Researchers develop way to strengthen proteins with polymers

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Proteins are widely used as drugs — insulin for diabetics is the best known example — and as reagents in research laboratories, but they react poorly to fluctuations in temperature and are known to degrade in storage.

Because of this instability, proteins must be shipped and stored at regulated temperatures, resulting in increased costs, and sometimes must be discarded because their "active" properties have been lost. Manufacturers of protein drugs will generally add substances known as excipients, like polyethylene glycol, to the proteins to prolong their activity.

In a new study published in the *Journal of the American Chemical Society*, investigators from the UCLA Department of Chemistry and Biochemistry and the California NanoSystems Institute at UCLA (CNSI) describe how they synthesized polymers to attach to proteins in order to stabilize them during shipping, storage and other activities. The study findings suggest that these polymers could be useful in stabilizing protein formulations.

The polymers consist of a polystyrene backbone and side chains of trehalose, a disaccharide found various plants and animals that can live for long periods with very little or no water. An example many people will recognize is Sea- Monkeys — the 'novelty aquarium pet' introduced in 1962. Sea–Monkeys can be purchased as kits that contain a white powder; when water is added, the powder becomes small shrimp whose

long tails are said to resemble those of monkeys.

Trehalose is known to stabilize proteins when water is removed, and as a result, it is an additive in several protein drug formulations approved by the Food and Drug Administration (FDA) to treat cancer and other conditions.

"Our polymers were synthesized by a controlled radical polymerization technique called reversible addition-fragmentation chain transfer (RAFT) polymerization in order to have end groups that can attach to proteins to form what is called a protein-polymer conjugate," said Heather Maynard, a UCLA associate professor of chemistry and biochemistry and a member of the CNSI. "We found that the polymers significantly stabilized the protein we used — lysozyme — better to lyophilization (freeze-drying, in which water is removed from the protein) and to heat than did the protein with no additives."

The research team found that attaching the polymer covalently to the protein — that is, forming a protein-polymer conjugate — stabilized the protein to lyophilization better than adding the non-conjugated polymer at the same concentration.

The team also found that the polymers stabilized lysozyme significantly better than the currently used excipients trehalose and polyethylene glycol, depending on the stress and conditions used.

The Maynard research group is currently exploring the use of their polymer as a stabilizer by attaching it or adding it to FDA–approved protein therapeutics. In addition, they are investigating the mechanism of how the polymer stabilizes proteins.

The research team included Rock J. Mancini and Juneyoung Lee, both graduate students of chemistry and biochemistry in the Maynard

research group.

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