UDC 577.29

DOI: 10.25808/08697698.2018.202.6S.040

A.N. KVETKINA, L.A. KALUZHSKIY, E.V. LEYCHENKO, E.A. ZELEPUGA, M.P. ISAEVA, A.S. IVANOV, E.P. KOZLOVSKAYA

The new *Heteractis magnifica* kunitz-peptide interacts with serine proteases

Key words: sea anemone, Kunitz-peptide, surface plasmon resonance

Proteolytic enzymes participate in all living processes, including food digestion, blood coagulation, hormone processing, apoptosis, and others. Deficiency in regulation of the significant molecules can result from the development of neurodegenerative, cardiovascular, and other disorders [3]. Therefore the investigation of protease inhibitors as protease activity regulators is the relevant task. Among the known protease inhibitors Kunitz-peptides are the most characterized due to their distribution in numerous living organisms [2]. They consist of about 60 amino acid residues and form the compact $\alpha+\beta$ structure, stabilized by three disulfide bonds [1]. The primary and first discovered function of Kunitz-peptides is an inhibition of serine proteases, but they also possess other biological activities, such as modulating of ion channel, exhibition of anti-inflammatory, antihistamine, antifibrinolytic, hemostatic activities, etc [2].

We investigated the interaction of Kunitz-peptide HMIQ3c1 of sea anemone *H. magnifica* with serine proteases by surface plasmon resonance method. This method permits to determine kinetic and thermodynamic parameters of protease-inhibitor complex formation. The results revealed a high affinity of HMIQ3c1 to trypsin (K_D 1.07×10⁻⁹ M), chymotrypsin (K_D 4.70×10⁻⁸M), kallikrein (K_D 2.81×10⁻⁸ M), and elastase (K_D 1.11×10⁻⁷ M). Moreover, the peptide has been shown recently inhibited trypsin with K_i 5.0×10⁻⁸ M. The interaction of HMIQ3c1with neutrophil elastase and kallikrein may indicate its anti-inflammatory activity. Thus, Kunitz-peptide HMIQ3c1 of *H. magnifica* makes strong enough complexes with serine proteases that allow us to consider it as potential pharmacological tool.

REFERENCES:

1. Berndt K.D., Güntert P., Orbons L.P., Wüthrich K. Determination of a high-quality nuclear magnetic resonance solution structure of the bovine pancreatic trypsin inhibitor and comparison with three crystal structures // J. Mol. Biol. 1992. Vol. 227, N 3. P. 757–775.

2. Mourão C.B., Schwartz E.F. Protease inhibitors from marine venomous animals and their counterparts in terrestrial venomous animals // Mar. Drugs. 2013. Vol. 11, N 6. P. 2069–2112.

3. Turk B. Targeting proteases: Successes, failures and future prospects // Nat. Rev. Drug Discov. 2006. Vol. 5, N 9. P. 785–799.

^{*} KVETKINA Aleksandra Nikolaevna – Junior Researcher, LEYCHENKO Elena Vladimirovna – PhD, Senior Researcher, ZELEPUGA Elena Alexandrovna – PhD, Senior Researcher, ISAEVA Marina Petrovna – PhD, The Head of The Laboratory, KOZLOVSKAYA Emma Pavlovna – DSc, The Head of The Laboratory(G.B. Elyakov Pacific Institute of Bioorganic Chemistry, FEB RAS, Vladivostok, Russia); KALUZHSKIY Leonid Alexandrovich – PhD, Junior Researcher, IVANOV Alexey Sergeevich – DSc, Prof. (V.N. Orekhovich Institute of Biomedical Chemistry of the Russian Academy of Medical Sciences, Moscow, Russia). *E-mail: sashaledy@gmail.com

This work was partially supported by the Presidium of Far Eastern Branch of the Russian Academy of Sciences (grant number RUS_ST2017-228).