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Changes in adhesive ingredients in continuous glucose monitoring systems may induce new contact allergy pattern

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Abstract

Background: Medical devices (MD) in close skin-contact for a prolonged time, such as glucose monitoring (CGM) systems, are a risk factor for contact allergy, and there has been an increase in patients using these. Correct diagnosis demands targeted testing.

Objectives: We report a new allergen in a continuous CGM system in which the adhesive was changed. The allergy pattern of the patients diagnosed is reported.

Methods: The three patients reported were patch tested with an MD series, own material, and possible allergens found through analysis with gas chromatography-mass spectrometry, comparing analysis from the CGM system before and after change.

Results: The patients were sensitized to isobornyl acrylate (IBOA), found in previously used devices and the present CGM. Apart from IBOA, the culprit allergen was found to be 2,2'-methylenebis(6-*tert*-butyl-4-methylphenol) monoacrylate.

Conclusion: Allergic contact dermatitis due to CGM systems and insulin pumps are difficult to investigate and require chemical analysis. Because of the lack of information on substances used in the production, and when changes with MDs are initiated, it is difficult to advise patients, especially since they risk sensitization to several allergens. The use of MDs has increased and, thus, the need for collaboration between manufacturers, clinicians, and patient organizations.

KEYWORDS

2,2'-methylenebis(6-*tert*-butyl-4-methylphenol) monoacrylate, allergic contact dermatitis, contact allergy, diabetes type I, gas chromatography-mass spectrometry glucose monitoring (CGM) systems, isobornyl acrylate medical device

1 | INTRODUCTION

Investigating patients with suspected allergic contact dermatitis to medical devices (MDs), such as continuous glucose monitoring (CGM) systems, intermittently scanned glucose monitoring (isCGM)/flash

glucose monitoring systems, and insulin pumps, is complicated.¹ The diagnosis has to be suspected and the patient must be patch tested with the right substances. The investigation should also include patch testing with the patient's own material. This testing may, however, result in false negative reactions since the concentration of allergens

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in the material may actually be too low to elicit a positive reaction at ordinary patch testing, even if an extract of the product is made.² Producing an extract can in itself be difficult because of the lack of material, especially if extraction solvents with different physico-chemical properties are desired.¹ The culprit contact allergens found have mainly been used in attachment areas, ie, where different materials must adhere to each other, but not necessarily primarily in the adhesive patch in direct contact with the skin. Therefore, identifying and finding the optimal patch test substance and dose has been complex, as the final dose on skin exposure is not necessarily the same as where the substance is identified used. The need for collaboration with the manufacturers of the devices has been emphasized,^{2,3} especially as the number of patients being sensitized to several allergens found in different MDs is increasing. As product ingredients may be changed without a change of brand name or notification to the clinicians or the users, helping the user find a reliable product is made even more difficult.

Here we report three patients who reacted to the Dexcom G6, CGM system (Dexcom, Inc.), who suddenly experienced symptoms after the composition of the adhesive was changed and in which a new allergen was found. The identification of the allergen was simplified by the fact that previous analyses of Dexcom G6 existed for comparison at our laboratory in Malmö.²

2 | MATERIAL AND METHODS

The three patients were all referred because of sudden onset of problems related to efforts made by the manufacturing company to improve the adhesive in Dexcom G6.

Case 1. This patient was a 40-year-old female office worker, with diabetes mellitus since the age of 8, rhinoconjunctivitis, but no atopic dermatitis nor asthma and no other skin diseases. She started to use an insulin pump in 2008 and had at first referral used three different brands (Medtronic, Animas Vibe, and Tandem t:slim) without the occurrence of dermatitis; however, because of dermatitis problems she had stopped using certain brands (Freestyle Libre and Dexcom G6). In 2015, she started to use the FreeStyle Libre glucose sensor. After 1 month she experienced an oozing dermatitis at the contact site for the sensor and, therefore, changed to Dexcom G4, then G5, without experiencing any problems. In October 2019 she started to use Dexcom G6. In March the following year the patient started getting an itchy dermatitis at the contact site of the sensor that gradually deteriorated. At that time she had received a new batch of sensors with an adhesive that was more difficult to remove from the skin. At referral she could only use the sensor for 2–3 days (normal wear: 10 days) before getting a severe dermatitis. She had started to use Tegaderm Transparent film style 9534 HP (3M) under the sensor adhesive, but even then she could not use the sensor for more than 5–7 days before the dermatitis

forced removal of the device. The patient was thus referred for patch testing.

