

ORIGINAL ARTICLE

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Contact dermatitis caused by glucose sensors—15 adult patients tested with a medical device patch test series

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Abstract

Background: Several cases of allergic contact dermatitis (ACD) to the glucose sensor FreeStyle Libre have been reported. Isobornyl acrylate (IBOA) and *N,N*-dimethylacrylamide (DMAA) are known culprit allergens.

Objectives: To evaluate patients with suspected ACD to FreeStyle Libre in a standardized manner, present causative allergens, and assess patient-reported implications.

Methods: A total of 15 patients with suspected ACD to FreeStyle Libre were patch tested with the Swedish baseline series and a new medical device series. IBOA and DMAA were tested at 0.1% and 0.3% in petrolatum (pet.). Readings were performed on day (D) 3 and D7. Background data, details on skin reactions, and associated implications were assessed using a questionnaire.

Results: Thirteen patients were sensitized to IBOA and four to DMAA. Two positive reactions to IBOA and one to DMAA were seen only at 0.3% concentration on D7. Median duration of sensor use before dermatitis onset was 6 months. Half the number of the patients took precautions in everyday life due to sensor-related skin reactions. Six patients discontinued sensor usage.

Conclusions: Patients with suspected ACD to glucose sensors should be evaluated with a relevant patch test series containing IBOA and DMAA. Adding the 0.3% pet. concentration is recommended. The reading on D7 is necessary.

KEYWORDS

adhesive, allergic contact dermatitis, diabetes mellitus, FreeStyle Libre, glucose sensor, isobornyl acrylate, medical device, *N,N*-dimethylacrylamide

1 | INTRODUCTION

The use of modern glucose sensors has improved glucose control in patients with type 1 diabetes.¹ However, adverse skin reactions at the site of application are reported by more than one-third of

adult users.² According to a recent study, skin reactions constitute one of the main causes of treatment discontinuation.³ When evaluating adverse skin reactions from medical devices, results from patch tests are necessary in differentiating allergic from irritant contact dermatitis.

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In recent years, several cases of allergic contact dermatitis (ACD) to the glucose sensor FreeStyle Libre (Abbott Diabetes Care, Witney, UK) have been reported. Isobornyl acrylate (IBOA) and *N,N*-dimethylacrylamide (DMAA) have been identified as major culprit allergens.^{4–9} Believed to derive from an adhesive used to join the top and bottom part of the plastic housing of the sensor, IBOA and DMAA have been identified in FreeStyle Libre through gas chromatography-mass spectrometry (GC-MS) analyses.^{4,8} Furthermore, a high proportion of simultaneous positive patch test reactions to sesquiterpene lactone mix (SLM) have previously been described in patients with contact allergy to IBOA and/or FreeStyle Libre.¹⁰ Studies addressing sensor-related ACD and its implications for affected patients are scarce. In addition, in prior studies different patch test procedures have been used in terms of allergens included and patch test reading days. In this report we present 15 patients with contact dermatitis to FreeStyle Libre, assessed in a standardized manner using both a medical device patch test series and a questionnaire addressing sensor-related problems.

2 | METHODS

In total, 15 adult patients with type 1 diabetes experiencing adverse skin reactions suggestive of ACD at the FreeStyle Libre application site were investigated. None of the patients had been using the second generation of the sensor (FreeStyle Libre 2). Patients were referred to a branch clinic of the Department of Occupational and Environmental Dermatology, Malmö, located in Karlshamn, Sweden, in autumn 2019. Demographic data are presented in Table 2.

All patients were patch tested with the Swedish baseline patch test series including SLM 0.1% in petrolatum (pet.) and a new medical device patch test series containing 35 test preparations. An overview of the medical device patch test series is presented in Table 1. Chemotechnique Diagnostics (Vellinge, Sweden) provided the patch test preparations unless stated otherwise. All other test preparations were prepared at the Department of Occupational and Environmental Dermatology in Malmö, Sweden.

