

ORIGINAL ARTICLE

# Patch testing with alkyl glucosides: Concomitant reactions are common but not ubiquitous

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**Background:** Alkyl glucosides constitute a family of mild surfactants that are increasingly being used in a wide range of cosmetics and household products. Contact allergy to alkyl glucosides may be more frequent than previously suspected, especially in atopic patients.

**Objectives:** To investigate the frequency of contact allergy to alkyl glucosides, and to identify concomitant reactivity.

**Method:** We retrospectively reviewed all cases of suspected allergic contact dermatitis (ACD) in which patients were patch tested with either a cosmetic series that includes five alkyl glucosides (decyl glucoside, lauryl glucoside, coco glucoside, cetearyl glucoside, and caprylyl/capryl glucoside) or a specific alkyl glucoside series from November 2013 to April 2017 in two UK centres.

**Results:** A total of 5775 patients were patch tested across the two centres. Twenty-nine (1.04%) of the 2796 patients tested with the cosmetic/alkyl glucoside series had a positive patch test reaction to at least one of the alkyl glucosides. Twenty-three (79.3%) patients were sensitized to multiple alkyl glucosides; 21 patients (72.4%) were female. The mean age was 43.5 years. Twelve patients (41.4%) had a background of atopic dermatitis.

**Conclusions:** The prevalence of alkyl glucoside-induced ACD is relatively high, and there are frequent concomitant reactions between different alkyl glucosides. We recommend the inclusion of alkyl glucosides in all cosmetic series.

**KEYWORDS**

alkyl glucoside, allergic contact dermatitis, caprylyl/capryl glucoside, cetearyl glucoside, coco glucoside, cosmetic, decyl glucoside, lauryl glucoside, patch test

## 1 | INTRODUCTION

Alkyl glucosides constitute a family of mild, non-ionic surfactants synthesized through the condensation of glucose with long-chain fatty alcohols. The fatty alcohols are primarily derived from palm, coconut and rapeseed oil, and the glucose is obtained from corn, potato or wheat starch.<sup>1</sup> Alkyl glucosides are therefore completely biodegradable. Alkyl glucosides were first introduced in the 1930s, but were superseded by synthetic products.<sup>1</sup> However, they have regained favour in recent years because of their eco-friendly properties.<sup>2</sup>

Alkyl glucosides have cleansing, foaming and emulsifying properties. Since the 1990s, they have been used in both rinse-off products, for example, shower gels, shampoos, soaps, cleansers, and hair dyes, and leave-on cosmetics, for example, sunscreens, fragrances, tanning

products, emollients, and deodorants.<sup>2</sup> They can also be found in certain baby products such as wipes and cleansers.<sup>1</sup> Alkyl glucosides are considered to have lower irritancy and allergenicity than harsher surfactants such as sodium lauryl sulfate and sodium laureth sulfate.<sup>3</sup> They are chemically stable and hardly protein-reactive; they do not contain chemically reactive sites or strongly polarized structures. Therefore, they were not predicted to have allergenic potential. In 2013, the Cosmetic Ingredient Review Expert Panel, which reviews and assesses the safety of ingredients used in cosmetics in the United States, concluded that the 19 alkyl glucosides were safe for use in cosmetics when formulated at low concentrations to be non-irritating.<sup>4</sup>

Allergic contact dermatitis (ACD) caused by alkyl glucosides is uncommon. Since the first cases of ACD were described in 2003,<sup>5-7</sup>

there has been a slow but steady increase in the frequency of sensitization. The North American Contact Dermatitis Group, for instance, which has been routinely patch testing patients with decyl glucoside since 2009, noted an increase in positive reactions from 1.5% in 2009 to 2012 to 1.7% in 2013 to 2014.<sup>8</sup> Routine patch testing with multiple alkyl glucosides has not been yet widely adopted. Therefore, the above figures are likely to represent an underestimate of the prevalence of contact allergy to this group of chemicals. Decyl glucoside is the most common alkyl glucoside causing ACD. Simultaneous reactions with other alkyl glucosides are common; thus, patch testing with multiple compounds is recommended.<sup>2</sup>

