

CONTACT DERMATITIS FROM GLUCOSE SENSORS IN SPAIN: A MULTICENTRIC APPROACH

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the [Version of Record](#). Please cite this article as doi: [10.1111/cod.13924](https://doi.org/10.1111/cod.13924)

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Authors do not have any conflicts of interests to declare.

ABSTRACT

Background: Allergic contact dermatitis from glucose sensors may interfere with their ongoing application.

Objective: To evaluate a series of Spanish patients with contact dermatitis to glucose sensors regarding former sources of contact allergens, patch test results and outcomes from the ongoing use of the device.

Methods: A series of patients with contact dermatitis from glucose sensors was investigated in eight dermatology departments across Spain (epidemiologic features, brands, latency time to develop dermatitis, the ability to continue using the devices as well as the patch test results).

Results: Thirty patients were evaluated (mean age: 20.93 years). 66.7% were children and 66.7% female. 90.0% used Freestyle Libre (FSL). 8/26 (30.8%) reacted to isobornyl acrylate (IBOA) and 2/20 (10.0%) to *N,N* dimethylacrylamide (DMAA). The mean latency time to develop dermatitis was 9 months. 16/29 (55.2%) patients continued using the same sensor causing the reaction. 13/29 (44.8%) were unable to continue using the sensor due to severe reactions. Of them, 5 were positive to IBOA, one to IBOA and DMAA; one to DMAA; one to colophony and 1 to isopropyl alcohol wipes. In one patient the outcome was unknown.

Conclusion: The frequency of sensitization to IBOA and DMAA, was lower than in other European series, but similar to a previously published Spanish article. Legislation requiring manufacturers to provide information regarding medical devices composition and cooperate with the investigation of contact dermatitis is urgently needed.

KEY WORDS

Allergic contact dermatitis; glucose sensor; insulin pump; medical devices; glucose sensor sets; patch test; acrylates; adhesives; isobornyl acrylate (CAS 5888-33-5); *N,N* dimethylacrylamide (CAS no. 2680-03-7).

1. INTRODUCTION

Proper control and treatment of diabetes mellitus is critical to prevent the multiple and potentially severe complications of this chronic metabolic disease in short and long term (particularly hypoglycemia)¹.

Glucose sensors and insulin pumps are sophisticated medical devices used to improve the treatment and the quality of life of patients with diabetes mellitus, especially diabetic children and their families. For example, by using this technology, parents are able to assess their children's glucose levels even when the child is away (e.g., at school or in a camp), or in bed at night without waking them up¹.

Unfortunately, using these devices have associated risks including many skin complications. In particular, several reports on allergic contact dermatitis to diverse brands of glucose sensors and insulin pumps have been published¹.

In a short period of time, the efforts of several dermatology professionals across Europe² have allowed the identification of the main culprits of said allergic contact dermatitis, including well-known allergens such as colophony³ and ethyl-cyanoacrylate^{4,5}; previous uncommon allergens such as isobornyl acrylate (IBOA)²; and new allergens such as *N,N* dimethylacrylamide (DMAA)⁶.

Additionally, ideal patch test concentrations have also been investigated and suggested⁷.

The progressive increase in the frequency of sensitization to these devices reaching alarming figures over the past 3 years, prompted us to perform this research to assess the situation in our region.

We evaluated a series of Spanish patients with contact dermatitis to glucose sensors with regards to possible former sources of contact allergens, patch test results and outcome of possible ongoing use of the device with protective dressings.

2. MATERIAL AND METHODS

A case series of suspected allergic contact dermatitis from glucose sensors studied by Spanish dermatologists in multiple centers across Spain, (depicted in Table 1) is reported. Participating researchers were invited to share cases in April 2019 and the collection of cases was completed in November 2020.

Written consent for participation, was provided by adult patients and by the parents or tutors in patients under 18 years old.

Clinical histories and patch test results were reviewed. Patients with typical clinical pictures who refused to undergo patch test investigation were also included.

Information regarding the age; sex; atopic constitution; age of DM onset; age at which the patch tests were performed; and available data regarding sensor brands; estimated latency time for sensitization (time passed from the first use of the sensor and the beginning of the symptoms) as well as the year and month the patients started to use the sensor; the ability to continue using it; the need for barrier dressings; use and tolerance to other devices such as insulin pumps, add-on transmitters, dressings and other acrylate sources; as well as patch test results were collected from the clinical histories. Patch testing was performed according to the criteria of the European Society of Contact

Dermatitis (ESCD)⁸. Two readings were performed in all patients (at D2 and 4) and three readings (also on D7) in some.

Statistical analyses were performed including Pearson's chi-squared test to evaluate the differences regarding the outcome of the patch testing with IBOA and DMDAA among participating centers, Fisher's exact test to evaluate the differences in positive reactions from the different IBOA patch tested preparations, and T-test (Student's test) to analyze possible differences regarding the mean latency time to sensitization between patients with and without sensitization to IBOA.

3. RESULTS

3.1 Patients characteristics

A series of thirty patients with contact dermatitis from glucose sensors were reported by eight participating centers across Spain (Table 1). The clinical histories were retrospectively reviewed. Three patients refused to pursue patch tests. The mean age (of the 30 patients) was 20.93 years (range: 3-64), 20/30 (66.7%) were children (≤ 16 years old), 20/30 (66.7%) were female, and 6/30 (20.0 %) had atopic dermatitis. 27/30 (90.0%) used Freestyle Libre (FSL) (Abbott, Chicago, Illinois, USA) and 3 used different models of Enlite (Medtronic, Dublin, Ireland) (Table 1). 5/26 FSL users also used add-on transmitters: 3 MiaoMiao (High Brilliant Health Technology, Shanghai, China), and 2 BluCon (GlucoNightWatch, Paterna, Spain). Fourteen patients also used insulin pumps. Information regarding year of first use of the sensor was available in 22 patients (Table 1): 7 patients started using FSL in 2016, 10 in 2017, 3 in 2018, 1 in 2019 and 2 in 2020.