Case 2. This case was a 35-year-old female, office worker, with diabetes mellitus since the age of 3, and no history of skin disease or atopy. She started to use Freestyle Libre in 2015 but developed dermatitis at the contact site for the sensor after a couple of months. In 2016 the patient started to use the insulin pump Omnipod. In March 2017, a dermatitis developed. The patient during this period used Dexcom G5 and G6 CGM without complications. The patient started in October 2017 to use the Medtronic A6 CGM and insulin patch pump system and immediately experienced problems. She was investigated because of contact dermatitis and found to have an allergic contact dermatitis.⁴ Because of the multiple contact allergies found in the earlier investigation (Table 1), and the fact that the patient now had started having symptoms from Dexcom G6, she was once more referred for patch testing.

Case 3. This patient was a 44-year-old, male office worker with diabetes mellitus since the age of 29 and no history of skin disease or atopy. He started to use Freestyle Libre in 2017, but developed dermatitis at the contact site after 9 months. He had previously used a Medtronic insulin pump without dermatitis problems and was in 2018 recommended CGM system Dexcom G5 and then Dexcom G6. At referral the patient used Dexcom G6 with a Dexcom overpatch. Initially, he had no dermatitis problems, but in the summer of 2020 developed an oozing dermatitis. At referral for patch testing he could only use his device for 2–3 days because of the dermatitis (Figure 1). He developed dermatitis both with and without the overpatch.

2.1 | Ethical approval

The patients gave written consent to the use of patch test results, report their case history and use of their photos. Patient data are registered and used with approval of the Ethical Review Board, Stockholm, Sweden (Dnr 2020-02190).

2.2 | Patch testing and reading

The patients were patch tested with the Swedish baseline patch test series, the extended Malmö baseline series, the in-house medical device patch test series used in 2020,⁵ and relevant patch test substances according to the updated chemical analysis (described below). Chemotechnique Diagnostics provided the patch test preparations, unless otherwise stated (Table 1). All other test preparations were prepared at the Department of Occupational and Environmental Dermatology in Malmö, Sweden. Case 1 and Case 3 were patch tested with the Dexcom G6 adhesive patch “as is” and with separate ethanol