## 2 | PATIENTS AND METHODS

We included all patients with suspected ACD who were patch tested at the Contact Dermatitis Investigation Units, Leeds Teaching Hospitals NHS Trust and Hillingdon Hospitals NHS Foundation Trust, from November 2013 to April 2017. Patch tests were performed with IQ Ultra Chambers (Chemotechnique Diagnostics, Vellinge, Sweden). The tests were occluded for 48 hours, and readings were performed on day (D) 2 and D4. The cosmetic series of both centres includes: decyl glucoside 10% aq., lauryl glucoside 10% aq., coco glucoside 10% aq., cetearyl glucoside 10% pet., and caprylyl/capryl glucoside 10% aq. The aqueous preparations were all diluted to 10% of the active surfactant, and were buffered to a neutral pH from the alkaline pH of the commercially supplied solutions (BCM Specials, Nottingham, UK). The level of activity of each alkyl glucoside in the raw materials is shown in Table 1. The Leeds patients were additionally tested with decyl glucoside 5% pet. (AllergEAZE, Bio-Diagnostics, Upton upon Severn, UK) and lauryl glucoside 3% pet. (Chemotechnique Diagnostics). All patients' details and patch test results were prospectively recorded in a departmental patch test database.

## 3 | RESULTS

In Leeds Teaching Hospitals, 3070 patients were patch tested between November 2013 and April 2017, with 1929 (62.8%) being tested with a cosmetic series. In the same period, 2705 patients were patch tested in Hillingdon Hospitals, with 867 (32.1%) being tested with an alkyl glucoside series. The MOAHLFA (male, occupational, atopic dermatitis, hand, face, leg dermatitis, age > 40 years) indices of both centres are shown in Table 2.

Twenty-nine patients (1.04% of those tested with a cosmetic series) had a positive patch test reaction to at least one of the alkyl

**TABLE 2** MOAHLFA indices (%) of Leeds Teaching Hospitals and Hillingdon Hospitals

|                       | Leeds Teaching Hospitals |                 | Hillingdon Hospitals |                        |
|-----------------------|--------------------------|-----------------|----------------------|------------------------|
|                       | Baseline series          | Cosmetic series | Baseline series      | Alkyl glucoside series |
| M (male)              | 30.5                     | 25.4            | 29.2                 | 22.7                   |
| O (occupational)      | 10.2                     | 9.2             | 1.3                  | 1.0                    |
| A (atopic dermatitis) | 41.8                     | 44.8            | 28.9                 | 35.1                   |
| H (hand)              | 30.0                     | 25.1            | 24.3                 | 25.7                   |
| L (leg)               | 5.1                      | 3.4             | 9.7                  | 6.6                    |
| F (face)              | 35.4                     | 49.0            | 33.7                 | 54.3                   |
| A (age > 40 years)    | 49.7                     | 48.1            | 54.5                 | 49.0                   |

glucosides (Tables 3 and 4). The most common positive reactions were to lauryl glucoside 3% aq. (20/29) and to decyl glucoside 5% pet. (18/29). Six patients (20.7%) had a positive reaction to only one alkyl glucoside. There were no clear-cut irritant reactions.

**TABLE 3** Patient sex, age, occupation, affected site and association with atopic eczema

| Patient | Sex | Age (years) | Occupation      | Site             | Atopic eczema |
|---------|-----|-------------|-----------------|------------------|---------------|
| 1       | M   | 48          | Cleaner         | Hand             | Yes           |
| 2       | F   | 22          | Office          | Face             | Yes           |
| 3       | M   | 56          | Unemployed      | Face             | No            |
| 4       | M   | 70          | Retired         | Hand             | No            |
| 5       | F   | 42          | Bakery          | Trunk            | No            |
| 6       | F   | 37          | Food and drink  | Face             | Yes           |
| 7       | F   | 15          | Student         | Flexures         | Yes           |
| 8       | F   | 22          | Midwife         | Perineal         | Yes           |
| 9       | F   | 20          | Childminder     | Face             | No            |
| 10      | F   | 51          | Research        | Head             | Yes           |
| 11      | F   | 29          | Nurse           | Hand             | No            |
| 12      | F   | 30          | Teaching        | Face             | No            |
| 13      | F   | 68          | Housewife       | Neck             | Yes           |
| 14      | F   | 67          | Retired         | Head             | Yes           |
| 15      | F   | 22          | Student         | Hand             | No            |
| 16      | F   | 33          | Clerk           | Face             | Yes           |
| 17      | F   | 60          | Housewife       | Neck             | Yes           |
| 18      | F   | 46          | Nurse           | Hand             | No            |
| 19      | M   | 75          | Retired         | Neck             | No            |
| 20      | F   | 33          | Hairdresser     | Face             | No            |
| 21      | F   | 32          | Hairdresser     | Hand             | No            |
| 22      | F   | 29          | Accountant      | Hand             | Yes           |
| 23      | F   | 82          | Retired         | Face             | No            |
| 24      | M   | 27          | Office          | Not recorded     | No            |
| 25      | M   | 74          | Retired         | Hand and foot    | No            |
| 26      | F   | 42          | Beauty          | Hand and forearm | Yes           |
| 27      | F   | 65          | Psychotherapist | Generalized      | No            |
| 28      | M   | 30          | Computers       | Hand             | No            |
| 29      | M   | 34          | Civil engineer  | Hand             | No            |

Abbreviations: F, female; M, male.

