TRIGGERED PROTEIN RELEASE FROM CALCIUM ALGINATE / CHITOSAN GASTRO-RESISTANT CAPSULES

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Therapeutic peptides and proteins are typically administered via parenteral routes due to their instability in the gastrointestinal tract, which causes degradation of these active components and limited absorption through the intestinal mucosa [1]. However, parenteral administration poses challenges when sustained therapeutic levels are needed or frequent dosing is required, often resulting in badly administered doses.

The oral route presents an alternative, offering benefits such as non-invasiveness, improved patient compliance, and ease of use, particularly for long-term treatments [2]. Despite these advantages, significant challenges remain in developing oral delivery systems for peptides and proteins, primarily due to the harsh environment of the gastrointestinal tract. Nonetheless, recent years have seen promising developments in oral delivery systems, with some advancing to clinical trials [3].

Following our previous studies [4], the aim of the present research was to investigate the encapsulation of BSA, a model protein, within calcium alginate and assess the potential of these capsules as a protein delivery system for the gastrointestinal tract. BSA was encapsulated in calcium alginate capsules, which were then coated with chitosan (Fig. 1).

The aqueous mixture of BSA and AlgLV resulted in the formation of coacervate droplets with a size of approximately 124 nm. Capsules were produced with dimensions of around 2.3 mm in width, 3.1 mm in length, and a water content of roughly 95.1 wt% [5]. A thin layer of chitosan was applied to coat the capsules, denoted as BSA-Alg/$CaCl_2$-CHT. These chitosan-coated capsules were evaluated for their potential as an oral delivery system, by investigating the release kinetics of BSA using an *in vitro* model that simulated both gastric and intestinal environments [5].

Release experiments indicated that these chitosan-coated capsules were highly effective at retaining most of the BSA within a simulated gastric fluid (SGF), showing minimal release at low pH. Interestingly, while the capsules remained stable in either SGF or simulated intestinal fluid (SIF) alone, they disintegrated rapidly when subjected to a two-step SGF-SIF treatment. BSA-Alg/$CaCl_2$ capsules, in the absence of chitosan, exhibited some swelling during the SGF stage and dissolved quickly in the subsequent SIF stage. In contrast, BSA-Alg/$CaCl_2$-CHT capsules, with chitosan, did not swell in SGF and took a longer time to disintegrate in SIF.

The results of the release experiments (Fig. 1), which simulated the digestion process, demonstrated that BSA remained encapsulated during the initial treatment with SGF. However, once the capsules were exposed to the SIF, all the BSA was released within less than one hour [5]. These findings indicated that the BSA-Alg/$CaCl_2$-CHT capsules are gastro-resistant and meet the in vitro requirements set by the European Pharmacopoeia. Consequently, Alg/$CaCl_2$-CHT capsules could be highly suitable for protecting proteins from the harsh conditions of the stomach and enabling their controlled release in the intestinal tract, showing promise as an oral delivery system for therapeutic proteins and peptides.

References

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Figures

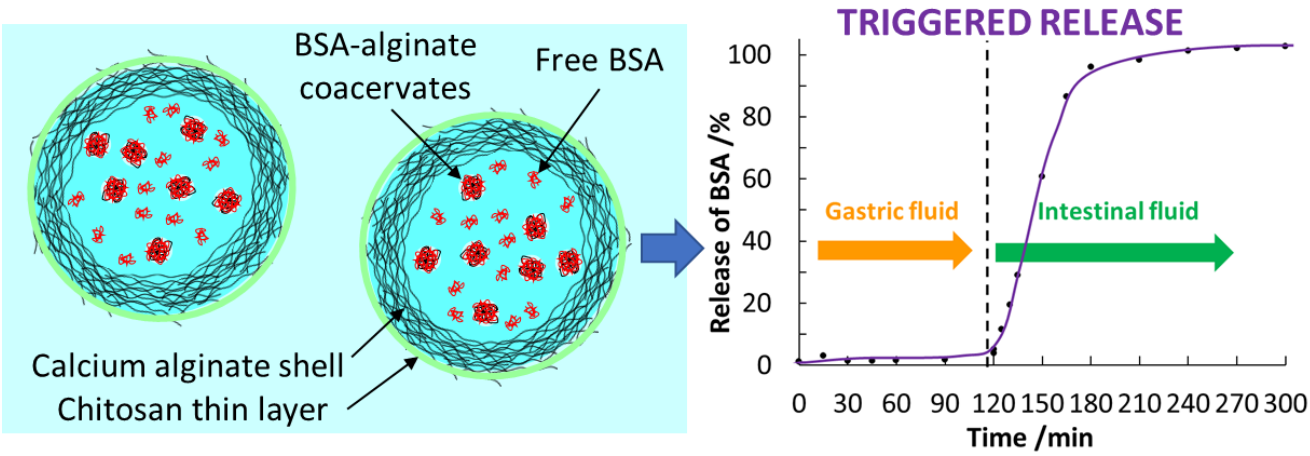

Figure 1. Structure of the BSA-Alg/$CaCl_2$-CHT capsules, and release of the BSA during the simulation of the digestion process (Reproduced from Ref. [5]).