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## **Can Collapse Freeze Drying Provide High Density Protein Sugar Particles for Ballistic Powder Injection?**

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Ballistic powder injection is an emerging needle-free technology. Powder particles are accelerated towards the skin and penetrate the superficial layers. Biopharmaceuticals like vaccines can be placed into the epidermal layer of the skin, widely known to be an attractive site for immunization [1]. Beneath avoiding hazards associated with needle-stick injuries using conventional needles and syringes, the use of dried sugar powders provides an enhanced stability for biopharmaceuticals [1]. In the literature the use of spray freeze drying to generate sugar particles for ballistic powder injection has been evaluated [2]. A ternary mixture of trehalose, mannitol and dextran was found to be appropriate to generate high density particles attributing appropriate characteristics for ballistic injection [2]. Dextran has an antiplasticizing effect on the formulation and leads to a partially collapsed, highly wrinkled morphology of the spray freeze dried particles. Nevertheless, the stabilising effect of this matrix for proteins still needs to be improved. A polymer like dextran is vital for the partial collapse of the spray freeze dried particles, but it is also responsible for the reduced stabilizing effect on the protein [2]. Our approach is to apply an aggressive freeze drying cycle as performed by Schersch et al. to evoke a collapse of the sugar matrix and generate a high density structure of the freeze dried cake [3]. Characteristics like high density and low specific surface area of the lyophilizates can provide protein stability and appropriate properties for ballistic powder injection. We investigated different sugar formulations with and without dextran and evaluated the effect of collapse freeze drying on particle morphology and protein stability. With this more in-depth information about particle morphology and protein stability we can introduce an improved formulation strategy for biopharmaceutics entrapped in a high density sugar matrix intended for ballistic powder injection.

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