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Spray-dried allicin/β-cyclodextrin inclusion complexes for antimicrobial applications

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Antimicrobial resistance is a rapidly growing threat to global medicine, primarily driven by the misuse and environmental accumulation of conventional antibiotics. Prolonged exposure of bacteria to subinhibitory concentrations facilitates the rapid development of resistance mechanisms. An innovative strategy to combat this challenge involves utilizing highly reactive antimicrobial agents with a short environmental half-life, thereby minimizing the evolutionary window for bacteria to develop resistance. A promising candidate is allicin, a natural broad-spectrum antimicrobial compound derived from garlic (*Allium sativum*). Allicin, natively not present in intact tissue, is synthesized upon cellular rupture when the precursor alliin and the enzyme alliinase, normally segregated in different cellular compartments, interact as a defense mechanism responding to immediate cell damage. However, allicin's inherent chemical instability poses a significant hurdle to its practical therapeutic application.

In light of these challenges, the primary objective of this research is to stabilize the allicin molecule via inclusion complexation with β-cyclodextrin (β-CD), a cyclic oligosaccharide whose hydrophobic cavity accommodates and shields the guest molecule from thermal and photochemical degradation. To isolate these complexes in a stable solid form, spray drying was employed, efficiently converting the liquid allicin/β-CD feed into a fine, dry powder. Crucially, although spray drying of aqueous solutions utilizes higher inlet gas temperatures, the rapid evaporative cooling effect ensures that the droplets and the resulting powder are mostly exposed to the significantly lower wet-bulb temperature. This thermodynamic mechanism makes the process highly suitable for preserving heat-sensitive compounds such as allicin.

The powder composition was optimized and subsequently evaluated for *in vitro* antimicrobial efficacy, along with comprehensive testing to assess its long-term stability under various storage conditions. Also, the performance of the allicin/β-CD powders was compared with previously developed spray-dried inhalable carriers co-encapsulating allicin precursors.