**TABLE 1** Level of activity of alkyl glucosides in raw materials

| Alkyl glucoside           | % Active in raw material                                |
|---------------------------|---------------------------------------------------------|
| Decyl glucoside           | 50% active (50% water)                                  |
| Lauryl glucoside          | 50% active (50% water)                                  |
| Coco glucoside            | 50% active (50% water)                                  |
| Cetearyl glucoside        | 100% active; not diluted in water (~0.8% water content) |
| Caprylyl/capryl glucoside | 60% active (40% water)                                  |

**TABLE 4** Patch test reactions to various alkyl glucosides

| Patient | Decyl 5% pet. |    |    | Decyl 10% aq. |    |    | Lauryl 3% pet. |    |    | Lauryl 10% aq. |     |    | Coco 10% aq. |    |    | Cetearyl 10% pet. |    |    | Caprylyl/capryl 10% aq. |    |    |
|---------|---------------|----|----|---------------|----|----|----------------|----|----|----------------|-----|----|--------------|----|----|-------------------|----|----|-------------------------|----|----|
|         | D2            | D4 | R  | D2            | D4 | R  | D2             | D4 | R  | D2             | D4  | R  | D2           | D4 | R  | D2                | D4 | R  | D2                      | D4 | R  |
| 1       | ++            | ++ | CR | —             | —  | —  | —              | —  | —  | —              | —   | —  | —            | —  | —  | —                 | —  | —  | —                       | —  | —  |
| 2       | ?+            | ?+ | CR | ?+            | ?+ | CR | ?+             | ?+ | CR | ?+             | ?+  | CR | ?+           | ?+ | CR | —                 | ?+ | CR | —                       | ?+ | CR |
| 3       | —             | —  | —  | —             | —  | —  | +              | +  | PR | —              | —   | —  | —            | —  | —  | —                 | —  | —  | —                       | —  | —  |
| 4       | +             | +  | CR | ?+            | —  | CR | +              | +  | CR | +              | +   | CR | ?+           | —  | CR | ?+                | —  | CR | —                       | —  | —  |
| 5       | ?+            | +  | CR | —             | —  | —  | ?+             | +  | CR | —              | —   | —  | —            | —  | CR | —                 | —  | —  | —                       | —  | —  |
| 6       | +             | +  | CR | —             | —  | —  | +              | +  | CR | —              | —   | —  | —            | —  | —  | —                 | —  | —  | —                       | —  | —  |
| 7       | +             | +  | CR | ?+            | ?+ | CR | +              | +  | CR | +              | ++  | CR | ?+           | ?+ | CR | —                 | —  | —  | ?+                      | ?+ | CR |
| 8       | —             | ?+ | CR | —             | ?+ | CR | —              | ?+ | CR | —              | ?+  | CR | —            | —  | —  | —                 | ?+ | CR | —                       | —  | —  |
| 9       | —             | ?+ | CR | —             | —  | —  | —              | ?+ | CR | —              | +   | CR | —            | +  | —  | —                 | +  | CR | —                       | +  | CR |
| 10      | +             | +  | CR | —             | —  | —  | —              | —  | —  | —              | —   | —  | —            | —  | —  | —                 | —  | —  | —                       | —  | —  |
| 11      | +             | +  | CR | —             | —  | —  | —              | —  | —  | —              | —   | —  | —            | —  | —  | —                 | —  | —  | —                       | —  | —  |
| 12      | —             | +  | CR | —             | ?+ | CR | —              | +  | CR | —              | ?+  | CR | —            | +  | CR | —                 | +  | CR | —                       | +  | CR |
| 13      | +             | +  | CR | —             | —  | —  | +              | +  | CR | —              | —   | —  | +            | +  | CR | —                 | —  | —  | —                       | ?+ | CR |
| 14      | ++            | ++ | CR | —             | —  | —  | +              | ++ | CR | ++             | ++  | CR | —            | —  | —  | —                 | —  | —  | —                       | —  | —  |
| 15      | ++            | ++ | CR | —             | —  | —  | ++             | ++ | CR | —              | +   | CR | —            | —  | —  | —                 | —  | —  | —                       | —  | —  |
| 16      | —             | ++ | CR | —             | +  | CR | —              | ++ | CR | —              | +   | CR | —            | —  | —  | —                 | —  | —  | —                       | —  | —  |
| 17      | +             | +  | CR | —             | —  | —  | +              | +  | CR | ?+             | +   | CR | —            | —  | —  | —                 | —  | —  | —                       | —  | —  |
| 18      | —             | +  | CR | —             | —  | —  | —              | +  | CR | —              | —   | —  | —            | —  | —  | —                 | —  | —  | —                       | —  | —  |
| 19      | +             | +  | CR | —             | +  | CR | +              | +  | CR | +              | +   | CR | +            | +  | CR | —                 | —  | —  | +                       | +  | CR |
| 20      | —             | —  | —  | +             | NR | CR | —              | —  | —  | —              | —   | —  | —            | —  | —  | +                 | NR | CR | —                       | —  | —  |
| 21      | —             | —  | —  | +             | +  | CR | —              | —  | —  | +              | +   | CR | +            | +  | CR | +                 | +  | CR | +                       | +  | CR |
| 22      | —             | —  | —  | —             | —  | —  | —              | —  | —  | —              | +++ | CR | —            | ++ | CR | —                 | +  | CR | —                       | —  | —  |
| 23      | —             | —  | —  | —             | ?+ | CR | —              | —  | —  | —              | ?+  | CR | —            | ?+ | CR | —                 | —  | —  | —                       | ?+ | CR |
| 24      | —             | —  | —  | +             | —  | CR | —              | —  | —  | +              | +   | CR | +            | —  | CR | —                 | —  | —  | —                       | —  | —  |
| 25      | —             | —  | —  | ?+            | +  | ?R | —              | —  | —  | ?+             | +   | ?R | ?+           | +  | ?R | —                 | —  | —  | ?+                      | +  | ?R |
| 26      | —             | —  | —  | —             | —  | —  | —              | —  | —  | —              | +   | CR | —            | —  | —  | —                 | —  | —  | —                       | —  | —  |
| 27      | —             | —  | —  | —             | —  | —  | —              | —  | —  | —              | +   | CR | —            | —  | —  | —                 | —  | —  | —                       | —  | —  |
| 28      | —             | —  | —  | ++            | +  | CR | —              | —  | —  | ++             | +   | CR | ++           | +  | CR | ++                | ++ | CR | ++                      | +  | CR |
| 29      | —             | —  | —  | ?+            | +  | ?R | —              | —  | —  | ?+             | +   | ?R | ?+           | +  | ?R | —                 | —  | —  | —                       | —  | —  |

