

**REVIEW**

**by Assoc. Dr. Delyan Delev, PhD**

**Head of the Department of Pharmacology and Clinical Pharmacology,**

**Faculty of Medicine, MU - Plovdiv**

of a dissertation for awarding the educational and scientific degree '**doctor**'

professional direction 7. *Health care and sports; 7.1. Medicine*

Doctoral Program "*Physiology*"

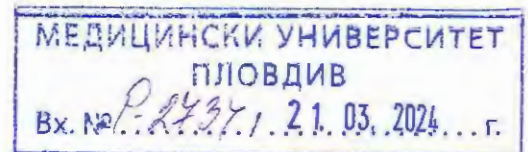
**Author** : Dr. Veselin Atanasov Vassilev

**Form of doctoral studies:** self-study basis

**Department:** Physiology

**Topic** : EFFECT OF SELECTIVE ANDROGEN RECEPTOR MODULATORS (SARM) ON PHYSICAL WORK CAPACITY AND SOME SIDE EFFECTS IN AN EXPERIMENTAL MODEL

**Research supervisor** : *Prof. Dr. Nikolay Boyadzhiev, MD, PhD*



**1. General presentation of the procedure and the doctoral student**

The presented set of materials on paper / electronic media is in accordance with Art. 70 ( 1 ) of I. Section. Acquisition of educational and scientific degree "DOCTOR" and scientific degree "DOCTOR OF SCIENCES" at MU-Plovdiv; Regulations of MU-Plovdiv dated 28.01.2021 and includes the following documents:

- Application to the Rector of MU-Plovdiv for disclosure of the procedure for the defense of a dissertation work
- curriculum vitae in European format with the doctoral student's signature
- a notarized copy of a higher education diploma
- orders for enrollment in doctoral studies, interruption of studies (due to maternity) and for continuation of studies; for deduction with right of defense
- order for conducting an exam from the individual plan and corresponding protocol for a passed exam or doctoral minimum in the specialty
- minutes of the departmental council for the preliminary discussion of the pre-dissertation work and the decisions made for the disclosure of the procedure and for the composition of the scientific jury
- dissertation work
- abstract
- list of scientific publications on the topic of the dissertation
- copies of scientific publications
- list of participations in scientific forums
- list of noticed citations
- declaration of originality and authenticity of the attached documents
- other documents related to the course of the procedure

The PhD student has attached 5 publications .

**I have no** notes or comments on the documents .

## **2. Brief biographical data of the PhD student**

Dr. Veselin Atanasov Vasilev was born on 06/04/1993. He graduated from the Language High School - "Plovdiv" in 2012. In the period 2012 - 2018, he studied at the Medical University - Plovdiv and acquired the qualification "Master degree in Medicine". Since 22.01.2019, he is an assistant in the Department of Physiology of MU-Plovdiv. He acquired a specialty in the discipline in 2023. He was enrolled in a doctoral course of independent preparation according to order P-425/27.02.2023 of the Rector. Successfully passed the candidate's minimum exam following the order of the Rector of MU-Plovdiv R-№1831/28.06.2023. with an overall score of Excellent (5.50). It was registered with the right of defense P-№3595/06.12.2023.

## **3. Actuality of the topic and appropriateness of the set goals and tasks**

The topic of the presented dissertation is relevant for specialists in various fields such as medicine, sports and public health. The data presented will significantly enrich the knowledge about the effects of SARMs. Some adverse effects of the mentioned group of substances are also reported. Non-steroidal SARMs are widely available online, typically used in doses many times higher than those used in various clinical trials. Abuse of them puts the health of their users at risk. There are data on positive doping samples and punishments resulting from their use, as well as data on their induced toxicity in various body systems. The obtained results can be used to improve public health, upgrade knowledge about SARMs as candidate therapeutics that could improve the therapeutic process and quality of life in a number of socially significant diseases. The reported data could also serve professional athletes with the aim of more carefully selecting the nutritional supplements used and avoiding the presence of SARMs in them.

