**α-Lactalbumin Nanotube as a Novel Delivery System for Food Bioactive Compounds**

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Food Sourced Protein nanotubes (PNTs) as biocompatible nanocarriers are promising to deliver functional ingredients in nutritional foods. α-Lactalbumin accounts for 20% of whey protein and has anti-inflammatory, anticancer, and immune-enhancing effects. In our Lab, the well-defined nanotubes were obtained by self-assembly of partially hydrolysed α-lactalbumin peptides by Bacillus licheniformis protease (BLP) specially at Glu and Asp sites, the amphiphilic peptides can form nanotubes through Ca2+ ions bridging coordination1. In this presentation, the molecular self-assembly mechanism and structural evolution of α-lactalbumin nanotubes will be discussed, laying a theoretical foundation for the application of α-lactalbumin nanotubes in nutritional delivery systems2. At the same time, it was also found that α-lactalbumin nanotubes can self-assemble to form nanospheres after removing Ca2+ or lowering pH. Nanospheres can also be transited into nanotubes under certain conditions, thereby realizing the reversible transformation between α-lactalbumin nanotubes and nanospheres3. This is conducive to the development and design of environmentally responsive delivery carriers with a variety of physical structures and physicochemical properties. We have developed different types of α-lactalbumin nanotubes for delivering bioactive compounds. For instance, we found that flexible tubular nanoparticles were effective at penetrating mucus, thereby improving the bioavailability and therapeutic efficacy of the administered compounds4. In another study, we found that a nanotube-based composite microsphere delivery system exhibited excellent mucoadhesive and mucus-penetrating properties, improving the bioavailability of hydrophobic capsaicin and maintaining the homeostasis of gut microbiota5. In addition, we also found that Mn2+ can induce the nanotubes formation bearing an nanozymes function which possessed the anti-rheumatoid arthritis effect with loaded capsaicin6. The information addressed in this presentation may provide inspirations for the future development of more advanced nanocarrier systems in functional food applications.

Reference

1 Liu, B.; Li, X.; Zhang, J. P.; Li, X.; Yuan, Y.; Hou, G. H.; Zhang, H. J.; Zhang, H.; Li, Y.; Mezzenga, R., Protein Nanotubes as Advanced Material Platforms and Delivery Systems. Advanced Materials 2024, 36 (6), 2307627.

2 Zhang, J.; Wang, Q.; Liu, B.; Li, D.; Zhang, H.; Wang, P.; Liu, J.; Hou, G.; Li, X.; Yuan, Y., The kinetic mechanism of cations induced protein nanotubes self-assembly and their application as delivery system. Biomaterials 2022, 286, 121600.

3 Zhang, J.; Liu, B.; Li, D.; Radiom, M.; Zhang, H.; Cohen Stuart, M. A.; Sagis, L. M. C.; Li, Z.; Chen, S.; Li, X., Ion-Induced Reassembly between Protein Nanotubes and Nanospheres. Biomacromolecules 2023, 24 (9), 3985-3995.

4 Bao, C.; Liu, B.; Li, B.; Chai, J.; Zhang, L.; Jiao, L.; Li, D.; Yu, Z.; Ren, F.; Shi, X., Enhanced transport of shape and rigidity-tuned α-lactalbumin nanotubes across intestinal mucus and cellular barriers. Nano Letters 2020, 20 (2), 1352-1361.

5 Yuan, Y.; Liu, Y.; He, Y.; Zhang, B.; Zhao, L.; Tian, S.; Wang, Q.; Chen, S.; Li, Z.; Liang, S., Intestinal-targeted nanotubes-in-microgels composite carriers for capsaicin delivery and their effect for alleviation of Salmonella induced enteritis. Biomaterials 2022, 287, 121613.

6 Hou, G.; Chen, S.; Ngai, T.; Miao, S.; Pang, J.; Zhang, L.; Hu, W.; Wang, X.; Liu, B.; Li, X., The nanozymes of protein nanotubes-constructed microspheres with dual peroxidase-and catalase-like properties for M1-to-M2 macrophages repolarization and the synergistic anti-rheumatoid arthritis effect with loaded capsaicin. Nano Today 2024, 56, 102290.