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Capryloyl glycine: a polyfunctional cosmetic ingredient and potential skin sensitizer.

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Running head: Contact allergy to capryloyl glycine.

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Amino acid alkyl amides (AAAA) are polyfunctional cosmetic ingredients, some also with preservative properties. Here we report a case of allergic contact dermatitis caused by a body lotion containing an AAAA, namely, capryloyl glycine (CG) (*syn*: caprylyl glycine, N-octanoylglycine; CAS no. 14246-53-8)(**Figure 1**).

Case report

A 50-year-old atopic man, known with hand dermatitis and recently diagnosed contact allergy to methylisothiazolinone (MI), methylchloroisothiazolinone/MI, fragrances (*Myroxylon perezii*, fragrance mix II) and ricinus oil, developed an itchy, papular skin eruption on his arms and legs after the application of a body lotion (**Figure 2A+B**). He had also suffered from a similar skin eruption after the use of two sunscreens. However, none of these products contained any of his known contact allergens and so he was referred to us for additional patch tests. These were performed with the three suspected products, tested “as is”, along with the separate ingredients of the body lotion, kindly provided by the manufacturer (L’Oréal, Clichy, France), a photopatch series (Chemotechnique Diagnostics, Vellinge, Sweden), and ingredients of the sunscreens that were commercially available as patch test preparations. Allergize patch test chambers (SmartPractice, Calgary, Canada) were used, and, following an occlusion of 2 days with Fixomull stretch (BSN Medical, Hamburg, Germany), all tests

were read, according to published guidelines, on day (D) 2, D4 and D7 [1]. The photopatch tests were occluded for two days, and, upon removal, one of two identical series was irradiated with 5 J/cm² UVA; readings were performed on D2, D4 and D7 following application of these tests. Positive patch test reactions were observed to the body lotion (++) and to its ingredient CG 1% 50% aq./50% alc. (+) (**Figure 3**). A repeated patch test with this allergen confirmed the positive reaction, with the same degree of reactivity (+). An additional patch test to CG 1% aq., retrieved from a different cosmetic company, gave only a doubtful reaction (?+). Twenty control patients tested completely negative to both CG 1% aq. and CG 1% 50% aq./50% alc. Our patient also had positive reactions to patch tests with the two sunscreens (+), to a lesser extent (?+) when these were irradiated with UVA, and to the chemical filter benzophenone-10 (+), which, according to the packagings, was not present in these products. As both sunscreens contained caprylic/capric triglyceride, i.e. glycerol esterified with 1 part capric acid and 2 parts caprylic acid, the latter being an acid also used in the manufacture of CG, additional tests were performed with caprylic/capric triglyceride (10% pet.; obtained from Pierre Fabre, Paris, France) however, this did not yield a positive reaction; the culprit ingredient(s) of the 2 sunscreens could thus not be identified. However, contact allergy to the body lotion, and its ingredient CG, was effectively detected and, out of interest, we additionally patch tested a “medical device” cream for psoriasis and a cream to treat scars, also containing CG, both resulting in positive reactions, ?+ and +, respectively, on D4. We thus advised the patient, in addition to his already known contact allergens and benzophenones to also avoid products containing CG. In our departmental database we retrieved five other patients who had developed dermatitis following the use of the same body

lotion. All these patients had reacted to the bodylotion “as is” (+ to ++), and some of them had also previously been tested with the separate ingredients, yielding, however, no positive reactions to CG 1% 50% aq./50% alc.