TABLE 1 Patch test results of the three cases

Patch test reactions at first or second reading	Case 1 D3/4/D7	Case 2 D3/4/D7	Case 3 D3/4/D7
In-house medical device series 2020 based on earlier used series ⁵			
IBOA 0.3% pet.	+(+)/++	−/++	+++/>++
IBOA 0.1% pet.	+/>+	−	++/>+
IBOA 0.01% pet.	−	−	+(+)/−
Ethyl acrylate	−	−	(+)/−
Colophony 20% pet.	−	+	−
Colophony 60% pet.	(+)/−	−	−
Hydroabietyl alcohol	−	++/>−	−
Alantolactone 0.1% alcohol	−	−	(+)/−
All other tested substances in the series	−	−	−
Sensor materials and substances deducted from clinic and analysis			
Dexcom G6 overpatch	NR	NT	−
Adhesive patch as is (outside)	(+)/−	NT	NT
Adhesive patch as is (inside)	++/>−	NT	++/>+
Sensor extract, ethanol	−	NT	+/>/(+)
Adhesive patch extract, ethanol	(+)/−	NT	+(+)/+
2,2'-Methylenebis(6-tert-butyl-4-methylphenol) monoacrylate	(+)/(+) ^a	−/− ^b	+/>+ ^b
0.1% acetone ^a / 0.1% pet. ^b			
2,2'-Methylenebis(6-tert-butyl-4-methylphenol) monoacrylate	+/>+ ^a	+/>− ^b	+/>+ ^b
0.3% acetone ^a / 0.3% pet. ^b			
2,2'-Methylenebis(6-tert-butyl-4-methylphenol) monoacrylate 0.5% pet.	NT	NT	+/>+
2,2'Methylenebis(6-tert-butyl-4-methylphenol) 0.3 and 1% pet.	−/−	−/−	−/−
Lauryl acrylate 0.1% pet.	−/−	−/−	−/−
Baseline series and extended baseline series			
Plastic related substances			
2-Hhydroxyethyl methacrylate	−	−	+
Preservatives			
Methylisothiazolinone	−/−	−	++/>+
TCMTB	−	−	+
Benzisothiazolinone	+/>−	−	+/>+
Fragrances/fragrance related			
<i>Myroxylon pereirae</i>	−	++	+++
Fragrance mix I	−	−	−
Fragrance mix II	−	++	−
Hexyl cinnamal	−	+	−
<i>Evernia prunastri</i>	−	++/>+	(+)
Hydroperoxides of linalool	−	+	(+)
Corticosteroids			
Tixocortolpivalate	−	−	+
Budesonide	+	−	−
Metals			
Potassium dichromate	−	−	+
Cobalt(II)hexahydrate	−	−	+
All other tested substances from the baseline series	−	−	−

Note: Case 2 had been previously investigated and the reactions highlighted in grey are those found positive at former investigation.

Abbreviations: IBOA, isobornylacrylate; NT, not tested; pet, petrolatum; TCMTB, 2-[thiocyanomethylthio]benzothiazole(Tolcide). a/b refers to the test dose and patch test finding of said patch test dose.



FIGURE 1 Allergic contact dermatitis in patient using Dexcom G6

extracts of the adhesive patches and the sensor housings. For case 1, materials from two sensors (LOT no 5268614) were used. The adhesive patches and the sensor housings were extracted in ~20 mL ethanol for 5 minutes in an ultrasonic bath. Thereafter, the extracts were concentrated to a volume of 0.5 mL. For case 3, extracts of the adhesive patch and sensor housing from one sensor (LOT no 7273137) were prepared in the same way. Case 3 was also tested with the Dexcom Overpatch both “as is” and as an ethanol extract.

All three patients were patch tested with two antioxidants detected in the chemical investigations. 2,2'-Methylenebis(6-*tert*-butyl-4-methylphenol) (Vulkanox BKF, CAS no 119-47-1, obtained as a gift from Trelleborg AB tested at 1.0% (w/w) in pet. 2,2'-methylenebis(6-*tert*-butyl-4-methylphenol) monoacrylate (>98%, CAS no 61167-58-6, Chemtronica) was tested at 0.3% and 0.1% in case 1 in acetone (w/v) and in cases 2 and 3 in pet. (w/w). Case 3 was also tested with a 0.5% pet. preparation in (w/w).

The Finn Chamber AQUA test chambers (SmartPractice) were used. Twenty milligrams of the pet. test preparations were applied on the chambers and 15 μ L of liquid preparations. The extracts tested in case 3 were applied in IQ Ultimate chambers (applied volume 20 μ L; Chemotechnique Diagnostics). 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 ICDRG and ESCD criteria.^{6,7} In order to discriminate differences in strength in between reactions and the patch test readings regarding the medical device series, the scoring system was further refined.⁸

2.3 | Controls

Twenty controls were patch tested with 2,2'-methylenebis(6-*tert*-butyl-4-methylphenol) monoacrylate pet. at 0.3% w/w. The controls were dermatitis patients referred for patch testing to the Department of Occupational and Environmental Dermatology in Malmö, who gave permission for additional patch testing with the substance. The testing

excluded children, those with known diabetes mellitus, and women with known pregnancy.

