

## Positive patch test reaction to *Lonicera japonica* extract in a patient sensitized to formaldehyde

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A 40-year-old female patient presented with generalized eczema resistant to oral and topical steroids. The dermatitis had started on her legs after use of postepilation soothing remedies, and had become worse following liberal applications of a body lotion for 'sensitive/allergic skin'. After remission, obtained by a short course of cyclosporin A and withdrawal from topical products, the patient was patch tested with the Società Italiana di Dermatologia Allergologica Professionale ed Ambientale (SIDAPA) Baseline series, a cosmetic series, and her own products. She reacted positively to formaldehyde (+ at D2 and ++ at D3), fragrance mix I (+ at both D2 and D4), nickel sulfate (+ at D2 and D3),

and to three of her products. Two of these contained formaldehyde-releasers and fragrances, whereas the third product, the body lotion, was free of them. Its patch test reactivity (+ at D2 and ++ at D3) was corroborated by a positive repeated open application test result within just two applications. Further patch testing with its individual ingredients, provided by the manufacturer and diluted according to existing guidelines (1), gave positive results only with *Lonicera japonica* flower extract 2% aqua (+ at D2 and D3) and 5% aqua (++ at D2 and D3) (Fig. 1). Patch testing with the *Lonicera* extract gave negative results in 15 controls. When patch testing was performed, the *Lonicera* extract sample was odourless, but 5 months later it had a pungent formaldehyde odour. Gas chromatography (GC) head space analysis, performed with a Hewlett Packard 5971 GC/mass spectrometry (MS) instrument, with a detection limit of 50 ppm, confirmed the presence of formaldehyde in the *Lonicera* extract but not in the body lotion. The

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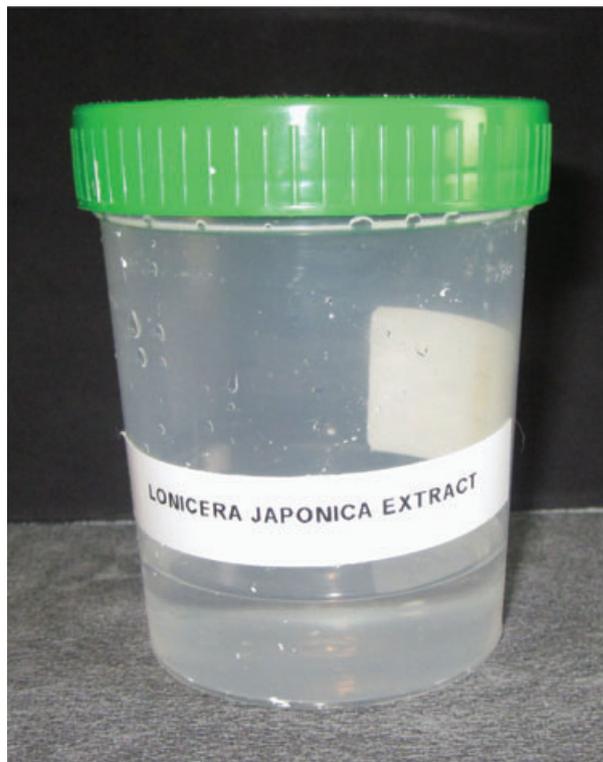


**Fig. 1.** Positive patch test reactions to *Lonicera japonica* extract (D3 reading).

*Lonicera* extract was also analysed for the presence of the individual components of fragrance mix I, with negative results.

## Discussion

*L. japonica* extract is the aqueous extract from the flowers of the Japanese honeysuckle (Caprifoliaceae), a popular remedy in traditional Chinese medicine. It has both anti-inflammatory and antimicrobial activity, the latter possibly attributable to a mixture of esters of lonicerin and natural *p*-hydroxybenzoic acid (2, 3). Because of these combined properties, it is used in cosmetic products for sensitive/allergic skin, where chemical preservatives are increasingly being replaced by natural antimicrobial ingredients not legislated as preservatives according to Annex VI of Commission Directive 76/768/EEC and the amending directives (2003/15/EC, 2007/17/EC, and 2007/22/EC) (4). Our patient was patch test-positive to the *L. japonica* extract present in the body lotion that had aggravated her allergic contact dermatitis caused by formaldehyde releasers and fragrances. Subsequent GC/MS analysis revealed the presence of formaldehyde in the tested *Lonicera* extract sample. According to its safety data sheet, the *Lonicera* extract may leach trace amounts of hexamine and other formaldehyde releasers from epoxy or phenolic-based plastic packaging. The data sheet specifies that such trace amounts are 'below Japan & EEC regulatory limits of formaldehyde' and recommend that the label should claim 'no preservative' or 'preservative-free'. However, the patch-tested *Lonicera*



**Fig. 2.** Plastic container of the *Lonicera japonica* extract sample that gave positive results for formaldehyde on gas chromatography/mass spectrometry analysis.

extract had leached formaldehyde from its plastic container (Fig. 2) to such an extent that a 2% dilution was sufficient to cause a positive reaction in our patient.

The package of the patient's body lotion was made of high-density polyethylene, a material that is not related to formaldehyde, and GC/MS analysis did not detect formaldehyde in it. The nature of the allergen(s) in the body lotion thus remains obscure. However, this case is noteworthy because it shows that *L. japonica* extract can leach amounts of formaldehyde sufficient to elicit eczema in sensitized patients, whereas the present cosmetic legislation allows it to be included in products labelled 'preservative-free'. Nardelli et al. recently suggested that products containing plant extracts that are potential perfume sensitizers should not be labelled as 'non-scented' or 'fragrance-free', because this may confuse consumers (5). Our case also shows that the statement 'preservative-free' can be misleading when plant-derived materials are used as preservatives.

## References

- 1 de Groot AC. *Patch testing. Test concentrations & vehicles for 3700 allergens*. Amsterdam: Elsevier Science, 1994.
- 2 Kang O H, Choi J G, Lee J H, Kwon D Y. Luteolin isolated from the flowers of *Lonicera japonica* suppresses inflammatory mediator release by blocking NF-kappaB and MAPKs activation pathways in HMC-1 cells. *Molecules* 2010; **15**: 385–398.
- 3 Papageorgiou S, Varvaresou A, Tsirivas E, Demetzos C. New alternatives to cosmetics preservation. *J Cosmet Sci* 2010; **61**: 107–123.
- 4 Varvaresou A, Papageorgiou S, Tsirivas E, Protopapa E, Kintziou H, Kefala V, Demetzos C. Self-preserving cosmetics. *Int J Cosmet Sci* 2009; **3**: 163–175.
- 5 Nardelli A, Thijs L, Janssen K, Goossens A. *Rosa centifolia* in a 'non-scented' moisturizing body lotion as a cause of allergic contact dermatitis. *Contact Dermatitis* 2009; **61**: 306–309.