

Intense skin reaction to a new glucose monitoring and insulin pump system

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Allergic contact dermatitis caused by flash or continuous glucose monitoring systems (CGM) and insulin pump systems is increasingly being reported. It is most often caused by contact allergy to isobornyl acrylate (IBOA), present in the medical device.¹⁻³ However, other contact sensitizers can be of importance.⁴⁻⁶

CASE REPORT

We present a case of a 34-year-old woman with type 1 diabetes from the age of 3 years. She had previously reacted with dermatitis to a flash glucose monitoring sensor (FreeStyle Libre, Abbott Diabetes Care, Witney, UK), which she had to stop using. She had, however, tolerated two CGM systems, the Dexcom G5 glucose sensor and Dexcom G6 glucose sensor (San Diego, California), but she had to give up use of an insulin patch pump (Omnipod, Insulet Corporation, Billerica, Massachusetts) because of dermatitis. In October 2019 she started to use a newly introduced CGM sensor and insulin patch pump system (Medtrum A6 TouchCare, Medtrum Technologies, Shanghai, China). Both the sensor and the insulin reservoir to which the pump is connected are attached with to the skin adhesive patches (Figure 1). Within a day, however, she had to remove the devices because of an intense dermatitis, initially confined to, but later spreading beyond the application sites of both the sensor and the insulin reservoir (Figure 2).

The patient was patch tested with our baseline series and a special medical device series.⁷ Patch testing was also performed with pieces of the adhesive patches removed from the sensor and the insulin reservoir and with extracts of different materials in the sensor and insulin reservoir. From the glucose sensor, separate acetone extracts were made from the adhesive patch, the sensor, and the plastic support material. From the insulin reservoir, separate acetone extracts were made from the adhesive patch and the reservoir itself

