissertation, the results achieved and the most important conclusions and contributions.

8. Recommendations for future use of dissertation contributions and results

I have no significant critical remarks on the dissertation and the quality of the results obtained.

CONCLUSION

The dissertation presented by assoc. prof. Petko Ivanov Bozov, PhD is an in-depth study that contains scientific and applied results, which represent an original contribution to science and meet the requirements of the RIASDARB and RPUIASD. The presented materials and dissertation results correspond to the specific requirements of the Faculty of Biology, adopted in connection with the RIASDARB and RPUIASD. The dissertation shows that Assoc. Prof. Dr. Petko Ivanov Bozov has in-depth theoretical knowledge and professional skills in the scientific specialty Organic Chemistry, demonstrating qualities and skills for conducting research with original and significant scientific contributions. Due to the above, I give my positive assessment of the research presented in the dissertation, summary, results and contributions, and I propose to the esteemed scientific jury to award the scientific degree "Doctor of Science" to Assoc. Prof. Dr. Petko Ivanov Bozov in the field of higher education: 4. Natural Sciences, Mathematics and Informatics, professional field 4.2. Chemical Sciences (Organic chemistry)

26.04.2021 г. **Opinion prepared by**: .....

Prof. Petko Denev, PhD