

Allergic contact dermatitis from pyoctanin

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Although pyoctanin is widely used in medicine, there are hardly any reports of contact allergy to it. Most reports of side-effects refer to irritant reactions after topical application. We describe 2 patients who developed pyoctanin contact dermatitis after long-term application on damaged skin. Positive patch test results down to concentrations of 0.0025% and 0.05% aqueous pyoctanin solution, respectively, were found.

Key words: allergic contact dermatitis; crystal violet; gentian violet; methylrosanilinium chloride; methyl violet; pyoctanin; medicaments; patch testing technique. © Munksgaard, 1997.

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Pyoctanin is methylrosanilinium chloride, a mixture of pentamethylpararosanolinium chloride and hexamethylpararosanolinium chloride (Fig. 1). The names crystal violet, methyl violet and gentian vi-

olet are used as synonyms. Rosalines are triphenylmethanes with 3 amino groups. Other triphenylmethane dyes are brilliant green, malachite green, methyl green and magenta II. Triphenylmethane dyes have been used in medicine as external antiseptics since Stilling described aniline dyes as antiseptics, and their subsequent use as a medical treatment, in 1890. Today they are still widely used in dermatology all over the world. Pyoctanin (gentian violet) belongs to the group of triphenylmethane dyes with mycostatic and antibacterial properties. As an antiseptic topical agent, it has been used to treat impetiginized eczema, infection in leg ulcers, mycosis and several mucous diseases, such as aphthae or stomatitis. As there are only few references to allergic reactions to triphenylmethane dyes, they are often preferred to other antibacterial substances, such as aminoglycosides or antiseptics like clioquinol, which are more potent allergens. We report 2 patients who developed pyoctanin contact dermatitis after long-term topical treatment.

Case Reports

Case no. 1

A 55-year-old Turkish worker had a 2-year history of persistent interdigital maceration and rhagades, as well as eroded lesions, papules and dyshidrosiform pustules of the forefeet and distal lower legs. Because previous therapies with topical antimycotics, antibiotics, triphenylmethane dyes and corticosteroids had not been successful, the patient was admitted to our hospital. Bacteriological investigation identified beta-hemolytic streptococcus

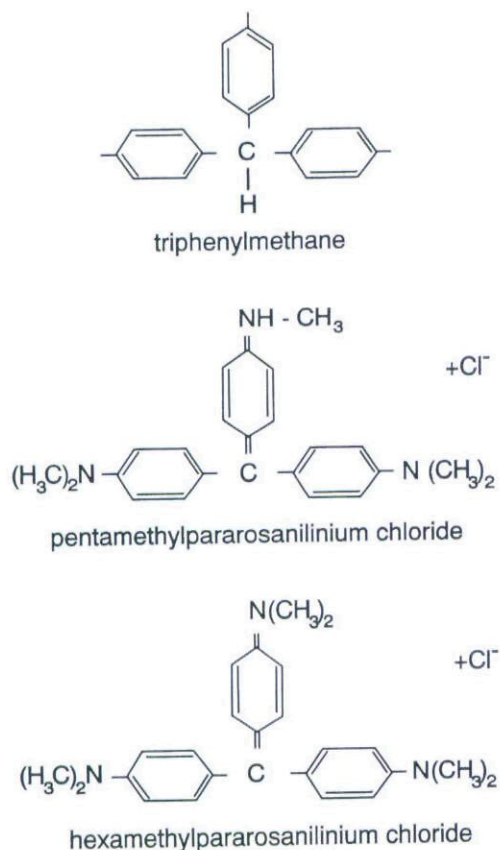


Fig. 1. Chemical structures of pyoctanin.



Fig. 2. Case no. 2: erosive contact dermatitis of the interdigital spaces of the feet.

type A, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and enterococcus. There was repeatedly no evidence of fungal infection. Laboratory tests were normal. Patch tests were performed in accordance with the standards of the DKG. There was evidence of contact allergy to neomycin, clioquinol and mercury amide-chloride.

After the patient had been admitted, systemic antibiotic therapy was administered. Local therapy included disinfecting dressings, dye solutions and footbaths, taking into consideration the allergy spectrum. After brief improvement of the skin condition, papules and pustules flared up again and erosions in the interdigital spaces reappeared, especially after the use of 0.25% aqueous pyoctanin solution. Patch testing with this substance revealed clearly positive reactions down to a concentration of 0.0025% aqueous pyoctanin solution. On therapy with topical corticosteroides, complete healing was achieved.

