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**Sensitization to modified colophonium in glucose sensors:
another problem for diabetes patients.**

Olivier Aerts¹, Ella Dendooven¹, Nadia Raison-Peyron²

¹Department of Dermatology, University Hospital Antwerp (UZA) and Research group Immunology, Infla-Med Centre of Excellence, University of Antwerp, Antwerp, Belgium.

²Department of Dermatology, Saint Eloi Hospital, Montpellier University, 80 avenue Augustin Fliche, 34295 Montpellier, France.

Corresponding author : Olivier Aerts, Department of Dermatology, University Hospital of Antwerp (UZA), Drie Eikenstraat 655, B-2650 Antwerp, Belgium. Tel: +3238214272 / E-mail: olivier.aerts@uza.be

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We report two diabetes type 1 patients with allergic contact dermatitis (ACD) from modified colophonium in glucose sensors.

Case reports

Case 1

A 12-year-old boy developed dermatitis on his arms following the application of a FreeStyle Libre I glucose sensor (Abbott Diabetes Care, Witney, UK), a few months after starting its use. Replacement by a Dexcom G6 sensor (Dexcom, San Diego, California) resulted in an immediate relapse of the eczema. Patch tests were performed with the European baseline, plastics and glues and a (meth)acrylate series (Chemotechnique Diagnostics, Vellinge, Sweden) including IBOA 0.1% pet. and N,N-dimethylacrylamide (DMAA) 0.1% pet. (both in-house prepared, raw materials from Sigma-Aldrich, Steinheim, Germany) mounted on IQ Ultra chambers. Additionally, 3 types of modified colophonium (provided by a manufacturer of adhesive bandages) were tested: methyl ester of rosin, hydrogenated rosin ester, and hydrogenated methyl abietate (all 20% pet.). Pieces of the adhesives from the two glucose sensors were patch tested 'as is', as well as a hydrocolloid dressing (Duoderm Extra Mince, ConvaTec, Deeside, UK), which he regularly placed between the devices and the skin to prevent skin reactions. All tests were occluded for 2 days with Oper tape (Iberhospitex, Innovative Health Technologies, Barcelona, Spain) and were read on day (D)2, D4 and D7 according to ESCD guidelines.

Positive reactions (D4) were observed to IBOA 0,1% pet. (+++), sesquiterpene lactone mix (SLM) 0,1% pet. (+), and linalool hydroperoxides 1% pet (+). Colophonium 20% pet. gave a doubtful reaction (?+) on D4, whereas the 3 modified rosins were positive (++). The adhesive from the Freestyle Libre glucose sensor gave a doubtful (?+) reaction, whereas the piece of the

hydrocolloid (Duoderm EM) dressing was positive (++) . The adhesive of the Dexcom sensor as well as abietic acid and hydroabietyl alcohol (Abitol) remained negative.

Case 2

A 56-year-old male developed eczema from his FreeStyle I glucose sensor during the first few weeks after starting its use. In order to improve the skin adhesion the patient had used Skin Tac wipes (Torbot Group Inc., Cranstone, Rhode Island), containing colophonium, which further aggravated his skin symptoms. Stopping the use of these wipes, and changing the device to the IBOA-free FreeStyle II sensor resulted in no improvement; another attempt by using the Dexcom G5 sensor brought no amelioration either. Patch tests, performed as in Case 1, showed sensitizations (D4) to nickel (+++), cobalt (?+), colophonium (++) , abietic acid (+), Abitol (+), and also to the modified colophonium methyl abietate 5% pet. (++) , as well as to several fragrances (*Myroxylon pereirae* resin, Fragrance mix I and II, and Lyrall: all +). IBOA 0.1% and 0.3%, and SLM 0.1% pet. showed no reactions.

Chemical analyses of his FreeStyle I sensor, using previously published protocols (1,2), could not identify the presence of methyl abietate, but confirmed the presence of methyl dehydroabietate in the housing of the sensor (3)(Supplementary file).

Discussion

Many diabetes patients with ACD from the FreeStyle I glucose sensor are sensitized to IBOA (4), sometimes with cross-reactivity to SLM (Case 1)(5). Although removal of IBOA from this particular glucose sensor (6) has led to a decline in IBOA-sensitization (2), ACD from other sensitizers in this device may still occur (7). Besides the presence of colophonium in some diabetes devices, and other products (e.g., adhesive wipes, Case 2), also modified colophonium, methyl dehydroabietate, in particular, is present in the FreeStyle sensor, which confirms the

findings of a previous report (8). The latter substance may, similar to IBOA, also induce primary skin sensitization (Cases 1 and 2). Methyl dehydroabietate, found in the device, is the rapidly formed auto-oxidation product of methyl abietate (positive in Case 2), which are chemically closely related to each other, and to hydrogenated methyl abietate (positive in Case 1)(Figure 2). Changing devices to (proclaimed) IBOA-free sensors, such as FreeStyle II (Case 2), or Dexcom G5/6 (9)(Case 1 and 2), might not be a solution, as methyl dehydroabietate could still be present in them (9). Moreover, hydrocolloid dressings, advised to prevent ACD in sensitized subjects (10), may not alleviate the problem (Case 1) as such dressings may equally contain modified colophonium (11).

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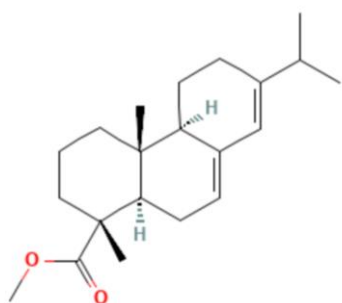
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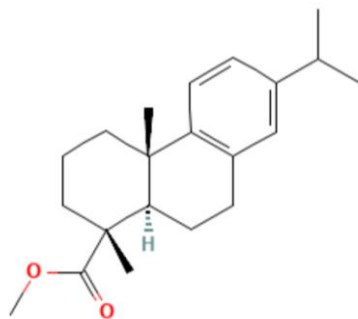
Figure 1. Positive patch test reaction to methyl abietate (*syn.* methyl rosinate) 5% pet. (++) on day (D)4 in Case 2. Methyl abietate rapidly auto-oxidizes to methyl dehydroabietate, and chemical analyses have confirmed the presence of the latter in FreeStyle Libre and Dexcom glucose sensors.



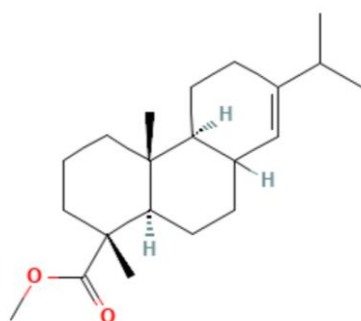
Figure 2. Chemical structures of 3 related forms of modified colophonium: (A) methyl abietate, which rapidly auto-oxidizes to (B) methyl dehydroabietate; (C) hydrogenated methyl abietate.



A



B



C

