Appendix 12a

REVIEW

of dissertation for the acquisition of:

educational and scientific degree " **doctor** "	X
scientific degree **"Doctor of Science"**	
	the true is indicated by the sign "X"

Author of the dissertation:

	Eng.	Maria	Tsvetanova	Mondeshka	
academic position	scientific degree	name	middle name	last name	workplace

Topic of the dissertation:

Combined methods for separation and concentration of extracts from natural raw materials using bio-based solvents

Scientific area:

5.	Technical Sciences
code	name

Professional area:

5.10.	Chemical Technologies
code	name

Scientific specialty:

Processes and Apparatuses in Chemical and Biochemical Technology

The review was written by:

Professor	D.Sc.	George	Angelov	Nickolov	Bulg. Acad. Sci'
academic position	scientific degree	name	middle name	last name	workplace

1. Completion of the provided documents:

A) The dissertation and the competition documents are in full compliance with the Regulations.	4 points	**X**
B) The documents are not completed in accordance with the requirements of the Regulations.	0 points	

		one of the answers given is marked with the sign "X"

Missing documents and violated standards must be described if response C is marked.

2. Meeting the minimum requirements under the Regulations:

A) The candidate meets the minimum requirements	20 points	X
B) The candidate doesn't meet the minimum requirements	0 points	
		one of the answers given is marked with the sign "X"

It must be filled in if answer B is marked. The publication activity of the candidate is analyzed. The response of the results achieved (quoted) is analyzed.

3. The relevance of the topic of the dissertation:

A) The topic is relevant and new (there are no known results on the topic by other authors)	8 points	
B) The topic is relevant and results from other authors are known	6 points	X
C) The topic is not relevant, but results from other authors are known	2 points	
D) The topic is not relevant and no results from other authors are known	1 point	
E) The topic does not correspond to the level of dissertation	0 points	
		one of the answers given is marked with the sign "X"

The evaluation of the relevance of the dissertation must be substantiated
The topic of the dissertation demonstrates a high degree of relevance and contemporary significance. On the one hand, the research focuses on natural extracts from medicinal plants, which constitutes an established and dynamically developing scientific field of increasing importance for both fundamental science and practical applications. On the other hand, the dissertation employs innovative approaches involving the use of non-conventional (bio)solvents, thereby contributing to the expansion of the range of valuable natural products. The results obtained make a valuable contribution to elucidating the potential for production and for pharmacological application of these products in accordance with their bioactive properties.

4. Knowledge of the problems, subject of research in the dissertation:

A) The doctoral student knows in detail the achievements of other authors on the topic of the dissertation	8 points	X
B) The doctoral student is partially familiar with the achieved results on the topic of the dissertation	4 points	
C) The doctoral student has no prior knowledge of the status of the problems in the dissertation	0 points	
		one of the answers given is marked with the sign "X"

The evaluation must be substantiated if answer C is marked.

5. Type of research:

A) Theoretical	4 points	
B) Applied	4 points	
C) Theoretical with application elements	4 points	X
D) It does not correspond to the level of dissertation	0 points	
		one of the answers given is marked with the sign "X"

The level of research must be substantiated if answer D is marked.

6. Objectives of the research:

A) Realistic and of scientific and / or applied interest	8 points	X
B) Realistic, but not of scientific and / or applied interest	3 points	
C) Unattainable (unrealistic)	0 points	
		one of the answers given is marked with the sign "X"

Objectives must be specified. The type of the set objectives must be justified.
The dissertation aims to develop an extended methodology for obtaining high-quality and safe extracts with medicinal properties that comply with pharmacopoeial requirements and standards, through the use of both conventional and non-conventional environmentally friendly solvents and the application of intensified extraction techniques. This objective is of scientific interest due to its comprehensive approach to the problem of obtaining valuable substances and expanding the range of applicable extractants. At the

same time, the nature of the resulting products and their orientation toward phytopharmaceutical formulations determine the applied relevance of the stated objectives.