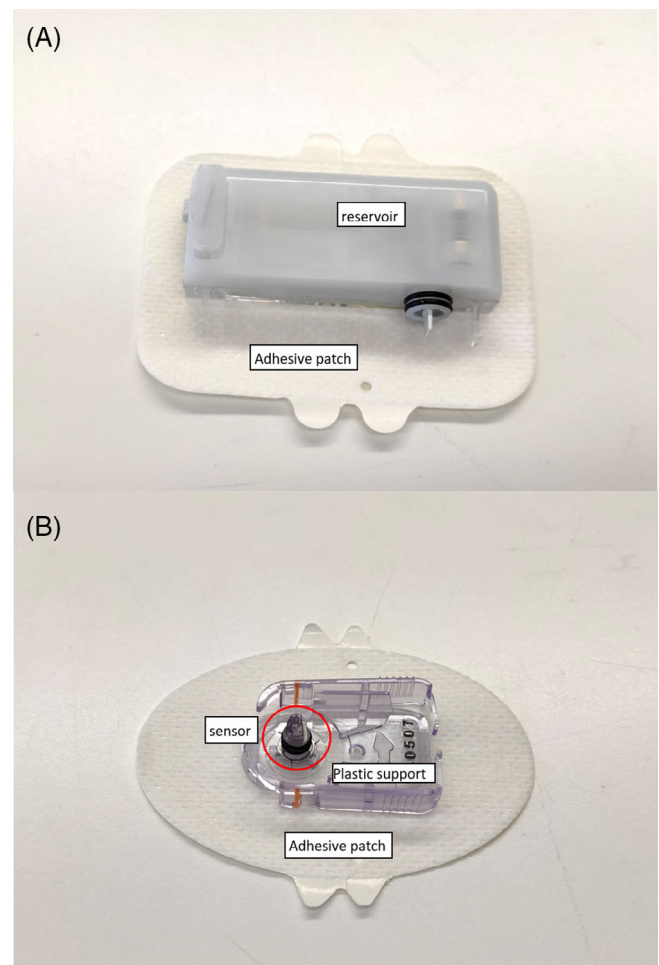


FIGURE 1 (A) Medtrum insulin reservoir and **(B)** glucose sensor B

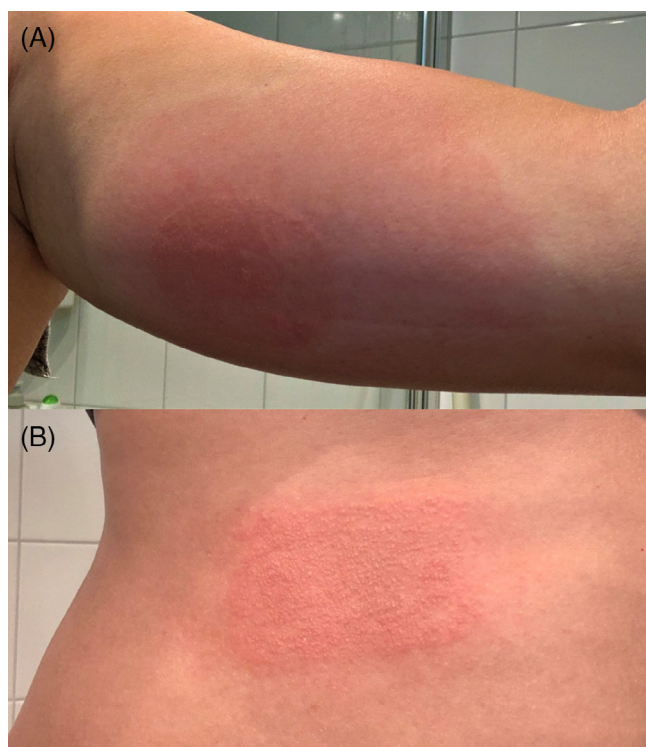


FIGURE 2 (A) Dermatitis at the site of sensor (arm) and (B) the site of the insulin reservoir (abdomen). Photographs provided by the patient

(Figure 1A,B). Each material was extracted in acetone in an ultrasonic bath for 5 minutes. Thereafter, all extracts were evaporated to a final volume of 0.5 mL.

Patch tests were applied to the patient's back with 8-mm Finn Chambers Aqua, (Smart Practice, Phoenix, Arizona) for 48 hours, and readings were made at day (D) 4 and D7.⁸ At the first reading on D4, the patient had extreme to strong reactions (+++/++) to the adhesive patches tested "as is" and as extract, and to the extract of the insulin reservoir. Furthermore, she had ++ reactions to hydroabietyl alcohol, *Myroxylon pereirae* resin, and fragrance mix II and + reactions to colophonium, hexyl cinnamal, and *Evernia prunastri*. At the second reading on D7, a positive reaction (++) to IBOA 0.3% pet. was noticed, while the test remained negative to IBOA 0.1% pet. On D4 additional patch testing was performed with a dilution series of the extracts, giving positive reactions, and with adhesive patches for the sensor and reservoir patch, which had not been mounted on the devices. The adhesive patches were tested "as is", but extracts were later prepared as described above for chemical analyses. The results from the patch testing with materials from the glucose sensor and insulin reservoir are summarized in Table 1.

The extracts of the different materials of the glucose sensor and insulin reservoir were analyzed by gas chromatography-mass spectrometry (GC-MS). Prior to the chemical investigations the extracts were diluted 10 times in acetone. The extracts of the unmounted adhesive patches were also analyzed undiluted. The GC-MS system consisted of an Agilent 8890 GC coupled to an Agilent 7250 GC/Q-

TABLE 1 Results from patch testing with materials from the glucose sensor and insulin reservoir

Sensor	Insulin reservoir
Adhesive patch from sensor	Adhesive patch from reservoir
"as is" +++/NR	"as is" ++
Ac extr 100% ++/–	Ac extr 100% ++/NR
Ac extr 32% ++	Ac extr 32% ++
Ac extr 10% +	Ac extr 10% +
Ac extr 3.2% +	Ac extr 3.2% +
Ac extr 1% +	Ac extr 1% +
Ac extr 0,32% -	Ac extr 0,32% -
Adhesive patch (new, unmounted)	Adhesive patch (new, unmounted)
"as is" +++	"as is" +++
Sensor part	Reservoir
Ac extr 100% –/–	Ac extr 100% ++/–
	Ac extr 32% ++
Plastic support ac extr 100% –/–	Ac extr 10% -
	Ac extr 3.2% -
	Ac extr 1% -
	Ac extr 0,32% -

Abbreviations: ac extr, acetone extract; NR, test not read.

