

OPINION

by Associate professor Diana Ilieva Pendicheva-Duhlena, MD, PhD
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Regarding: A dissertation for awarding the educational and scientific degree "Doctor" in the field of higher education 7. Health care and sports, professional direction 7.1. Medicine, doctoral program "Pharmacology (incl. Pharmacokinetics and Chemotherapy)"

Author: Elis Rafailova Gasanzadeeva

Form of doctoral studies: Full-time

Department: "Pharmacology and Clinical Pharmacology and Therapy", Medical University "Prof. Dr. Paraskev Stoyanov" – Varna

Title: "Pharmacological studies with anethole in an experimental model of obesity"

Scientific supervisor: Prof. Stefka Vasileva Valcheva-Kuzmanova, MD, PhD, DSc, MU-Varna

By Order No. R-109-168/22.05.2024 of the Rector of Medical University "Prof. Dr. Paraskev Stoyanov" – Varna, I have been appointed as a member of the Scientific Jury under the procedure for acquiring the educational and scientific degree "Doctor" by Elis Rafailova Gasanzadeeva, MD. At the first non-attendance Meeting of the Scientific Jury (Protocol No. 1/31.05.2024) I was appointed to prepare an opinion regarding the candidate's dissertation work.

General presentation of the procedure

All documents and materials provided in electronic and print formats are in accordance with the requirements laid down in the Law on the Development of the Academic Staff in the Republic of Bulgaria (DASRBA), the Regulations for the Application of DASRBA and the Section III, art.69 of the Regulations for the Development of the Academic staff at the Medical University – Varna. The order and conditions of the procedure for the acquisition of the ESD "Doctor" in MU-Varna have been observed and comply with the current normative documents. I declare that I have no conflict of interest with the candidate.

Brief biographical data and professional development

Dr. Elis Rafailova Gasanzadeeva was born in Shumen on March 15, 1993. She graduated with a Master's of Medicine (MD) from the Medical University "Prof. Dr Paraskev Stoyanov-Varna" in 2018. During her studies, she participated in practical training under the "Student Practices" project in the Endoscopy Office (March-July 2014) and the First Surgery Clinic

(June-October 2017) in St. Anna Medical Center – Varna. In 2018, she was a student demonstrator in practical training in Pharmacology of medical students at MU-Varna during her studies. From January to March 2019, Dr. Gasanzadeeva worked as a physician in the Department of Medical Oncology at the University Hospital "Deva Maria", Burgas. During March-October 2019, she was a part-time assistant in the Department of "Pharmacology and Clinical Pharmacology and Therapy" at the MU-Varna. After a successful competition in October 2019, she was appointed and has been working as a full-time assistant in the same department until now. She is involved in practical teaching in Pharmacology for students of medicine and dentistry and Clinical pharmacology for students in medicine in Bulgarian and English programs. Dr. Gasanzadeeva is fluent in English and Russian. From 24.07 to 04.08.2023, she conducted a short-term specialization at Ovidius University, Constanta, Romania. She was trained in the "Protection and Humane Treatment of Experimental Animals Used for Scientific or Educational Purposes" course. She is a member of the Bulgarian Society of Pharmacology, Clinical Pharmacology and Therapy and the European Association of Clinical Pharmacology and Therapeutics (EACPT). Dr. Gasanzadeeva was enrolled as a full-time doctoral student at the Department of Pharmacology and Clinical Pharmacology and Therapy at MU-Varna by Order No. P-109-450/28.10.2020 of the Rector of MU-Varna, with a scientific supervisor – Prof. Stefka Valcheva-Kuzmanova, MD, PhD, DSc. She was dismissed with the right of defense by order No.P-109-168/22.05.2024 of the Rector of MU-Varna.

Relevance of the dissertation

Obesity is a heterogeneous and multifactorial metabolic disease associated with a serious risk of developing chronic cardiovascular and other diseases and a leading cause of disability and mortality worldwide. In the therapy, control and prevention of obesity, non-medicinal, medicinal and surgical approaches are applied with varying degrees of efficacy and long-term maintenance of the clinical outcomes. Regardless of the efforts of researchers and specialists, definitive success in the overall disease control of the various risk profiles has not yet been achieved, which determines the importance of scientific research in this direction. The search for new plant sources and expanded investigation of already known biologically active substances of natural origin with potential beneficial effects on the consequences of obesity continues to be within the scope of scientific interests regarding the expected health benefits and preventing the disease. Dr. Gasanzadeeva's dissertation is focused on an experimental study of the plant monoterpene anethole (Sigma-Aldrich, Germany) administered orally in increasing doses to rats in a model of obesity induced by a high-calorie diet, for which there is insufficient data in the literature to date. Innovative is the approach to following the effects of anethole on motor activity and spatial memory in the applied experimental models. In support of the significance of the problem are the international awards of the doctoral student for her investigations on the influence of anethole on lipid peroxidation and spatial memory in rats on a high-calorie diet.