Discussion

We describe, to our knowledge, a first case of contact allergy caused by CG, a polyfunctional ingredient in cosmetic leave-on and rinse-off products, and household detergents. It is a N-acyl alpha amino acid, comprised of glycine acylated with caprylic acid chloride in aqueous medium [2, 3]. In cosmetics, besides being a skin and hair conditioning agent, it is also a surfactant and has antimicrobial properties. Despite the fact that CG inhibits the proliferation of *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Propionibacterium acnes* and *Pityrosporum ovale* and is thus included in products marketed for the treatment of acne-prone skin and dandruff, it is not considered a full-fledged preservative. However, this glycine derivative is often used together with other preservative agents to obtain a synergistic preservative effect [3, 5]. With regard to the test results obtained with CG 1% aq. (?+), as opposed to CG 1% in 50% aq./50% alc. (+) in our patient, we hypothesize that the vehicle might have influenced the test results: CG has a pKa around 4.0 and in the CG 1% aq. solution, with a pH of 7.0, most of the molecule is then negatively charged, hence negatively influencing skin penetration and possibly resulting in a weaker, or potentially even false-negative patch test [2, 3, 6]; we could not find out whether this solution had been neutralised to obtain a pH of 7. However, CG 1% in 50% aq./50% alc., as received by the manufacturer of the body lotion, has a low pH of 3.3, indicating that a smaller amount of negatively charged CG is present, hence ensuring better skin penetration and thus potentially provoking a

(possibly stronger) positive patch test reaction. Moreover, bearing in mind that CG is used in cosmetics up to a maximum concentration of approximately 2%, higher test concentrations than 1% might be necessary [3, 4]. Altogether, when performing patch tests in general, and with CG in particular, it is useful to question which particular vehicle and concentration might be the most appropriate one to use. Although we were unable to obtain the raw material of CG, it might be worthwhile, in the work-up of future cases, to patch test CG in petrolatum, a lipophilic vehicle, and then preferably at 2%, as it would correlate with an almost 100% uncharged CG, making skin penetration and possible detection of contact allergy to CG more reliable. Moreover, taking into account its surfactant properties, petrolatum-based vehicles might also be less irritating, although none of our control patients showed any irritant patch test reactions to the aqueous or aqueous/alcohol preparations. Our patient presented with a clinically very pronounced allergic contact dermatitis, reflecting a potentially strong sensitization, which probably led him to react even to potentially less adequate patch tests containing CG, at only 1%, and in a pure aqueous solution. In retrospect, we can not exclude that the negative patch-test reactions to CG 1% 50% aq./50% alc. in some of the other patients who had previously experienced a skin reaction from the same bodylotion, were false-negative reactions, possibly related to the abovementioned factors concentration and vehicle. We have no clue what ingredient was potentially the culprit sensitizer in the two sunscreens our patient could not tolerate. Although we suspected a potential link with the caprylic/capric triglyceride contained in these, a substance that, like CG, is manufactured with the use of caprylic acid, patch tests with caprylic/capric triglyceride 10% pet. remained negative, making a possible relationship between CG and caprylic/capric triglyceride unlikely.

References

1. Johansen J D, 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: 195–221.
2. KOSHTI, Nirmal, et al. Microemulsions of lipidated glycines and phenoxy ethanol for preservation of personal care products. U.S. Patent Application No 10/015,963, 2018.
3. BURNETT, Christina L., et al. Safety Assessment of Amino Acid Alkyl Amides as Used in Cosmetics. *International journal of toxicology*, 2017, 36.1_suppl: 17S-56S.
4. DUPRAT-DE-PAULE, Sébastien, et al. Augmented bio-based lipids for cosmetics. *OCL*, 2018.
5. PEREDA, Maria Del Carmen Velazquez, et al. Xylitol esters and ethers applied as alternative emulsifiers, solvents, co-emulsifiers and preservative systems for pharmaceutical and cosmetic products. U.S. Patent No 8,716,506, 2014.
6. DAYAN, Nava. Pathways for skin penetration. *Cosmetics and toiletries*, 2005, 120.6: 67-76.

Figure legends

Figure 1. Capryloyl glycine.

Figure 2A+B. Acute, papular rash on the arms following the use of a capryloyl glycine (CG)-containing body lotion.

Figure 3. Positive patch-test reaction (+) to capryloyl glycine 1% in 50% aq./50% alc. on day 4 (D4).