3.2 Patch test results

Patch tests were performed between 2018 and November 2020 with the Spanish Contact Dermatitis Research Group (GEIDAC) baseline series in 26 cases; acrylate series in 26 cases (Supplemental online Table 2); DMAA 0.1% pet. obtained from Dept of Occupational and Environmental Dermatology, Malmö (Sweden) in 20; IBOA 0.1% pet. obtained from Dept of Occupational and Environmental Dermatology, Malmö (Sweden) in 15; IBOA 0.1% pet. Chemotechnique Diagnostics (Vellinge, Sweden) custom made preparations in 8 patients at 2 centers before 2020 and commercialized preparations by the same company in 2020 for three patients from one center; and plant series (Chemotechnique Diagnostics, Vellinge, Sweden) in 10. In one child, baseline series were not tested, and, in another child, the complete acrylate series was not tested).

Positive reactions to IBOA were observed in 8/26 (30.8%) including 3/15 (20.0%) tested with IBOA 0.1% pet. obtained from Dept of Occupational and Environmental Dermatology, Malmö (Sweden) and 5/11 (45.4%) tested with IBOA 0.1% pet. (Chemotechnique). Additionally, a doubtful (?+) reaction on D2 involving one case with a typical clinical picture of allergic contact dermatitis was also observed. The reaction in this particular patient could be reproduced within a second investigation performed 3 months later. The reproduced reaction also scored as ?+ on D2.

Five patients with positive IBOA (5/8, 62.5%) were also positive to sesquiterpene lactone mix (SLM) (Figure 1). None of the patients with negative IBOA were positive to SLM. The plant series were applied to 3 SLM-positive

patients, testing positive in two (one to alantolactone; and another one to alantolactone plus parthenolide). The other individual constituents of SLM (costunolide and dehydrocostus lactone) are not included in the plant series and thus, were not tested.

Additionally, among IBOA-sensitized patients, two reacted to colophony and one reacted to *Myroxylon Pereirae* (MP), fragrance mix (FM) I, FM II and linalool hydroperoxides (LinOH). Among 18 IBOA-negative patients, one reacted to colophony, two to MP, two to FM I, one to linalool hydroperoxides (LinOH) only, one to limonene hydroperoxides (LimOH) only, one to both LimOH and LinOH, and one to the adhesive of the Finn Chambers Acqua (containing modified colophony).

DMAA was positive in 2/20 (10.0%) patients (one of them also reacting to IBOA) and doubtful (?+ on D4) in one.

Four patients were positive for (meth)acrylates other than IBOA. Positive (meth)acrylates were numerous and varied (Table 1). One 61-year-old man (case17, Figure 2) with long-term diabetes was sensitized to 2-hydroxypropyl methacrylate (HPMA), 1,6-hexanediol diacrylate (HDA), ethylhexyl acrylate (EHA), 2,2-bis(4-(2-methacryl-oxyethoxy)phenyl)propane (bis-EMA) and tetrahydrofurfuryl methacrylate (THFMA). This patient had been exposed to several diabetes devices including different types of sensors and pumps since 1983 when he participated in a clinical trial studying a pump. Additionally, two cases developed allergic contact dermatitis from acrylic manicure materials prior to the use of the sensors including a nail technician, sensitized to 2-hydroxyethyl acrylate (HEA), ethylene glycol dimethacrylate (EGDMA), 2-hydroxyethyl methacrylate (2-HEMA), and 2-hydroxypropyl methacrylate (2-

HPMA) (case 19); and one patient sensitized to several acrylates who applied acrylic manicure materials on herself (case 18).

A 9-year-old girl user of FSL and Minimed (Medtronic, Dublin, Ireland) pump consulting with reactions to the sensor was sensitized to several uncommon acrylates, namely, trimethylolpropane triacrylate (TMPTA), pentaerythritol triacrylate (PETA) and epoxy acrylate (EA) (case 25). Prior exposure to other acrylate sources could not be identified in this particular case and the manufacturer of the sensor claimed that none of these acrylates were contained in the device.

Pearson's chi-squared test showed that there were not significant statistical differences regarding the outcome of the patch testing with IBOA in the 8 centers P -value (P)= .467). Pearson's chi-squared test showed a significant association between positive patch tests to DMDAA and tests performed at the Hospital of Santiago de Compostela (P <.001). Fisher's exact test showed that the differences in positive reactions from preparations obtained from Dept. of Occupational and Environmental Dermatology, Malmö (Sweden) and Chemotechnique preparations (21.4% vs. 45.5%, respectively) were not statistically significant (P = .389).

3.3 Contact Dermatitis management and outcome

The median duration of use before the beginning of the dermatitis (latency) was 9 months. Mean latency periods of 8 patients with sensitization to IBOA and 16 patients without sensitization to IBOA were 10.75 and 8.94 months, respectively. Eight patients were excluded from statistical analysis due to missing values (not tested, doubtful patch test reactions or unknown latency). T-

test (Student's test) showed that there were no statistically significant differences regarding the mean latency between patients with or without sensitization to IBOA, difference in the mean latency being 1.81 months (Confidence Interval 95% (CI 95%): -7.26 to +10.89); $P=.68$.

Information regarding the ability to continue using the sensor was available in 29/30 patients. 16/29 (55.2%) patients were able to continue using the sensor, including two IBOA-positive patients; one patient with a doubtful reaction to IBOA (?+); 5 patients positive to other allergens, most of them being of past or unknown relevance (Table 1); 5 patients with negative patch tests; and 3 not tested. Of them, 8/16 (50.0%) needed barrier dressings (any materials applied between the sensor and the skin with the aim of preventing allergens to reach the skin including hydrocolloid plasters or dressing films); two required removal of the sensor before the end of the 14-day-period of using time (including one not patch tested-child using hydrocolloid tapes who required removal before 7 days; and one IBOA-positive patient using Tegaderm (ST. Paul, Minnesota, U.S.A) dressing film who required removal before 8-12 days); and 7 patients continued its use without any barrier materials but with the persistence of dermatitis. The remaining patient was lost to follow-up. Only colophony was considered relevant in this group. The relevance of the other positive allergens was either unknown or unavailable.

