

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, LDASRB, Decision of the Faculty Council of the Faculty of
"Pharmacy" at the MU - Varna and Rector's order No. P-109-545/05.12.2023 r.

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 aspects of the pharmaceutical analysis of quinine and some of its
oxidation products**"

Author: mag.-pharm. Ivalina Valerieva Vasileva, full-time doctoral student in the
"Pharmaceutical Chemistry" doctoral program, enrolled by order No.
R-109-391/09.10.2020 at the Department of Pharmaceutical Chemistry at the
Faculty of Pharmacy, MU - Varna.

Scientific supervisors: Assoc. Prof. Svetlana Georgieva, Ph.D.
Assoc. Prof. Iliyan Kolev, 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
- ✓ Order to change the topic of the dissertation work

The doctoral student has attached 2 (two) scientific publications related to the topic of the developed dissertation work, of which 1 (one) in a journal in refereed and indexed in world-renowned databases with scientific information and 1 (one) in a peer-reviewed journal and not referenced in world-renowned databases data with scientific information. One of the supervisors is not involved in the publications.

I have the following remark about the documents - the attached autobiography signed by the doctoral student contains scant information and does not allow to see her overall development. This prevents the reviewer from getting a full picture of the PhD student.

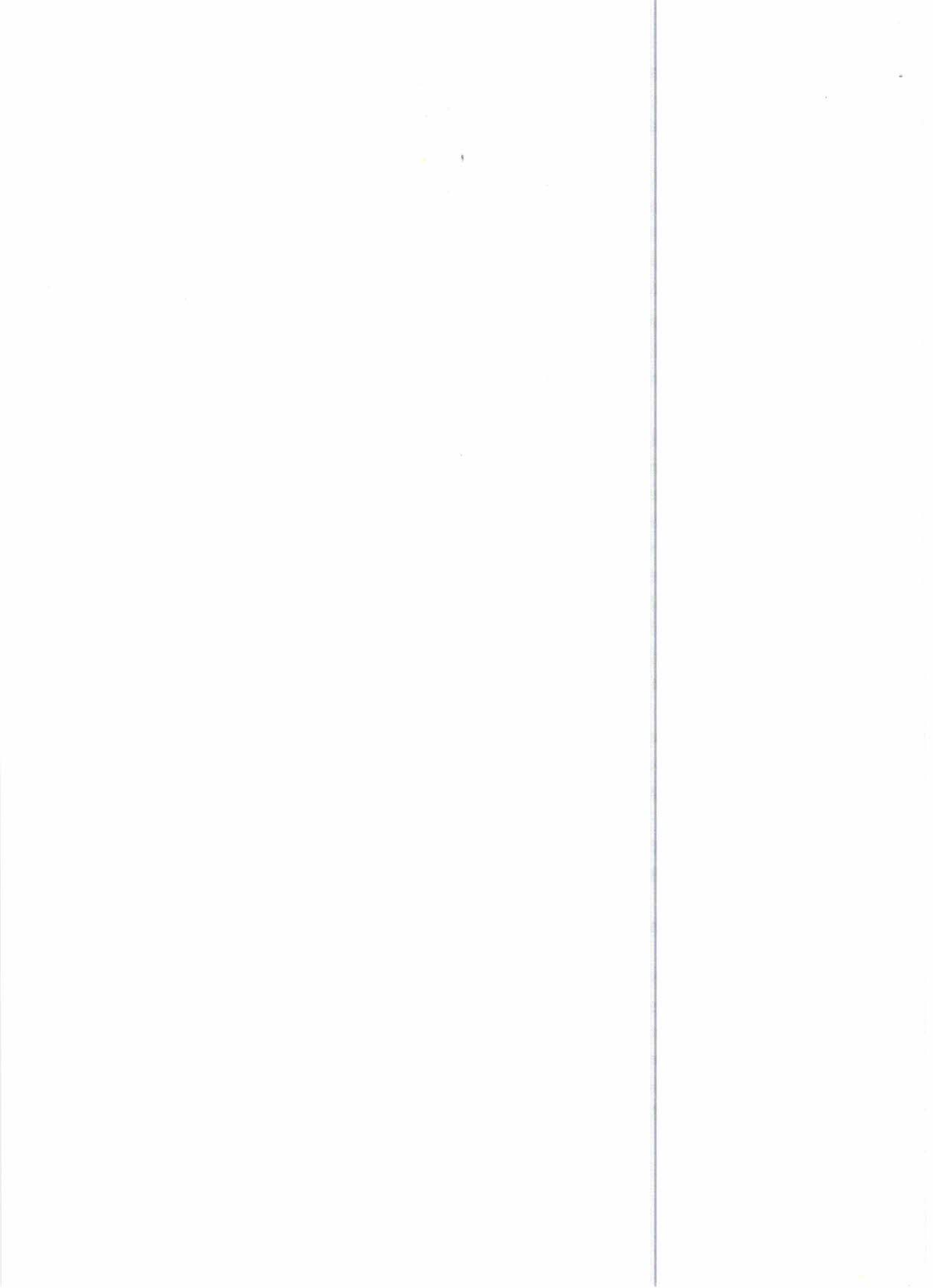
Ivalina Valerieva Vasileva graduated from the Medical College of the MU-Varna University and obtained the qualification of assistant pharmacist, as well as the Faculty of Pharmacy at the MU-Varna University and obtained the Master's degree (years not specified). By Order No. R-109-391/09.10.2020, she 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 research supervisor Assoc. Svetlana Georgieva, Ph.D. and Assoc. Iliyan Kolev, Ph.D. at the Department of Pharmaceutical Chemistry of the Faculty of "Pharmacy" at the University of 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 work has a total of 95 pages, of which 1 page of introduction, 28 pages of literature review, 1 page of purpose and tasks, 10 pages of experimental part, 38 pages of results and discussion, 1 page of conclusions, 1 page of contributions, 12 pages of literature. The work includes 4 tables (the last one is unnumbered), 42 diagrams and 24 figures.