2.4 | Chemical investigation

The extracts of the adhesive patches and sensor housings tested in case 1 and case 3 were diluted 10-2000 times and thereafter, analyzed by gas chromatography-mass spectrometry (GC-MS).⁵ Furthermore, ethanol extracts of the adhesive patch and sensor housing from another sensor (LOT no 5266562), as well as an acetone extract of the adhesive patch from yet another sensor (LOT no 5267489) were analyzed. Previous analysis using the GC-MS² existed making comparison with the extracts of the changed adhesive possible. The comparison yielded several possible substances for further investigation, but it was clear that a major change in the adhesive had been made and, thus, this substance was the first to be identified (Figure 3).

3 | RESULTS

The chemical investigations showed the presence of 2,2'-methylenebis(6-*tert*-butyl-4-methylphenol) monoacrylate (Figure 2) in all extracts. For all samples, the concentrations found corresponded to a total amount of approximately 1 mg per adhesive patch and 0.03-0.08 mg per sensor housing. Figure 3 shows chromatograms and mass spectra of an adhesive patch extract and a 2,2'-methylenebis(6-*tert*-butyl-4-methylphenol) monoacrylate reference sample. All extracts also contained isobornyl acrylate (IBOA) at estimated concentrations in the same order of magnitude as those found in previously analyzed sensors from older batches,² corresponding to a total IBOA content of ≤ 1 μ g/patch and ≤ 1 μ g/sensor housing. Furthermore, all sensors were also found to contain 2,2'-methylenebis(6-*tert*-butyl-4-methylphenol).

Table 1 summarizes the positive reactions found in the three patients.

All three patients were found positive to 2,2'-methylenebis(6-*tert*-butyl-4-methylphenol) monoacrylate, 0.3% with a + reaction. Case 1 was patch tested in acetone because acetone had been used in the initial analysis. When found positive in acetone the allergen was prepared in pet. and the following patients and controls were thus patch tested in pet. as the vehicle.

Case 1 was found positive for IBOA at 0.1% w/w in pet. with a + reaction and to IBOA 0.3% with a +(+) reaction, ie, a weak to moderate reactivity. Case 2 was positive to IBOA only at 0.3% with a + reaction and only on D7, ie, a weak reactivity. Case 3 had a +++ reaction to IBOA 0.3% and a positive reaction in dilution series of the same allergen down to 0.01%. Cases 1 and 2 both reacted to colophony, case 1 with a doubtful reaction at 60% pet.⁹ and case 2 with a + reaction to colophony in 20% pet. Case 2 was further positive to hydroabeityl alcohol. Moreover, case 1 reacted with a ++ reaction to the adhesive “as is”, and with a doubtful reaction to the adhesive in the alcohol extract, case 3 with a ++ positive reaction to the adhesive “as is”, + to the alcohol extract and to the extract of the sensor.

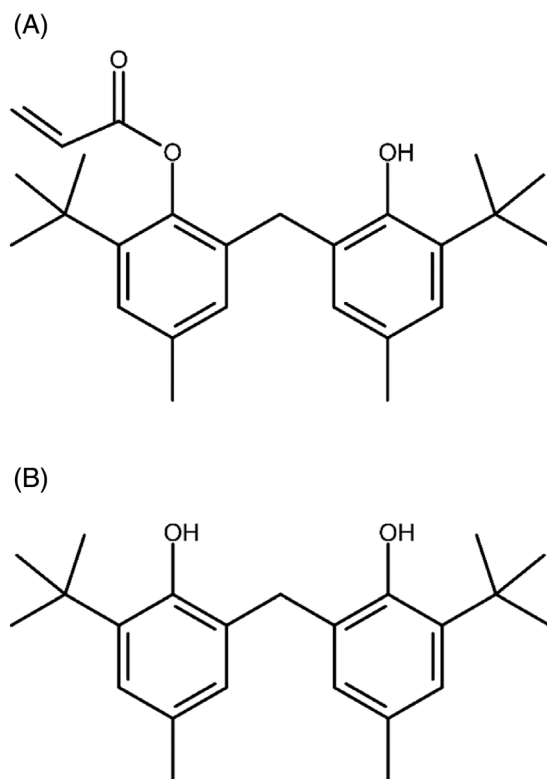


FIGURE 2 Molecular structure of (A) 2,2'-methylenebis(6-tert-butyl-4-methylphenol) monoacrylate and (B) 2,2'-methylenebis(6-tert-butyl-4-methylphenol)

