



INTERNATIONAL CONFERENCE

PROCESS MANAGEMENT AND SCIENTIFIC DEVELOPMENTS



Birmingham
United Kingdom



International Conference “Process Management and Scientific Developments”

Birmingham, United Kingdom
(Novotel Birmingham Centre, November 14, 2019)



Materials of the International Conference
"Process Management and Scientific Developments"
(Birmingham, United Kingdom, November 14, 2019)

M67

ISBN 978-5-905695-67-4

These Conference Proceedings combine materials of the conference – research papers and thesis reports of scientific workers. They examines technical and sociological issues of research issues. Some articles deal with theoretical and methodological approaches and principles of research questions of personality professionalization.

Authors are responsible for the accuracy of cited publications, facts, figures, quotations, statistics, proper names and other information.

UDC 330

ISBN 978-5-905695-67-4 ©Scientific publishing house Infinity, 2019
©Group of authors, 2019

CONTENTS

ECONOMICS

Legislation unification on registration of scientific discovers and intellectual properties as a reserve for economic growth of countries which are participated in “New Silk Road of Innovations”

Balashova Mariia Alexandrovna, Popova Julia Sergeevna.....9

Marketing risks of the digital economy

Chernyakov Mikhail Konstantinovich, Akberov Kamal Cholu-ogly,

Chernyakova Maria Mikhailovna.....18

Quality indicators of innovative products in the light industry

Humbatov Yusuf Abulfat, Nasibova Ayshan Viladdin, Mammadov Seymur Ceyhun.....26

JURISPRUDENCE

Forecasting the effectiveness of the penal system

Terekhin Valery Ilyich, Chernyshov Victor Valentinovich.....32

Appointment of judges in the Russian Federation

Kurchenko Viacheslav Nikolaevich.....43

Lawmaking Specificity in the Common Law System

Petrova Ekaterina Alexeevna.....53

The Institutionalization of Social Demands as an Instrument of the Law State

Smirnova Marina Gennad'evna.....62

Compliance with reasonable time limits in criminal proceedings

Senyk Taras Bohdanovych.....71

PEDAGOGICAL SCIENCES

Experience in the use of «Flipped classroom» technology in teaching physics at a university

Vaganova Vladislava Gennadievna.....76

The role of the teacher in the updated curriculum

Chulkova Natalya Yurevna, Shestak Yekaterina Sergeevna.....88

PHILOLOGY

Mythical-mystical nature of «Ukok princess»

Aimukhambet Zhanat Askerbekkyzy, Mussabekova Saule Elemeskyzy, Seiputanova Aiyngul Kamzanovna.....	94
---	----

PSYCHOLOGY

Features of adaptive responses of students to physical activity

Vorobeva Tamara Georgievna, Kharchenko Lubov Valerievna, Shamshualeeva Elena Faritovna.....	105
---	-----

Objectification of assessment of mental States of primary school students

Menzul Elena Vladimirovna, Ryazantseva Natalya Mikhailovna, Kuvshinova Natalia Yuryevna.....	111
---	-----

POLITICAL SCIENCES

Taliban: on the way to Central Asia

Archakov Mikhail Konstantinovich.....	120
---------------------------------------	-----

MEDICAL SCIENCES

Acute heart failure at prehospital stage in patients of older age groups

Khusainova Dilyara Featovna, Sokolova Lyudmila Aleksandrovna, Davydova Nadezhda Stepanovna.....	127
--	-----

Four years of experience with laparoscopic appendectomy in a district hospital

Teuvov Aslan Alekseevich, Baziev Arthur Mukharbievich, Teuvov Islam Aslanovich, Teuvova Alina Aslanovna.....	132
---	-----

Pancreatic blood perfusion in vascular model of acute pancreatitis versus abdominal organs blood perfusion after deep ischemia episode

Alekhin Sergey Aleksandrovich, Orlova Anzhelika Yur'evna, Firsova Tatiana Ivanovna.....	139
---	-----

Comparative analysis of the methods indirect revascularization in treatment of the critical ischemia lower extremities

Orlova Anzhelika Yur'evna, Alekhin Sergey Aleksandrovich, Abramova Svetlana Albertovna.....	144
---	-----

PHARMACEUTICAL SCIENCES

Search strategy for new drugs for the treatment of cognitive impairment and patient rehabilitation

