Moreover, it is known, that biologically active substances from Linseeds assist inhibition of atherosclerotic lesion growth and improve rheologic properties of blood.

Conclusions. Thus, the collection, analysis and systematization of scientific information concerning anti-atherosclerotic activity of Linseeds were done. Taking these data into account it is possible to conclude that Linseeds have anti-atherosclerotic and hypolipidemic effects, normalize lipid metabolism (decreasing level of atherogenic and increasing level of anti-atherogenic lipoproteins in blood), suppress the development of atherosclerotic lesions. In the same time Linseeds have very low toxicity, are well tolerated, have sufficient raw material source. All of this allows to say that Linseeds are perspective as plant origin material for creation of new anti-atherosclerotic phytomedicines necessary for today.

THE CYCLIC KYOTORPHIN (CYCLO(TYR-ARG) IS A HIGH-POTENTIAL NEUROPROTECTIVE DIPEPTIDE

Deiko R.D.
Scientific supervisor: Doctor of medical sciences, professor Shtrygol' S.Yu.
National University of Pharmacy, Kharkiv, Ukraine
roman.deyko@gmail.com

Introduction. The endogenous peptide kyotorphin (H-Tyr-Arg-OH) has been extensively studied since it was discovered in 1979. To date, it's well-known, that the neuropeptide kyotorphin is a promising neuroprotective agent. Particularly, its protective activity in the model of lipopolysaccharide-induced glucocorticoid-mediated inflammatory disturbance of brain, Alzheimer's disease model, cerebral hypoperfusion rat model, using animal models of cerebral resuscitation and of epilepsy (i.e., picrotoxin- or pentylenetetrazole-induced seizures) were demonstrated.

But it is aware that native kyotorphin is a potent neuroprotector and analgesic if administered directly into the brain. To date, it's possible to administrate many regulatory peptides, using intranasal or the other route. In connection with the high therapeutic potential of kyotorphin, as well as its pharmacokinetic deficiencies, a cyclic analogue of it was created at State Research Institute of Highly Pure Biopreparations (St. Petersburg) under the leadership of doctor of biological sciences Alexander Kolobov.

The aim of investigation. To evaluate the neuroprotective and nootropic properties of cyclic kyotorphin (laboratory code KRP(c)) in the models of normobaric hypoxic hypoxia with hypercapnia (NHHH), scopolamine-induced amnesia in mice, as well as acute cerebral disease (ACD) in rats under the conditions of intraperitoneal and intranasal administration.

Materials and methods. For this purpose, we used 69 white randomised male mice and 30 male Wistar rats. The NHHH was made in the hermetic chambers in the volume 200 sm^3. The ACD was modelled using irreversible bilateral carotid occlusion. The anterograde amnesia was reproduced administering scopolamine intraperitoneally (i.p.) in a dose of 1.5 mg/kg body weight. For the last 2 tests, peptide KRP(c) was administered i.p. in the doses of 0.1 or 1.0 or 10.0 mg/kg of body weight. In the ACD model, the peptide was administered i.p. in a dose of 0.1 mg/kg or intranasally (i.n.) in a dose of 0.02 mg/kg.

The heptapeptide semax (Met-Glu-His-Phe-Pro-Gly-Pro) (i.n. in a dose of 0.02 mg/kg) and piracetam (i.p., 400 mg/kg) were used as reference-drugs.

Results. In the NHHH test cyclic kyotorphin demonstrated the pronounced anti-hypoxic action. It increased mice's lifetime in average by 43.4% compared with untreated animals ($p<0.05$). The most anti-hypoxic effective dose of KRP(c) was 0.1 mg/kg (i.p.). In the same conditions, the reference-drugs piracetam and semax increased this index by 18.2% ($p<0.05$) and 10.1% respectively ($p>0.05$).

Under the conditions of irreversible cerebral ischemia, the investigated peptide cyclo(Tyr-Arg) increased rats' survival for the acute period – the first 4 days – up to 71.4% if was administered i.n. (0.02 mg/kg, $p>0.05$ vs control-group). According to this index peptide cyclo(Tyr-Arg) exceeded the reference drug semax (66.7% survived rats). On the other hand, if the peptide KRP(c) was administered i.p. (in a higher dose – 0.1 mg/kg), the rats' survival index reached 42.9% only. Thus, it should be concluded that the cyclic kyotorphin is the high-potential anti-hypoxic agent if it administered i.p., and the anti-ischemic medicine in the case of i.n. administration.