7.Methods of research:

A) Adequate to research and set objectives	8 points	X
B) Partially appropriate, enabling part of the scientific objectives and / or applications to be achieved	4 points	
C) Inappropriate methods	0 points	
		one of the answers given is marked with the sign "X"

Methods must be specified. The type of methods used is justified.
A diverse set of methods, varying in type and purpose, has been applied: Granulometry – for classifying the raw material according to particle size; Gravimetric methods – for determining moisture content, yields, and liquid density; Classical extraction methods – serving as a basis for comparison; Methods for influencing the system, such as stirring, temperature control, etc., in order to assess their impact; Application of ultrasound and analysis of its effect for process intensification, with the aim of increasing yields or reducing processing time; Kinetic study methods – for monitoring the development of the process over time; Optimization methods – for determining the most appropriate process parameters; UV and IR spectroscopy – for the analysis of solid, liquid, and oily fractions; Colorimetric cytotoxicity assay – for evaluating the potential harmful effects of the extracts. The methods employed are essential for the implementation of the research, have been applied appropriately, and contribute to the successful achievement of the stated objectives.

8. Contributions of the dissertation:

A) With lasting scientific and / or applied response, they form the basis for new research and applications	20 points	
B) They are of significant scientific and / or applied interest, complete and / or summarize previous research	16 points	X
C) They are of scientific and / or applied interest	12 points	
D) Lack of significant contributions	8 points	
E) Lack of contributions	0 points	
		one of the answers given is marked with the sign "X"

Contributions must be specified. The type of results achieved must be justified.

Only the most significant contributions of this research are highlighted below.

The principal scientific contribution lies in the proposed methodology for preliminary screening and selection of solvents based on Hansen solubility parameters. In contrast to the conventional approach relying primarily on molecular polarity, this methodology evaluates molecular structure, intra- and intermolecular interactions, as well as the affinity between solvents and solutes. This approach broadens the range of potential solvents, enables more rigorous selection based on selectivity, and allows the replacement of traditional organic extractants with more environmentally friendly solvents.

A Bulgarian raw material has been thoroughly investigated, and the necessary conditions for its collection, sorting, and blending have been established with a view to meeting international pharmacopoeial standards. Non-conventional, environmentally friendly oleum extractants have been investigated. The processes have been optimized with respect to key parameters such as temperature, hydromodule, granulometry, and extraction time. Extracts with medicinal properties suitable for direct application have been obtained without the need for solvent removal, thereby eliminating one technological step.

Through kinetic studies, the suitability of a two-parameter model for describing the process dynamics under real conditions of heterogeneous, polydisperse granulometry has been established.

The investigation of ultrasonic treatment has identified mechanisms contributing to process intensification, namely increased yield and reduced contact time, achieved under mild, low-temperature conditions.

With a view to practical application, the cytotoxicity of the newly obtained extracts has been evaluated, confirming their safety.

The obtained results are of both scientific and applied significance and are characterized by high quality and reliability.

9. Evaluation of the compliance of the dissertation summary with the dissertation:

A) Full compliance	4 points	X
B) Compliance of the main parts	2 points	
C) Lack of compliance of the main parts	0 points	
		one of the answers given is marked with the sign "X"

The evaluation must be substantiated if answer C is marked.

10. Participation of the doctoral student in the achievement of the results of the dissertation:

A) The doctoral student has at least an equal participation	8 points	X
B) The doctoral student has secondary participation	5 points	
C) The participation of the doctoral student is unnoticeable	0 points	
		one of the answers given is marked with the sign "X"

Critical notes must be provided if one of the items B or C is marked.

11. Critical notes:

A) Lack of critical notes	8 points	
B) Critical notes of a technical nature	7 points	X
C) Critical notes that would partially improve the results achieved	4 points	
D) Significant critical notes	0 points	
		one of the answers given is marked with the sign "X"

Critical notes must be provided if one of the answers C or D is marked.

12. Conclusion

A) The evaluation of the dissertation is **POSITIVE**	This evaluation is assigned to a total number of at least 65 points	X (93 p.)
B) The evaluation of the dissertation is **NEGATIVE**	This evaluation is assigned to a total number below 65 points	
		one of the answers given is marked with the sign "X"

To be filled in at the request of the reviewer
The dissertation is impressive in terms of the volume of work performed and the scope of the results obtained. Evidence of the relevance of the topic is also provided by the literature review, which is very comprehensive and includes more than 170 references, predominantly from recent years.