Brkich Galina Eduardovna, Zyryanov Oleg Anatolievich, Pyatigorskaya Natalia Valeryevna, Lavrov Mstislav Igorevich, Palyulin Vladimir Alexandrovich.....	153
--	-----

BIOLOGY

Main principles for the development of biophysical research

Tursymatova Orazkul Isaevna, Ibadullayeva Saltanat Zharylkasynovna.....	159
---	-----

CHEMICAL SCIENCES

Thermal analysis method for the study of condensed matter

Iskenderov Eldar Gadzhimuradovich, Dvoryanchikov Vasily Ivanovich, Dibirov Yahya Alievich.....165

Modified carbon graphite electrode by nano particles of manganese dioxide and its analytical application

Narmaeva Gavkhar Zarifovna, Aronbaev Sergey Dmitrievich,

Aronbaev Dmitry Markielovich.....176

TECHNICAL SCIENCES

Weather forecasts in aviation and the use of modern methods of transmission of weather forecasts in airports and airfields. METAR, Internet and other types of weather forecast transmission methods

Dmitrieva Tatyana Vasilevna.....185

SEARCH STRATEGY FOR NEW DRUGS FOR THE TREATMENT OF COGNITIVE IMPAIRMENT AND PATIENT REHABILITATION

Brkich Galina Eduardovna ¹
Zyryanov Oleg Anatolievich ¹
Pyatigorskaya Natalia Valeryevna ¹
Lavrov Mstislav Igorevich ²
Palyulin Vladimir Alexandrovich ²

¹Sechenov First Moscow State Medical University,
Moscow, Russia

²Department of Chemistry, Lomonosov Moscow State University,
Moscow, Russia

Abstract. Approaches to the synthesis of tricyclic derivatives of 3, 7-diazabicyclo [3.3.1] nonane have been developed, according to docking data that have well bind to allosteric sites of the AMPA receptor. Based on a study of the spatial model of the AMPA receptor, its complexes with known AMPA modulators, and the results of their molecular docking, it was shown that compounds based on tricyclic derivatives of 3,7-diazabicyclo [3.3.1] nonane bind to AMPA receptors in a fundamentally different place than ampakines from other known groups. While studying compounds capable of positively modulating the function of AMPA receptors, it was found that positive allosteric AMPA modulators have a number of useful properties that improve memory and cognitive functions of humans and animals. These compounds are true modulators, and not agonists, since they themselves do not cause synaptic currents in any concentrations. Their unique property is the ability to slow down (inhibit) or block the transition of the receptor to a desensitized state, this ability mediates the improvement of learning and memory by activating BDNF and NGF.

Keywords: AMPA-receptors, derivatives of 3, 7-diazabicyclo [3.3.1] nonane, BDNF, NGF, positive allosteric modulators, rehabilitation of patients after brain damage.

Introduction

Nootropic drugs is a special group of neuropsychotropics which possess the possibility to enhance memory and cognitive processes, improve learning ability, and positively affect intellectual capacity of both healthy individuals and those suffering from various disorders. Throughout the literature sources, "smart drugs" and "cognitive enhancers" are often used as synonyms for nootropics [1].

These medicinal products are used for treatment of class V disorders – mental and behavior disorders. Nootropics have widespread list of indications: ageing cognitive problems, psychoorganic syndromes of neurodegenerative or vascular origin (including Alzheimer's disease), acute or chronic cerebral blood circulation disturbance (including those after stroke or encephalopathy), craniocerebral injuries, neuroinfections, acute and chronic fatigue, chronic fatigue syndrome, stress, pain syndrome, diseases caused by prolonged alcohol and drug intake, conditions due to prolonged central nervous system (CNS) depressants administration (anxiolytics, antipsychotics, etc.), asthenic, astheno-depressive, and depressive syndromes, neurotic disorders, vegetovascular dystonia, dizziness. In pediatric practice nootropic medicinal products are used for treatment of cerebroasthenic and encephalopathic disorders, memory defects, mental and lexical retardation, perinatal CNS damage consequences, and attention deficit hyperactivity disorder (ADHD). Healthy individuals usually use nootropics in case there is a certain need to increase mental capacity, improve mental alertness, work productivity, planning and decision-making ability, and speed up processes of memory recall [2].

