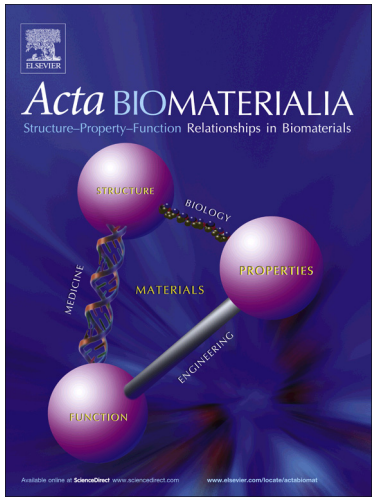

Full length article

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Controlled Release of an HDAC Inhibitor for Reduction of Inflammation in Dry Eye Disease

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Key Words: HDACi, SAHA, Microspheres, PLGA, dry eye disease

Abstract

Dry eye disease (DED), also known as keratoconjunctivitis sicca, is an ocular surface disease characterized by T-cell-mediated inflammation. Current therapeutics, such as immunosuppressive agents, act to suppress the clinical signs and inflammation. However, long-term usage of these treatments can cause severe side effects. In this study, we present an alternative therapeutic approach that utilizes a histone deacetylase inhibitor (HDACi) to regulate transcription of a variety of immunomodulatory genes. Specifically, HDACi have emerged as a potential anti-inflammatory agent, which can modulate the functions of a subset of suppressive T lymphocytes known as regulatory T cells (Tregs), enhancing FoxP3 acetylation and subsequently guarding the transcription factor from proteasomal degradation. Here, a specific HDACi known as SAHA (suberoylanilide hydroxamic acid) was formulated to controllably release in the lacrimal gland. Intralacrimal gland injection of PLGA-based SAHA microspheres prevented