Dissertation structure

The dissertation presented by Dr. Elis Gasanzadeeva consists of 157 standard pages and is designed according to the accepted requirements for obtaining the ESD "Doctor". The text is well distributed and structured in the following sections: Abbreviations used – 1 page, Content – 6 pages, Introduction – 2 pages, Literature review – 33 pages, Aim and objectives – 2 pages, Materials and methods – 9 pages, Own results and discussion – 72 pages, Conclusions – 4 pages, Contributions – 1 page, List of publications and scientific forum participations related to the dissertation – 4 pages and Bibliography – 23 pages. The bibliography includes 311 literary sources, of which 309 are in English, and two are in Bulgarian. The dissertation is illustrated with 40 figures and 27 tables.

Literature review

The detailed literature review shows the author's good awareness of chronology and contemporary aspects of research on the dissertation topic. In the three parts of the review, known-to-date problems, risks and methods of obesity treatment, main physicochemical and pharmacological characteristics of anethole, and the experimental methods and models for induction of obesity have been presented consistently and logically. Two figures illustrated obesity according to body mass index and the chemical structure of anethole. Textual emphasis is understandably placed on the nature, synthesis, effects and inclusion in foods and phytopreparations of monoterpenes and essential oils of natural origin. The literature analysis strongly emphasizes the need for expanded studies of anethole in experimental models of obesity.

Aim and tasks

The dissertation aim is clearly and precisely formulated – to investigate and summarize the pharmacological effects of anethole administered orally in increasing doses in rats in a model of obesity induced by a high-calorie diet. The tasks adequately serve the aim and are divided into two groups, which include induction of obesity in healthy experimental animals through a high-calorie diet and study of the effects of anethole on physical, behavioral, biochemical and laboratory indicators, histological changes, deviations in tissue indices and immunohistochemical markers..

Materials and methods

The materials and methods are described in detail and appropriately selected to implement the set tasks. The origin of the experimental animals is declared, and the standard conditions for their rearing are described. It is guaranteed that the experiments will be conducted by national and international laws and policies based on the EU Directive on the protection of animals used for science (Directive 2010/63/EU) and with ethical approval by the Bulgarian Food Safety Agency (Document No. 177/07.07.2017). A wide range of classical and modern

methods was used, which is understandable given the need for additional and new research on the subject. The statistical analysis of the results is adequately selected and described.

Results and discussion

The results are original scientific and applied developments declared by the author and meet the set tasks. Seven main groups of effects of anethole are presented: on body weight, calorie and fluid intake; on behavior in a four-test model of obesity; on biochemical and laboratory indicators (metabolism, antioxidant protection and oxidative stress); on adipose tissue (adipose tissue indices, histology and immunohistochemistry of retroperitoneal adipose tissue); on myocardium and coronary vessels; on liver; on carrageenan-induced hind paw edema. Of interest are the observations regarding the effects of high doses of anethole on spatial memory, symptoms of anxiety and depression, eating behavior, total caloric intake, and visceral adiposity. The results are illustrated with 27 tables and 38 figures. The discussion follows the presentation of the results by groups and is not summarized in a separate section.

Conclusions and contributions

Based on the results obtained, two main conclusions are drawn, separated, and described in detail in subsections. The conclusions fully correspond to the tasks set. Six original contributions are formulated and substantiated regarding the effects of anethole in rats in an experimental model of diet-induced obesity, with a reported increase in food consumption, fluid and caloric intake, reduction of anxiety, improvement of spatial memory, improvement of glucose tolerance, suppression of brain lipid peroxidation, antagonizing effect on high-calorie diet-induced adipocyte enlargement; increase in the proapoptotic phenotype in retroperitoneal adipose tissue and the liver and decreased expression of the inflammatory marker MAC387 in the liver.

Publications and participation in scientific events

Dr. Gasanzadeeva presented a list of five publications related to the dissertation, in which she is the lead author. She participated in 11 national scientific forums and presented three scientific developments at ECNP congresses in Vienna, Austria (2022) and Barcelona, Spain (2023). It is impressive that she has been awarded a doctoral student award from the Scientific and Practical Conference "Faculty of Pharmacy – 15 years of traditions, innovations and perspectives" on 20-21 October 2023 in Varna, and two international awards for excellence (Excellence award) at ECNP congresses. The articles published in connection with the dissertation meet the quantitative criteria for publication activity of the doctoral students specified in the current normative documents.

Abstract

The abstract is 100 pages long, structured according to the requirements, and fully corresponds to the content of the dissertation.

Conclusion

The PhD thesis of Dr. Elis Gasanzadeeva "Pharmacological studies with anethole in an experimental model of obesity" is up-to-date and interesting, with an original creative character and scientific applied contributions. The scientific indicators correspond to the requirements for awarding the ESD "Doctor" laid down in the DASRBA, the Regulations for the Application of the DASRBA and the Regulations for the Development of the Academic Staff at the Medical University – Varna.

Based on the above, I give my positive assessment of the candidate and suggest that the respected members of the scientific jury vote positively for awarding the educational and scientific degree "Doctor" in the field of higher education 7. Health care and sports, professional direction 7.1. Medicine, doctoral program "Pharmacology (incl. Pharmacokinetics and Chemotherapy)" to Dr. Elis Rafailova Gasanzadeeva

26.06.2024 г.
Pleven

Prepared by:



/Assoc. prof. Diana Pendicheva-Duhlenska, MD, PhD./