The aim of this work was study of systematic analysis of the ampakine nomenclature for the treatment of cognitive impairment and rehabilitation of patients undergoing acute brain hypoxia due to ischemia.

Results and Discussion

The strategy for the search for new drugs for the treatment of cognitive impairment and rehabilitation of patients undergoing acute brain hypoxia due to ischemia or other brain injuries includes the search for substances with synaptic plasticity and the ability to increase the production of neurotrophic factors. Many substances with neuroprotective

activity either act in large doses or have increased toxicity. Of undoubted interest are substances of a relatively new class of ampakines (ampakines™), which in their physiological effect are positive allosteric modulators of AMPA receptors (PAM AMPA) [3, 4]. About 500 abstracts and full-text versions of patents were selected, selected for various options of queries using the most comprehensive European Patent Office database, in the Worldwide search collection, as well as electronic patent databases of the Russian Patent Office, Patent Office US USPTO: Searching Full Text, Patents (Since 1976) and USPTO Patent Application Full-Text and Image Database (AppFT) and other available databases included in the search policy [5]. 81 patents were selected for a more detailed development.

When analyzing the submitted patents, it should be noted that the selected patents belong to such countries as the USA, Japan, Germany, Luxembourg, Denmark, France, Poland, Norway, Canada, Great Britain. These countries have submitted international and European applications. Should be also noted that there is significant number of patenting countries, which indicates the high need and importance of research in this area.

As a result of a patent search were not found analogues of the proposed product. The difference between the proposed works and innovative research from existing projects is that in the proposed project a drug based on derivatives of 3,7-diazabicyclo [3.3.1] nonane to restore motor and cognitive functions after brain damage. The presented data indicate the relevance of the chosen research path and the high competitiveness of the proposed drug. During the patent search process, it was confirmed that there are no foreign and Russian objects of technology similar to the developed technologies in the world, no applications were registered that would consider the prospects for the potential use of 6- [4-methoxy-3- (1H-pyrazol-1-ylmethyl) benzyl] -1,11-dimethyl-3,6,9-triazatricyclo [7.3.1.1] tetradecane-4,8,12-trion as a pharmacologically active pharmaceutical substance or as part of dosage forms. No applications were found that reflected the possibility of using tricyclic derivatives of 3,7-diazabicyclo [3.3.1] nonane for the restoration of motor and cognitive functions after brain damage [4, 6].

Thus, the priority of this topic is currently fully owned by the participants in this project. An innovative drug with the chemical name 6- [4-methoxy-3- [1H-pyrazol-1-ylmethyl] benzyl] -1,11-dimethyl-3,6,9-triazatricyclo [7.3.1.1] tetradecane-4, 8, 12-trion is synthesized by project participants.

An important issue in the study of new pharmacologically active compounds is the determination of their potential toxicological activity. Thus, the test substance from a number of ampakines of an innovative class of tricyclic derivatives of 3,7-diazabicyclo [3.3.1] nonane (bispidine) is promising as a "candidate" for the development of an innovative drug with a "cognitive effect", including those prescribed for rehabilitation cognitive and motor functions after brain damage caused by trauma and acute ischemia.

As a result of studies carried out by the developers of the project, computer modeling and optimization of 260 new ampakine structures - derivatives of 3,7-diazabicyclo [3.3.1] nonane and 4,4'-biphenyl, potentially possessing positive modulatory activity with respect to AMPA receptors and the synthesis of the most promising of them (selected according to the simulation results) is carried out. Approaches to the synthesis of tricyclic derivatives of 3,7-diazabicyclo [3.3.1] nonane have been developed, which, according to docking data, bind well to modulator sites of the AMPA receptor. Based on the analysis of the spatial structure of the AMPA receptor, its complexes with the known PAM AMPA and the results of their molecular docking, it was shown that compounds based on tricyclic derivatives of 3,7-diazabicyclo [3.3.1] nonane bind to AMPA receptors in a fundamentally different place, then ampakines from other known groups of PAM AMPA [6,7].

