Poly(Lactide-*co*-Glycolide) Nanoparticles, Layer by Layer Engineered for the Sustainable Delivery of AntiTNF-α[a]

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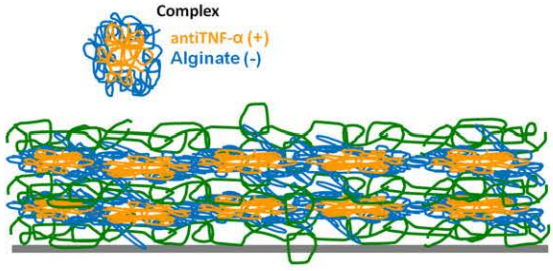
A strategy of encapsulation of the antiTNF-α antibody on top of poly(lactide-*co*-glycolide) nanoparticles (PLGA NPs) is presented on the basis of the complexation of antiTNF-α with alginate (Alg) and subsequent assembly layer by layer with poly(L-lysine) (PLL). The assembly of the antiTNF-α/Alg complex with PLL and its stability in PBS and lysozymes are monitored on a planar support using a quartz crystal microbalance with dissipation. The assembly of the antiTNF-α/Alg complex on PLGA NPs is followed by zeta potential measurements. AntiTNF-α release from the PLGA NPs is measured in PBS at 37 and 60 °C and in the HepG2 cell line following NP uptake, using the Q-ADA kit detection kit. The release follows first-order kinetics with an initial burst. Intracellular release of antiTNF-α is confirmed by confocal Raman microscopy.



1. Introduction

In recent years, biomedical research has been highly focused in the development of effective and specific therapeutic agents. Among the novel therapeutic agents, the current sales volume of therapeutic monoclonal antibodies is the largest, underlining their great importance for curing complex diseases, such as autoimmune diseases and cancer.[1] Adalimumab, also known as Humira or antiTNF-α, was one of the first monoclonal antibodies in the market. This antibody binds to tumor necrosis factor alpha (TNF-α), thereby down-regulating inflammatory reactions in autoimmune diseases.[2] Meanwhile, there are more than one hundred different antibodies or antibody fragments undergoing trials or even on the market. The administration of therapeutic antibodies is generally done by means of injection or infusion, since oral administration is not possible. The drawbacks of this systemic administration route are that they include non-specific off-target binding resulting in adverse effects, caused by the required high doses of the antibodies. Any reduction in the doses by controlling the release on the targeted site would decrease adverse effects and also the costs of these comparatively highly priced medications. Local-delivery systems with prolonged controlled release are thus highly desirable. In addition, it is necessary to find ways of protecting the antibodies from the proteolytic enzymes active at inflammation sites.

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[a] **Supporting Information** is available from the Wiley Online Library or from the author.