All 20 controls patch tested negatively and with no irritant reactions to 2,2'-methylenebis(6-tert-butyl-4-methylphenol) monoacrylate, 0.3% pet., and no reported late reactions (2/2 vs 0/20; $P = .0043$; Fisher's exact test, two-sided).

4 | DISCUSSION

For the clinician it is interesting to note the fact that the three patients were all what is usually called polysensitized.¹⁰ The term is complex and here, in the definition, we include allergens other than those found in the baseline series. They had as a mean nine contact allergies. Multiple allergies have been discussed previously with regard to patients using the medical device Freestyle Libre,¹¹ but that using a medical device, ie a glucose sensor or insulin pump, should be a risk factor for polysensitization can, of course, not be argued from case reports. The patients had been patch tested in a targeted manner with substances that also might be found in the same products. The finding does, however, point to the fact that the group, because of exposure, may possibly be prone to polysensitization.

Case 3 was positive to 2-hydroxyethyl methacrylate without any known exposure, and had a doubtful reaction to ethyl acrylate, to which an association has been indicated in Freestyle Libre-sensitized patients.¹² All three patients when patch tested were found to be sensitized not only to allergens from different groups related to MDs;

acrylates, and colophony, but also to corticosteroids, preservatives, metals, and fragrance substances. The possible association with regard to preservatives, metals, and fragrance allergens and the MD exposure could not be determined. Neither did the patients have any other clear relevance, present or past, for these identified contact allergies. With regard to corticosteroids, it could not be determined whether the sensitization was related to treatment of medical device-related dermatitis. Among patients with contact allergy to IBOA, sensitized due to the use of MDs (Freestyle Libre), contact allergy to sesquiterpene lactones has also been found to be overrepresented.^{12,13} In these cases this was not found, however, case 1 had a doubtful reaction to alantolactone.

We have previously reported on the finding of IBOA in Dexcom G6.² Not only was IBOA found to be a possible culprit allergen, but also possible derivatives of colophony.² As Dexcom Inc. and their Swedish distributors contacted us because users had reported dermatitis during the spring of 2020, we knew that some alteration had been made in the adhesive. The three patients reported here had previously been able to use Dexcom products, but now showed a reaction pattern with contact allergy to IBOA, in case 2 contact allergy to colophony and hydroabietyl alcohol and in case 1 a doubtful reaction to colophony. All showed positive reactions to 2,2'-methylenebis(6-tert-butyl-4-methylphenol) monoacrylate 0.3%, while there was no reaction in the 20 controls ($P = .0043$). The latter substance has, to the best of our knowledge, not previously been described as an irritant or as an allergen in man nor animal.

2,2'-methylenebis(6-tert-butyl-4-methylphenol) monoacrylate, (also known under the trade names Sumilizer GM, BNX 3052, and Irganox 3052), is a heat and light stabilizer and an antioxidant used in a wide range of adhesive, plastic, and elastomer materials. Unlike traditional phenolic stabilizers/antioxidants, this substance is an effective alkyl radical scavenger.^{14,15} This property is especially useful in processes at high temperatures and in low oxygen environments, such as during the initial mixing of adhesives.^{14,16} The stabilizing mechanism involves trapping of polymer alkyl radicals at the double bond of the acrylate group, and subsequent hydrogen transfer from the intramolecular hydrogen-bonded phenolic hydroxyl group, which results in a stable phenoxyl radical.¹⁷ 2,2'-methylenebis(6-tert-butyl-4-methylphenol) monoacrylate may also be grafted using the acrylate moiety.¹⁶