Abbreviations: CR, current relevance; D, day; NR, not recorded; PR, past relevance; R, relevance; ?R, possible relevance.

Twenty-one patients (72.4%) were female. The mean age was 43.5 years. The head and neck were the most commonly affected sites (44.8%). Twelve patients (41.4%) had a history of atopic dermatitis. Occupations associated with the 11 cases of hand eczema in our study included nursing, cleaning, hairdressing, and beauty therapy.

## 4 | DISCUSSION

Since the 1990s, alkyl glucosides have been increasingly used in cosmetics and household products. Although most alkyl glucosides in cosmetics have surfactant properties, a few have been reported to work as skin-conditioning agents, hair-conditioning agents, or emulsion stabilizers. As of 2011, decyl glucoside was an ingredient in 492 cosmetic formulations. The most frequently used alkyl glucosides in leave-on and rinse-off formulations are cetearyl glucoside and decyl glucoside, respectively.<sup>4</sup>

Alkyl glucosides were not expected to be allergenic at the low concentrations used in personal care products. In vivo methods have been used to estimate the allergenic potencies of glucosides with

varying alkyl chain lengths. In a guinea-pig maximization test, alkyl glucosides were neither irritating nor sensitizing. On the other hand, a murine local lymph node assay indicated that one C12-C18 glucoside, C14 glucoside and C18 branched glucoside were potential sensitizers. However, in repeated insult patch tests on human volunteers, no skin reactions suggestive of sensitization were detected.<sup>9</sup>

Since 2003, more than 20 patients with ACD caused by alkyl glucosides have been described in case reports and case series. Furthermore, in a retrospective study that reviewed 19 years of data in a Belgian centre, 30 patients had positive patch test reactions to one or more alkyl glucosides.<sup>10</sup> Seventy-four per cent of the patients affected in the published reports were female, possibly because of their higher use of cosmetics.<sup>2</sup> This figure is similar to ours (72.4%). The distribution of the rash associated with ACD secondary to alkyl glucosides depends on the area(s) targeted by the offending product. With sunscreens and shampoos, the face, scalp and neck are most commonly affected. In contrast, the hands are mainly involved in patients with occupational exposures.<sup>2</sup>

