

Allergic Contact Dermatitis from the Vehicle Components of Topical Pharmaceutical Products



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KEYWORDS

- Allergic contact dermatitis • Iatrogenic • Topical pharmaceutical products
- Excipients • Preservatives • Fragrances

KEY POINTS

- The different categories in which the most important allergens can be classified are excipients, preservative agents, antioxidants, and fragrance components.
- The most frequently encountered allergens among the excipients are wool alcohols, propylene glycol, sorbitan oleate esters, and cetyl- en stearyl alcohol.
- The most frequently encountered allergens among the preservative agents are thimerosal, parabens, benzoic acid, and mercurials.
- The most frequently encountered allergens among the antioxidants are ethylene diamine (complexing agent) and (bi) sulfites.
- The most frequently encountered allergens among the fragrance components found in topical drugs are essential oils.

INTRODUCTION

The local application of pharmaceutical products may induce allergic and photo-allergic contact dermatitis (and, in some cases, skin reactions after systemic administration of the allergen or a chemically related compound), contact urticaria (immediate-type reactions), irritation, and systemic adverse effects caused by drug absorption. This article will only discuss allergic contact dermatitis.

ALLERGIC CONTACT DERMATITIS FROM TOPICAL PHARMACEUTICAL PRODUCTS

Topical pharmaceutical products are, in general, applied to diseased or inflamed skin, the barrier function of which is often incapacitated, leading to enhanced skin penetration of the applied chemicals. In such cases, even weak allergens are able to induce

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sensitization. Hence, contact allergy to topical pharmaceutical products is common, particularly in subjects suffering from stasis eczema and/or leg ulcers, perianal dermatitis, and otitis externa, but also in individuals with irritant and/or other pre-existing eczematous conditions.¹⁻⁴

NATURE OF THE CONTACT ALLERGENS

The contact allergens in topical pharmaceutical products concern active principles and vehicle components. Not only products such as creams, ointments, and solutions, but also wound dressings may be involved.

This article will concentrate on the vehicle components. **Box 1** gives the number of cases with positive patch-test reactions to vehicle components of topical pharmaceutical products (ie, excipients, preservative agents, and fragrances). The allergens have been identified in a total population of 17,367 patients tested between 1990 and 2013, of whom 2513 (14.5%) presented with an allergic iatrogenic contact dermatitis.

The different categories in which the most important allergens can be classified are listed in **Box 1**.^{1,2}

Excipients

Excipients include wool alcohols (eg, eucerin and lanolin), propylene glycol, sorbitan oleate esters, and cetyl- en stearyl alcohol. **Fig. 1** shows a positive reaction to isopropyl myristate. **Fig. 2** shows clinical symptoms and positive patch-test reaction to cetyl alcohol in a 15-month-old atopic baby, due to its presence in a pharmaceutical cream.

Preservative Agents

Preservative agents include thimerosal, parabens, benzoic acid, mercurial, and benzalkonium chloride. **Fig. 3:** shows contact dermatitis from a combination preparation containing a local antibiotic and corticosteroid caused by the preservative potassium sorbate (sorbic acid also positive).

Antioxidants

Antioxidants include ethylene diamine (complexing agent), previously the main allergen in a combined antimycotic/antibiotic/anti-inflammatory widely used cream, (b) sulfites (test substance sodium metabisulfite),⁵ and butylhydroxyanisole.

Perfume Components

Previously these were often present in historical wound-healing preparations, but they actually are still used in many preparations, including nonsteroidal anti-inflammatory products, which for example contain lavender, geranium-, or other essential oils. Indeed, in a previous study, the author could demonstrate that 10% of the topical pharmaceutical products in Belgium were found to contain fragrance components.⁶ **Fig. 4** shows allergic contact dermatitis from fragrance components, including lavender oil in a nonsteroidal anti-inflammatory product.

Wound dressings

In general, wound dressings mainly contain higher molecular (polymeric) compounds that are less likely to induce sensitization, and thus seem to be safer than the previously used creams and ointments; however, some additives, particularly in hydrocolloids, such as modified colophony or antioxidants, may still be the allergenic culprits.^{7,8}

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