Escin Inhibits Type I Allergic Dermatitis in a Novel Porcine Model

Wolfgang Sipos a Benjamin Reutterer c Maria Frank c Hermann Unger b Andreas Grassauer c Eva Prieschl-Grassauer c Petra Doerfler c

a Clinical Department for Farm Animals and b Laboratory of Tropical Veterinary Medicine, University of Veterinary Medicine, and c Marinomed Biotechnologie GmbH, Vienna, Austria

Key Words
Allergy • Type I hypersensitivity • Escin • Skin prick test • Pig • Compound 48/80 • Glucocorticoid receptor

Abstract
Background: Current standard medications for the treatment of allergic inflammation consist primarily of glucocorticoids and anti-histamines, but adverse side effects or insufficient responsiveness by patient subpopulations illustrate the need for safe and novel alternatives. Thus, there is a demand to develop a porcine model that is able to mimic mast cell-mediated type I hypersensitivity. Previously, we found that escin, a pharmacologically active mix of triterpene saponins from horse chestnut extracts, exerts anti-allergic effects in murine models and merits further investigation as an anti-allergic therapeutic. Methods: We developed a new porcine model of allergic dermatitis based on a clinical prick test protocol. Histamine clearly provoked erythema and swelling at the prick site, whereas the mast cell-degranulating compound 48/80 even more pronounced caused wheal and flare reactions known from the human prick response. This model was used to test the anti-allergic efficacy of orally applied escin. Results: Oral pretreatment of animals with escin strongly inhibited the allergic skin response induced by compound 48/80 in a dose-dependent manner. Additional in vitro data from murine mast cells indicate an engagement of the glucocorticoid receptor pathway upon treatment with escin. Conclusions: This model provides a valuable and easy-to-set-up tool for preclinical studies of mast cell-inhibiting compounds. The successful implementation of this model supports the development of oral escin applications as a novel anti-allergic therapy.

Introduction

Type I hypersensitivity is an increasing health threat in Western civilization [1]. It is characterized by excessive activation of immune cells, primarily mast cells, basophils, and T helper cells, in response to contact with diverse environmental agents, such as pollen, house dust mite excreta, or ingredients of food or cosmetics [2]. Fce receptors on mast cells or basophils are activated by cross-linking via allergens that are bound to IgE antibodies in sensitized individuals. Within minutes of allergen exposure, these activated cells release various preformed or rapidly synthesized mediators such as histamine and serotonin, which elicit vasodilation, increased vascular