

Allergic contact dermatitis from *Dittrichia graveolens* (L.) Greuter (stinkwort)

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Case Report

A 56-year-old man was referred with episodes of blistering of his dorsal hands, gradually progressing to marked extensive hyperkeratosis for 5 years. He had been treated with several courses of systemic corticosteroids, but the treatment did not result in complete skin lesion resolution. He reported to be clinically intolerant to leather gloves and plants. His past medical history was remarkable for psoriasis. There was no personal or family history of atopy. As he is a heavy-equipment hauler, his job depends on his ability to come in contact with plants. He brought in a sample of the plant that he believed was responsible, and it was identified as *Dittrichia graveolens* (stinkwort).

Physical examination showed hand dermatitis with marked erythema and hyperkeratosis on the dorsum of hands and, in lesser degree, hyperkeratosis at the elbows and knees. Patch tests were performed with the North American Contact Dermatitis Research Group standard series and the plant series (Chemotechnique, Malmo, Sweden), left occlusive for 48 h, and a fragment of *D. graveolens*, which was left under a non-occlusive tape, microphore for 30 min then removed. No controls were tested.

The sites were read on 48 and 96 h. The International Contact Dermatitis Research Group (ICDRG) grading scale was utilized (1). Positive reactions are summarized in Table 1.

On further review of history, he did not have clinical history of intolerance to fragrance. The positive reaction to potassium dichromate confirmed his history of intolerance to leather gloves. His reactions to multiple plant species (i.e. the last 5 Compositae reactions in Table 1) suggested that he might have developed a hypersensitivity to chemicals in these 'related' plants. We advised the patient to avoid leather gloves and to use protective vinyl gloves with cotton lining or undergloves every time during work when handling the plants. His skin lesions were also treated with class I topical corticoid (clobetasol cream) with vinyl glove occlusion at bedtime. He was clear on follow-up 2 months later.

Comment

Cases of allergic contact dermatitis from *Dittrichia viscosa* (*Inula viscosa*), a closely related species to *D. graveolens* had been reported (2, 3). Older literature reported both allergic and irritant contact dermatitis from *D. graveolens*, mostly in Australia (4). However, cases of allergic contact dermatitis due to *D. graveolens* have rarely been reported in the USA because it is a relatively new invasive plant in this country.

Dittrichia graveolens (syn. *Inula graveolens* (L.) Desf., common name: stinkwort) is a multibranched, fall-blooming annual, which may superficially resemble a tarweed (Fig. 1) (5). It is usually small and branched from the base, but can grow up to 3 ft high. *Dittrichia graveolens* is sticky, has fine hairs, and smells strongly of camphor. It has alternate narrow and grayish-green leaves. Its ray flowers are small and yellow with tiny petals.

Its seeds look like the typical spherical fluffy daisy seed heads (6).

Dittrichia graveolens, a Compositae, is a weed native to the Mediterranean region but has become naturalized in many parts of southern Australia. It was first identified in California on a levee at the San Francisco Bay Wildlife Refuge in Alameda County in 1995 and thus is a fairly new invasive plant. It is now found in at least 6 counties in northern California including Alameda, Contra Costa, and Santa Clara, San Mateo, Solano, and Yolo Counties (6, 7).

Dittrichia graveolens can spread rapidly as an invasive weed. The fine hairs of the seeds help with wind dispersal, and this explains the airborne pattern of allergic contact dermatitis (3). They also stick to clothing, wool, hair, and machinery and spread in contaminated soil. Pyogranulomatous enteritis in sheep due to penetrating seed heads of *D. graveolens* has been reported (8). There is scant literature on the human effect of *D. graveolens*.

This plant has been chemically investigated and several pharmacologically active sesquiterpenes (9–12), flavonoids (13), and aromatic compounds (9) have been isolated. The constituents of the plant included (i) eudesmanolides: 11,13-dihydroivalin (9) and 3 α -hydroxy-eudesm-4-en-12,6 β -olide (10); (ii) sesquiterpene lactones: ivalin, inuviscolide, 8-epi-inuviscolide, 8-epi-xanthatin-1 β , 5 β -epoxide (9) and 4 α ,5 α -epoxyinuviscolide; (iii) the xanthanolides: tomentosin and 4H-tomentosin; (iv) the carabrones: carabrone and 4H-carabrone; (v) the sesquiterpene acids: costic acid, 2 α -hydroxycostic acid, 3 α -hydroxycostic acid, 1 β -hydroxycostic acid, isocostic acid, and ilicic acid; (vi) the flavonone: sakuranetin; (vii) the dihydroflavonols: aromadendrin, 7-O-methylaromadendrin, 3-O-acetyl-7-O-methylaromadendrin, 3-O-acetyl-taxifolin, padmatin, 3-O-acetylpadmatin,

Table 1. Positive patch test reactions

	% pet.	48 h	96 h
Potassium dichromate	0.25	+	++
Balsam of Peru	25	+	++
Fragrance mix	8	+	++
Compositae mix	5	+	++
<i>Chrysanthemum cinerariaefolium</i>	1	+	++
<i>Tanacetum vulgare</i>	1	–	++
Parthenolide	0.1	+	++
<i>Dittrichia graveolens</i> (leaf, 30 min)		+++	+++



Fig. 1. *Dittrichia graveolens*.