IBOA and DMAA were both tested in pet. at two concentrations (0.1% wt/wt and 0.3% wt/wt). The SLM constituents alantolactone, costunolide, and dehydrocostus lactone were tested at 0.1% wt/vol in ethanol. Patch testing also included substances indicated to be present in glucose sensors and insulin pumps according to GC-MS analyses at our department and substances believed to occur in ultraviolet-cured adhesives used in medical devices according to safety data sheets or previous publications.^{11–13}

For patch testing, IQ Ultimate Chambers (Chemotechnique Diagnostics) were used. Twenty-five mg of the pet. test preparations were applied on the chambers and 20 µL of liquid preparations. The tests were occluded on the back for 2 days. Reading of the tests was performed on day (D) 3 and D7. The tests were read and scored according to the ICDRG (International Contact Dermatitis Research Group) and ESCD criteria.^{14,15}

All patients completed a 15-item questionnaire prior to patch testing. Atopy, atopic eczema, skin reactions to FreeStyle Libre, their associated implications, and treatment attempts were assessed. Skin reactions to other medical devices, plastics, perfumed products, and plants were also assessed.

3 | RESULTS

Patch test results are summarized in Table 2. Thirteen patients (87%) were sensitized to IBOA. Two of the IBOA-sensitized patients (15%) had positive patch test reactions only on D7 and when tested with a concentration of 0.3%. Four patients had positive patch test reactions to DMAA, one of whom presented positive only to DMAA 0.3% on D7.

Positive patch test reactions to SLM were observed in four patients, one of whom was positive to alantolactone and costunolide and one to alantolactone alone. Two patients presented negative or doubtful reactions to SLM constituents. Three patients had positive reactions to fragrance mix I or II, with two patients being positive to *Myroxylon pereirae* (balsam of Peru) at the same time. One patient showed a strong positive reaction to colophonium and presented a simultaneous positive reaction to abietic acid. Positive reactions to 2,4-di-*tert*-butylphenol (2,4-DTBP) and butylated hydroxytoluene (BHT) were seen in one patient. One patient reacted positive to 2-carboxyethyl acrylate and one patient to tetrahydrofurfuryl acrylate (THF-A). In total, 58 positive patch test reactions were seen, and nine of these only on the D7 reading.

In total, two of the 15 patients had a history of atopic eczema. Median duration of sensor use before the onset of skin reaction was 6 months (range 0–29). As much as 12 of 13 patients were able to use the sensor for at least 1 month and five patients for more than a year before the development of adverse skin reactions. Nine patients (60%) reported a need to replace the sensor more often than every other week due to adverse skin reactions. Six patients (40%) discontinued FreeStyle Libre usage, all of them contact allergic to IBOA and/or DMAA. Half of the patients reported taking precautions in everyday life due to sensor-related skin reactions and difficulties in sensor usage.

Eleven of the patients (73%) reported attempts to treat skin reactions, including all patients later discontinuing sensor usage. Local treatments used were corticosteroid-containing cream or ointment; corticosteroid-containing nasal spray, barrier spray, or solutions; and barrier dressings. Three of five patients who reported treatment attempts with barrier dressings discontinued FreeStyle Libre usage. Table 3 summarizes reported skin reactions from products other than FreeStyle Libre. One patient reported adverse skin reactions from Omnipod insulin pump and from catheters. Both reactions appeared after the onset of ACD to FreeStyle Libre. None of the patients who reported skin reactions after contact with perfumed products showed positive patch test reactions to fragrance mix I or II, colophonium, or *Myroxylon pereirae*. No patient reported skin reactions upon exposure to plants.