2,2'-methylenebis(6-tert-butyl-4-methylphenol) monoacrylate has no harmonized classification according to the Classification, Labelling and Packaging (CLP) regulations. In the vast majority of CLP notifications provided by companies to the European Chemicals Agency (ECHA) no hazards (including skin sensitization) have been classified.¹⁸ According to data in ECHA's dossier on the substance, no irritancy was described in animal testing with the Draize test method; and it has been classified as a non-allergen in a local lymph node assay.¹⁹ The highest tested concentration in the local lymph node assay was 25%, although neither local irritation nor systemic toxicity were reported at this concentration.

The sensors were also found to contain 2,2'-methylenebis(6-tert-butyl-4-methylphenol), a structurally related antioxidant which, however, lacks the acrylate group present in 2,2'-methylenebis(6-tert-

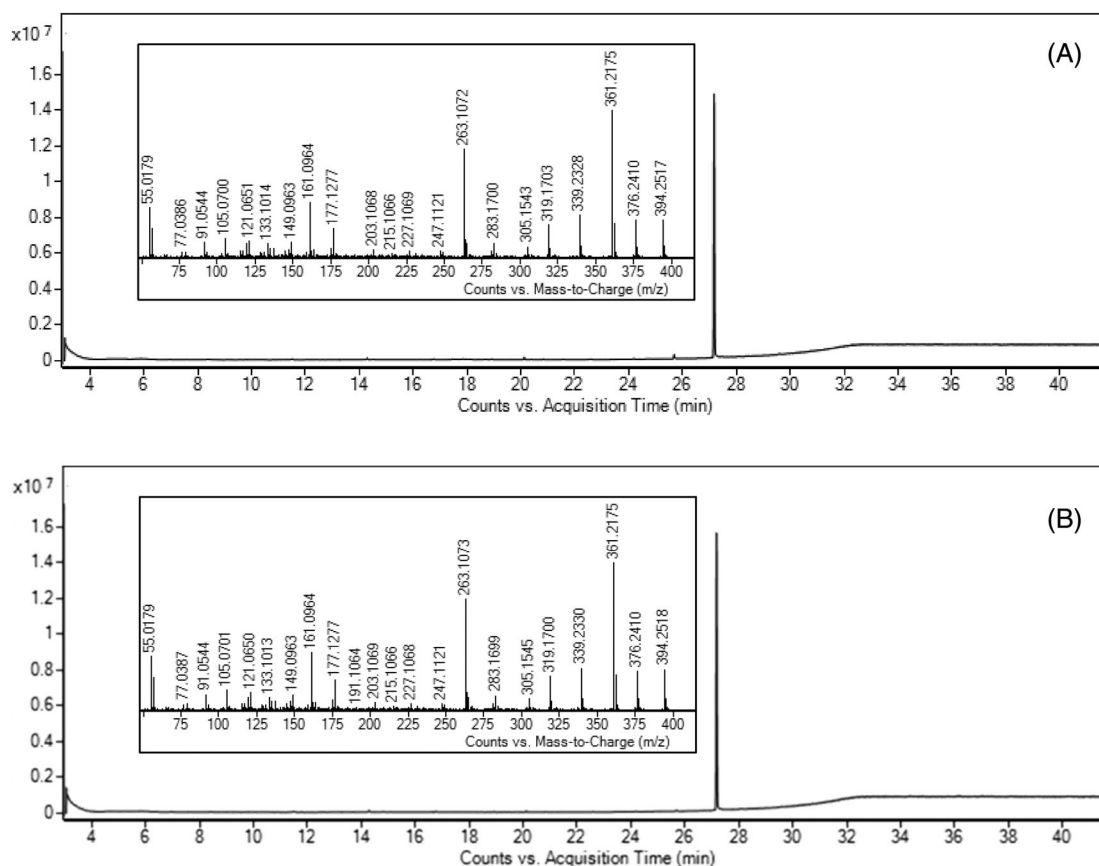


FIGURE 3 Total ion chromatogram of (A) an ethanol extract of an adhesive patch from a Dexcom G6 sensor (0.5 mL diluted 1000 times) and (B) a 3 ppm reference sample of 2,2'-methylenebis(6-tert-butyl-4-methylphenol) monoacrylate. The mass spectra of the 2,2'-methylenebis(6-tert-butyl-4-methylphenol) monoacrylate peaks at 27.2 minutes are shown in each chromatogram

butyl-4-methylphenol) monoacrylate (Figure 2). The content of 2,2'-methylenebis(6-tert-butyl-4-methylphenol) in the adhesive patches was approximately 20 times lower than the content of methylenebis(6-tert-butyl-4-methylphenol) monoacrylate. Because of the structural similarities, simultaneous reactions based on cross-reactivity could be expected, and at least theoretically, an enzymatic hydrolysis of 2,2'-methylenebis(6-tert-butyl-4-methylphenol) monoacrylate in the skin generating 2,2'-methylenebis(6-tert-butyl-4-methylphenol) and acrylic acid, could occur.²⁰ Interestingly, none of the patients reacted to 2,2'-methylenebis(6-tert-butyl-4-methylphenol) tested at 1.0%, although this corresponds to a molar concentration which is 3 times higher than that of 0.3% 2,2'-methylenebis(6-tert-butyl-4-methylphenol) monoacrylate. This may indicate that the presence of an acrylate group is crucial for the sensitizing potential of 2,2'-methylenebis(6-tert-butyl-4-methylphenol) monoacrylate.