## **4. Knowing the problem**

From the documents presented to me, incl. project for a dissertation and abstract shows that the doctoral student knows the state of the problem in detail and creatively evaluates the literary material. The literature review is up-to-date, contains 256 sources and is extremely well selected.

## **5. Research methodology**

The chosen research methodology allows fully achieving the set goal and obtaining an adequate answer to the tasks solved in the dissertation work . The aim of the dissertation work is to investigate the isolated effects and the combined action of two main factors: administration of a non-steroidal

representative of SARM (ostarine or liandrol) and systemic submaximal training, on physical work capacity and different body systems, in rats.

In order to achieve the goal, clear tasks have been set that examine its implementation:

To investigate the effects of selective androgen receptor modulators on endurance, maximal sprint speed and VO<sub>2</sub>max.

To investigate the effects of selective androgen receptor modulators on some markers of muscle oxidative capacity and carbohydrate metabolism.

To investigate the effects of SARMS on lipid profile and gene expression in m. gastrocnemius.

To study the adverse effects of selective androgen receptor modulators.

To investigate changes in the concentration of hormones – LH, FSH and testosterone in response to systemic submaximal training combined with SARMS intake.

Statistical methods are appropriately chosen for this type of study.

## **6. Characterization and evaluation of the dissertation work**

The dissertation contains 174 pages and is illustrated with 90 figures and 53 tables. follows a classical structure and is composed as follows: List of abbreviations (1 page); Introduction (1 page); Literature review (29 pages); Purpose and tasks (1 page); Material and methods (9 pages); Results and Discussion (93 pages); Conclusions (2 pages) ; Statement of contributions (1 page); Bibliography (32 pages); Scientific publications related to the topic and participation in scientific forums related to the topic (2 pages).

Two experiments were conducted with a total of 80 rats to perform the tasks. Each of the experiments included 4 groups of 10 animals reared in individual metabolic cells. The allocation of groups made by the doctoral student was appropriate because in each experiment there was a training and a non-training group receiving an active substance, as well as a training and a non-training group treated with a placebo. Body weight and food consumption of the rats were monitored weekly. Dr. Veselin Vasilev has researched different groups of indicators to achieve the goal. Appropriate authorities were selected for the purposes of the study. The methods used by the doctoral student are modern and suitable for the implementation of the tasks. Survey data were processed using appropriate statistical methods. As a result of the conducted experiments, Dr. Vesselin Vasilev makes some important conclusions that reflect the results obtained:

The 8-week intake of ostarine significantly increased the concentration of total cholesterol in the blood plasma.

Treatment with ostarine does not cause significant changes in the concentration of gonadotropic hormones and testosterone.

It found a decrease in glucose plasma concentration in animals receiving ostarine.



Administration of ostarine decreases submaximal endurance but does not alter maximal oxygen consumption.

The administration of ostarine does not change the number of different types of blood cells as well as the hemoglobin concentration.

Ostarin treatment increased myostatin gene expression in m. gastrocnemius.

A two-month intake of ligandrol increases the plasma concentration of triglycerides.

Administration of ligandrol decreased maximal oxygen consumption but did not affect maximal sprint speed.

Both of the non-steroidal SARMs used increase the time spent in sleep.

Treatment with ligandrol increased the grip strength of the rats but did not change the maximal time to exhaustion.

Dr. Vassilev also found a decrease in follicle-stimulating hormone induced by taking ligandrol. The results are presented correctly, in the form of graphs and tables. The discussion is correctly presented and reflects the results of the doctoral student in the light of modern literary sources on the problem.

