

A case of contact dermatitis due to impurities of cetyl alcohol

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A 29-year-old man being treated for itchy lesions on the amputation stump of the thigh became allergic to betamethasone valerate and gentamicin sulfate cream (Rinderon VG®). Closed patch tests with all the ingredients of the cream revealed positive reactions to cetyl alcohol 30% to 5% pet. Gas chromatographic analysis of the cetyl alcohol in the cream base detected stearyl alcohol (C₁₈), myristyl alcohol (C₁₄) and lauryl alcohol (C₁₂) in addition to the main component of cetyl alcohol (C₁₆). Patch testing with 99% pure analytical reagent grade saturated alcohols (C₁₀, C₁₁, C₁₂, C₁₃, C₁₄, C₁₅, C₁₆, C₁₇, C₁₈, C₁₉, C₂₀) showed negative reactions. Thus, it is concluded that some minor impurities in cetyl alcohol not detected by gas chromatography might be the cause of this dermatitis.

Key words: allergic contact dermatitis; topical medicaments; cetyl alcohol; impurities; Rinderon VG®, © Munksgaard, 1997.

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Cetyl alcohol is a liquid, primary, branched chain, C₁₆ alcohol, made up of an array of isomeric compounds maintained in constant proportion by a complex manufacturing process. It is used in cosmetics as an emollient, emulsion modifier and coupling agent, and in pharmaceuticals as an emulsifying and stiffening agent. This is a report of a case of contact dermatitis possibly due to impurities in the cetyl alcohol used in Rinderon VG® cream base.

Method and Materials

Case report

A 29-year-old man underwent a left above-knee amputation for osteosarcoma in 1981 and had since used an artificial limb. In the summer of 1995, he developed itchy lesions on the amputation stump and was treated with erythromycin (Ilotycin®) and gentamicin sulfate ointments (Gentacin®), and betamethasone valerate and gentamicin sulfate creams (Rinderon VG®), but the lesions got worse.

Patch testing

The patient was patch tested with plastic parts of artificial limb, smoothing powder, topical medicaments that he had used, including Rinderon VG®

cream, the European standard series (Trolab®), all the ingredients of Rinderon VG® cream supplied by the manufacturer, and 99% pure analytical reagent grade saturated alcohols (C₁₀, C₁₁, C₁₂, C₁₃, C₁₄, C₁₅, C₁₆, C₁₇, C₁₈, C₁₉, C₂₀) purchased from Nacalai Tesque. Closed patch tests were performed with Finn Chamber® technique. Reactions were read at D2 and D3 according to the recommendations of ICDRG.

10 normal control subjects were patch tested with the cetyl alcohol used in the cream base and petrolatum.

Gas chromatographic analysis of cetyl alcohol

The cetyl alcohol (C₁₆) analysed was that used in the Rinderon VG® cream. The 100% pure cetyl alcohol (C₁₆), stearyl alcohol (C₁₈) and the 99.8% pure myristyl alcohol (C₁₄) were purchased from Wako Pure Chemical and the 99.6% pure lauryl alcohol (C₁₂) from Nacalai Tesque and used as standards. Organic solvents used were of analytical reagent grade.

0.5 g of cetyl alcohol was dissolved in 50 ml of dehydrated ethanol. The gas chromatographic separation was carried out on a model GC-9A gas chromatograph (chromatopac C-R5A, Shimadzu,

Ltd.) with a 2.1 m×3 mm i.d. glass column packed with 5% OV-101 on g-Q 80–100 mesh.

Results

Patch testing

The patch tests revealed positive reactions to Rinderon VG[®] cream, but negative reactions to plastic parts of artificial limb, smoothing powder, other topical medicaments (Table 1). European standard series allergens (Trolab[®]) were negative except wool wax alcohols (Table 1). The patch tests with ingredients of Rinderon VG[®] cream revealed positive reactions to Rinderon VG[®] cream base and cetyl alcohol 30% to 5% pet., but negative reactions to other ingredients of Rinderon VG[®] cream (Table 2). Patch testing with 99% pure analytical reagent grade saturated alcohols (C₁₀, C₁₁, C₁₂, C₁₃, C₁₄, C₁₅, C₁₆, C₁₇, C₁₈, C₁₉, C₂₀) purchased from Nacalai Tesque revealed negative reactions (Table 3). 10 normal control subjects showed negative reactions to the cetyl alcohol used in the cream base and petrolatum.