TABLE 1 Medical device patch test series

Substance	Vehicle	Concentration (wt/wt) or (wt/vol)	Manufacturer
1	Isobornyl acrylate	Pet.	S-A
2	2,4-Di- <i>tert</i> -butylphenol	Pet.	S-A
3	Butylated hydroxytoluene	Pet.	C
4	4- <i>tert</i> -Butylphenol	Pet.	C
5	Isobornyl acrylate	Pet.	S-A
6	2-Hydroxyethyl methacrylate	Pet.	C
7	Isophorone diisocyanate	Pet.	C
8	Isophorone diamine	Pet.	C
9	Urethane diacrylate, aliphatic	Pet.	C
10	Urethane dimethacrylate	Pet.	C
11	<i>N,N</i> -dimethylacrylamide	Pet.	S-A
12	2-Hydroxyethyl acrylate	Pet.	C
13	Ethyl cyanoacrylate	Pet.	C
14	Tetrahydrofurfuryl acrylate	Pet.	S-A
15	<i>N,N</i> -dimethylacrylamide	Pet.	S-A
16	2-Carboxyethyl acrylate	Pet.	S-A
17	2-Ethylhexyl acrylate	Pet.	C
18	Di(ethylene glycol) ethyl ether acrylate	Pet.	S-A
19	Hydroxypropyl methacrylate	Pet.	C
20	Acrylic acid	Pet.	A
21	1,6-Hexanediol diacrylate	Pet.	C
22	Tri(propylene glycol) diacrylate	Pet.	C
23	2-Phenoxyethyl acrylate	Pet.	P
24	Lauryl acrylate	Pet.	S-A
25	2,2-Dimethoxy-2-phenylacetophenone	Pet.	S-A
26	(3-Glycidyloxypropyl)trimethoxysilane	Pet.	S-A
27	Diphenyl(2,4,6-trimethylbenzoyl)phosphine oxide	Pet.	S-A
28	Hydroxycyclohexyl phenyl ketone	Pet.	S-A
29	Compositae mix II	Pet.	C
30	Hydroabietyl alcohol	Pet.	C
31	Abietic acid	Pet.	C
32	Camphene	Pet.	S-A
33	Alantolactone	EtOH	S-A
34	Costunolide	EtOH	S-A
35	Dehydrocostus lactone	EtOH	S-A

Abbreviations: A, Acros Organics, Geel, Belgium; C, Chemotechnique Diagnostics, Vellinge, Sweden; EtOH, ethanol (Kemetyl, Haninge, Sweden); P, Polysciences, Inc. Warrington, Pennsylvania; pet., petrolatum (vaselin, vitt; APL, Stockholm, Sweden), used in all pet. preparations not delivered by C; S-A, Sigma-Aldrich, Steinheim, Germany; wt/vol, weight/volume; wt/wt, weight/weight.

4 | DISCUSSION

In recent years, medical devices have assumed ever-greater importance in treatment and disease monitoring. For intracoronary stents, dental implants, glucose sensors, and insulin pumps, all capable of releasing haptens and with long-term attachment to the skin, endothelium, or mucosa, usage is associated with a risk of developing contact allergic reactions.^{16,17} ACD generally disappears as exposure to

the culprit allergen ceases. However, contact allergies remain throughout life along with an associated risk of renewed allergen exposure and subsequent ACD elicitation. Although medical devices offer many potential benefits for a majority of users, recent studies have highlighted the risk of associated ACD. Given its implications for those affected, an increased awareness of ACD to medical devices is called for, not only in specialized dermatology clinics but also among healthcare professionals in general.

