Micro-sized capsules for targeted drug delivery inspired by Russian pelmeni

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An international team led by a Skoltech researcher has developed a method of fabrication for biodegradable polymer microcapsules, made more efficient by turning to an unusual source of inspiration—traditional

Russian dumpling, or pelmeni, making. The two papers were published in *Materials and Design* and *ACS Applied Materials and Interfaces*.

Micro-sized capsules, which can be tailored to a variety of purposes, have proven very useful in targeted delivery of drugs and other bioactive compounds. To ensure optimal functioning, these have to be designed and manufactured with precision and in particular shapes, as non-spherical capsules turned out to be more efficient and effective than spherical ones.

"Non-spherical capsules could have side directed release as one side could degrade first and let the cargo release, they also could be navigated in flow with magnetic field. But the most important advantage is that biological cells more readily internalize non-spherical objects, however, this phenomenon is not yet understood," Gleb Sukhorukov of Skoltech and Queen Mary University of London, the papers' lead author, explains.

In the two papers, Sukhorukov and his colleagues describe a way to create micrometer-sized pyramid, rectangular and torpedo-shaped capsules by using soft lithography. In this method, a template is coated with a polymer, then cargo (a drug, for instance) is loaded onto the polymer and sealed by a top polymer layer, ending up sandwiched between the two layers. The capsules are then printed onto gelatin and harvested by dissolving it in water.

"The approach is not only inspired by Russian pelmeni making process, but in fact really reproduces on a microstructure level the trick that allows us to wrap various components inside, like proteins (meat in proper pelmeni) or natural healthy components (like berries or mashed potatoes in case of vareniki, a similar product)," Sukhorukov notes.

In the first paper, the team demonstrated two approaches, based on polyelectrolyte multilayer and polylactic acid, that resulted in

7-micrometer-long torpedo-shaped capsules. These had a high loading capacity, retained hydrophilic molecules well and were internalized by cells without causing toxic effects. "The proposed method offers great flexibility for the choice of active substances, regardless of their solubility and molecular weight," the authors write.

In the second paper, the researchers described pyramid and rectangular capsules made of polylactic acid, which are respectively about 1 and 11 micrometers in size. These capsules proved sufficiently stable to encapsulate small water-soluble molecules and to retain them for several days for subsequent intracellular delivery and/or serve as depot for controlled release.

"So far we created the capsules from polylactic acid, and we plan to explore these principles with other polymers which undergo degradation and hence release of cargo under specific conditions such as temperature, enzymes, pH and so on," Sukhorukov says.

More information: Valeriya Kudryavtseva et al. Biodegradable Defined Shaped Printed Polymer Microcapsules for Drug Delivery, *ACS Applied Materials & Interfaces* (2021). DOI: 10.1021/acsami.0c21607

Valeriya Kudryavtseva et al. Micro-sized "pelmeni" - A universal microencapsulation approach overview, *Materials & Design* (2021). DOI: 10.1016/j.matdes.2021.109527

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