Table 1. Patch test results with plastic parts of artificial limb, smoothing powder, topical medicaments and the European standard series (Trolab[®])

Substance	D2	D3
plastic parts of artificial limb	??	–
smoothing powder	??	–
Rinderon VG [®] cream	–	+
other topical medicaments (2 kinds)	–	–
standard series allergens		
wool wax alcohols	+	+
others	–	–
white petrolatum as is	–	–
distilled water as is	–	–

Table 2. Patch test results with ingredients of Rinderon VG[®] cream

Substance	D2	D3
Rinderon VG [®] cream	–	+
betamethasone valerate 0.12% pet.	–	–
gentamicin sulfate 20% pet.	–	–
Rinderon VG [®] cream base	++	++
cetyl alcohol ^{a)} 30% pet.	++	++
cetyl alcohol 10% pet.	++	++
cetyl alcohol 5% pet.	+	+
cetyl alcohol 1% pet.	–	–
ingredients of cream base other than cetyl alcohol	–	–
white petrolatum as is	–	–
distilled water as is	–	–

pet. : petrolatum.

^{a)} Cetyl alcohol is a product used in the cream base without purification.

Table 3. Patch test results with 99% pure analytical reagent grade saturated alcohols

Substance	D2	D3
C ₁₀ 19.6% pet. (1.24 mol/kg)	–	–
C ₁₁ 21.3% pet. (1.24 mol/kg)	–	–
C ₁₂ 23.1% pet. (1.24 mol/kg)	–	–
C ₁₃ 24.8% pet. (1.24 mol/kg)	–	–
C ₁₄ 26.5% pet. (1.24 mol/kg)	–	–
C ₁₅ 28.3% pet. (1.24 mol/kg)	–	–
C ₁₆ 30.0% pet. (1.24 mol/kg)	–	–
C ₁₇ 31.7% pet. (1.24 mol/kg)	–	–
C ₁₈ 33.5% pet. (1.24 mol/kg)	–	–
C ₁₉ 35.2% pet. (1.24 mol/kg)	–	–
C ₂₀ 37.0% pet. (1.24 mol/kg)	–	–
white petrolatum as is	–	–

pet. : petrolatum.

Gas chromatographic analysis of cetyl alcohol

In the gas chromatogram of the cetyl alcohol (C₁₆) in the cream base, 4 isolated peaks at the retention time corresponding to the standard samples, i.e., cetyl alcohol (C₁₆), stearyl alcohol (C₁₈), myristyl alcohol (C₁₄) and lauryl alcohol (C₁₂), were detected (Fig. 1).

Discussion

The skin of the amputation stump while using an artificial limb often becomes macerated from long-lasting friction, pressure and sweating (1). Such conditions predisposed the patient to the development of allergic contact dermatitis due to topical medicaments.

The results of patch testing in our case revealed positive reactions to the cetyl alcohol used in the cream base. According to the manufacturer, cetyl alcohol used in cosmetics contains 50–60% cetyl alcohol (C₁₆), 30–35% stearyl alcohol (C₁₈) and 10% myristyl alcohol (C₁₄) (2). Gas chromatographic analysis of the cetyl alcohol used in the cream base detected cetyl alcohol (C₁₆), small peaks of stearyl alcohol (C₁₈), myristyl alcohol (C₁₄) and lauryl alcohol (C₁₂). Hence, we patch tested with 99% pure analytical reagent grade saturated alcohols (C₁₀, C₁₁, C₁₂, C₁₃, C₁₄, C₁₅, C₁₆, C₁₇, C₁₈, C₁₉, C₂₀) and observed totally negative reactions. We have to speculate that 1 or more substances not detected under our experimental conditions could be the cause of the allergic reaction in our case.