TABLE 2 Demographic data and patch test results

Patient number	Sex	Age (years)	IBOA 0.1% pet.		IBOA 0.3% pet.		DMAA 0.1% pet.		DMAA 0.3% pet.		SLM 0.1% pet.		Alantolactone 0.1% ethanol		Costunolide 0.1% ethanol		Dehydrocostus lactone 0.1% ethanol		Other positive substances
			D3	D7	D3	D7	D3	D7	D3	D7	D3	D7	D3	D7	D3	D7	D3	D7	
1	F	36	+++	++	+++	++	–	–	–	–	++	++	+++	+++	++	+	?+	–	–/–
2	F	28	+++	++	+++	++	–	–	–	–	?+	?+	–	–	–	–	–	–	FM II –/+ Ni ?+/+
3	M	52	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	BHT +/?+ Black rubber mix +/- Cr +/- 2,4-DTBP +/-
4	M	64	+++	+++	+++	+++	++	++	+++	+++	+++	++	+	++	–	?+	–	?+	FM I ++/+++ MP +++/+++ THF-A +/THF-A +
5	M	73	++	+	+++	+	–	–	–	–	+	+	–	?+	–	?+	–	–	–/–
6	M	57	–	?+	–	+	–	–	–	+	–	–	–	–	–	–	–	–	2-Carboxyethyl acrylate -/+
7	F	42	+++	++	+++	++	–	–	–	–	–	–	–	–	–	–	–	–	Abietic acid +/- Co -/+ Colophonium +++/+ Ni +++/+++
8	F	45	++	++	+++	++	++	++	++	++	–	–	–	–	–	–	–	–	–/–
9	F	67	++	?+	++	+	+	?+	++	+	+	?+	–	–	–	–	–	–	MI +/-+ Ni +/-+
10	M	66	?+	+	+	+	–	–	–	–	–	–	–	–	–	–	–	–	–/–
11	F	72	+	+	+	+	–	–	–	–	–	–	–	–	–	–	–	–	–/–
12	F	34	–	–	?+	+	–	–	–	–	–	–	–	–	–	–	–	–	–/–
13	M	19	++	++	++	++	–	–	–	–	–	–	–	–	–	–	–	–	–/–
14	M	68	++	+	++	++	–	–	–	–	–	–	–	–	–	–	–	–	FM II +/-+ MDBGN +/-+ MP +/-+
15	F	54	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	Ni ?+/+

Abbreviations: 2,4-DTBP, 2,4-di-*tert*-butylphenol; BHT, butylated hydroxytoluene; Co, cobalt; Cr, chromium; DMAA, *N,N*-dimethylacrylamide; F, female; FM I, fragrance mix I; FM II, fragrance mix II; IBOA, iso-bornyl acrylate; M, male; MDBGN, methyldibromo glutaronitrile; MI, methylisothiazolinone; MP, Myroxylon *pereirae*; Ni, nickel; pet., petrolatum; SLM, sesquiterpene lactone mix; THF-A, tetrahydrofurfuryl acrylate; –, negative; ?+, doubtful; + to +++, positive.

TABLE 3 Skin reactions to products other than FreeStyle Libre

Product	Other diabetes equipment	Other healthcare products	Plaster, tape, patches	Plastics	Perfumed products	Plants contact during eating/drinking ^c
Patient/case number	1 ^a	1 ^a , 15 ^b	1 ^a , 8 ^{a,b} , 12 ^b , 13 ^b , 15 ^b	15 ^b	5 ^{a,b} , 13 ^b , 15 ^b	—

^aAfter onset of skin reactions to FreeStyle Libre.^bBefore onset of skin reactions to FreeStyle Libre.^cFor example salad or herbal tea.

4.1 | Patch testing

In recent years IBOA has gained increased attention as a contact allergen causing ACD to medical devices used in diabetes monitoring and treatment.¹⁸ IBOA has been identified in the glucose sensors FreeStyle Libre and Enlite (Medtronic MiniMed, Northridge, California), Omnipod insulin pump (Insulet Corporation, Billerica, Massachusetts), and the insulin infusion set Paradigm MiniMed Quick-set (Medtronic, Minneapolis, Minnesota).^{4-7,9} DMAA has been identified as an additional sensitizer in FreeStyle Libre and Enlite.^{6,8} IBOA and DMAA are two monomeric reactive diluents, used in ultraviolet-cured adhesives.¹⁹

In this report, 87% of the patients were sensitized to IBOA. In previous studies, IBOA sensitization prevalence has been estimated to be 68%-83.3%^{7,9,20} among FreeStyle Libre users with sensor-related adverse skin reactions. In those studies, IBOA was patch tested at a maximum concentration of 0.1% and patch test readings on D7 were not routinely performed.

