

REVIEW

By Prof. Dr. Rumen Pavlov Nikolov, MD
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Member of a scientific jury (order of the Rector of the University of Medicine - Plovdiv No. R-983/19.04.2023 in connection with the procedure for the defense of a dissertation on the topic "EXPERIMENTAL PHARMACOLOGICAL STUDY OF SIDERITIS SCARDICA EXTRACT, LAMIACEAE" by Master Pharmacist Nikolai Yanchev, full-time doctoral student in a doctoral program in pharmacology (incl. pharmacokinetics and chemotherapy) at the Department of Pharmacology and Clinical Pharmacology at the Faculty of Medicine, Medical University - Plovdiv, professional direction "7.1. Medicine" and field of higher education 7. Health and sports". Scientific supervisor of the doctoral student: Assoc. Prof. Dr. Delyan Delev, PhD. Scientific consultant: Assoc. Prof. Dr. Ilia Kostadinov, PhD.

All documents in accordance with the requirements of the Regulations for the conditions and procedures for acquiring scientific degrees and holding academic positions at the Medical University - Plovdiv were provided to me.

Master Pharmacist Nikolai Yanchev has successfully passed the required exams: doctoral minimum (pharmacology) and doctoral school.

Biographical data

Master Pharmacist Nikolay Yanchev completed his secondary education in 2007 at the Language School - Plovdiv. He obtained a master's degree in pharmacy from the Free University - Berlin, Germany in 2014. He works as a

pharmacist in public pharmacies in the city of Berlin. Since 2022, he has been working as a health communication and drug information expert.

Dr. Yanchev is fluent in written and spoken German and English. Has very good computer skills with basic office programs and statistics.

Assessment of the submitted dissertation

Structure of the dissertation

Presented dissertation contains 151 pages and is illustrated with 46 figures, 39 tables and one appendix. 303 literary sources in Latin are cited in the dissertation.

The scientific work is properly structured in the following sections: introduction - 2 pages, literature review - 30 pages, summarizing conclusion - 1 page, goal and tasks - 1 page, scientific idea and working hypothesis - 1 page, materials and methods – 11 pages, results – 27 pages, discussion – 18 pages, conclusion – 1 page, conclusions – 1 page, contributions – 1 page, appendix with a list of publications and participations related to the dissertation work – 15 pages, and bibliography – 30 pages.

Relevance of the dissertation topic

The dissertation is competently and comprehensively written. The topic of the dissertation is dedicated to a current problem related to the study of the toxicity and some pharmacological effects (anti-inflammatory, anxiolytic and neuroprotective) of a dry extract of *Sideritis scardica* (popularly known as Greek mountain tea, mursal tea, or pyrrhic tea).

The present study represents the first systematic pharmacological study of this species endemic to Bulgaria.

The presence of polyphenols such as ferulic acid, chlorogenic acid and apigenin in *Sideritis scardica* ("mountain tea") is most likely responsible for the

effects on mood and cognition, which is due to the ability of certain polyphenols such as hydroxy-cinnamic acids and flavonoids to prevent the opposite uptake of monoamine neurotransmitters and to increase cerebral blood flow.

Gastroprotective and anti-inflammatory effects of mountain tea extract have been reported in the literature, as well as a correlation between antioxidant activity and phenolic content of mountain tea extracts.

Literature review

The literature review is competently written and includes contemporary sources related to the topic of this dissertation. The literature review presents data on the distribution and botanical characterization of *Sideritis scardica*, the content of active principles in the aerial part of mountain tea, the established pharmacological effects of active substances in mountain tea extracts, experimental models of chronic stress, models of cognitive deficits and neurodegenerative changes. The review concludes with a general conclusion and conclusions from the literature review. Research over the past decade has focused interest on the neuroprotective and anti-stress effects of dry mountain tea extracts.

The literature review shows that the doctoral student is thoroughly familiar with the issues related to the dissertation work, incl., and the latest studies in this direction.

