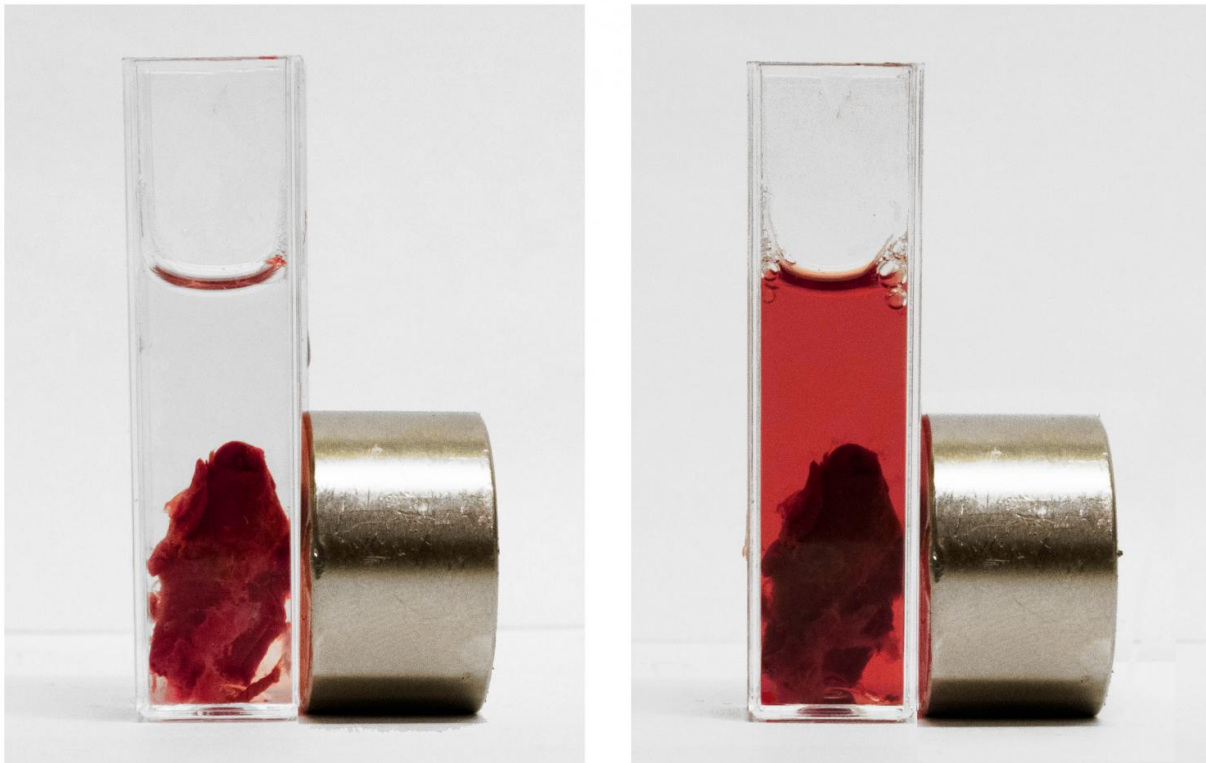


New targeted drug effectively dissolves blood clots, has fewer side effects

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The influence of developed thrombolytic system on vascular thrombus extracted during the operation. Credit: ITMO University

Critical conditions associated with the blockage of blood vessels comprise a primary health concern worldwide. The main objective of emergency assistance in such conditions is to induce thrombolysis, i. e.,

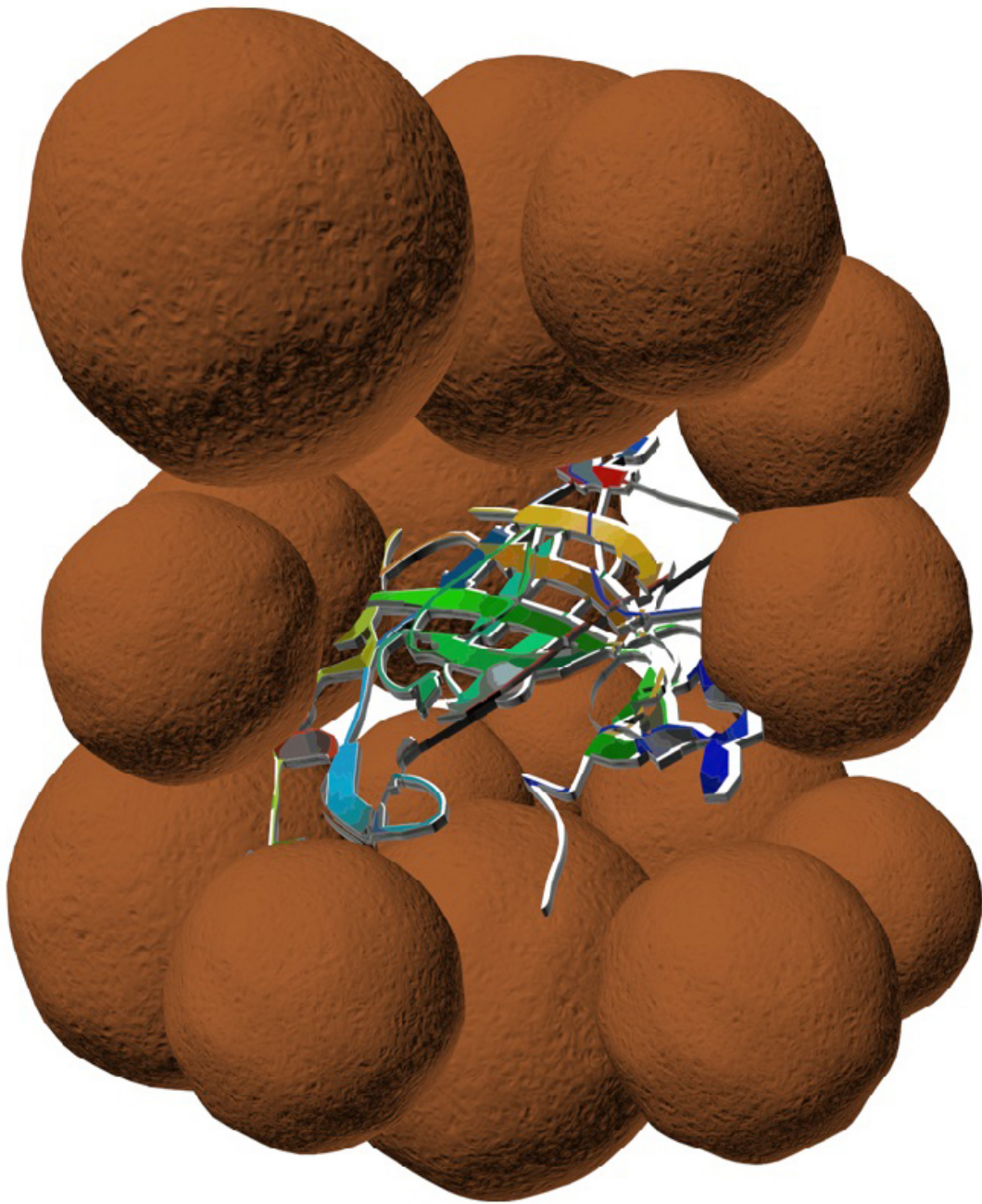
to quickly dissolve the clot. To this end, scientists from ITMO University in cooperation with Mariinsky Hospital in Saint Petersburg have developed a magnetically controlled drug that can be condensed on a blood clot by means of a magnetic field. The new drug is safe for intravenous injection and can dissolve clots up to 4000 times more efficiently than ordinary enzyme-based drugs. The new study will also help reduce drug dosage, thus avoiding numerous side effects. The results of the research were published in *Scientific Reports*.