On the other hand, 13/29 (44.8%) patients were unable to continue using the sensor due to severe reactions. In 9/13 (69.2%), positive patch tests of likely current relevance were obtained including 5 patients positive to IBOA, one to IBOA and DMAA, one to DMAA, one to colophony, and one to isopropyl alcohol wipes (supplied in the FSL container). In the remaining 4/13, either the tests

were negative or sensitization was of past or unknown relevance. Thus, sensitization to several uncommon acrylates (case 25, Table 1) of unknown relevance was observed involving one girl; and sensitization to epoxy resin and black rubber of possible past relevance, was observed to involve a teenager (case 3) who used multiple traditional and semipermanent nail polishes and who declared pruritus upon the contact with a bicycle and a motorcycle black rubber handle grips. However, epoxy resin was not identified in any of the products brought in by her.

All patients who had to discontinue the use of the sensor were diagnosed with likely allergic contact dermatitis according to the typical clinical picture (intense pruritic reactions, sometimes edematous, developing within several weeks/months from the first application, and, sometimes, requiring to apply dressing barriers) regardless of the patch tests results.

Three previously published users of MiaoMiao developed contact dermatitis to both the glucose sensor and the add-on transmitter⁹. Two patients applied the transmitter BluCon without recalling any reactions from it.

Six patients developed reactions from insulin pumps as well. One child reacted to up to three devices (FSL and Enlite glucose sensors and Minimed 640G insulin pump).

Regarding the exposure to other potential sources of (meth)acrylates, 5 patients had been exposed to acrylic manicure materials, 2 of them developing reactions from them as mentioned prior-to the first use of the sensor. One additional patient recalled reactions from kinesitherapy plasters.

4. DISCUSSION

Despite the significant benefits of glucose sensors and insulin pumps, their use must often be interrupted due to sensitization and allergic contact dermatitis. This side effect has become a significant challenge for the diabetic patients who use these devices.

4.1 Sensitization to IBOA in Spanish diabetic patients using glucose sensors

In Spain, the FSL flash system was marketed for the first time in 2014. Ever since, it has been the most frequently used glucose monitoring device. In 2017, it was included in the portfolio of products financed by the Spanish Health-Care National System (Sistema Nacional de Salud; SNS) for insulin-dependent DM pediatric patients (between 4 and 17 years of age) and, in 2019, it was approved also to be applied in adults. This may explain the predominance of the FSL sensor over other brands 27/30 (90.0%) and that the majority of patient (66.7%) in our series were children.

Insulin pumps, on the other hand, had been financed by the SNS since 2004 throughout the Spanish territory for all risk groups of insulin-dependent DM by decree of the Spanish Ministry of Health¹⁰. Some of our patients developed contact dermatitis reactions also from the insulin pumps. However, most did not consult us for contact dermatitis in these instances. This may be due to the replacement times for insulin pumps (2-3 days), shorter than for glucose sensors (14 days) making it easier for the patients to tolerate them. In our opinion, the fact that some patients do not complain, does not mean that they are not suffering mild-to-moderate forms of contact dermatitis from these devices. In many patients who did not recall any reactions from the insulin

pumps, we noticed multiple rounded eczematous lesions involving the abdomen or lower back reproducing the silhouette of the insulin pumps when they were patch tested.

IBOA has been detected in different parts of glucose sensors (both FSL and Enlite) and insulin pumps by means of gas chromatography-mass spectrometry^{2,11-14}. In published case series of allergic contact dermatitis from glucose sensors, IBOA was the most common allergen involved. Interestingly, in our series, the frequency of sensitization to IBOA (30.8%), was similar to the previously reported rates by other Spanish authors, (35.7%)¹⁵, however much lower than the frequency detected by authors in other European countries, such as Belgium (69.2% currently and ~80% in the past)¹⁶, Portugal (80.0%)¹⁷ and Finland (80.9%)¹⁸.

An explanation for these striking regional differences is lacking. All our cases were systematically read on both D2 and D4 and most on D7, in accordance with the latest recommendations to increase the sensitivity of the test^{7,19} (two patch test readings as well as D7 readings). Positive reactions were observed at D2 and D4 readings in all and performing readings on D7 did not allow to diagnose further cases. The most likely explanation is that the patch test concentration of IBOA in our series (0.1% pet.) may underestimate sensitization to it (currently, higher concentrations (0.3% pet.) are recommended to increase sensitivity⁷). However, 0.1% pet. IBOA was also tested in other European series with much higher positivity rates¹⁶⁻¹⁹, which may imply that other factors are possibly implicated.

An additional hypothetical explanation could be, that in Spain, the available batches of devices have a different composition with lower concentrations of the culprit allergens and/or with other non-tested unknown allergens. Unfortunately, the exact batches of the devices were no longer available at the time we performed the evaluation of the clinical histories of our cases. It has been shown that composition changes have been made to both FSL and FSL 2^{20,24}. However, most of our patients started using FSL and developed reactions before these changes were made (likely in 2018). The fact that, in some patients, no relevant contact allergy was demonstrated, may indicate that other unknown allergens may be involved. Interestingly, two patients reacting to FSL, tolerated FSL2 and we have not dealt with any patients reacting to FSL2.

A statistical analysis was performed to study a possible impact of inter-center differences in the outcome of the testing. Unfortunately, since each center contributed with a small number of cases, statistical significance could not be reached with regards to IBOA. However, we found a significant association between those having positive patch tests to DMCAA and those being studied at the center of Hospital of Santiago de Compostela (both positive patch tests to DMAA were detected there). The reason for it is unknown, however we could hypothesize whether the amount of DMAA in the batches used in that regional area is higher.

The lower rate of IBOA cases could also be due to a selection bias noting that participating centers provided cases concerning patients with suspected contact dermatitis from the sensors and the diagnostic criteria applied in the different centers may not be homogeneous. Some researchers likely apply stricter criteria and may omit some patients with suspected allergic contact dermatitis to

glucose sensors (when patch tests are not definitely positive), while other researchers are possibly laxer and include some patients that may actually have irritant contact dermatitis.

