The structural stability of oral insulin nanoencapsulations studied by SANS

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The oral delivery of insulin in diabetes treatment can improve patient compliance and avoid peripheral hyperinsulinemia. The main barriers faced by oral insulin are degradation by low pH and proteolytic enzymes in the gastrointestinal tract. In this context, it is of great significance to understand the fundamental principles of insulin assembly within nanoencapsulations and to identify the effects of temperature, salt composition, pH of the medium, and other factors on the stability of oral insulin nanoencapsulations.

Systematic investigation of temperature and pH effects helps to elucidate the conformational changes and aggregation behavior of insulin in nanocarriers, providing a theoretical basis for optimizing formulation compositions and process parameters. Moreover, such studies enable the prediction of nanoencapsulations stability in different segments of the gastrointestinal tract. Furthermore, temperature and pH stability studies can also provide scientific support for establishing storage conditions and quality control standards for the formulations. [1].

To evaluate the protective effect of nanoencapsulation on insulin against acidic environments, free insulin and insulin-loaded nanoencapsulations were incubated at pH 7.0 (physiological condition) and pH 3.0 (simulated gastric fluid), respectively, and their status changes were monitored. At pH 7.0, both free insulin and encapsulated insulin remained well-dispersed. In contrast, at pH 3.0, free insulin rapidly exhibited significant aggregation and precipitation, whereas the encapsulated insulin showed no notable aggregation, with stable particle size and dispersion. These results demonstrate that the nanoencapsulation system can effectively protect insulin from acid-induced aggregation and inactivation, providing a critical barrier function for oral insulin delivery.

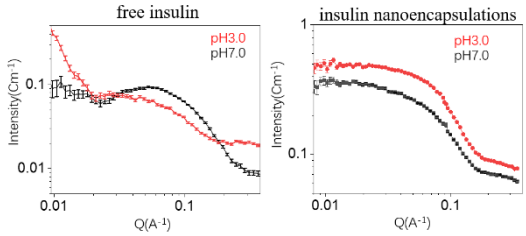

Fig. 1. Comparison of SANS curves of free insulin and insulin nanoencapsulations at at pH 7.0 (black) and pH 3.0 (red).

To further investigate the effect of temperature on insulin stability, free insulin and insulin-loaded nanoencapsulations were incubated at 10, 20, 35, 50, and 60 °C, respectively, and their status changes were monitored. The results showed that within the tested temperature range (10–60 °C), the insulin nanoencapsulations exhibited no obvious aggregation or structural changes, indicating good thermal stability. In contrast, free insulin displayed significant aggregation at 50 °C, as evidenced by increased turbidity and enlarged particle size; the aggregation became more pronounced as the temperature rose to 60 °C. These findings demonstrate that nanoencapsulation can substantially enhance the thermal stability of insulin, effectively delaying or inhibiting heat-induced aggregation and inactivation.

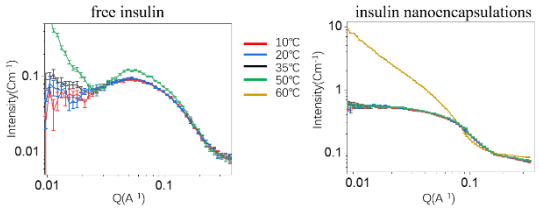

Fig. 2. Comparison of thermal stability of free insulin and insulin nanoencapsulations at at 10, 20, 35, 50 and 60 °C.

Reference

[1] Xiao Y, Tang Z, Wang J, Liu C, Kong N, Farokhzad OC, Tao W. Oral Insulin Delivery Platforms: Strategies To Address the Biological Barriers. Angew Chem Int Ed Engl. 2020 Nov 2;59(45):19787-19795.