ACD induced by alkyl glucosides is known to be more common in patients with a history of atopy.<sup>3</sup> This is in keeping with the

proportion of patients who had pre-existing atopic eczema in our study (41.4%). It has been suggested that atopic dermatitis and occupation-related irritation increase the risk of contact allergy to alkyl glucosides by disrupting the epidermal barrier, thereby allowing greater penetration of the allergen. In addition, patients with atopic eczema are probably more likely to purchase products marketed as hypoallergenic or suitable for sensitive skin, many of which contain alkyl glucosides.<sup>1</sup> A survey of the 20 best-selling sunscreens and facial moisturizers on Amazon, the largest online retailer in the world, showed that 15% contained alkyl glucosides in their list of ingredients.<sup>3</sup> There have been multiple reports of ACD caused by decyl glucoside in the sunscreen ingredient Tinosorb M.<sup>11–14</sup> Although decyl glucoside is present in the final preparation, its name does not appear on the ingredient labels of some sunscreens. Therefore, it is considered to be the “hidden allergen” within Tinosorb M.<sup>15</sup> In recent years, alkyl glucosides have been identified as culprit allergens in wound dressings, prompting authors to recommend their inclusion in leg ulcer series.<sup>16–18</sup>

Positive patch test reactions to multiple structurally related alkyl glucosides are common, but not systematic.<sup>15</sup> In a retrospective analysis of suspected cases of cosmetic-related ACD, 65% of the alkyl glucoside-allergic patients showed co-reactions to decyl glucoside and lauryl glucoside.<sup>19</sup> Twenty-three of the 29 patients (79.3%) in our study had positive reactions to more than one alkyl glucoside. Simultaneous reactions, such as those found in our study, may be attributable to structural similarities at the molecular level. The industrial manufacturing process results in blends of different alkyl glucosides; positive patch test reactions to different alkyl glucosides may therefore represent concomitant reactions.<sup>15</sup> A recent study, which aimed to identify possible allergenic impurities in commercial samples of alkyl glucosides, found that isobornyl acrylate (IBOA) may represent a hidden allergen in the form of an impurity generated during the industrial process. IBOA is used as a plasticizer in various plastic materials, and could be leached out of the container because of the extraction power of alkyl glucosides.<sup>20</sup> In the last few years, a number of cases of ACD caused by IBOA in diabetic patients using insulin pumps and glucose sensors have been described.<sup>21–23</sup> However, in a recent report of ACD caused by alkyl glucosides in a foam dressing, IBOA was not detected on chemical analysis, either in the foam dressing or in the patch test materials of decyl glucoside and lauryl glucoside.<sup>17</sup> This would suggest that it is unlikely to be responsible for the positive reactions to alkyl glucoside patch test materials. We have previously described a case of contact allergy to octyldodecyl xyloside, a constituent of cosmetic serum. This allergen is structurally closely related to alkyl glucosides.<sup>24</sup>

On the basis of our findings, we recommend patch testing with other alkyl glucosides besides lauryl and decyl glucoside, for example, coco glucoside, cetearyl glucoside, and caprylyl/capryl glucoside. There are only a few case reports of contact allergy to these additional alkyl glucosides, probably because they are neither commercially available nor tested routinely.<sup>11</sup> Additionally, a case of contact allergy to arachidyl glucoside in a facial cream has recently been described, with associated positive patch test reactions to four other alkyl glucosides.<sup>25</sup> Eight of the patients in our series reacted to a lower concentration of decyl glucoside (5%) or lauryl glucoside (3%) when

pet. was used as the vehicle, but not to the corresponding 10% aqueous solutions, suggesting that the pet. preparations may be more sensitive. Decyl glucoside 5% pet. and lauryl glucoside 3% pet. have both been recognized as common cosmetic haptens in North America, and the former is already included in the American Contact Dermatitis Society Core Allergen Series.<sup>26</sup> Furthermore, the addition of both compounds as an extension to the European baseline series has been recommended in a recent publication.<sup>27</sup> It has been suggested that failure to correct the pH of pet. samples by suppliers of commercial allergens could render them irritant.<sup>28</sup>

In conclusion, alkyl glucosides represent an emerging group of allergens that dermatologists should be aware of. It is becoming apparent that their skin-sensitizing potential may have been underestimated. We suggest that they should be included in all cosmetic series. As there is a high rate of simultaneous reactions, it is prudent for sensitized patients to avoid all the alkyl glucosides. However, because concomitant reactions do not systematically occur, we recommend testing multiple compounds.

## CONFLICTS OF INTEREST

The authors have no conflicts of interest to report.

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