4.2. Allergic versus irritant contact dermatitis

We wonder whether there is a bias involving a potential inclusion of a high number of cases with irritant contact dermatitis in our series. However, most patients, even IBOA-negative cases, developed reactions only after using the sensor for a few weeks/months; in most, reactions consisted of severe exudative lesions causing early device detachment; and some could only tolerate the devices with different types of dressings; all features being more consistent with an allergic rather than irritant contact dermatitis. This is in accordance with the advice provided in the literature¹⁹ on how to classify the cases with regards to the results of the patch testing investigations in conjunction with the time between first use and first symptoms. We believe that the patients' clinical history is crucial and the fact that a patient tolerates the sensor for some time and then suddenly develops lasting dermatitis may be a signal that the reaction is actually allergic. However, it is also true that in the clinical practice, the application of these criteria may not be easy and patients may have difficulties recalling time of onset of symptoms after the first use. Interestingly, statistical analysis did not find significant differences between the mean latency (time passed between first use of the sensor and the beginning of the reactions) between IBOA-positive and IBOA-negative patients. This may indirectly further confirm that, in our series, patients with a clinical picture compatible with allergic contact dermatitis are likely truly allergic regardless of

the results of patch tests. This may possibly be due to either false negative tests to IBOA or sensitization to other allergens.

Hydrocolloids tapes have proved more efficient than film dressings in preventing reactions from glucose sensors allowing their application during the 14-day time period²⁵.

The fact that some IBOA-negative patients were able to use the sensor with persistent mild dermatitis from the Tegaderm film dressing (case 9) and without any dressings (cases 4, 6, 7, 8 and 24) could likely indicate that the reactions involving these cases were actually irritant. However, allergic contact dermatitis cannot be excluded either, especially in case 6, when the patient reacted to a piece of the adhesive from a used FSL sensor.

Although, it has been published that prevention of allergic contact dermatitis from FSL is not possible beyond 72 hours by using film dressings²⁵, three patients sensitized to IBOA tolerated the sensors for longer periods of time with Tegaderm (5, 8-12 and 14 days respectively). Unfortunately, these patients did not use hydrocolloids which possibly could have enabled extension of the using period of the sensor.

4.3 Sensitization to other allergens

We found that, among patients with severe reactions jeopardizing the use of the sensor, sensitization to likely relevant allergens was frequent (IBOA in half of them, and more sporadically others such as DMAA or colophony). However, some patients reacted to allergens apparently unrelated to the sensor and

others tested negative. We hypothesize that, in some of our patients with a clearcut clinical picture of severe allergic contact dermatitis to the sensor, negative patch tests with IBOA and/or DMAA were likely false negative although sensitization to other allergens could not be excluded. In addition, we also identified sensitization to MCI/MI (methylchloroisothiazolinone/methylisothiazolinone), MI (methylisothiazolinone) as well as fragrance markers (in both patients who could go on using the sensor and patients who needed to discontinue its use). In these cases, a possible contribution of sensitization to components of hygiene products, disinfectants, wipes or dressings cannot be completely ruled out. The occlusion of said products from the sensor/dressings and their subsequent application on top of an already damaged skin could easily facilitate the sensitization and the eventual elicitation of the contact dermatitis reaction. The dressings could also contain preservatives, acrylates as well as other relevant allergens.

We observed a high percentage of IBOA-sensitized patients with positive reactions to SLM (62.5%) like in previous case series^{2,7,16}. Only 12.5% (1/8) of IBOA-sensitized patients also reacted to terpenes and other fragrances, unlike previously published research with a higher frequency of sensitization to these chemicals (61.1%)¹⁶.

As previously reported²¹, our patients rarely showed positive patch test reactions to other (meth)acrylates (15.4%), and most of them recalled exposure and intolerance to other sources of (meth)acrylates prior to the application of the sensor (mainly other diabetes medical devices and manicure materials). The exception was a 9-year-old girl who used FSL and Minimed pump, who

was sensitized to several uncommon acrylates (TMPTA, PETA and epoxy acrylate) in whom previous exposure to acrylates was not proven (case 25).

We have recommended Dexcom (San Diego, U.S.A) glucose sensors in patients sensitized to IBOA because this brand was supposed to be free of this allergen²². However, recently, small amounts of IBOA have been detected in both the Dexcom sensors and their adhesive patches²³. Possible technical differences preparing the extracts, how analysis was performed or differences in the composition among different batches may explain why IBOA was not previously detected in this specific brand up until recently²³. It is uncertain whether this finding may impact the tolerance to this device among patients reacting to other brands such as FSL or Enlite. In our series, five patients were changed to Dexcom. However, unfortunately, information regarding tolerance to it was only available in a minority of them (Table 1).

In mid-2020, presumably IBOA-free Freestyle Libre 2 was launched. Some of our patients changed from FSL to FSL 2 with good tolerance (including some who tested negative to IBOA) (Figure 1). In FSL 2, a potential allergen already known in cosmetics, namely butyl hydroxy toluene (BHT), has also been detected²⁴.

4.4 Addressing the advantages of international research networks as well as the need to build legislation

In many cases, information was requested from the manufacturers. However, neither information regarding the composition nor cooperation providing materials to further patch test our patients was provided. This makes it extremely complex to study these patients. An additional drawback has been

the lack of available commercial allergens (IBOA has recently become marketed, but DMAA is still unavailable). For these reasons, many doctors and patients may become discouraged to complete any patch tests believing that the investigations will be ineffective. In our opinion, it is our duty to investigate suspected cases with available means and to report/notify them to the scientific community and competent authorities.

However, in order to investigate these patients correctly the investigating clinician needs sample material (i.e. devices to perform extracts with), chemical knowledge as well as the possibility to perform chemical analysis and the possibility to investigate several patients having similar problems so that doses and patch test substances can be standardised and optimised. As dermatology clinics work today this is only made possible through the use of the national and international research societies so that information can be quickly transmitted and help with analysing enabled.

Like other authors, we also believe that there is a dire need for the competent authorities to build legislation accordingly. The systematic declaration of components in medical devices should be mandatory. In addition, manufacturers should be responsible to collaborate in the investigation of the potential harm their products may provoke. Only a collaborative approach amongst doctors, manufacturers and authorities will redound to the benefit of our patients with contact dermatitis from medical devices.