Purpose and tasks of the study

The purpose of the study is precisely and clearly formulated. The tasks for its implementation are well defined, specific and correspond to the set goal.

The aim of the dissertation is to carry out a systematic study of the toxicity and various pharmacological effects of Mursal tea extract (*Sideritis scardica*) - anti-inflammatory, anxiolytic and neuroprotective.

To achieve this goal, mag. Pharm. Nikolay Yanchev has set himself 7 tasks that are well formulated and exactly correspond to the set goal.

Materials and methods

The experimental studies were carried out on male Wistar rats. Experimental models of cold and chronic stress and models of acute inflammation induced by injection of carrageenan or lipopolysaccharide have been established.

Phytochemical analysis, acute and subchronic toxicity research methods, antioxidant activity assessment methods, pharmacological tests for behavioral and memory research (e.g., cross-maze test, social interaction test, forced swimming test, recognition of the location of objects, a test for the study of spatial orientation and working memory, methods of active learning and methods of passive learning of experimental animals), laboratory, histological, immunological, and statistical methods.

The methodical approach is modern and sufficient to fulfill the set goals and tasks.

Results

The results of the conducted experimental studies are in-depth and illustrated in detail.

The data obtained from the toxicological study of a dry extract of mountain tea did not establish mortality in the experimental animals after administration of an extract of *Sideritis scardica* in doses up to 5000 mg/kg. In the study of subchronic toxicity after treatment of experimental animals with the extract for 12 weeks, no pathological changes were found in histological studies, as well as disorders in hematological and biochemical parameters.

Experiments on cold and chronic stress models found a reduction in alertness after mountain tea extract administration, as well as an improvement in

short-term and long-term memory in behavioral tests in a scopolamine- and diazepam-induced amnesia model by mountain tea extract administration. Administration of mountain tea extract reduced hind paw edema in a rat carrageenan model of acute inflammation and significant anti-inflammatory activity with systemic injection of lipopolysaccharide.

Conclusions and scientific contributions

The main conclusions reached by the doctoral student are 7 and represent a logical sequence of the in-depth and competent analysis of the obtained results.

There are 6 contributions in the dissertation, which are divided into two groups: with scientific-theoretical significance (3) and with scientific-practical significance (3). The scientific contributions have significant theoretical and methodological value, as well as potential clinical-applied significance of the effects of mountain tea studied in the dissertation work.

Scientometric indicators related to the dissertation work

In connection with his dissertation, M.Sc. Pharm. Nikolay Yanchev has presented a list of 6 publications, 1 of which is in a journal with IF. He is the first author in all the publications presented.

Master Pharmacist Nikolay Yanchev has presented a list of 6 participations in congresses and conferences.

Doctoral Thesis

The doctoral thesis contains 54 pages, 35 figures and 6 tables. The attached abstract adequately reflects the main content of the dissertation and the results obtained.

Recommendations and critical remarks: I recommend the doctoral student to continue his publication activity related to the dissertation topic.

Conclusion

The dissertation contains scientific, scientific-applied, and applied results, which represent an original contribution to science and meet all the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (ZRASRB), the Regulations for the Implementation of ZRASRB and the Regulations of the Medical University of Plovdiv. The presented materials and dissertation results fully correspond to the specific requirements adopted in connection with the Regulations of the Medical University - Plovdiv for the application of the ZRASRB.

I believe that the presented dissertation work is well designed, impressing the use of adequately selected experimental methods and excellent implementation of the set goals and tasks, which is confirmed by the results obtained.

Based on the detailed positive aspects of the dissertation submitted to me for review, I strongly recommend to the respected members of the scientific jury to vote positively for awarding the educational and scientific degree "Doctor" in the doctoral program in pharmacology (incl. pharmacokinetics and chemotherapy) to Master Pharmacist Nikolay Borisov Yanchev.

05/14/2023

Prepared the review:

/Prof. Dr. Rumen Nikolov, PhD/

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