

Allergic contact dermatitis from carbomers: two case report

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Carbomer is the trade name for polyacrylic acid (PAA), a group of synthetic high-molecular-weight polymers of acrylic acid. They are widely used as a thickening, emulsifying, emulsion-stabilizing, dispersing, and suspending agent in topical pharmaceutical products, cosmetics, personal care products, nutrients, and detergents. The safety of carbomers has been assessed by the Cosmetic Ingredient Review (CIR) Expert Panel¹ who concluded that "acute oral and dermal clinical studies with carbomer polymers have demonstrated that these ingredients have a low potential for phototoxicity, photo-contact sensitization, skin irritation, and sensitization at concentrations up to 100%". Hence, it was decided that carbomer polymers were safe to be used as ingredients in cosmetics and personal care products. Herein, we report two cases of allergic contact dermatitis (ACD) caused by carbomers.

CASE REPORTS

Case 1: A 64-year-old woman presented with facial dermatitis of 4-month duration, consisting of pruritic, erythematous and scaly plaques on both cheeks and on the chin (Figure 1). Six months earlier she had started daily application of brimonidine topical gel, 0.33% (Mirvaso, Galderma, France) for the treatment of erythema on the cheeks. She also regularly used a "rejuvenating" night cream, although her dermatitis was exactly localized at the application site of Mirvaso gel.

The patient was patch tested with the European baseline and a cosmetic series, as well as her own products, including Mirvaso gel. All tests were performed using IQ Ultra patch-test chambers (Chemotechnique Diagnostics, Vellinge, Sweden), covered with Fixomull stretch (BSN, Hamburg, Germany), and read at day (D) 2 and D4, according to the ESCD guidelines. This resulted in a positive reaction (+ D2, ++ D4) only to the Mirvaso gel.

The patient was then tested with the ingredients, namely, brimonidine tartrate 0.5% aq., carbomer homopolymers 10% aq. (Carbomer 934P NF Polymer; CAS no. 9003-01-04, and Carbopol 974P NF Polymer; CAS no. 151687-96-6; Lubrizol, Oevel, Belgium), glycerol 1% aq., methyl paraben 3% pet., phenoxyethanol 1% pet., propylene glycol 5% aq., and titanium dioxide 1% pet, prepared in appropriate concentrations by Galderma (Galderma Benelux, Breda, The Netherlands).

This resulted in a ++ positive reaction at D2 and D4 to Carbopol 974P. Further testing with acrylic acid 0.1% pet. and 0.1% aq., as well as with a limited series of acrylates remained negative.

Case 2: A 59-year-old man who had worked as an ophthalmologist for 30 years, presented with chronic eczema on his hands and forearms that had lasted for several months. He used vinyl gloves while working and was in contact with a hydro-alcoholic gel (Phago'rub SPS, Christeyns, Vertou, France), chlorhexidine wipes, as well as various topical anaesthetics (oxybuprocaine, tetracaine hydrochloride), and antibiotics (tobramycin, azithromycin) on a daily basis.

A self-performed repeated open application test (ROAT) was carried out by the patient, twice daily, on the volar aspect of his forearm, with the suspected hydro-alcoholic Phago'rub SPS gel. Readings showed a positive reaction in terms of erythema and vesicles at D2. Patch tests were then performed with the European baseline series, with a series of photo-allergens (Chemotechnique Diagnostics) supplemented with additional series, including preservatives and excipients, as well as the products used "as is". Patch tests were positive (++) at D2 and D3 to cobalt chloride, budesonide 0.01%, and tetracaine hydrochloride 1% and 5%. A patch test with the neutralized carbomer provided by the manufacturer was also positive (+) (Figure 2).

