

- CONTRIBUTIONS TO THIS SECTION MAY NOT UNDERGO PEER REVIEW, BUT WILL BE REVIEWED BY THE EDITOR •

Allergic contact dermatitis caused by aftershave creams containing *Glycyrrhiza inflata*

Laura Wuyts, Tom van Hoof, Julien Lambert and Olivier Aerts

Department of Dermatology, University Hospital Antwerp (UZA) and University of Antwerp (UA), 2650 Antwerp, Belgium

doi:10.1111/cod.12725

Key words: aftershave creams; allergic contact dermatitis; case report; cosmetics; facial dermatitis; *Glycyrrhiza inflata*; herbal extracts; liquorice; patch tests.

Herbal extracts, which are often perceived by consumers as innocuous, may cause allergic contact dermatitis. We describe 2 male patients suffering from facial dermatitis following the use of aftershave creams containing *Glycyrrhiza inflata*.

Case Reports

Case 1

A 60-year-old atopic male who presented with facial dermatitis, extending down his neckline, that had been present for 6 months. A skin biopsy identified spongiotic dermatitis, and patch tests were performed on the upper back with his own cosmetics (including an after-shave cream, tested 'as is'), a baseline series, and a cosmetic series (Chemotechnique, Vellinge, Sweden), all with patch test chambers from Allergeaze® (SmartPractice, Calgary, Canada). After an occlusion time of 2 days with Fixomull® stretch (BSN Medical, Hamburg, Germany), reactions were read according to ESCD guidelines. On day (D) 4, reactions were seen to *Myroxylon pereirae* (balsam of Peru; +), which was considered to account for previous axillary dermatitis resulting from the use of a deodorant, and to his own aftershave cream (++), explaining his facial dermatitis. No later reactions were reported. Additional patch tests were performed with the individual ingredients of the cream obtained from the manufacturer, including *G. inflata* (delivered as a dry, brown powder and



Fig. 1. A (++) reaction to *Glycyrrhiza inflata* 1% eth. on day 4 in Case 1.

diluted in-house to 1% in pet. and 1% in eth.), for both of which ++ reactions were scored on D4 (Fig. 1). Twenty control patients did not react to this allergen when it was patch tested 1% pet. The patient's rash healed after treatment with a topical corticosteroid, and, following our advice to avoid both liquorice-containing products and fragranced cosmetics, has not recurred since.

Case 2

A 70-year-old atopic male who developed pruritic dermatitis of the beard region several hours after shaving, sometimes accompanied by papulovesicular lesions in his neck, on his hands, and on his legs. Patch tests were performed as in Case 1, and showed positive reactions on D4

Correspondence: Dr Olivier Aerts, Department of Dermatology, University Hospital Antwerp (UZA) and University of Antwerp (UA), Wilrijkstraat 10, B-2650 Antwerp, Belgium. Tel: +32 38214272; Fax: +32 38253428. E-mail: olivier.aerts@uza.be

Conflicts of interest: The authors declare no conflict of interests.

to methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) 0.02% aq. (++), MI 0.2% aq. (++), and benzoic acid 5% pet. (+), all three of which were present in his own personal care products; MI was also found in a shoe polish, contributing to his hand dermatitis. He also reacted to methyldibromo glutaronitrile 0.3% pet. (+), for which no relevance was found, and to *G. inflata* 1% pet. (+), found in an aftershave cream that the patient brought in on D4. His skin condition healed following avoidance of all identified contact allergens. An additional patch test with dipotassium glycyrrhizate 1% pet. (kindly provided by Professor An Goossens) gave a negative result.

Discussion and Conclusion

Liquorice is the root of plants belonging to the genus *Glycyrrhiza*, comprising at least 30 species, including *Glycyrrhiza glabra*, *Glycyrrhiza uralensis*, and *G. inflata*. Oil-soluble (ethanolic) extracts mainly contain flavonoids (e.g. glabridin), whereas water-soluble (dry) extracts typically contain saponins such as glycyrrhizin, a mixture of potassium and calcium salts of 18 β -glycyrrhizic acid (glycyrrhizate), which may be hydrolysed to form 18 β -glycyrrhetinic acid (syn. glycyrrhizinate; enoxolone) (1–6). Enoxolone possesses (mild) anti-inflammatory properties, which is why it has been included in a medical specialty to treat atopic and allergic contact dermatitis (Atopiclair®; Graceway Pharmaceuticals, Bristol, TN, USA) (2).

Other applications include use as flavouring agents in pharmaceuticals, tobacco, beer, candy, food supplements, and herbal teas. Moreover, these extracts are popular in Chinese and modern folk medicine (e.g. as an expectorant, to relieve throat irritation, for peptic ulcers, and for digestive problems) (3). Furthermore, oil-soluble liquorice extracts inhibit tyrosinase activity *in vitro* and promote depigmentation (4, 6, 7), making them popular ingredients in skin-lightening cosmetics in Asia. Glycyrrhizin

is also used as an adhesive agent in insecticides, and as a surfactant (1). *G. inflata* root extract, the variant specifically reported here, can be present as a skin conditioning agent in sunscreens and in cosmetics marketed for use in individuals with acne, or with 'sensitive' and rosacea-prone skin.

