
Bydgoszcz, July 21, 2022.

EVALUATION OF DOCTORAL DISSERTATION

by **Sinemyiz Atalay Ekiner**

entitled *Protective Effects of Cannabidiol on Skin Keratinocytes in an Oxidative Microcellular Environment Induced by UVA/B Radiation or Exposure to Hydrogen Peroxide*

written under the direction of Prof. Elżbieta Skrzydlewska, Ph.D. (supervisor), Faculty of Pharmacy, Medical University of Białystok, Poland

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The doctoral dissertation presented for evaluation focuses on the evaluation of the effects of cannabidiol (CBD) on skin keratinocytes in an oxidative microenvironment induced by UVA/UVB or exposure to hydrogen peroxide.

The dissertation proper is presented in the form of five publications. All those papers have been assigned by the Polish Ministry of Education and Sciences to the pharmaceutical sciences category, and the Doctoral Student is listed as the first author in them. It is evident from the documentation presented and the attached statements that the Doctoral Student had a leading role in the research which informed the dissertation. The first of these publications is a review paper, the others are original (research) papers:

1. Antioxidative and anti-inflammatory properties of cannabidiol. Atalay S., Jarocka-Karpowicz I., Skrzydlewska E. *Antioxidants*, 2020, 9, 21.
2. Cannabidiol protects keratinocyte cell membranes following exposure to UVB and hydrogen peroxide. Atalay S., Dobrzynska I., Gęgotek A., Skrzydlewska E. *Redox Biology*; 2020, 36, 101613.
3. Protective effects of cannabidiol on the membrane proteins of skin keratinocytes exposed to hydrogen peroxide via participation in the proteostasis network. Atalay S., Gęgotek A., Domingues P., Skrzydlewska E. *Redox Biology*, 2021, 46, 102074.
4. Protective effects of cannabidiol on the membrane proteome of UVB-irradiated keratinocytes. Atalay S., Gęgotek A., Skrzydlewska E. *Antioxidants* 2021, 10, 402.

5. Therapeutic application of cannabidiol on UVA and UVB irradiated rat skin. A proteomic study. Atalay S., Gęgotek A., Wroński A., Domigues P., Skrzydlewska E. . *Journal of Pharmaceutical and Biomedical Analysis* 2021, 192, 113656.

I would like to mention that due to the extensive research and the fact that the papers included in the dissertation have already been published and are available to those interested, I will not describe them in detail. Instead, I will focus on the achievements of Sinemyiz Atalay Ekiner, M.D. and will refer to the main objective she set for herself. The main objective of the dissertation was to evaluate the effect of CBD on cellular metabolism related to redox homeostasis in relation to changes in the phospholipid and protein profile of the cell membrane of keratinocytes under UV or hydrogen peroxide-induced oxidative microenvironment. The Doctoral Student studied the effect of CBD under two scenarios – where CBD was administered only after exposure to stressors and where CBD was administered both before and after exposure to stressors. In the first publication, the Doctoral Student summarized the biological effects of CBD and its natural and synthetic derivatives. She paid particular attention to the antioxidant and anti-inflammatory effects of CBD and its derivatives, having regard to the potential for using CBD to protect against oxidative stress and the consequences associated with oxidative modifications of proteins and lipids [1]. It should be emphasized that this publication is a good introduction to the subject matter the doctoral dissertation deals with. It also testifies to Sinemyiz Atalay Ekiner's very good theoretical preparation for her experimental work, which she presented in four subsequent publications. In three of those papers, she presented the results of research conducted on human keratinocyte cell lines (CCD 1102 KERTr, American type Culture Collection, Virginia, USA). In the fifth paper, she presented the results of studies conducted on nude rats (RH-FOXN1RNU). At the first stage of her experimental work, she evaluated the effect of CBD on the structure and function of cell membranes of keratinocytes exposed to oxidative stress. She used UVB radiation and hydrogen peroxide as physical and chemical agents [2]. In a subsequent publication, she reported on the outcome of CBD's protective effect on the proteome of membranes of keratinocytes exposed to hydrogen peroxide [3]. In her next publication, the Doctoral Student evaluated the effects of short-term (24 hours) and long-term (48 hours) CBD application on the proteomic profile of biological membranes in keratinocytes exposed to UVB [4]. The final stage of the research presented in the doctoral dissertation was the analysis of the proteomic profile of keratinocytes in the skin of nude rats exposed to chronic UVA or UVB irradiation and the application of cannabidiol treatment [5]. Noteworthy is not only the consistent theme of the research, reflected

in the title of the dissertation, but also the state-of-the-art research technique employed by the Doctoral Student.

Studies conducted by Sinemyiz Atalay Ekiner have shown that CBD prevents the overproduction of reactive oxygen species (ROS) and lipid peroxidation products and their adducts with proteins. They also showed that administration of CBD before and after exposure to the stressors tested yields better protective results than administration after exposure alone. The results suggest that CBD can be used as a compound to protect skin cells from damaging effects of oxidative stress induced by skin exposure to harmful hydrogen peroxide or UV radiation.

After carefully reviewing the entire dissertation, I conclude that the dissertation was written properly and represents an original achievement of Sinemyiz Atalay Ekiner, M.D., contributing new relevant data to the subject matter of the research concerned. The purpose of the dissertation was clearly specified, the experiments were correctly planned and executed. What deserves to be emphasized is the sound research technique employed by the Doctoral Student. The discussion of the results is balanced, supported by the results of the experiments and the current literature, which clearly demonstrates very good preparation of the Candidate seeking a doctoral degree in the discipline of pharmaceutical sciences. The fact that the research results have been published in internationally recognized peer-reviewed specialized journals clearly confirms this.

Considering the above, I conclude that the doctoral dissertation submitted for evaluation by Sinemyiz Atalay Ekiner entitled *Protective Effects of Cannabidiol on Skin Keratinocytes in an Oxidative Microcellular Environment Induced by UVA/B radiation or Exposure to Hydrogen Peroxide* satisfies the statutory requirements to be met by dissertations for the degree of Doctor of Pharmaceutical Sciences. Therefore, I move that the High College of Pharmaceutical Sciences of the Medical University of Białystok should admit Sinemyiz Atalay Ekiner, M.D. to further stages of the doctoral degree conferment procedure. At the same time, given the high overall rating of the dissertation, its topicality and relevance of the subject matter it deals with, I request that it be awarded a distinction.

Kierownik
Katedry Biofarmacji

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