There are several reports of contact dermatitis due to cetyl alcohol (3–7). Hannuksela et al. (5) reported that the real cause of contact hypersensitivity could be impurities in commercial batches sold as cetyl alcohol (C₁₆), because chemically pure cetyl alcohol (C₁₆) had not produced a positive patch test

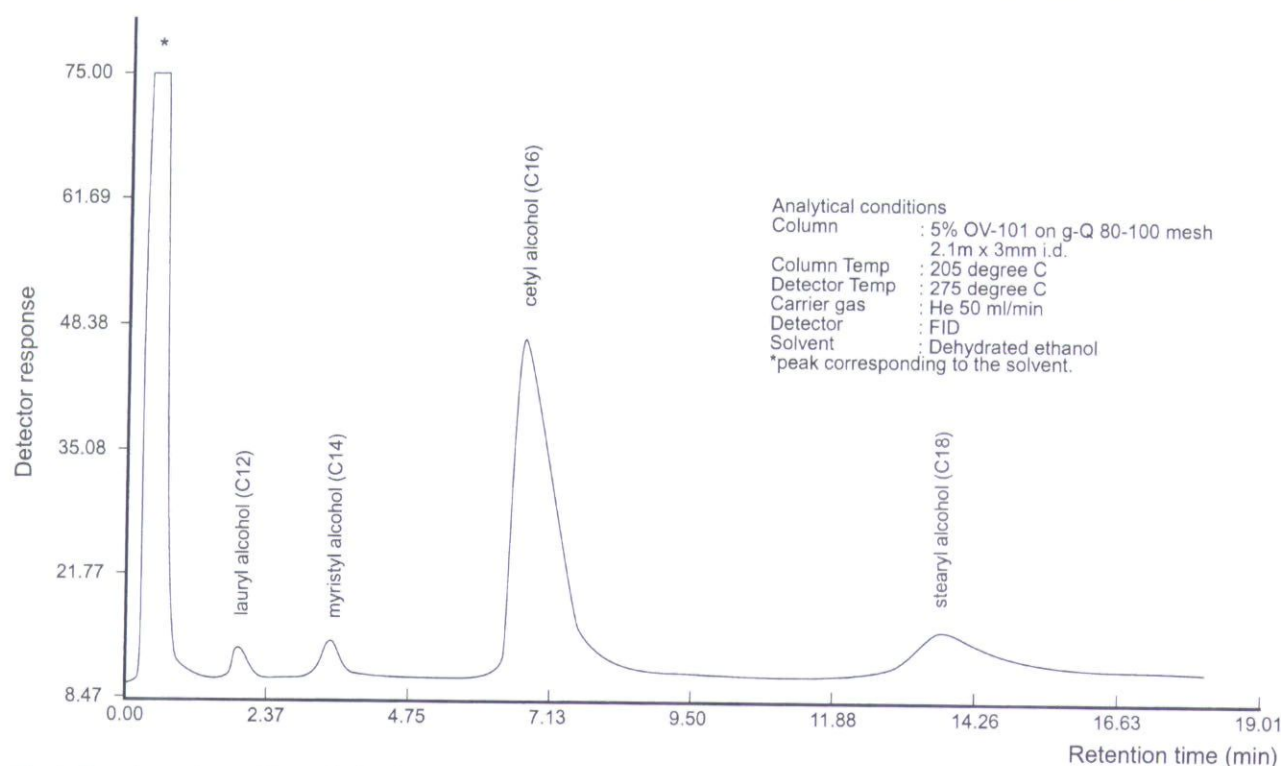


Fig. 1. Gas chromatographic analysis of the cetyl alcohol used in the cream base.

reaction in 6 of their 7 patients with an allergic patch test reaction to Lanette N[®] (90% cetylstearyl alcohol and 10% sodium cetylstearyl sulfate) or Lanette 16[®] (92.1% cetyl alcohol (C₁₆), 3.3% stearyl alcohol (C₁₈) and small quantities of C₈-C₁₄ alcohols) and, moreover, the particular patient with a positive patch test reaction to chemically pure cetyl alcohol (C₁₆) had not reacted to this chemical in the repeated open application test (ROAT).

Non-specific irritation by the alcohols themselves could be ruled out for 3 reasons. 1st, 30% pet. is the standard concentration for patch testing suggested by Fisher et al. (8) and the results of patch testing in our case revealed positive reactions to it at as low as 5% pet. 2nd, the cetyl alcohol used in the cream base produced a positive patch test reaction 3×, that is, December 1995, February 1996 and March 1996, respectively. 3rd, no positive reactions occurred in 10 normal control subjects.

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