Interestingly, in this report, positive patch test results to IBOA 0.1% on D3 were seen in only 67% of the patients. The prevalence of IBOA sensitization among all FreeStyle Libre users has previously been estimated to 0.7%⁷ and 3.8%,²⁰ respectively, among adults and 4.2%⁹ among children. However, because not all users are patch tested the true frequency is most likely higher.

Cases of suspected ACD to FreeStyle Libre and similar devices with negative patch test results to IBOA 0.1% pet. have previously been reported.^{4,7,21,22} By including the concentration 0.3% pet., additionally two patients in this report presented positive reactions to IBOA on D7 and one to DMAA on D7. This concentration is higher than the usual patch test concentration for acrylates (0.1%). However, for induction of sensitization and elicitation, the number of molecules per skin surface is the crucial factor.²³ The molar concentration of IBOA patch tested at the concentration 0.3% is only 1.4 times higher than that of ethyl acrylate (with a lower molecular weight) when tested at 0.1%.

In this report, patients presenting positive reactions to IBOA 0.3% on D7 presented + reactions. Possibly, patch testing at a higher concentration in patients with negative reactions to IBOA 0.3% could further reduce the number of false-negative reactions. However, to find an optimal patch test concentration, the risk of false-negative reactions must be weighed against the risk of irritant reactions and active sensitization. In a previous study,²⁴ three cases of irritant reactions to IBOA 0.3% were reported among 19 patients tested. However, among the 15 patients with diabetes in the present report, no

irritant reactions to IBOA 0.3% were seen. In addition, 100 consecutive patients with dermatitis in Malmö were patch tested with IBOA 0.3% without any doubtful or irritant reactions. Patients were informed to contact our department in case of late appearing reactions beyond D7 and no patient did; thus, there was no indication of patients with active sensitization.

In previous studies around 10% of positive reactions to (meth)acrylates were seen only on reading D7 or later.^{24,25} Including a late reading on D7 as recommended by ESCD-guidelines¹⁵ is crucial for achieving accurate patch test results, also with regard to (meth)acrylates.

In this report, one patient with negative patch test reactions to IBOA and DMAA had positive reactions to the antioxidants 2,4-DTBP and BHT 1% pet. and 2% pet., respectively. BHT can be found in plastics, adhesives/glues as well as cosmetics.^{26,27} GC-MS analyses (carried out at the Department of Occupational and Environmental Dermatology, Skåne University Hospital in Malmö) have indicated the presence of BHT and 2,4-DTBP in FreeStyle Libre. Possibly, a primary sensitization to BHT with a cross allergy to 2,4-DTBP or vice versa could explain the simultaneous positive reactions. In another 60 patients with adverse skin reactions to medical devices, all patch tested with 2,4-DTBP 1% in pet. at the Department in Malmö, no positive, doubtful, or irritant reactions were observed. To the best of our knowledge, contact allergy to 2,4-DTBP and/or BHT has not previously been described in patients with contact dermatitis to FreeStyle Libre.

One of the patients showed simultaneous positive reactions to IBOA, DMAA, and THF-A 0.1% pet. Two occupational cases of contact allergy to THF-A found in a medical device adhesive used at a factory assembling surgical needles have previously been described.¹³ One of these patients showed a simultaneous positive reaction to DMAA (1% pet.) that was also part of the adhesive. A third, non-occupational case, involving an adhesive of a clip-on earring, was recently reported.²⁸

One of the patients in this report presented simultaneous positive reactions to IBOA and DMAA 0.3% pet. and 2-carboxyethyl acrylate 0.1% pet. Interestingly, all three substances were positive only on D7. Two previous cases with simultaneous positive patch test reactions to IBOA and 2-carboxyethyl acrylate contained in a glue used in insulin infusion sets have been reported.¹¹ Positive patch test reactions to 2-carboxyethyl acrylate have also been reported in workers from a factory producing television receivers. An acrylic glue used in the working process contained 2-carboxyethyl acrylate, IBOA, and DMAA.²⁹

The presence of THF-A and 2-carboxyethyl acrylate in FreeStyle Libre has not been confirmed and the significance of these sensitizations among users is unclear.

