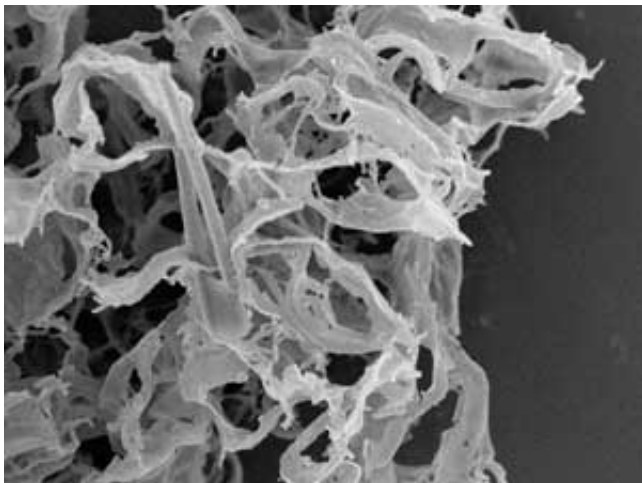


Nanoparticle drugs can make it easier for medications to reach their targets

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Nanoscale, cross-linked polymer scaffolds can help deliver a surprisingly high amount of drugs with poor water solubility to aqueous targets. Credit: Elsevier

The huge doses of drugs required to combat cancer could be reduced thanks to the work of A*STAR researchers, and the drugs themselves may become more effective. The researchers have developed a polymeric 'scaffold' that helps drugs that often have trouble entering the bloodstream, such as anti-cancer agents, form highly stable nanoparticles with improved bioavailability.

Many medications that target tumor cells are made from water-repelling hydrocarbon molecules, which require extra processing or high doses rates to enter aqueous biological environments. A safer alternative is to 'nanosize' pharmaceuticals into 10 to 1,000 nanometer particles using either mechanical grinding or special crystallization techniques. These extra-small medications easily slip into water and are effective against tumors, but it is hard to prevent them from agglomerating into larger precipitates with less potency.

Ulrike Wais and Alexander Jackson from the A*STAR Institute of Chemical and Engineering

Sciences and Haifei Zhang at the University of Liverpool have developed a way to lessen agglomeration problems by using poly(ethylene glycol) and acrylamide (PEG-PNIPAM)—biocompatible polymers that are highly water soluble and can stabilize water-repelling molecules because they have similar surfactant-like hydrocarbon chains.

The team synthesized PEG-PNIPAM into 'hyperbranched' spheres that are reinforced with short carbon cross-linking molecules. They then mixed the spheres with test drug compounds such as ibuprofen and blended them together to create an emulsion between the water-repelling and water-attracting components.

The next step required a way to freeze-dry the emulsion so it could be pulverized into nanoparticles, but this involved solving a tricky processing problem. "If [phase separation](#) occurs before the sample is completely frozen, drug crystals form that are neither nanosized nor stabilized against agglomeration by the scaffold," explains Wais.

The researchers prevented phase separation during freeze-drying by ensuring the emulsification was extremely uniform before spraying it as tiny droplets into a pool of liquid nitrogen. Dynamic light scattering and scanning electron microscopy analysis of the solidified emulsion revealed that the drugs and polymer spheres had integrated into a porous, scaffold-like structure.

After mechanically grinding the freeze-dried emulsion into drug nanostructures, the researchers found their open framework made it simple to dissolve them into water. Furthermore, the drugs could be transformed into nanoparticles with yields of 100 per cent using surprisingly low levels of PEG-PNIPAM spheres.

"The polymer structure and level of branching

directly affect drug nanoparticle stabilization. This method gives us a way to investigate it systematically," says Jackson. He notes that this method is synthetically straightforward and could be applied to a wide range of pharmaceuticals.

More information: Ulrike Wais et al. Drug nanoparticles by emulsion-freeze-drying via the employment of branched block copolymer nanoparticles, *Journal of Controlled Release* (2016). [DOI: 10.1016/j.jconrel.2015.12.022](https://doi.org/10.1016/j.jconrel.2015.12.022)

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