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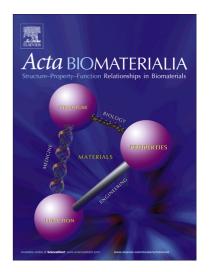
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ACCEPTED MANUSCRIPT

Controlled Release of an HDAC Inhibitor for Reduction of Inflammation in Dry Eve 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

T-cell-mediated characterized bv 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

1

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