Nanozymes—efficient antidote against pesticides

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Members of the Faculty of Chemistry of the Lomonosov Moscow State University have developed novel nanosized agents that could be used as efficient protective and antidote modalities against the impact of neurotoxic organophosphorus compounds such as pesticides and chemical warfare agents. The research results are published in the *Journal of Controlled Release*.

Development of the first nanosized drugs started more than 30 years ago, and in the 1990s, the first nanomedicines for cancer treatment entered the market. These medicines were based on liposomes—spherical vesicles made of lipid bilayers. The new technology, developed by Kabanov and his colleagues, uses an enzyme encapsulated into a biodegradable polymer coat based on an amino acid (glutamic acid).

Alexander Kabanov of Lomonosov Moscow State University, one of the authors, says, "At the end of the 1980s, my team (at that time in Moscow) and Japanese colleagues led by Prof. Kazunori Kataoka from Tokyo began using polymer micelles for small molecule delivery. Soon, the nanomedicine field exploded. Currently, hundreds of laboratories across the globe work in this area, applying a wide variety of approaches to the creation of such nanosized agents. A medicine based on polymeric micelles, developed by a Korean company Samyang Biopharm, was approved for human use in 2006."

Professor Kabanov's team, after moving to the U.S. in 1994, focused on development of polymer micelles, which could include biopolymers due

to electrostatic interactions. Initially, chemists were interested in the usage of micelles for RNA and DNA delivery, but later, scientists started actively utilizing this approach for delivery of proteins and enzymes to the brain and other organs.

Alexander Kabanov says, "At the time, I worked at the University of Nebraska Medical Center, in Omaha, and by 2010, we had a lot of results in this area. That's why, when my colleague from the Chemical Enzymology Department of the Lomonosov Moscow State University, Prof. Natalia Klyachko, asked me to apply for a mega-grant, the research theme of the new laboratory was quite obvious. Specifically, to use our delivery approach, which we've called a 'nanozyme,' for medical applications."

Scientists together with the group of enzymologists from the Lomonosov Moscow State University under the leadership of biological researcher Elena Efremenko, have chosen organophosphorus hydrolase as a one of the delivered enzymes. Organophosphorus hydrolase is capable of degrading toxic pesticides and chemical warfare agents. However, it has disadvantages. Because of its bacterial origin, an immune response is observed as a result of its delivery to mammals. Moreover, organophosphorus hydrolase is quickly removed from the body. Chemists have solved this problem with the help of a "self-assembly" approach. The inclusion of the organophosphorus hydrolase enzyme in a nanozyme particles causes the immune response to become weaker, and both the storage stability of the enzyme and its lifetime after delivery to an organism increase considerably. Rat experiments have proved that the nanozyme efficiently protects organisms against lethal doses of highly toxic pesticides and even chemical warfare agents such as VX nerve gas.

Alexander Kabanov says, "The simplicity of our approach is very important. You could get an organophosphorus hydrolase nanozyme by simple mixing of aqueous solutions of anenzyme and a safe

biocompatible polymer. This nanozyme is self-assembled via electrostatic interaction between a protein (enzyme) and polymer."

According to the scientist, the simplicity and technological effectiveness of the approach, along with the promising results of animal experiments, bring hope that this modality could be successful in clinical use.

More information: Elena N. Efremenko et al, A simple and highly effective catalytic nanozyme scavenger for organophosphorus neurotoxins, *Journal of Controlled Release* (2017). DOI: 10.1016/j.jconrel.2016.12.037

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