Liquorice derivatives may be used in cosmetics in varying concentrations, usually from 0.1% to 5%. They are probably only poorly absorbed through the (intact) skin, and they are considered to be relatively safe, that is, without obvious irritant or (photo-)sensitizing properties (1). Interestingly, weaker reactions to higher concentrations of the steroid-like enoxolone have been observed during patch testing, which (similarly to the situation with corticosteroids) may be attributable to a dominating anti-inflammatory effect (2). A summary of previously published cases of allergic contact dermatitis caused by liquorice derivatives is given in Table S1 (3–16).

To conclude, although allergic contact dermatitis caused by cosmetics is mostly observed in female patients, and is only rarely attributable to liquorice derivatives, we have reported 2 male patients in whom *G. inflata*-containing creams, applied onto damaged (shaved) skin, induced contact allergy and subsequent allergic contact dermatitis.

Acknowledgements

We are grateful to Professor An Goossens and Ms Liesbeth Gilissen, RPharm (KU Leuven, Belgium) for sending us patch test material of dipotassium glycyrrhizate.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Previously published cases of allergic contact dermatitis caused by liquorice derivatives.

References

- 1 Cosmetic Ingredient Review Expert Panel. Final report on the safety assessment of Glycyrrhetinic Acid, Potassium Glycyrrhetinate, Disodium Succinoyl Glycyrrhetinate, Glyceryl Glycyrrhetinate, Glycyrrhetinyl Stearate, Stearyl Glycyrrhetinate, Glycyrrhizic Acid, Ammonium Glycyrrhizate, Dipotassium Glycyrrhizate, Disodium Glycyrrhizate, Trisodium Glycyrrhizate, Methyl Glycyrrhizate, and Potassium Glycyrrhizinate. *Int J Toxicol* 2007; **26**: 79–112.
- 2 Sasseeville D, Desjardins M, Almutawa F. Allergic contact dermatitis caused by glycyrrhetinic acid and castor oil. *Contact Dermatitis* 2011; **64**: 168–169.
- 3 Cabrita S F, Silva R, Correia M P. Allergic contact dermatitis due to glycyrrhizic acid as an ingredient of a hair restorer. *Contact Dermatitis* 2003; **49**: 46.
- 4 Nishioka K, Seguchi T. Contact allergy due to oil-soluble licorice extracts in cosmetic products. *Contact Dermatitis* 1999; **40**: 56.
- 5 Kanoh H, Banno Y, Nakamura M, Seishima M. Contact allergy to liquorice flavonoids: analysis with liquid chromatography–mass spectrometry. *Contact Dermatitis* 2016; **74**: 191–192.
- 6 Numata T, Kobayashi Y, Ito T et al. Two cases of allergic contact dermatitis due to skin-whitening cosmetics. *Allergol Int* 2015; **64**: 194–195.
- 7 Madhogaria S, Ahmed I. Leucoderma after use of a skin-lightening cream containing kojicdipalmitate, liquorice root extract

- and Mitracarpusscaber extract. *Clin Exp Dermatol* 2010; **35**: 103–105.
- 8 Matsunaga K, Fujisawa Y. Two cases with allergic contact dermatitis due to whitening agents. *Aesthet Dermatol* 1995; **5**: 81–86.
 - 9 Kuriyama Y, Takano T, Okada F, Nukada T. Hypersensitivity to glycyrrhizin. A case report. *Med J Osaka Univ* 1975; **26**: 75–78.
 - 10 Fernández J, Gamboa P, Jáuregui I et al. Concomitant sensitization to enoxolone and mafenide in a topical medicament. *Contact Dermatitis* 1992; **27**: 262.
 - 11 Tanaka S, Otsuki T, Matsumoto Y. Allergic contact dermatitis from enoxolone. *Contact Dermatitis* 2001; **44**: 192.
 - 12 Oiso N, Ota T, Yoshinaga E et al. Allergic contact dermatitis mimicking atopic dermatitis due to enoxolone in a topical medicament. *Contact Dermatitis* 2006; **54**: 351.
 - 13 Villas-Martinez F, Joral Badas A, Garmendia Goitia J F, Aguirre I. Sensitization to oral enoxolone. *Contact Dermatitis* 1994; **30**: 124.
 - 14 Benomar S, Ismaili N, Koufane J et al. Fixed food eruption caused by liquorice. *Ann Dermatol Venereol* 2010; **137**: 121–123.
 - 15 Benomar S, Frémont G, Hassam B, Dubertret L. Une cause inhabituelle d'érythème pigmenté fixe. *La lettre du Gerda* 2008; **20**: 1.
 - 16 Cartier A, Malo J-L, Labrecque M. Occupational asthma due to liquorice roots. *Allergy* 2002; **57**: 863.

Table S1: Previously published cases of allergic contact dermatitis from liquorice-derivatives.

Reference	Clinical presentation	Culprit allergen source and/or liquorice-derivative
3	Scalp allergic contact dermatitis	A hair-restoring preparation containing glycyrrhizic acid
4-8	Facial allergic contact dermatitis (sometimes with leukoderma)	Skin whitening agents based on oil-soluble liquorice-extracts (usually containing glabridine or licoflavone A)
9	“Skin hypersensitivity reaction” (unspecified)	Glycyrrhizin
2; 10-12	Allergic contact dermatitis (various locations, depending on the culprit product used)	Enoxolone, present in deodorants, after-sun creams, pharmaceutical ointments for atopic dermatitis, and in hemorrhoidal creams
13	Delayed-onset facial angioedema	Oral ingestion of enoxolone
14-15	Exanthema and fixed drug (fixed food) eruption	Oral ingestion of liquorice candy
16	IgE-mediated occupational asthma and rhinoconjunctivitis	Powder from liquorice roots