## **7. Contributions and significance of the development for science and practice**

The dissertation work has a contributing character, as the conclusions from its implementation will significantly enrich the knowledge about the effects of non-steroidal SARMs on adaptation changes in the body during systematic endurance training. The paper presents, for the first time, the effects of nonsteroidal androgen receptor modulators on maximal oxygen consumption, running economy, maximal sprint speed, submaximal endurance, and maximal exhaustion time in rats. Specific effects on carbohydrate metabolism, lipid profile, on muscle gene expression, on indices of muscle oxidative capacity, on basic hematological parameters and some hormonal parameters are also reported.

The results of the development of the topic "Influence of selective androgen receptor modulators (SARM) on physical work capacity and some side effects in an experimental model" will bring theoretical and practical contributions to specialists in various fields such as medicine, sports and public health.

In conclusion, Dr. Vassilev formulated 5 scientific contributions, namely:

1. For the first time, the effects of non-steroidal AR modulators are being investigated on the indicators of physical work capacity - MCC, SMI,  $VO_{2\max}$ , MVI, in training and non-training rats.

2. For the first time it was found that non-steroidal SARMs reduce submaximal endurance in conditions of submaximal training, do not affect MVI and MCC, but may have cross-directional effects regarding  $VO_{2\max}$ .
3. Some adverse effects of nonsteroidal SARMs have been reported on the lipid and hormonal profile of rats.
4. Effects of non-steroidal AR modulators have been established on carbohydrate metabolism and gene expression of myostatin, VEGF-A, IGF-1 in m. gastrocnemius.
5. An effect of non-steroidal SARMs was found on sleep duration in trained and non-trained rats.

### **8. Evaluation of publications on the dissertation work**

The doctoral student presents 5 publications, of which: one in a journal with an Impact factor, 2 referenced in internationally recognized databases (Scopus, WoS) and 2 in refereed journals. They are all in English. He is the first author of 3 of them, and equal co-author of the others, which speaks of the personal participation of the doctoral student in the conducted dissertation research and proves that the formulated contributions and obtained results are his personal merit. Dr. Vassilev also participated in 5 scientific forums related to the topic of the dissertation, 4 abroad and one in Bulgaria.

### **9. Personal participation of the doctoral student**

The presented materials undoubtedly show the personal participation of the doctoral student in the conducted dissertation research, as well as that the formulated contributions and obtained results are his personal merit.

### **10. Abstract**

The abstract contains 55 pages, is illustrated with 30 figures and 14 tables, is made according to the requirements of the relevant regulations and reflects the main results achieved in the dissertation.

### **11. Critical remarks and recommendations**

critical remarks and recommendations to the conducted research and set of materials.

### **12. Personal impressions**

Dr. Vasilev is an ambitious young scientist and teacher, dedicated to his profession with high knowledge of the discipline "Physiology".

### **13. Recommendations for future use of dissertation contributions and results**

I recommend Dr. Vassilev to continue and further develop his scientific research in this interesting field.

## CONCLUSION

The dissertation *contains scientific, scientific-applied and applied results, which represent an original contribution to science* fully meets the requirements of the Act on Development of the Academic Staff in the Republic of Bulgaria (ADASRB), the Regulations for its implementation and the Regulations of the Medical University of Plovdiv. The presented materials and dissertation results fully correspond to the specific requirements regarding the Regulations of the Medical University of Plovdiv for implementation of the ADASRB.

The dissertation shows that the doctoral student Dr. Veselin Atanasov Vassilev **possesses** in-depth theoretical knowledge and professional skills in the scientific specialty of Physiology, **demonstrating** qualities and skills for independent conduct of scientific research.

I confidently **give my positive assessment** of the research, presented by the above peer-reviewed dissertation, author's abstract, obtained results and scientific contributions, and would recommend to the honorable members of the scientific jury to award the educational and scientific degree "Doctor" to Dr. Veselin Atanasov Vassilev in the doctoral program in "Physiology", professional direction 7. Health and sports; 7.1. Medicine.

18.03. 2024

Reviewer: 

Associate Professor Delyan Penev Delev, Ph.D

Заличено на основание  
Чл.5 §1, б. "В" Регламент (ЕС)2016/679