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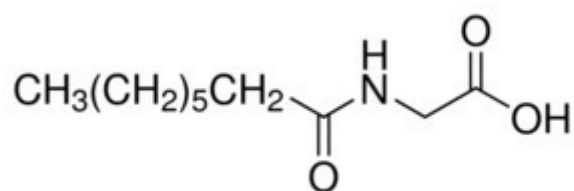


Fig1.jpg



Fig2A.jpg



Fig2B.jpg

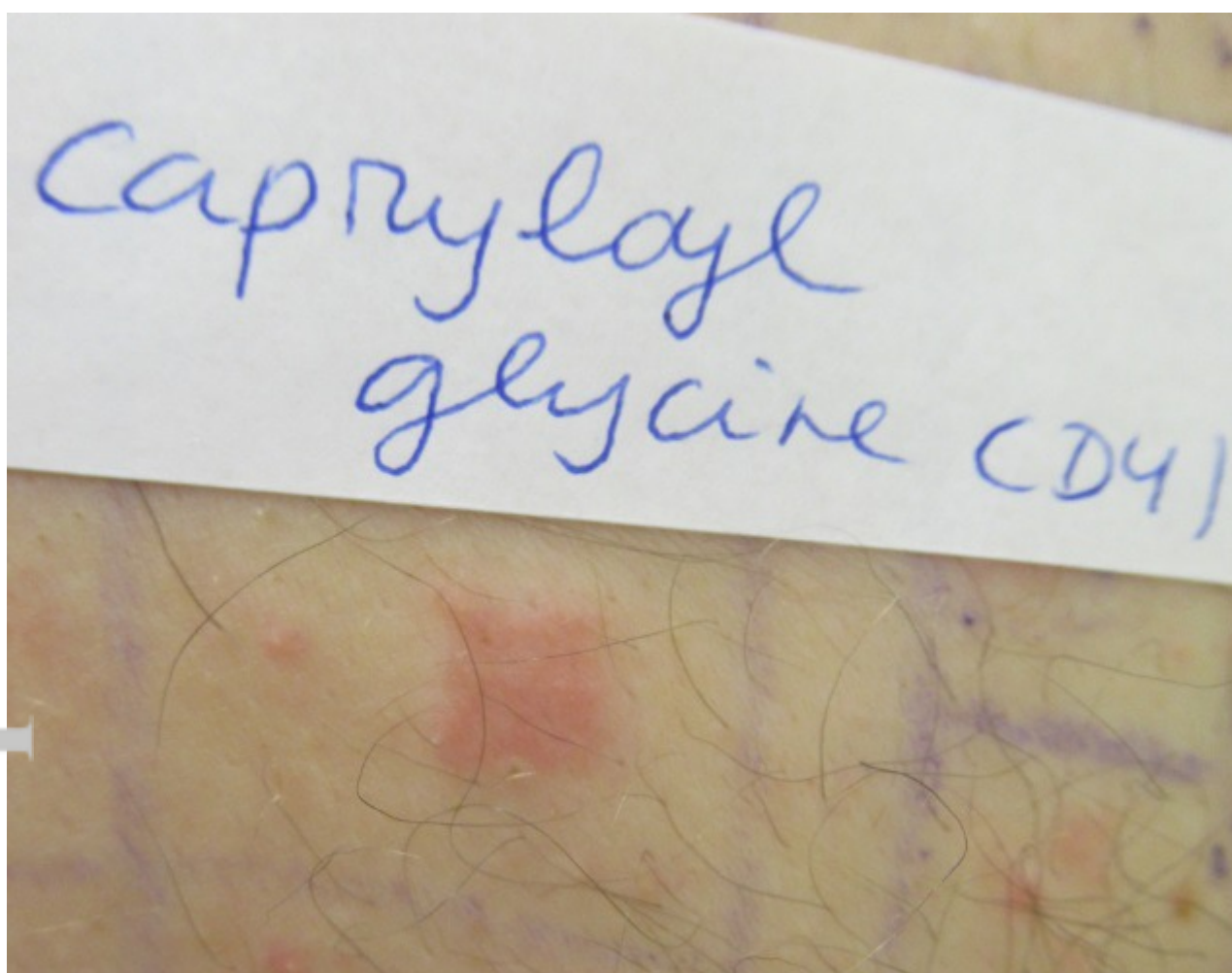


Fig3.jpg