III. Relevance and dissertationability of the development

The topic of the dissertation work developed by the PhD student I. Vasileva concerns various aspects in the analysis of the quinoline alkaloid quinine, which is a pharmacopoeia according to the European Pharmacopoeia. In this sense, the topic could be considered as relevant and dissertable. On the other hand, the targeted search for various analytical methods that can be applied to its derivatives would expand the knowledge related to the properties of quinolines.



IV. Critical analysis of the dissertation

The **literature review** (28 pages in total) is based on 159 literary sources. It shows the doctoral student's good knowledge of the developed problem, it is written with understanding, but at the same time it is thorough and reflects the theoretical foundations of the analysis of quinoline alkaloids and their semi-synthetic derivatives in general. However, the question arises as to why quinine was chosen as the subject of research, given that, despite being a pharmacopoeia, quinine and its derivatives are of increasingly limited use. The latter is evident from the quinine preparations listed at the end of the literature review, the majority of which are from the end of the 19th and the beginning of the 20th century.

The **purpose** of the dissertation, determined by the literature review, is clearly stated. For its implementation, 5 specific **tasks** have been formulated.

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. The methodology does not raise doubts and is a prerequisite for obtaining the results discussed below.

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

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

The dissertation offers developments on several analytical procedures: use of the oxidation potential of sulfur melted together with the analyzed substance; preparation of phenothiazine dye; the so-called herapatite test; chemiluminescent method based on a process of reduction of Ce(IV) to Ce(III) ions accompanied by the release of electromagnetic radiation; as well as investigation of sorption behavior of quinine-imprinted quartz-crystal microbalance towards (+)- and (-)-carvone. However, I did not find an explanation why carvone is used, and I would like the doctoral student to give more explanations on this matter. There is considerable theoretical potential in the research done in this way, but I personally doubt their practical applicability in analytical practice. Everywhere the dissertation talks about a putative reaction path, I did not find convincing evidence for the structure of the resulting compounds, for example, the phenothiazine dye.

No doubt, herapatite is a very interesting compound showing dichroic properties similar to tourmaline, but what applicability can be expected from this test for the qualitative analysis of quinoline alkaloids when, in the words of the doctoral student,



"the expected analytical result is realized smoothly, within a relatively short period of time (one hour)"? More interesting is the obtaining of a "red insoluble product" in the words of the dissertation, which is assumed to most likely represent a molecular complex of the introduced alkaloid with iodine. It has been suggested but not proven, and proof of its structure and/or composition would have been a significant contribution.

The **conclusions** (5 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, 2 (two) scientific publications have been published related to the topic of the developed dissertation work, of which 1 (one) in a journal in refereed and indexed world-famous databases with scientific information and 1 (one) in a peer-reviewed journal and unreferenced in world-renowned databases of scientific information. There is no evidence that parts of the dissertation have been presented at national and international scientific forums. Based on the critical reading of the presented dissertation and related publications, it is clear that the obtained results are largely the personal work of the doctoral student.

With regard to these scientometric indicators, the dissertation student meets the requirements for awarding the educational and scientific degree "Doctor", laid down in the Rules of the MU - Varna. The doctoral student does not submit a reference for citation of the presented scientific publications.

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.

VII. Critical remarks and recommendations

As I noted above, the claim of easy adaptability and applicability in qualitative analysis of the proposed analytical methods at this stage is too bold. I agree, however, that theoretically there is rationality in them, although there is a degree of self-servingness in theoretical research.

I have a question as follows:

Which of the proposed methods can certainly be claimed to be specific for quinine and structurally similar quinoline compounds?



CONCLUSION

The dissertation is written in relatively 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 synthetic and analytical methods.

The dissertation mainly contains scientific and theoretical results, which represent an original contribution to the research of the properties of quinine and its structural analogues and meet the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), the Regulations for the Implementation of LDASRB and the Regulations 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 it can be assumed that the doctoral student mag.-pharm. Ivalina Valerieva Vasileva has acquired theoretical knowledge and professional skills for independent conduct of scientific research.

In view of 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 mag.-pharm. Ivalina Valerieva Vasileva in a PhD program in Pharmaceutical Chemistry.

София.

21 February 2024

Reviewer:

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

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