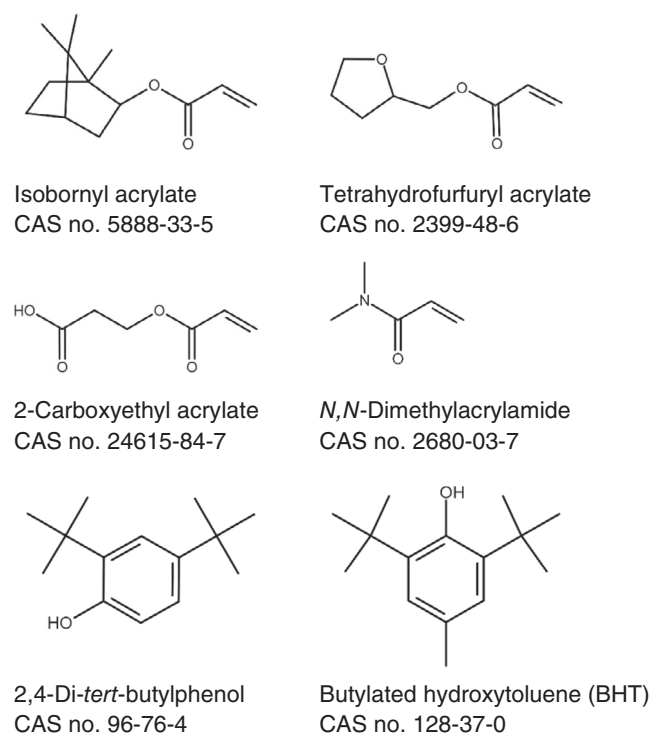


FIGURE 1 Molecular structures of selected allergens to which positive reactions were observed

All patients in this report had at least one positive patch test reaction (see Figure 1 for molecular structures of selected allergens). Half of the patients had one or more positive reaction(s) to allergens in the Swedish baseline series on reading at D3. In comparison, based on patch test results from a section of the European general population, only 27% of the population were estimated to have at least one positive reaction to allergens in the European baseline series.³⁰

In this study, four of the 15 patients, all of them contact allergic to IBOA, presented with positive patch test reactions to SLM. Positive reactions were seen in particular to alantolactone, consistent with findings from a previous study in which more than half of the patients sensitized to IBOA showed simultaneous positive reactions to SLM and/or its individual components.¹⁰ Camphene is a building block in the synthesis of IBOA¹⁰ and a substance found in plants containing sesquiterpene lactones.³¹ Camphene being an impurity in IBOA and SLM has been proposed as an explanation for the simultaneous positive reactions.¹⁰ However, in the absence of positive patch test reactions to camphene among patients in this report, this explanation is unlikely.

4.2 | Questionnaire

Worldwide, usage of continuous glucose monitoring and flash glucose monitoring is increasing.³² Among users, improved treatment

outcomes^{33,34} and high treatment satisfaction are seen.³⁵⁻³⁷ However, adverse skin reactions to continuous glucose monitoring and/or insulin pumps have been reported as a persistent health issue affecting diabetes-specific emotional distress among those affected.³⁸ Half of the patients in the present report were taking precautions in everyday life due to adverse skin reactions and difficulties in sensor usage (eg, avoiding physical activity or putting tape over the sensor as an extra fixation).

In line with previous findings by Hyry et al,⁷ median duration of reported sensor usage before the onset of dermatitis was 6 months. This time lag from first exposure to the development of skin reactions is suggestive of ACD. Among patients discontinuing sensor usage, one or more different treatments of ACD had been attempted (Figure 2). According to case reports, the use of hydrocolloid-based dressings between the sensor and skin can enable continued sensor usage (Figure 2).^{39,40} However, in our report, three of five patients using barrier materials (patches/plaster) discontinued sensor usage. Figure 3 shows a severe case of ACD to FreeStyle Libre occurring despite the use of barrier materials. As it may affect device performance, the Medicines and Healthcare products Regulatory Agency in the United Kingdom has advised against the application of creams and sprays and the use of patches under the sensor.⁴¹

