International Science Group

ISG-KONF.COM

THEORY, SCIENCE AND PRACTICE

III

SCIENTIFIC AND PRACTICAL CONFERENCE

05-08 October

Tokyo, Japan

DOI 10.46299/ISG.2020.II.III

ISBN 978-1-64945-868-1

THEORY, SCIENCE AND PRACTICE

Abstracts of III International Scientific and Practical Conference

Tokyo, Japan
October 05-08, 2020

Library of Congress Cataloging-in-Publication Data

UDC 01.1
The III th International scientific and practical conference «Theory, science and practice» (October 05-08, 2020). Tokyo, Japan 2020. 450 p.

ISBN - 978-1-64945-868-1
DOI - 10.46299/ISG.2020.II.III

EDITORIAL BOARD

EXPERIMENTAL STUDY OF POSSIBLE MECHANISMS OF 1,3-OXAZOLE-4-YL-PHOSPHONIC ACID DERIVATIVE ANTIHYPERTENSIVE PROPERTIES

Nizhenkovska Iryna,
MD, PhD, professor,
head of the pharmaceutical, biological and toxicological chemistry department of
Bogomolets National Medical University

Matskevych Kateryna
PhD,
ass.professor of the pharmaceutical, biological and toxicological chemistry
department of
Bogomolets National Medical University

One of the most common diseases of the cardiovascular system is arterial hypertension (AH). According to official WHO statistics, hypertension has affected approximately 1.1 billion people worldwide, while the disease causes the death of more than 9 million people annually [1]. There are many genetic and other factors which determine the further increase in the prevalence of pathology in our time [2]. Despite the presence of a significant arsenal of drugs, modern antihypertensive pharmacotherapy has a number of disadvantages, the main of which are: polypragmatism and reluctance of patients to adhere to complex treatment regimens, the presence of resistant forms of hypertension, short-acting antihypertensive drugs, the phenomenon of morning increase in blood pressure (morning "pharmacological deficit"), irrational combination of antihypertensive drugs, uncontrolled consumption of antihypertensive drugs with nonsteroidal anti-inflammatory drugs, etc. [3]. Given the lack of efficacy and unsatisfactory tolerability of antihypertensive drugs, resulting in low motivation of patients to treat, the study of new compounds capable of antihypertensive effects is an important area of modern pharmacological science and pharmacy.

One of the promising groups of compounds which are able to reduce vascular tone are phosphorylated oxazole derivatives. Previously, we studied the safety of this group and identified the antihypertensive effect of the leader compound OVP-1 in models of acute and persistent hypertension in animals, and confirmed the mediation of vasodilating action of OVP-1 by nitric oxide system [4].

The aim of the study was to investigate the possible mechanisms of antihypertensive action of the compound-leader of phosphorylated oxazole derivatives OVP-1 due to the effect on phosphodiesterase activity and calcium ion content in the model of stable hypertension in rats.

Materials and methods. The study was performed on Wistar rats. Stable AH was

modeled by saline drinking 1% NaCl solution for 21 days [5]. Determination of phosphodiesterase (PDE) activity was performed by fluorimetric method on a fluorometer RF-510 ("Shimadzu", Japan) using umbelliferon, determination of calcium ions was performed using a biochemical analyzer Biochem SA ("HTI", USA) in blood aorta and myocardium of rats.

Results. Because the antihypertensive activity of OVP-1 may be related to its effect on the synthesis of vasodilating factor cGMP, which is also affected by the signaling action of NO, we investigated the effect of the oxazole derivative on the change in the activity of its regulator, the PDE enzyme. In rats with saline hypertension, PDE activity was increased by 73.4% ($P < 0.05$) in the aorta, by 61.1% ($P < 0.05$) in the heart and by 34.8% ($P < 0.05$)) in the serum in relation to the intact group of animals. Under the influence of OVP-1 at a dose of 25 mg / kg (ED_{50}) was observed a decrease in the studied parameter in the aorta by 24.5% ($P < 0,05$), in the myocardium - by 22,7% ($P < 0,05$), in serum - by 14.6% ($P < 0.05$) compared with the group of control pathology rats. The established data may indicate the possibility of implementing the vasodilating effect of OVP-1 by influencing the latter to increase the synthesis of cGMP due to inhibition of PDE activity.

In view of the results obtained, it was advisable to continue to study the mechanism of antihypertensive action of the oxazole derivative associated with the regulation of Ca^{2+} ions in the aorta and serum, the increase of which may lead to the activation of Ca-dependent PDE. It was found that under the influence of OVP-1 25 mg/kg Ca^{2+} content decreased by 47.3% ($P < 0.05$) in the aorta and 59.5% ($P < 0.05$) in the serum compared with the control pathology group, which may indicate the participation of calcium-mediated component in the mechanism of vasodilating action of oxazole derivative, in particular by reducing the activity of Ca-dependent PDE, that can stimulate the hydrolysis of cAMP and cGMP, resulting in increased sensitivity of myofilaments to calcium and vasoconstriction [6].

Conclusions. The obtained results of experimental studies could indicate that the mechanism of antihypertensive action of OVP-1 is mediated by the effect on the guanylate cyclase system (reduction of phosphodiesterase activity by 24.5% ($P < 0.05$) and reduction of Ca^{2+} content by 47.3% ($P < 0.05$) in the aortic wall). These results are the basis for further in-depth preclinical and clinical studies to develop a new original antihypertensive drug for preventing the development and treatment of hypertension.

Literature:

1. URL: https://www.who.int/cardiovascular_diseases/publications/global_brief_hypertension/en/

2. Bouchy A., Weatherald J., Savale L., et al. Risk assessment, prognosis and guideline implementation in pulmonary arterial hypertension. European Respiratory Journal Aug. 2017. 50 (2). 1700889.

3. Whelton PK, Carey RM, Aronow WS, et al. ACC/AHA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults. Hypertension. 2018. 71: e-13-e115.

4. Nizhenkovska I., Sedko K., Golovchenko O. I., Golovchenko O. V. Efficiency of the application of the 1.3-oxazole-4-il-phosphonic acid derivative on the sustained arterial hypertension model in rats. Current Topics in Pharmacology. 2018. №22. P. 63-68.

5. Badyal D.K. Animal models of hypertension and effect of drugs. Indian Journal of pharmacology. 2003. 35 (6). P. 349-362.

6. Fan P., Ning C., Shenghui X, et al. Calcium intake, calcium homeostasis and health. Food Science and Human Wellness. 2016. 5 (1). P. 8-16.