From the patients' histories it is quite clear that the initial sensitization was to IBOA and that previous use of Freestyle Libre² was the medical device that sensitized. Case 2 was further exposed to IBOA through the use of Omnipod²¹ and was most likely thereby sensitized to colophony and hydroabietyl alcohol, causing allergic contact dermatitis almost instantly when using the Medtronic devices.⁴ The three cases are particularly interesting since they could at first use the

device without experiencing any skin problems, in cases 2 and 3, even for a prolonged time, and then experienced dermatitis. The fact that we know from previous investigations and the investigations reported here that in Dexcom G6² both IBOA and possibly colophony-related substances are present, but presumably in our cases the concentration did not initially initiate an elicitation. It was most probably the change in adhesive components that actually caused dermatitis, which could at least be partially explained by contact allergy to 2,2'-methylenebis(6-tert-butyl-4-methylphenol) monoacrylate. This substance has not been observed in our previous analyses of older Dexcom G6 sensors, but was now found in sensors from newer production batches in relatively high concentrations, while the IBOA content was approximately the same as in the sensors from previous batches.² If the patients would have been sensitized to 2,2'-methylenebis(6-tert-butyl-4-methylphenol) monoacrylate had they not had contact allergy for substances already found in the products, cannot be clarified in retrospect. The cases underline two possibly contradictory general principles when using substances which are biologically active and that may give rise to contact allergy (ie sensitization) and allergic contact reactions, ie, elicitation: (a) by keeping the concentration of substances low and possibly using different substances concomitantly, thus achieving the wanted effect, the risk of sensitization decreases- which

