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Impact of Change of Matrix Crystallinity and Polymorphism on Ovalbumin Release from Lipid-based Implants

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Keywords

Lipid implants; Hot melt extrusion; Polymorphism; Crystallinity; Protein formulation; Protein sustained release

Abstract

The objectives of this study were to prepare lipid-based implants by hot melt extrusion (HME) for the prolonged release of ovalbumin (OVA), and to relate protein release to crystallinity and polymorphic changes of the lipid matrix. Two lipids, glycerol tristearate and hydrogenated palm oil, with different composition and degree of crystallinity were studied. Solid OVA was dispersed within the lipid matrixes and it preserved its stability during extrusion. This was partially attributed to a protective effect of the lipidic matrix. The incorporation of OVA decreased the mechanical strength of the implants prepared with the more crystalline matrix, glycerol tristearate, whereas it remained comparable for the hydrogenated palm oil because of stronger physical and non-covalent interactions between the protein and this lipid. This was also the reason for the faster release of OVA from the glycerol tristearate matrix when compared to the hydrogenated palm oil (8 vs. 28 weeks). Curing induced and increased crystallinity, and changes in the release rate, especially for the more crystalline matrix. In this case, both an increase and a decrease in release, were observed depending on the tempering condition. Curing at higher temperatures induced a melt-mediated crystallization and solid state transformation of the glycerol tristearate matrix and led to rearrangements of the inner structure with the formation of larger pores, which accelerated the release. In contrast, changes in the hydrogenated palm oil under the same curing conditions were less noticeable leading to a more robust formulation, because of less polymorphic changes over time. This study helps to understand the effect of lipid matrix composition and crystallinity degree on the performance of protein-loaded implants and to establish criteria for the selection of a lipid carrier depending on the release profile desired.

1. Introduction

Controlled release delivery systems for peptides and proteins have been developed not only to have an extended drug release, but also to protect these labile compounds from detrimental conditions during preparation, storage and upon administration (i.e. pH variations and