3-*epi*-padmatin, and 3-*epi*-acetyl-7-*O*-methyларomadendrin; (viii) the flavones: scutellarein-6-methylether, kaempferol, kaempferol-3-methylether, and 6-hydroxykaempferol-3, 6-dimethylether; (ix) the aromatics: *p*-hydroxybenzoic acid and 2-(*p*-hydroxyphenyl)ethylstearate; and also (x) *epi*-acadinol and bornyl acetate (14).

Similar to *D. viscosa*, the main allergens of *D. graveolens* are sesquiterpene lactones, namely inuviscolide (3, 15). Because multiple simultaneous positive reactions to sesquiterpene lactones with different structures have been reported (16, 17), as well as positive patch tests to *Frullania*, *Laurus nobilis*, and other Compositae due to cross-reaction (18, 19), this explains the multiple positive patch test reactions in our patient. The volatile oils isolated from the plants might also cross-react to fragrance mix and Balsam of Peru, producing the positive patch test reactions.

A patch test with extracts diluted to 0.5% or 1% in pet. or patch testing with the leaf as we did in this patient is recommended (3, 20). Short-term application of dried leaf without

occlusion appears not to give false-positive irritant reactions (20). Lowell (20) suggested that such application is not irritating, and we accepted this as our control. Because *D. graveolens* is a relatively new invasive plant in the USA, its ability to colonize a range of sites is unknown. We believe most patients can continue their occupational activities, using appropriate protection of the hands.

An algorithm for defining primary sensitization to a plant chemical may be readily performed in a virgin guinea-pig. Unfortunately, the highly variable adult human exposure prevents identifying the primary allergenic exposure. Details of diagnostic patch testing with plant parts are found in Mitchell (21).

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References

1. Wilkinson D S, Fregert S, Magnusson B et al. Terminology of contact dermatitis. *Acta Derm Venereol* 1970; 50: 287–292.
2. Estrela F, Tapadinhas C, Pereira F. Allergic contact dermatitis from *Dittrichia viscosa* (L.) Greuter. *Contact Dermatitis* 1995; 32: 108–109.
3. Goncalo M, Goncalo S. Allergic contact dermatitis from *Dittrichia viscosa* (L.) Greuter. *Contact Dermatitis* 1991; 24: 40–44.
4. Mitchell J, Rook A. *Botanical Dermatology. Plants and Plants Products Injurious to the Human Skin*. Greengrass, Vancouver, 1979: 209.
5. Herbario Virtual del Mediterraneo Occidental, Avea de Botanica, Departament de Biologia, Universitat de les Illes Balears. (Available from <http://herbarivirtual.uib.es/eng-med/especie/4448.html>).
6. Barry S. Keeping Landscapes Working. *Newsl Managers Bay Area Rangeland* 2005; 2: 7.
7. United States Department of Agriculture Natural Resource Conservation Service. (Available from <http://plants.usda.gov>).
8. Philbey A W, Morton A G. Pyogranulomatous enteritis in sheep due to penetrating seed heads of *Dittrichia graveolens*. *Aust Vet J* 2000; 78: 858–860.
9. Topçu G, Öksüz S, Shieh H L, Cordell G A, Pezzuto J M, Bozok-Johansson C. Cytotoxic and antibacterial sesquiterpenes from *Inula graveolens*. *Phytochemistry* 1993; 33: 407–410.
10. Öksüz S, Topçu G. A eudesmanolide and other constituents from *Inula graveolens*. *Phytochemistry* 1992; 31: 195–197.
11. Lanzetta R, Lama G, Mauriello G, Parrilli M, Racioppi R, Sodano G. Ichthyotoxic sesquiterpenes and anthranolides from *Dittrichia graveolens*. *Phytochemistry* 1991; 30: 1121–1124.
12. Rustaiyan A, Jakupovic J, Chau-Thi T V, Bohlmann F, Sadjadi A. Further sesquiterpene lactones from the genus *Dittrichia*. *Phytochemistry* 1987; 26: 2603–2606.
13. Souleles Ch, Philianos S. Chemical constituents of *Inula graveolens* Dest. *Fitoterapia* 1979; L: 251–254.
14. Petropoulou A, Tzakou O, Verykokidou E. Volatile constituents of *Dittrichia graveolens* (L.) greuter from Greece. *J Essential Oil Research* 2004; 16: 400–401.
15. Pinedo J M, De Canales F G, Hinojosa J L, Llamas P, Hausen B

- M. Contact dermatitis to sesquiterpene lactones in *Inula viscosa* Aiton. *Contact Dermatitis* 1986; 17: 322–323.
16. Epstein W L, Reynold G W, Rodriguez E. Sesquiterpene lactone dermatitis. Cross-sensitivity in costus-sensitized patients. *Arch Dermatol* 1980; 116: 59–60.
 17. Benezra C, Epstein W L. Molecular recognition patterns of sesquiterpene lactones in costus-sensitive patients. *Contact Dermatitis* 1986; 15: 223–230.
 18. Pecegheiro M, Brandao F M. Airborne contact dermatitis to plant. *Contact Dermatitis* 1985; 13: 277–279.
 19. Benezra C, Ducombs G, Sell Y, Foussereau J. *Plant Contact Dermatitis*. Toronto, Decker Inc., 1985: 105–149.
 20. Lowell C R. *Plants and the Skin*. Oxford, Blackwell Scientific Publications, 1993: 165.
 21. Mitchell J C, Maibach H I. Diagnosis and patch testing of plant dermatitis. In: *Dermatologic Botany*, Vol. 4, Avalos J, Maibach H I (eds): Boca Raton, CRC Press, 2000: 39–44.

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