The doctoral candidate demonstrates a detailed knowledge of previous research, as well as an in-depth understanding of mass transfer mechanisms in solid–liquid systems and the influence of process parameters on them.

With regard to the discussion of the influence of raw material granulometry, it should be noted that, on the one hand, the increase in interfacial surface area due to particle size reduction has a positive effect on mass transfer; on the other hand, technological limitations may arise from excessive comminution, such as clogging of process openings, difficulties in filtration, or impeded penetration and wetting in fixed-bed extraction. While these limitations can be overcome in stirred systems, granulometry generally requires optimization depending on the specific technology and equipment used.

A comprehensive study of the content of active compounds in the raw material has been conducted under a wide range of conditions: different plant parts, different locations, different harvests, various stages of development, as well as storage and processing conditions, with the aim of determining the state in which the raw material exhibits maximum content of active components.

A significant contribution is the investigation of vegetable oils as extractants and the application of the Hansen approach in such systems. Oils are considered environmentally friendly solvents, and in the case of oil extracts, the technology is simplified due to the absence of a solvent removal step. Emphasis is placed on the theoretical approach to evaluating the ability of oils to exhibit selectivity toward specific functional groups.

Hansen analysis has led to the important conclusion that oils are broader-spectrum solvents than hexane; they exhibit extraction properties comparable to a number of conventional solvents such as dichloromethane, chloroform, and diethyl ether, and can replace them as safer extractants.

Kinetic studies have identified conditions under which the processes can be described by a single-parameter model; however, in the more common case of polydisperse raw materials, the use of a two-parameter model is required, corresponding to the fast and slow process stages and to a variable effective diffusion coefficient.

The analytical proficiency of the doctoral candidate is also at a high level. A variety of necessary and appropriate analytical methods have been employed, yielding reliable results. A thorough understanding of the complex mechanisms of interaction and structural transformations, as well as their identification through spectrometric methods, is demonstrated.

For part of the studies involving external energy input for process intensification, ultrasonic treatment has been selected. This is an appropriate choice due to the absence of significant thermal effects, efficient energy utilization at low temperatures, safety of the method, and its applicability in fixed-bed extraction systems where mechanical stirring is not feasible. Suitable operating conditions for maximizing yield have been established, and the mechanisms of ultrasonic action on both the plant matrix and the solvent have been correctly discussed.

Through an optimization procedure, an appropriate set of process parameters has been determined, ensuring conditions for maximum yield of the target extract.

A stepwise extraction scheme has been developed, enabling separation and selective extraction of components with different functional groups and bioactivity.

A conclusion of practical importance is the finding that the quality of the Bulgarian raw material used meets existing international pharmacopoeial requirements.

I also note the very good linguistic and grammatical proficiency of the doctoral candidate. The dissertation is written clearly and coherently, with logical connections between its individual parts.

Some technical remarks:
The inclusion of common (trivial) names of the herbs alongside their Latin names would make the text more accessible to a non-specialist audience.
It should be noted that, in my opinion, one publication and one poster presentation listed among the author's outputs, dealing with nanofiltration of extracts, are not directly related to the dissertation, and their results are not included in it.
I also observe some incompleteness in the list of conference presentations and posters, as the institutional and town locations of the scientific events are not indicated.

Conclusion:
The presented work constitutes a comprehensive and well-developed study with both scientific and applied contributions. In the course of this research, the doctoral candidate has acquired in-depth knowledge of mass transfer mechanisms and the interactions between plant matrices and solvents. In addition, the candidate has gained experience with a wide range of extraction and analytical techniques. The educational component of the doctoral program has thus been successfully fulfilled. The personal experimental work and the application of various specific methods and laboratory procedures have contributed to the candidate's advanced qualification in scientific research practice. Through this dissertation and its results, the full set of requirements for awarding the Doctoral degree has been met, and I recommend that the PhD degree be conferred upon the candidate.

	The review was written by:	
Date 31.03.2026	**Prof. DSc. George Angelov Nickolov**	Signature