REFERENCES

1. Gatica-Ortega ME, Pastor-Nieto MA. Dermatitis alérgica de contacto y otras dermatosis asociadas al uso de bombas de insulina y sensores de glucosa. Allergic contact dermatitis and other dermatosis related to the use of insulin pumps and glucose sensor sets. *Piel*. 2020;35(8):500-508.
2. Herman A, Aerts O, Baeck M, et al. Allergic contact dermatitis caused by isobornyl acrylate in Freestyle® Libre, a newly introduced glucose sensor. *Contact Dermatitis*. 2017;77(6):367-373.
3. Passanisi S, Lombardo F, Barbalace A et al. Allergic contact dermatitis and diabetes medical devices: 2 clinical cases. *Contact Dermatitis*. 2018;79(2):115–7.
4. Schwensen JF, Friis UF, Zachariae C, Johansen JD. Sensitization to cyanoacrylates caused by prolonged exposure to a glucose sensor set in a diabetic child. *Contact Dermatitis*. 2016;74(2):124-125.
5. Peeters C, Herman A, Goosens A, Bruze M, Mowitz M, Baeck M. Allergic contact dermatitis caused by 2-ethyl cyanoacrylate contained in glucose sensor sets in two diabetic adults. *Contact Dermatitis*. 2017;77(6):406-429.
6. Mowitz M, Herman A, Baeck M, et al. N,N-dimethylacrylamide—A new sensitizer in the FreeStyle Libre glucose sensor. *Contact Dermatitis*. 2019;81(1):27–31.

7. Ulriksdotter J, Svedman C, Bruze M, Glimsjö J, Källberg K, Sukakul T et al. Contact dermatitis caused by glucose sensors-15 adult patients tested with a medical device patch test series. *Contact Dermatitis*. 2020;83(4):301-309.
8. Johansen JD, Aalto-Korte K, Agner T, et al. European Society of Contact Dermatitis guideline for diagnostic patch testing - recommendations on best practice. *Contact Dermatitis*. 2015;73(4):195–221.
9. Gatica-Ortega M, Pastor-Nieto M, Torres-Aranda R, Luna-Bastante L, Pérez-Hortet C. Contact dermatitis from Miaomiao (an add-on transmitter to FreeStyle Libre Flash glucose monitoring system). *Contact Dermatitis*. 2021;doi:10.1111/cod.13788.
10. Boletín Oficial del Estado 0685053 Orden SCO/710/2004, de 12 de marzo. <https://www.boe.es/eli/es/o/2004/03/12/sco710>. Accessed January 28, 2021.
11. Oppel E, Högg C, Summer B, Ruëff F, Reichl FX, Kamann S. Isobornyl acrylate contained in the insulin patch pump OmniPod as the cause of severe allergic contact dermatitis. *Contact Dermatitis*. 2018;79(3):178–80.
12. Raison-Peyron N, Mowitz M, Bonardel N, Aerts O, Bruze M. Allergic contact dermatitis caused by isobornyl acrylate in OmniPod, an innovative tubeless insulin pump. *Contact Dermatitis*. 2018;79(2):76–80.
13. Herman A, Baeck M, de Montjoye L. et al. Allergic contact dermatitis caused by isobornyl acrylate in the Enlite glucose sensor and the

- Paradigm MiniMed Quickset insulin infusion set. *Contact Dermatitis*. 2019;8(6):432–7.
14. Kamann S, Oppel E, Liu F, Reichl FX, Heinemann L, Högg C. Evaluation of isobornyl acrylate content in medical devices for diabetes treatment. *Diabetes Technol Ther*. 2019;21:533– 7.
15. Vidal-Albareda C, Yelmo-Valverde R, Solórzano-Zepeda C, Rodríguez-Muñoz N, de-la-HozCaballer B, González-de-Olano D. Prevalence of contact dermatitis to glucose sensors in pediatric population and the main allergens involved. *Contact Dermatitis*. 2020;83(1):47–49.
16. Dendooven E, Foubert K, Goossens A, et al. Concomitant positive patch test reactions in FreeStyle-allergic patients sensitized to isobornyl acrylate. *Contact Dermatitis*. 2020; doi: 10.1111/cod.13706. Online ahead of print.
17. Queirós CS, Alexandre MI, Garrido PM, Correia TE, Filipe PL. Allergic contact dermatitis to IBOA in FreeStyle Libre: Experience from a tertiary care Portuguese hospital. *Contact Dermatitis*. 2020;83(2):154–157.
18. Hyry HSI, Liippo JP, Virtanen HM. Allergic contact dermatitis caused by glucose sensors in type 1 diabetes patients. *Contact Dermatitis*. 2019;81(3):161–166.
19. Ulriksdotter J, Mowitz M, Svedman C, Bruze M. Patch testing and diagnosis when suspecting allergic contact dermatitis from medical devices. *Contact Dermatitis*. 2020;83(4):333–335.

20. Aerts O, Herman A, Mowitz M, Bruze M, Goossens A. Isobornyl Acrylate. *Dermatitis*. 2020; 31(1): 4-12.
21. Herman A, de Montjoye L, Tromme I, Goossens A, Baeck M. Allergic contact dermatitis caused by medical devices for diabetes patients: A review. *Contact Dermatitis*. 2018;79(6):331-335.
22. Oppel E, Kamann S, Reichl F-X, Högg C. The Dexcom glucose monitoring system—An isobornyl acrylate-free alternative for diabetic patients. *Contact Dermatitis*. 2019;81(1):32–36.
23. Svedman C, Bruze M, Antelmi A, et al. Continuous glucose monitoring systems give contact dermatitis in children and adults despite efforts of providing less "allergy- prone" devices Investigation and advice hampered by insufficient material for optimized patch test investigations. *J Eur Acad Dermatol Venereol*. 2020 doi: 10.1111/jdv.16981. Online ahead of print.
24. Oppel E, Kamann S, Heinemann L, Klein A, Reichl F-X, Högg C. Freestyle libre 2: The new isobornyl acrylate free generation. *Contact Dermatitis*. 2020;83(5):429–431.
25. Kamann S, Oppel E. Hydrocolloid blister plaster decreases allergic contact dermatitis caused by Freestyle Libre and isobornyl acrylate. *Contact Dermatitis*. 2019;81(5):380–381.

TABLES

TABLE 1. CONTACT DERMATITIS FROM GLUCOSE SENSOR SETS: EPIDEMIOLOGICAL FEATURES, TYPE OF DEVICE, PATCH TESTS RESULTS AND CLINICAL EVOLUTION.