In emergency situations caused by thrombosis, the clot has to be destroyed within a very short period of time—about 3 to 4.5 hours. After that, tissues lacking [blood](#) flow will die. But even if the patient was lucky enough to receive thrombolysis treatment, she could develop numerous complications caused by the thrombolytic drug—a specific enzyme injected intravenously to dissolve blood clots. In developed countries, thrombolysis is effectively carried out in 15 percent of cases on average. In countries like Russia, the figure is much lower: Out of a hundred people brought to the hospital, only two are likely to benefit significantly from the procedure. In other cases, the patient faces the risk of disability or death.

The challenge is that thrombolytic drugs do not target the clot, but rather spread throughout the entire circulatory system. The immune system responds to the drug as a foreign enzyme, quickly diminishing its activity. Therefore, the drugs are injected in knock-out doses in the hope that at least a small portion will reach the blood clot on time. "Now, we are using a sledgehammer to crack a nut," says Ivan Dudanov, head of the regional cardiovascular center of Mariinsky hospital. "Dissolving a little blood clot that blocked a vessel of only one to two millimeters in diameter, thrombolytic drugs negatively affect the entire network of blood vessels. In order to improve the situation, we decided to develop a method of targeted drug delivery that would allow us to considerably reduce the dosage and ensure that the whole therapeutic effect is focused

on the clot."

The scientists produced a composite material that can deliver thrombolytic enzymes in a safe and targeted manner. The new material is composed of a porous magnetite framework containing molecules of urokinase, an enzyme frequently used in medicine as a thrombolytic agent. The composite can be used to create thrombolytic coating for artificial blood vessels and stable injectable solutions made of nanosized particles that can be easily localized near the clot by means of an external magnetic field.



Schematic image of thrombolytic drug nanoparticles. The enzyme is surrounded by magnetite framework. Credit: ITMO University

Importantly, the magnetite framework also protects enzymes from various inhibitors that are present in the blood and can deactivate thrombolytic medications. Andrey Drozdov, first author of the study and researcher at the Laboratory of Solution Chemistry of Advanced Materials and Technologies says, "Usually, in order to achieve a prolonged effect for such drugs, the enzyme is placed inside a polymeric matrix. The enzyme is then gradually released from the matrix and eventually loses all activity. We, on the other hand, experimentally demonstrated that enzymes protected using our approach do not lose therapeutic properties over extended periods of time, and even after repeated use. The rate at which the new drug can dissolve the clot outperforms unprotected enzymes by about 4000 times."

The material is potentially safe for humans because it is made of components already approved for intravenous injection. According to professor Dudanov, future drugs based on the new composite could be used not only for thrombosis treatment, but also for its prevention. Circulating in the blood even in small amounts, the enzyme can gently clean the vessels and will remain active for a very long time until it is naturally excreted through the liver like an ordinary metabolite.

This work became a logical continuation of earlier studies devoted to enzyme entrapment in sol-gel magnetite matrices and the production of magnetically controlled bioactive systems.

"In this phase of our project, we have demonstrated how the concept we developed works for more specific objects. We prepared a thrombolytic colloid and tested its effects on artificial blood clots obtained from the plasma and blood of humans, and thrombus extracted from patients. The results may soon allow us to try out the new thrombolytic system on mammals. Now we are preparing for preclinical studies," concludes Vladimir Vinogradov, head of the Laboratory of Solution Chemistry of Advanced Materials and Technologies.

More information: Andrey S. Drozdov et al, Leach-proof magnetic thrombolytic nanoparticles and coatings of enhanced activity, *Scientific Reports* (2016). [DOI: 10.1038/srep28119](https://doi.org/10.1038/srep28119)

Provided by ITMO University

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