can be done with cosmetic consumer products; (b) in an individual already sensitized to allergens in a mixture, the more possible contact allergens there are at the same skin surface area, the higher the risk of elicitation of contact allergy.²² In the Dexcom G6, IBOA has been found in low concentration and the patients could previously use the devices. In the devices used by these patients, alterations in the adhesive patch had been made and after this they experienced an oozing dermatitis leaving hyperpigmentation for a prolonged time. However, all patch test reactions, apart from that of IBOA in case 3, were at the most found with a moderate reactivity. With regard to colophony in case 1 nothing but a doubtful reaction to colophony at 60%²² could be verified. In this patient it cannot be clarified in retrospect if colophony-related allergens in Dexcom caused the allergy or if the patient had been exposed to the allergens elsewhere. The patient had been recommended to use Tegaderm Transparent film dressing frame style 9534 HP (3M) under the adhesive and next to the skin. Tegaderm products have been found to contain abietic acid–colophony;²³ however, as far as we know, not in the product recommended. How can the very strong reaction to the adhesive when using the device be explained when there were no strong (+++) reactions to 2,2'-methylenebis(6-*tert*-butyl-4-methylphenol) monoacrylate in anyone of the patients? The most obvious explanation is, of course, the application time. Another possible explanation is that the substance 2,2'-methylenebis(6-*tert*-butyl-4-methylphenol) monoacrylate, found in a quite high concentration in the product, was patch tested at too low a concentration. In the adhesive the concentration was calculated to 40 µg/cm², this can be compared to the epicutaneous patch test concentrations, where a 0.3% acetone preparation gives a dose of 90 µg/cm² and a 0.3% pet. preparation gives a dose of 120 µg/cm².

The patch test concentration was, thus, only 3–4 times higher than the concentration in the product. For many sensitizers, including preservatives, the required patch test concentration is around 20 times higher than in leave-on products, – which at patch testing may give false negative reactions.¹ Whether an optimal patch test concentration for 2,2'-methylenebis(6-*tert*-butyl-4-methylphenol) monoacrylate would be around 1.5% needs to be carefully investigated in order to avoid active sensitization.²⁴ A third possible explanation is that a low grade inflammatory reaction to IBOA, and in 2 cases colophony and colophony-related substances, caused enhanced penetration of allergens, thus inducing a greater total reaction. Another explanation could be that the reaction pattern can be defined as an example of the cocktail effect;²⁵ that is, additional low reactivity allergens in a mix will enhance the reactivity by immunological mechanisms and thereby produce a reaction greater than the reactivity of the different components in themselves.

The last explanation is, of course, that the major culprit allergen has not so far been identified.

With regard to patch test results for testing with own material and extracts²⁶ the patients did not always react, or react with stronger reactions to the extracts, as compared to the material “as is,” which is in agreement with previous results with regard to medical devices.

The reaction pattern of the patients with regard to extract vs material “as is” indicates that also in these cases, the extracts used

were not concentrated enough.¹ In these cases the analysis of the material and the knowledge that the substance found was an acrylate made us, out of precaution, limit the amount of adhesive used for extracts.

5 | CONCLUSION

In the reported cases a new allergen in the CGM system Dexcom G6 is presented: 2,2'-methylenebis(6-*tert*-butyl-4-methylphenol) monoacrylate. The three cases showed multiple allergies at the investigation, some with low reactivity. This emphasizes the need for re-testing and re-analysing the devices chemically² if a patient suddenly appears to have problems to material that has previously been negative at testing. Besides sensitization to an already known sensitizer in the device, the possibility of increased reactivity due to exposure and sensitization at same area to a presently unknown allergen in the device should be considered. The reactivity pattern with weak and moderate reactivity to the allergens emphasizes the need for optimal test concentrations^{1,2,20} and the need for two patch test readings.^{1,2} From the three cases, where two were actually patch tested with the allergen in pet. and one in acetone, we cannot exclude the possibility that we were not patch testing at the optimal concentration. These cases emphasise the importance of occlusion time when using CGMs.^{2,5,27,28}

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AUTHOR CONTRIBUTIONS

Cecilia Svedman: Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; resources; writing-original draft; writing-review and editing. **Josefin Ulriksdotter:** Conceptualization; data curation; formal analysis; funding acquisition; investigation; writing-original draft; writing-review and editing. **Tina Lejding:** Data curation; investigation; writing-review and editing. **Magnus Bruze:** Conceptualization; methodology; supervision; writing-original draft; writing-review and editing. **Martin Mowitz:** Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; writing-original draft; writing-review and editing.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data available on request from the authors

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