Case number	Center	Sex/age (years old)	Glucose sensor brand/ month-year of introduction	Latency (months)	IBOA (D2/D4/D7)	DMAA (D2/D4/D7)	Positive reactions to GEIDAC baseline as well as additional series and materials	Previous exposure to acrylate sources/ reaction	Ability to go on using the sensor/ outcome
1	HUT	M/12	FSL/ 03-2016	8	++/++/+	-/-/-	Colophony, PTBP, FMI, FMII, MP, SLM, LinOH, JA, SWO, BP, used Enlite and FSL sensor adhesive, deodorant	Tapes/ NR.	No/ Change to Enlite requiring Tegaderm and early removal (5 days). Use discontinued during the summer

2	HUT	F/ 9	FSL/01-2017	7	++/+/+	-/-	SLM, alantolactone	-	No/ Change to Dexcom G6 since 12-2020
3	HUT	F/ 14	FSL/09-2017	12	-/-	-/-	ER, BR	Semipermanent nail polish/ NR.	No
4	HUT	F/ 9	FSL/10-2017	2	-/-	-/-	-	-	Yes/ Dermatitis persists
5	HUT	M/ 64	FSL/2016	5	-/-	-/-	-	Dental procedures/ NR	Yes/ Requires Compeed dressing
6	HUT	F/11	FSL/04-2016	24	-/-	-/-	Used sensor adhesive FSL	-	Yes/ Dermatitis persists
7	HUT	M/7	FSL/2018	-	-/-	-/-	LimOH, LinOH	-	Yes/ Dermatitis persists
8	HUT	M/9	FSL/10-2017	12	-/-	-/-	Co, Dermaplast	-	Yes/ Dermatitis

							adhesive		persists
9	HUT	F/16	FSL/2016	12	-/-	-/-	MP, BIT	-	Yes/ Dermatitis persists with Tegaderm.
10	HUT	M/ 12	FSL/2016	1	NT		NT	-	Yes/ Requires hydrocolloid tape and early removal (7 days). Use discontinued during the summer
11	HUT	F/ 3	Enlite/2019	1	-/-/NP	-/-/NP	MP, ER, Finn Chambers Aqua with modified colophonium, LinOH, Enlite sensor, Overtape dressing,	-	Yes/ Requires Leukoplast tape

							moisturizing cream, plastic support of sensor grated		
12	HUS C	F/ 13	FSL/07-2017	24	++/+++/N P	NT	-	-	Yes/ Requires Tegaderm tape and early removal (8-12 days)
13	HUS C	M/ 29	FSL/04-2019	2	++/+++/N P	NT	-	-	No/ Change to Dexcom G5 mobile
14	HUS C	M/ 10	FSL/08-2017	24	-/-/ NP	NT	-	-	Yes/ Dermatitis persists
15	HUS C	M/ 12	FSL/09-2018	7	-/-/ NP	NT	-	-	No/ Change to Dexcom G5 mobile
16	HUS	F/ 34	FSL/10-2016	36	++/+++/	NT	Ni	-	No/ Change to

	C				NP				Dexcom G5 mobile
17	HUS	M/ 61	FSL/2017	2	++/++/NP	++/++/NP	SLM, ER, HPMA, HDA, EHA, bis-EMA, THFMA, parthenolide, alantolactone	-	No
18	HUS	F/ 33	FSL/unknown	0	-/- NP	++/ ++/ NP	MCI-MI, MI, propolis, several unknown acrylates	Acrylic nails user/ reaction (removal needed in 2 days)	No
19	HUS	F/ 39	FSL/unknown	1	-/- NP	NT	MCI-MI, HEA, EGDMA, 2-HEMA, HPMA	Nail technician and acrylate manicure user/fissured pulpitis	Unknown
20	HUG	F/14	FSL/11-2017	1	-/-/-	-/-/-	-	-	Yes/ Mild intermittent reactions likely irritant

									Changed to Enlite in late 2019
21	HUG	F/ 9	FSL/06-2018	6	?+/-/- (tested twice with same outcome)	-/-/-	-	Kinesiotherapy plasters/reaction	Yes/ Requires hydrocolloid dressing. Resolution after changing to FSL 2.
22	HUG	F/ 45	FSL/08-2017 (stops in 2018 and re-starts in 06-2020)	6	++/+++/ NP	-/- NP	SLM	Semipermanent nail polish and dental prosthesis/NR	No/ Resolution after changing to FSL 2
23	HUG	F/18	FSL/12-2017	6	-/-/-	-/-/-	Isopropyl alcohol wipes (++ on D4)		No
24	HUG	F/37	FSL/01-2016	0	-/-/-	?/-/-	PTBPF, Thiomersal, FMI, LimOH	-	Yes/ Mild dermatitis persists

25	HLP	F/9	FSL/unknown	12	NT	NT	TMPTA, PETA, epoxy acrylate	NT	No
26	HLP	F/16	Enlite/unknown	1	-/+ NP	-/-NP	SLM, colophony	-	Yes/ Requires Tegaderm tape
27	HA	F/7	FSL/unknown	24	-/- NP	-/-NP	-	-	No/ Good tolerance of different models of Dexcom (G4, G5, G6)
28	HDM	F/9	Enlite/unknown	12	-/- NP	-/?+/NP (patch tested twice)	Colophony, MI, FMI	-	No/ Requires Tegaderm
29	HIGC	F/10	FSL/unknown	4	NT		NT	-	Yes/ Requires Askina barrier cream
30	HIGC	M/ 62	FSL/unknown	unkno wn	NT		NT		Yes/ Requires Comfeel dressing and