Conclusion

The synthesized derivatives of bispidine possess the properties of positive allosteric AMPA modulators due to the tricyclic framework, the bispidine scaffold was chosen due to the rigidity and high hydrophobicity of the molecule [8,9]. Tricyclic derivatives of 3,7-diazabicyclo [3.3.1] nonane are positive allosteric modulators of glutamate AMPA receptors,

or ampakines. Glutamate receptors are expressed at the synapses of neurons and are activated by glutamic acid, the most common neurotransmitter that transmits signals that stimulate nerve cells. PAM AMPA either slows down the rate at which the AMPA receptors lose their sensitivity to the prolonged exposure to glutamate, or they slow down the deactivation of the AMPA receptor after termination of glutamate exposure [3,7].

It is assumed that indications for the use of this drug, a positive modulator of AMPA receptors, but not an agonist or antagonist, will include acceleration and improvement of the quality of convalescence after brain disorders, since the acute phase and the phase of convalescence are provided by various pathogenetic mechanisms. For the developed innovative drug, a high safety of use and a "prognitive effect" are predicted to exceed the first-generation ampakines analogs from other structural classes, and the oral route of administration is in the form of capsules or coated tablets.

In addition, the combination of ampakines with antipsychotics and narcotic analgesics is expected to be very effective in order to mitigate the side effects of the latter (for example, respiratory depression without suppressing the analgesic effect of drugs). Possibly promising application of ampakines is in emergency care for received patients with overdose of drugs or barbiturates.

Thus, ampakines currently attract the interest of many scientists, the range of areas of research is very diverse. The mechanism of pharmacological effects of ampakines is associated with their ability to influence neuroplasticity and express neurotrophic factors BDNF and NGF by modeling AMPA receptors of the glutamatergic mediator system.

References

1. Zakharov, V.V. Glutamatergic therapy in the recovery period after ischemic stroke/ V.V. Zakharov // Effective pharmacotherapy.- 2016.-No. 42.- P.6-14.2.Neurotrophic and metabotropic potential of nerve growth factor and brain-derived neurotrophic factor: Linking cardiometabolic and neuropsychiatric diseases / S.Yanev [et al.] // World J Pharmacol. - 2013. - Vol. 2. - No4. - P.92-99.
2. Lavrov, M.I. Novel AMPA receptor modulators: design and assessment. : PhD thesis [chemistry, 02.00.03, 02.00.16] / Mstislav Igorevich Lavrov; scientific advisers N.S.Zefirov, V.A.Palyulin. - Moscow, 2011.- P.150-169.
3. Tricyclic derivatives of 3,7-diazabicyclo [3.3.1] nonanes potentially possessing pharmacological activity, pharmaceutical compositions based on them and method of their use: RF patent No. RU 2480470 C2 / Authors: Zefirov NS, Palyulin V.A ., Lavrov M.I., Zapolsky M.E. - Publ. 04/27/2013 Bull. No. 12.
4. Federal Institute of industrial property: [electronic resource]. M., 1997-2012. URL: www.fips.ru. [electronic resource: 18.09.2018].
5. Enomoto, T. Synthetic study toward ecteinascidin 743: concise construction of the diazabicyclo[3.3.1]nonane skeleton and assembly of the pentacyclic core / T.Enomoto, Y.Yasui, Y. Takemoto // J. Org. Chem. - 2016. - Vol. 75. - P. 4876-4879.
6. Cycloprolylglycine neuropeptide is an endogenous AMPA receptor positive modulator / T.A. Gudasheva [et al.] // Academy of Science Proceedings. - 2016. - Vol. 471. - No. 1. - P. 106-108.
7. Bispidine-Amino Acid Conjugates Act as a Novel Scaffold for the Design of Antivirals That Block Japanese Encephalitis Virus Replication/ V. Haridas [et al.] // PLOS Neglected Tropical diseases. - 2013. - Vol. 7.-No 1. - P. 1-11.
8. Synthesis, stereochemistry and in vitro antimicrobial evaluation of novel 2-[[2,4-diaryl-3-azabicyclo[3.3.1]nonan-9-ylidene]hydrazono]-4-phenyl-2,3-dihydrothiazoles/ R.Ramachandran [et al.] // Bioorganic & Medicinal Chemistry Letters. - 2015. - V. 21. - P. 6301-6304.

Scientific publication

**International Conference
“Process Management and Scientific Developments”**

Birmingham, United Kingdom
(Novotel Birmingham Centre, November 14, 2019)

Signed in print 18.11.2019 г. 60x84/16.
Ed. No. 2. Order 182. Circulation of 500 copies.
Scientific publishing house Infinity, 2019.