Furthermore, when the anterograde scopolamine-induced amnesia was reproduced in the mice, the cyclo(Tyr-Arg) demonstrated moderate nootropic properties. This compound had an anti-amnestic activity (AA) that reached up to 23.0% ($p<0.05$ compared with untreated mice). In contrast, the action of the classical nootropic agent piracetam was more pronounced (AA – 60%). The effective dose of the cyclo(Tyr-Arg) in this case was 10.0 mg/kg (i.p.).

Conclusions. According to the mentioned data, we should conclude that the cyclic kyotorphin is the new original dipeptide, that's capable to promote rats' survival under the conditions of acute cerebral ischemia; increase the mice' lifetime in the hypoxia model; and finally, to be a moderate nootropic agent. It is worth noting that, this peptide is useful for intranasal and intraperitoneal administration, what is beneficial for clinical practice. The obtained results complement the known facts about the protective properties of the cyclo(Tyr-Arg). In our opinion, it's needed the future pre-clinical studying and the clinical trials.

PHARMACOLOGICAL CORRECTION OF ALZHEIMER'S DISEASE

Didenko O. Yu.
Scientific supervisor: prof. Derymedvid L. V.
National University of Pharmacy, Kharkiv, Ukraine
olegdidenko465@gmail.com

Introduction. In our time, there are many diseases that impair the perception of information and memory. These include Alzheimer's (AD) disease, as well as various forms of dementia. Alzheimer's disease affects about 6% of people 65 years of age and older. WHO experts predict that the number of patients with dementia will triple by 2050 and make 115.4 million people, 70% of them will be residents of developing countries. There are several theories of the development of this pathology: the cholinergic hypothesis (this disease is supposed to be due to the decreasing synthesis of the acetylcholine neurotransmitter), beta-amyloid (the main cause of the disease is extracellular deposition of beta-amyloid (Aβ). In 2009, this theory was updated, assuming now , which is not necessarily the beta-amyloid itself, and a close relative of the beta-amyloid protein may be one of the main causes of the disease) Tau hypothesis (based on the detection of neurofibrillary tusks in the brain tissues arising from because of the violations in the structure of tau protein).

Aim. Analyze the range of medicines to treat Alzheimer's disease, the results of randomized clinical trials and preclinical studies.

Results and discussion. At present, acetylcholinesterase inhibitors (rivastigmine, tacrine, donepezil and galantamine), an NMDA receptor antagonist – memantine, are used to treat cognitive problems in AD. I also use the introduction of mono- or polyclonal antibodies. Choline alphospherate is used to further enhance the activity of acetylcholinesterase inhibitors and to replenish the cerebral acetylcholine deficiency.

As is known, enzymes involved in the metabolism of cerebral acetylcholine accelerate the deposition of amyloid protein in the brain, so it is initially deposited in structures rich in acetylcholine, the mediastasis of the frontal cortex and the core of the Meynert. These structures, in turn, are largely involved in memory processes. Thus, memory impairment becomes first and then - with further development of the disease - the most significant symptom of AD.

The peculiarity of the action of antichildinesterases in AD, in particular, galanthamine, is the phagocytosis of the microglial Aβ. In July 2013, the FDA approved a patch based on rivastigmine acetylcholinesterase inhibitor - Excelone as a remedy for treating patients with severe AD.

Memantadine as an NMDA receptor antagonist blocks NMDA receptors, thus blocking the access of calcium to the cell and decreases the pathologically increased content of glutamate, which has a damaging effect on the nerve cells (toxic excitation), which leads to dysfunction of the neurons.

The most promising method of pathogenetic treatment of AD is passive immunization. This method is based on the introduction of mono- or polyclonal antibodies that bind and remove amyloid protein from the brain. Hantenerumab is the first drug based on fully human antiAβ monoclonal antibodies. The drug has a high ability to bind and remove beta-amyloid from the substance of the brain. Hantenerumab easily penetrates the blood-brain barrier, binds to amyloid protein and activates microglia. The microglial-mediated mechanism of plaque phagocytosis can act as the main mechanism of action of this drug.