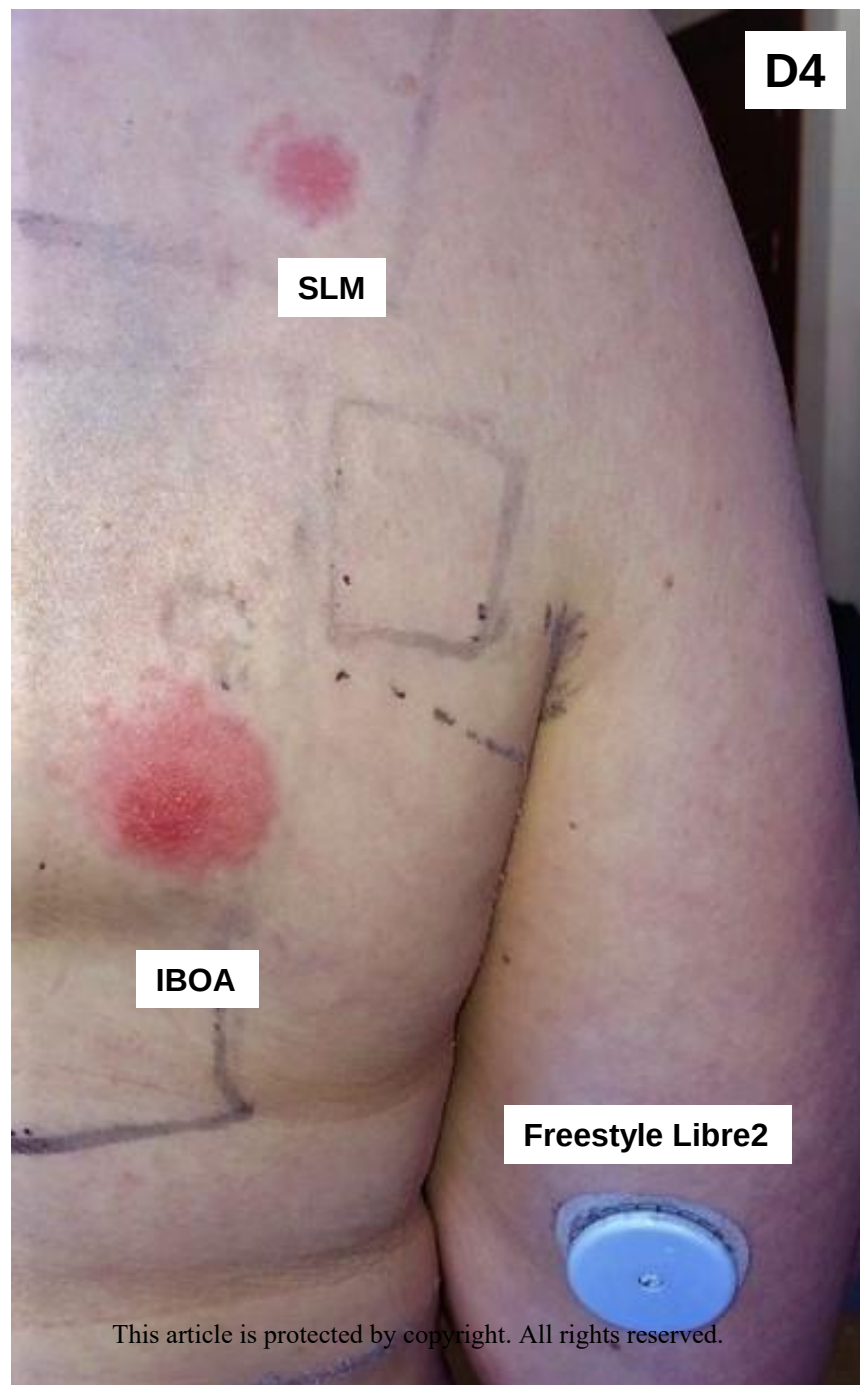
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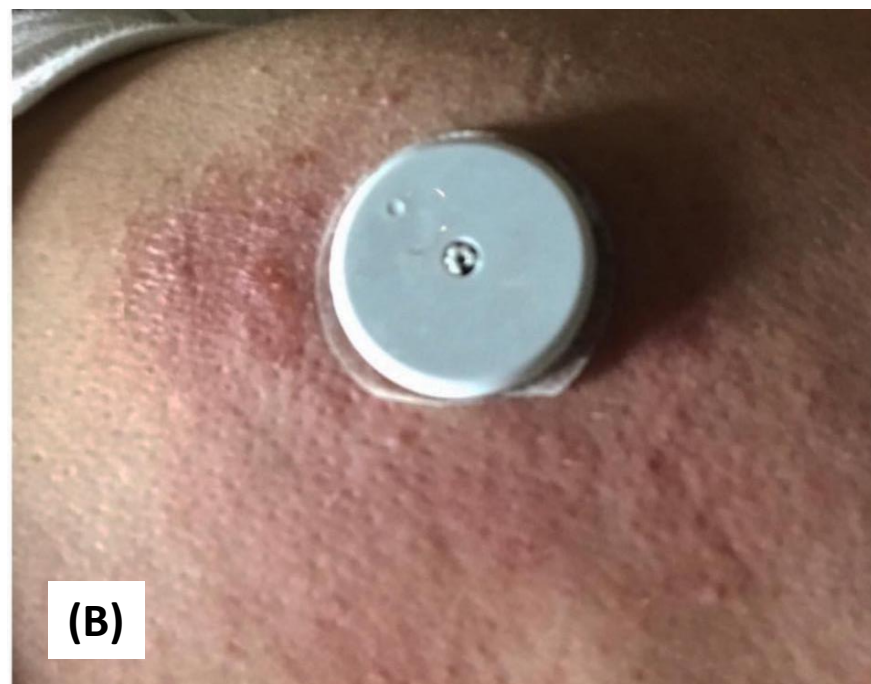
Abbreviations: bis-EMA: bis- ethyl methacrylate; BIT: benzisothiazolinone; BP: Benzoyl peroxide; BR: Black rubber; Co: Cobalt chloride; DMAA: N,N dimethylacrylamide 0.1% pet; EGDMA: Ethylene glycol dimethacrylate; EHA: etylhexyl acrylate; ER: Epoxy resin; FM: fragrance mix; F: female; FSL : FreeStyle Libre ; GEIDAC: Spanish Contact Dermatitis Research Group; GST: gold sodium thiosulfate; HDA: 1,6 hexanediol diacrylate; HEA: 2-Hydroxyethyl acrylate; HEMA: hydroxyethyl methacrylate; HPMA: 2-Hydroxypropyl methacrylate; IBOA: Isobornyl acrylate 0.1% pet; JA: Jasmine absolute; LimOH: limonene hydroperoxides; LinOH: linalool hydroperoxides; M: male; MCI/MI: methylchloroisothiazolinone/ methylisothiazolinone; MI: methylisothiazolinone; MP: *Myroxylon pereirae*; Ni: Nickel sulfate; NP : not performed ; NR: no reaction; NT: non tested; PETA: pentaerythritol triacrylate; PTBP: p—ter-Buthylphenolformaldehyde resin; SLM: Sesquiterpene lactone mix; SWO: Sandalwood oil; THFMA: Tetrahydrofurfuryl methacrylate; TMPTA: trimethylolpropane triacrylate.