TOF MS controlled by Mass Hunter 10.0 software (Agilent Technologies, Santa Clara, California). The GC was equipped with an HP-5MS UI capillary column (Agilent Technologies) with a length of 30 m, an internal diameter of 0.25 mm, and a film thickness of 0.25 μ m. The carrier gas was helium (Air Liquide, Malmö, Sweden) with a flow rate of 1.0 mL/min. The injection was splitless and the inlet was heated to 250°C. The injection volume was 1 μ L. The temperature programme was as follows: isothermal at 70°C for 3 minutes, raised by 8°C/min to a final temperature of 300°C, and isothermal at this temperature for 10 minutes. Electron-ionization mass spectra were collected in scan mode recording ions with m/z from 50–500 with a spectral acquisition rate of 5 Hz. The transfer line temperature was 200°C, the ion source temperature was 200°C, and the quadrupole temperature was 150°C. The electron energy was 70 eV. The library of mass spectra of the National Institute of Standards and Technology (Gaithersburg, Maryland) was used for identification of substances. Dilutions of IBOA in acetone were used as reference standards.

The GC-MS analyses indicated the presence of colophonium-related substances, such as methyldehydroabietate, in all extracts and ethyl-2-cyanoacrylate in the extracts of the sensor and the reservoir. IBOA was observed in the extracts of the adhesive patches, which had been removed from the sensor and reservoir, respectively, and in the extracts of the sensor and the reservoir. The estimated IBOA concentrations in the extracts corresponded to a total IBOA content of 1 μ g in the sensor, 3 μ g in the sensor adhesive patch, 30 μ g in the reservoir, and 6 μ g in the reservoir adhesive patch. For the adhesive patches this corresponds to a surface concentration of 0.1 μ g/cm² in the

patch from the sensor and $0.2 \mu\text{g}/\text{cm}^2$ in the patch from the reservoir. In the extracts of the unmounted adhesive patches IBOA was found in concentrations corresponding to $0.005 \mu\text{g}/\text{cm}^2$ in the sensor patch and $0.01 \mu\text{g}/\text{cm}^2$ in the reservoir patch.

The supplier of the products (Medtrum) confirmed the presence of up to 15% of modified colophonium in the adhesive used on the adhesive patches, but could not give any information on the presence of IBOA or other acrylates in the products.

DISCUSSION

The patient's history and results from the patch tests and chemical investigations suggest that the patient had previously been sensitized to IBOA (reported in the flash glucose monitoring sensor and the insulin pump she had used previously) and colophonium (present in the previously used insulin pump). Therefore, she reacted at the first application of the new products from another supplier. As seen in some recent cases, IBOA was only positive when tested at a higher concentration (0.3% w/w in pet.) and when read on D7.⁷

In the cases of both the FreeStyle Libre¹ and Omnipod,² IBOA is thought to originate from a UV-curing acrylate containing adhesives used in other parts of the devices. This may also be the case for the Medtrum devices, where higher amounts of IBOA were found in the adhesive patches removed from the devices, compared to the adhesive patches which had not been mounted on any device. However, as the patient reacted with similar strength to all adhesive patches tested "as is", we suspect the reactions to be caused mainly by the presence of colophonium-related substances in the adhesives. As both IBOA and colophonium may be present in several different medical devices, this case is a clear illustration of the difficulties sensitized patients could have in finding devices that do not cause allergic reactions.

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AUTHOR CONTRIBUTIONS

Nils Hamnerius: Conceptualization; data curation; formal analysis; investigation; methodology; writing-original draft. **Martin Mowitz:**

Conceptualization; data curation; formal analysis; investigation; methodology; writing-review and editing.

CONFLICTS OF INTERESTS

The authors declare no conflict of interests.

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