Highly concentrated clusters dissociate when diluted in vitro

Protein nanoclusters could provide a new method of drug administration, allowing patients to self-administer drugs that could previously be given only intravenously, researchers in Texas reported. The nanoclusters are a new physical form of highly concentrated protein, not dependent on a nanoparticle vehicle, the lead researcher said.

“There are other approaches where one might encapsulate proteins in bioerodable polymers and so forth, but we’re just trying to go from the concentrated protein itself. If we can achieve syringe-able viscosities at higher concentrations than are possible for solutions, this would be helpful to be able to do subcutaneous injection instead of intravenous delivery of monoclonal antibodies and proteins,” said Keith P. Johnston, PhD, a professor of chemical engineering at the University of Texas at Austin.

Dr. Johnston is first author of a paper describing the technology (Johnston KP, Maynard JA, Truskett TM, et al. [Published online ahead of print Jan. 30, 2012.] ACS Nano). He led the research, along with Thomas M. Truskett, PhD, and Jennifer Maynard, PhD, professor and assistant professor, respectively, at UT Austin.

The researchers developed the highly concentrated nanoclusters by adding trehalose as a cosolute to strengthen the attraction between protein monomers and adjusting the pH to lower the protein charge. The nanoclusters dissociate into stable, biologically active protein monomers after injection into mice. Subcutaneous injection in vivo yielded pharmacokinetics indistinguishable from standard antibody solution, the researchers reported.

The concept of forming nanoclusters by tuning colloid interactions can potentially be used with any protein drug, Dr. Johnston told PFQ.

“We’d like to see next how these nanoclusters will work for therapeutic proteins and if they will be of interest for human clinical trials. I think this could be developed quite rapidly,” he said.