FIGURES

FIGURE 1. Patch tests reactions to sesquiterpene lactone mix (SLM) (+) and isobornyl acrylate 0.1% pet. (IBOA) (++) on day 4 in a 45-year-old female patient (case 22) who reacted to Freestyle libre (FSL) (after 6 months of use). Due to the intensity of the reactions the patient had to discontinue its use and switched to FSL 2 which was well tolerated as seen in the picture.

FIGURE 2. Patient (case 17) with eczematous circular reactions circumscribed to the areas the MiniMed 640G insulin pump had been recently applied (A). Pruritic reaction in the same patient at the glucose sensor Freestyle libre site with spreading beyond the contact area (B).





ONLINE SUPPLEMENTAL TABLE 2. (METH)ACRYLIC ALLERGENS PATCH TESTED BY THE PARTICIPANT CENTERS

Allergens*	Abbreviations	(Dilution/ vehicle)	HUT	HUSC	HUS	HUG	HLP	HA	HDM
2-Hydroxypropyl methacrylate	HPMA	(2% pet)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2-Hydroxyethyl-methacrylate	HEMA	(2% pet)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Tetrahydrofurfurylmethacrylate	THFMA	(2% pet)	Yes	Yes	Yes	Yes	NT	Yes	Yes
2-hydroxy-ethylacrylate	HEA	(0.1% pet)	Yes	NT	Yes	Yes	Yes	Yes	NT
Ethyleneglycol-dimethacrylate	EGDMA	(2% pet)	Yes	Yes	Yes	Yes	Yes	Yes	NT
Ethylacrylate	EA	(0.1% pet)	Yes	NT	Yes	Yes	Yes	Yes	NT
Triethyleneglycol-dimethacrylate	TEGDMA	(2% pet)	Yes	Yes	Yes	Yes	Yes	Yes	NT
Butylacrylate	BA	(0.1% pet)	Yes	NT	Yes	Yes	NT	Yes	NT
Methylmethacrylate	MMA	(2% pet)	Yes	Yes	Yes	Yes	Yes	Yes	NT
Urethanedimethacrylate	UDMA	(2% pet)	Yes	Yes	Yes	Yes	NT	NT	NT
1,4-butanediol-dimethacrylate	1,4-BDMA	(0.1% pet)	yes	Yes	Yes	NT	Yes	NT	NT
1,3-butanediol-dimethacrylate	1,3-BDMA	(2% pet)	NT	NT	NT	Yes	NT	NT	NT
Ethylmethacrylate	EMA	(2% pet)	Yes	NT	Yes	Yes	Yes	Yes	NT

Urethanediacylate (Aliphatic)	UDA(AL)	(0.1% pet)	Yes	NT	Yes	NT	NT	NT	NT
Urethanediacylate (Aromatic)	UDA(AR)	(0.05% pet)	Yes	NT	Yes	NT	NT	NT	NT
Benzoylperoxide	BP	(1% pet)	Yes	NT	NT	NT	NT	NT	NT
Bisphenol-A-dimethacrylate	BIS-MA	(2% pet)	Yes	Yes	Yes	NT	NT	Yes	NT
Ethylcyanoacrylate	ECA	(10% pet)	Yes	Yes	Yes	Yes	NT	Yes	NT
Bisphenol A	-	(1% pet)	Yes	NT	NT	Yes	NT	NT	NT
Hydroquinone	-	(1% pet)	Yes	NT	NT	NT	NT	NT	NT
Bisphenol A glycerolate dimethacrylate	BIS-GMA	(2% pet)	NT	Yes	NT	Yes	NT	NT	NT
Butyl methacrylate	BMA	(2% pet)	NT	Yes	Yes	NT	Yes	NT	NT
Tetraethylene glycol dimethacrylate	TEGDMA	(2% pet)	NT	Yes	Yes	Yes	NT	NT	NT
Dimethylaminoethyl methacrylate	DMAEMA	(0.2% pet)	NT	Yes	Yes	Yes	NT	NT	NT
1,6 hexanediol diacrylate	HDA	(0.1% pet)	NT	Yes	Yes	Yes	Yes	NT	NT
trimethylolpropane triacrylate	TMPTA	(0.1%pet)	NT	NT	Yes	NT	Yes	NT	NT
pentaerythritol triacrylate	PETA	(0.1%pet)	NT	NT	Yes	NT	Yes	NT	NT
2-ethylhexyl acrylate	EHA	(0.1% pet)	NT	NT	Yes	NT	Yes	NT	NT

Hidroxypropyl acrylate	HPA	(0.1% pet)	NT	NT	Yes	NT	Yes	NT	NT
2,2-Bis (4-(2-methacryl-oxyethoxy) phenyl) propane	Bis-EMA	(2.0% pet)	NT	NT	Yes	NT	Yes	NT	NT
Diethylenglycol diacrylate	DEGDA	(0.1% pet)	NT	NT	Yes	NT	Yes	NT	NT
Tripropylenglycol diacrylate	TPGDA	(0.1% pet)	NT	NT	Yes	NT	Yes	NT	NT
Oligoa triacrylate	(OTA 480)	(0.1% pet)	NT	NT	Yes	NT	Yes	NT	NT
Triethylenglycol diacrylate	TEGDA	(0.1% pet)	NT	NT	Yes	NT	Yes	NT	NT
N,N-Methylene-Bisacrylamide	MBAA	(1.0% pet)	NT	NT	Yes	NT	Yes	NT	NT

Abbreviations: HA: Hospital Alcorcón. Madrid; HDM: Hospital del Mar. Barcelona; HLP: Hospital La Paz, Madrid; HUG: Hospital Universitario de Guadalajara; HUS: Hospital Universitario de Santiago de Compostela; HUSC: Hospital Universitario San Cecilio (Granada); HUT: Hospital Universitario de Toledo; NT, not tested.

*Allergens supplied by Chemotechnique Diagnostics (Vellinge, Sweden) in all centers except for HA (Hospital Alcorcón. Madrid) that patch tested allergens supplied by AllergEaze, SmartPractice (Calgary, Canada).