

Statement

Of Pavlina Gateva, MD, PhD

Department of Pharmacology and Toxicology, Medical University of Sofia

Concerning the procedure of thesis defense

Of Zlatina Petrova Nenchovska

With the title: Study of the effects of hormone melatonin on behavioral and biochemical changes accompanying epileptogenesis in the kainate model of temporal lobe epilepsy

Scientific specialty: Pharmacology (including pharmacokinetics and pharmacotherapy) code 03.01.24

Scientific supervisor: prof. Yana Tchekalarova

The Thesis which is presented for evaluation is written on 132 pages A4 format. It is well structured.

In the introduction, which is written on three pages, the main topic of the Thesis is described. The temporal lobe epilepsy (TLE), is the most common form of pharmacoresistant epilepsy. The impact of the kainate model of TLE is discussed as widely used in experimental practice.

The review of the literature is written on 26 pages and demonstrates that the PhD-student knows very well the problematics. She mentions a general definition of the well-known mechanisms of the seizures as a prerequisite for subsequent pharmacological treatment. A brief description is made of the existing models of TLE, and the choice of young-adult rats is justified. The PhD-student analyzes the link among epilepsy, the plasticity of the hippocampus, oxidative stress and arterial hypertension. The second part of the review of the literature examines melatonin in detail. It presupposes the hypothesis of the PhD-student about its role in epilepsy. The paragraph for agomelatine is not necessary because the PhD-student does not present any results with agomelatine. The review of the literature logically reaches to the formulation of the scientific hypothesis of the Thesis.

The aim and tasks of the Thesis are clearly stated.

Methods which were used by the PhD-student are explained in 13 pages. There is a declaration about the respect of the ethics during the experiments with animals. The PhD-student attempts to present the intricate design of the experiments in the Thesis

schematically. Both Wistar and SHR strains were used. EEG and video records are analyzed. A broad spectrum of behavioral tests as performed. Remarkably, they were executed twice – at 3 p.m. and 3 a.m. Histology, biochemistry, and statistics are also presented.

Own results are described in 48 pages and 29 figures with an exhaustive explanation. In the label of the fig. 4.9.4.1 it is written “hsp70” which seems to be a mistake (instead of “hsp72”). This figure is missing in the Summary of Thesis.

The discussion comprises 12 pages, and its structure is composed as a comparison of the effects of melatonin in Wistar vs. SHR.

The PhD-student draws seven conclusions about the species-specific effects of the chronical application of pharmacological doses of melatonin. The findings are well formulated allowing to project further experiments, i.e., for testing the link between the seizure frequency and oxidative stress; neuroprotective effects of melatonin under different conditions; the role of the serotonergic system and others.

The self-assessment for the merits of the Thesis is correct, and I am accepting it.


The Thesis-related achievements are published in 5 articles. Three of the publications are with IF. In two of the papers, the PhD-student is the first author. **The score of the PhD-student resulting from her articles is 37 points, and this is satisfying the legal requirement for PhD-achievement.** There are no additional requirements from the BAS regulations 2018 concerning the scientific staff promotion.

A long list is applied with the participation of the scientific forums. The PhD-student declares two awards she was received as an outstanding young scientist. Additionally, a one-year bursary she was obtained from the International Federation of Scientists. A travel grant for participation in a workshop from the European College of neuropsychopharmacology was also received.

The bibliography of the Thesis comprises 256 papers, four of them from Bulgarian teams.

The Summary of Thesis correctly reflects the containing of the Thesis.

The PhD-student is a biologist by education. She is working in the Institute of Neurobiology of BAS since 2010. Since 2011 she is an assistant, and since 2013 she is a PhD-student in the same institute. As a result of many years of working in the institute, the PhD-student succeeded to develop her skills to handle the complicated experimental tasks. Also, she was developed her sense of acquiring new scientific knowledge. The mission of the Thesis preparing is indeed accomplished. I recommend, and I am convinced to vote for the assignment of the scientific and educational title “doctor” of Zlatina Petrova Nenčovska.


N. Tazebek
04.09.2019 r