Skin reactions from plasters, tape, and patches were reported by five patients, one of whom reported onset after the occurrence of ACD to FreeStyle Libre. Alkyl glucosides, generally classified as low-risk allergens, have recently been identified as allergens in foam wound dressings.⁴² In alkyl glucosides, IBOA has been identified as a possible hidden allergen.⁴³ However, IBOA has not been identified in the glucoside-containing dressings.⁴²

One patient in this report, with allergy to IBOA, developed ACD to Freestyle Libre in 2016. Two years later the patient started treatment with Omnipod insulin pump, resulting in contact dermatitis at its application site. As IBOA is contained in both devices, sensitization was probably from FreeStyle Libre usage with later elicitation of ACD from Omnipod usage.

A report form aiding the clinician in assessing patients with diabetes experiencing adverse skin reactions to medical devices in a standardized manner has recently been published.⁴⁴ Hopefully, this report form can prove useful especially for nondermatologists in identifying patients where further diagnostic evaluation regarding ACD is necessary. Patch testing patients with contact dermatitis to Freestyle Libre and similar devices is a cornerstone in the diagnostic workup. Contact allergies can only be detected upon patch testing with relevant substances in suitable concentrations. Obtaining information about device contents is hampered by the fact that product labelling of medical devices is not required. Device contents can be modified without any visible changes to the products and without this being communicated to the users or healthcare professionals. Several reports also indicate difficulties in collaborating with the manufacturers.^{4,7} Hence, healthcare professionals guiding patients with ACD to Freestyle Libre and similar devices are limited to a trial-and-error method to find suitable device alternatives. Current state of knowledge regarding contact allergen contents originate from time-consuming and expensive

FIGURE 2 Different products used in treatment attempts of allergic contact dermatitis reported by the patient seen in Figure 3



FIGURE 3 Severe allergic contact dermatitis, despite the use of a physical barrier (plaster/patch), in a patient later discontinuing FreeStyle Libre usage

analyses of sensor, pump, and infusion set extracts. To ensure an up-to-date patch test series reflecting current allergen exposure, continuous chemical analyses are necessary.

Because known culprit allergens are believed to derive from medical adhesives, IBOA and DMAA should be tested when ACD to adhesives/glues is suspected, in order not to miss new potential sources of sensitization. As a result of careful product inventories, IBOA has been identified in multiple medical devices used by patients with diabetes and can be suspected to be a constituent in other medical devices as well. In addition, hitherto unknown allergens can be involved.

The medical device patch test series used in this report is tested in a limited patient population. Before a suitable medical device patch test series can be established, and to further assess the magnitude of ACD to glucose sensors and/or insulin pumps, larger inventories among patients with diabetes are required.

5 | CONCLUSION

ACD to glucose sensors has recently been discovered. Larger inventories are required to assess the magnitude of the problem. Patch testing including IBOA and DMAA at concentration 0.3% pet. should be recommended. The late reading at D7 is necessary to minimize the number of false-negative reactions.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

AUTHOR CONTRIBUTIONS

Josefin Ulrikdotter: Data curation; investigation; writing-original draft; writing-review and editing. **Cecilia Svedman:** Conceptualization; data curation; investigation; methodology; resources; supervision; writing-review and editing. **Magnus Bruze:** Conceptualization; data curation; investigation; methodology; supervision; writing-review and editing. **Jenny Glimsjö:** Conceptualization; project administration; writing-review and editing. **Kajsa Källberg:** Data curation; investigation; project administration; writing-review and editing. **Thanisorn Sukakul:** Data curation; investigation; writing-review and editing. **Martin Mowitz:** Conceptualization; data curation; investigation; methodology; supervision; writing-review and editing.

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How to cite this article: Ulrikssdotter J, Svedman C, Bruze M, et al. Contact dermatitis caused by glucose sensors—15 adult patients tested with a medical device patch test series. *Contact Dermatitis*. 2020;1–9. <https://doi.org/10.1111/cod.13649>