

LETTER TO THE EDITOR

Rhododendrol-induced leukoderma accompanied by allergic contact dermatitis caused by a non-rhododendrol skin-lightening agent, 5,5'-dipropylbiphenyl-2,2'-diol

Dear Editor,

In 2013, a number of consumers who used rhododendrol-containing cosmetics developed leukoderma at the site of application of the cosmetic in Japan and Taiwan.¹ Here, we report the first case of rhododendrol (4-[4-hydroxyphenyl]-2-butanol; C₁₀H₁₄O₂, Chemical Abstracts Service [CAS] no. 501-96-2, molecular weight [MW] = 166.22)-induced leukoderma accompanied by allergic contact dermatitis caused by 5,5'-dipropylbiphenyl-2,2'-diol (C₁₈H₂₂O₂, CAS no. 20601-85-8, MW = 270.37).

A 64-year-old housewife suffered from itchy erythema on the face for 2 years and noticed leukoderma at the same sites. The leukoderma gradually extended to her neck and forearms. For 2 years, she had been using skin-lightening cosmetics that contained 5,5'-dipropylbiphenyl-2,2'-diol or rhododendrol. When she presented at our hospital, she had leukoderma surrounded by pigmentation and itchy erythema on her face. The leukoderma was prominent on the face, and also affected her neck and forearms. Because we initially suspected allergic contact dermatitis caused by the cosmetics, we performed patch testing using her cosmetics and patch test allergens related to cosmetics after obtaining written informed consent. Finn Chambers (Smart Practice, Phoenix, AZ, USA) were used for the test, and the results were read according to the International Contact Dermatitis Research Group standards. On days 3, 4 and 7, the patient showed a positive reaction (+) to her skin lotion (as is) containing 5,5'-dipropylbiphenyl-2,2'-diol. In the ingredient patch test of this skin lotion, she also showed positive reactions ([+?] on day 4 and [+] on day 7) to 5,5'-dipropylbiphenyl-2,2'-diol (0.5% pet.) and negative reactions to rhododendrol (2% pet). All three healthy control subjects did not react to 5,5'-dipropylbiphenyl-2,2'-diol and rhododendrol.

Rhododendrol was synthesized in Japan as a new skin-lightening agent that suppresses melanogenesis formation.^{2,3} Cosmetics that contained 2% rhododendrol had been sold in 10 Asian countries. The symptoms of depigmentation had been confirmed in approximately 16 000 (2%) of 800 000 estimated users of cosmetic products containing rhododendrol (The Japanese Dermatological Association Special Committee on the Safety of Cosmetics Containing Rhododendrol, 2014 [in Japanese]). On the other hand, Suzuki *et al.*⁴ reported the first case of allergic contact dermatitis caused by the skin-lightening agent, 5,5'-dipropylbiphenyl-2,2'-diol.

Because 5,5'-dipropylbiphenyl-2,2'-diol was a skin lightening agent as well as rhododendrol, we could not deny the possibility that the leukoderma of our patient's face and neck was caused



Figure 1. Clinical course of leukoderma in the patient. (Top) Clinical appearance of her neck at the first visit to our department. There was leukoderma surrounded by pigmentation on her neck. (Bottom) Clinical appearance of the neck 1 year after the first visit. The leukoderma had gradually improved.

by 5,5'-dipropylbiphenyl-2,2'-diol. However, based on the sites of her lesions of leukoderma, we reached the diagnosis of rhododendrol-induced leukoderma accompanied by allergic contact dermatitis from 5,5'-dipropylbiphenyl-2,2'-diol.

After discontinuing the cosmetics containing 5,5'-dipropylbiphenyl-2,2'-diol and rhododendrol, her erythema and leukoderma improved (Fig. 1). Sasaki *et al.*⁵ elucidated that rhododendrol

caused cytotoxicity in melanocytes via a tyrosinase-dependent mechanism. They revealed the occurrence of melanocyte cytotoxicity that might have been triggered by the tyrosinase-dependent conversion of rhododendrol to active product(s). In this present case, we considered that the inflammation of the skin due to repeated allergic contact dermatitis caused by 5,5'-dipropylbiphenyl-2,2'-diol might have increased the percutaneous absorption of rhododendrol. It was necessary for us to consider that the cosmetics caused not only contact dermatitis but also leukoderma.

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CONFLICT OF INTEREST: None declared.

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