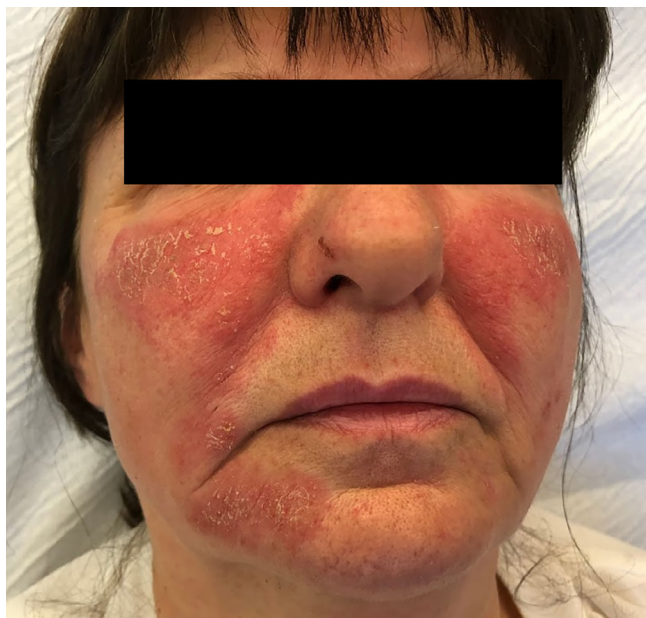


FIGURE 1 Case 1: A 53-year-old woman with facial eczema after daily application of brimonidine topical gel, 0.33%



FIGURE 2 Case 2: Positive patch test to the neutralized carbomer included in the hydro-alcoholic Phago'rub SPS gel

In order to determine which component of the hydro-alcoholic gel the patient was sensitized to, its ingredients, Carbopol Ultrez 20 Polymer 0.25% aq. (Lubrizol, Oevel, Belgium, CAS no. 96827-24-6) and 2-Amino-2-methyl-1-propanol 0.1% aq. (Merck, Darmstadt, Germany, CAS no. 124-68-5), kindly prepared at appropriate concentrations by the manufacturer, were additionally patch tested. All tests remained negative, except the patch test with Carbopol Ultrez 20 Polymer, showing a positive (+) reaction.

DISCUSSION

Carbomers are synthetic, high-molecular-weight polyacrylic acids, cross-linked with allyl sucrose or allyl pentaerythritol, which contain between 56% and 68% w/w carboxylic acid groups. Depending upon the degree of cross-linking and manufacturing conditions, various grades of carbomers are available, each grade having its own significance and applicability in pharmaceutical dosage forms. Carbopol 934 is cross-linked with allyl sucrose and polymerized in benzene, while Carbopol 71, 971, and 974 are cross-linked with allyl pentaerythritol and polymerized in ethyl acetate.² Carbomers are large molecules with good biocompatibility that are known to be well tolerated and to cause no skin irritation.³

Among residual chemicals present in polyacrylic acids, acrylic acid, being the molecule from which their production starts, is a potential allergen. Although it was reported as an unlikely allergen by Bruze et al,⁴ it has been responsible for some cases of ACD due to its presence in ECG electrodes and in transcutaneous electrical nerve stimulation apparatus.^{5,6} Moreover, more recently, Hansel et al⁷ advised it should be tested in cases of contact allergy to other acrylates. Altogether, these data suggest the possibility of cross-reactivity between acrylic acid and carbomers. However, this was not confirmed in our first case, where acrylic acid had been tested.

The low sensitization potential of carbomers may be explained by their high molecular weights that limit skin penetration and, thus, prevent contact with the skin-associated immune system, which might explain why ACD seems to be rare, and to our knowledge, not previously reported. ACD from brimonidine gel has been previously reported, but except for one case with a positive test to brimonidine tartrate (diluted in pet. 1%, 5% and 10%), no other ingredients were tested, hence, carbomers could not be excluded as potential culprits.⁸ In conclusion, although ACD from carbomers is rare, it should be highlighted because of possible cross-reactions with other metacrylates.

CONFLICTS OF INTEREST

The authors declare no conflict of interests.

AUTHOR CONTRIBUTIONS

Florence Castelain: Conceptualization; data curation; investigation; methodology; resources; supervision; validation; visualization; writing-review and editing. **Kerre Stefan:** Data curation; formal analysis; methodology; resources; supervision; validation; writing-original draft; writing-review and editing. **Clémentine Carlet:** Conceptualization; data curation; formal analysis; investigation; methodology; writing-review and editing. **An Goossens:** Supervision; validation; visualization; writing-original draft; writing-review and editing. **Pascal Girardin:** Conceptualization; data curation; resources; validation; writing-review and editing. **Fabien Pelletier:** Conceptualization; formal analysis; methodology; validation; writing-review and editing. **Francois Aubin:** Formal analysis; investigation; visualization; writing-original draft; writing-review and editing.

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