Case no. 2

A 48-year-old painter had been treated in numerous hospitals, as an out-patient as well as an in-patient, for recurring skin conditions on the feet, diagnosed as tinea pedis and bacterial infections. He was first admitted to our department after suffering 3 days of chills and an erythema with swelling of the right foot and calf. There was massive maceration, weeping lesions and fissures in the interdigital spaces of both feet, which spread to the underside of the toes and feet (Fig. 2). There was scaly hyperkeratosis on both soles. Our diagnosis was erysipelas and tinea pedis combined with bacterial infection of the feet. Bacterial investigation identified hemolytic streptococcus type B, *Staphylococcus aureus*, enterococcus and *Pseudomonas aeruginosa*. *Candida albicans* was isolated from the interdigital spaces. Patch testing in accordance

with the standards of DKG revealed contact allergy to perfume mix, triphenylphosphate, butylcatechin and quinoline mix.

Using a combination of systemic antibiotics, there was quick healing of the erysipelas. However, the interdigital lesions remained, despite consequent treatment with disinfecting dressings and dye solutions, taking into consideration the allergy spectrum. Even after several changes of topical treatment and systemic itraconazole therapy, there were recurrent skin lesions in the interdigital spaces. As the skin condition appeared to worsen, particularly after use of pyoctanin and solutio Castellani (=fuchsin 0.8, isopropanol 10.0, resorcinol 10.0, acetone 5.0, aqua destillata ad 100.0), a new patch test series was run with these suspicious substances. Patch tests showed positive results to pyoctanin down to a concentration of 0.05%, to a 1:8 diluted solutio Castellani (Fig. 3) and to resorcinol 2.5%. Treatment avoiding these allergens, combined with application of topical corticosteroids and consequent foot care, led to complete healing of the skin condition.

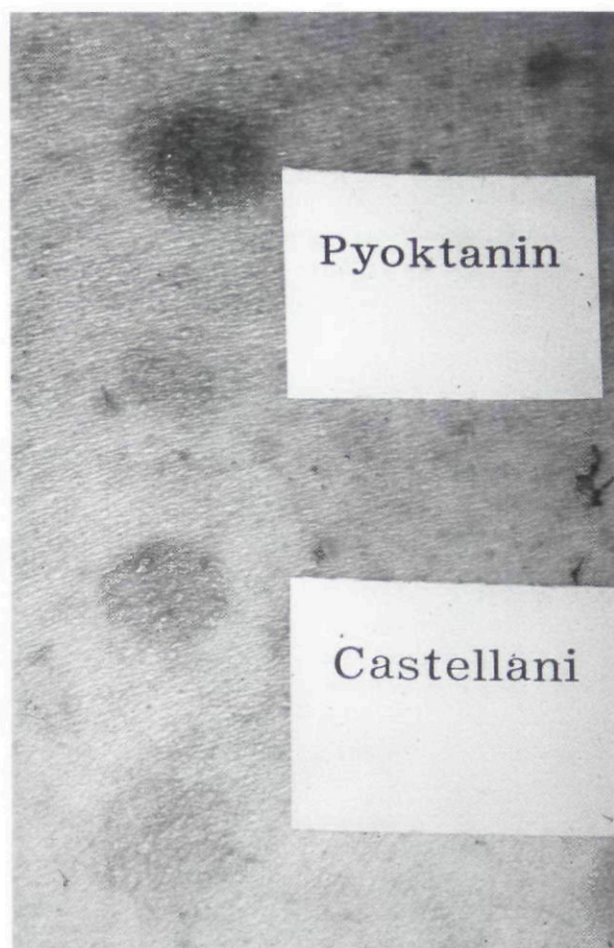


Fig. 3. Case no. 2: positive patch test results to pyoctanin and solutio Castellani.

Discussion

Most reports on local side-effects from the use of pyoctanin (gentian violet) deal with irritant or toxic reactions to this substance. In 1966, Slotkowski & Redondo (1) described irritation of the mucous membranes of the mouth after a wash with 1% gentian violet solution. In 1972, Björnberg & Mobacken (2) published several cases with painful and slowly healing skin necrosis in intertriginous spaces after the use of a 1% pyoctanin solution. In 1972, Wilkinson & Cronin (3) described mucous necrosis after application of 1% gentian violet in a patient with vaginitis. In 1977, Meurer & Konz (4) and Sommer & Happle (5) reported skin necrosis after treating intertriginous spaces with 2% and 1% pyoctanin solutions, respectively. They claimed that in intertriginous spaces, triphenylmethane dyes should only be used at a lower concentration, due to the possibly harmful effects resulting from the astringent capacity of the dye solutions on local application.

The 1st publication on sensitization to gentian violet was published in 1940 by Goldstein (6). However, the author referred to a 3% gentian violet solution applied in intertriginous spaces. In all probability, this was a toxic reaction rather than an allergic reaction. There are only a few other publications of presumed contact allergy to pyoctanin. In 1958, Michel et al. (7) reported on a 64-year-old patient, who suffered a shock reaction on therapy with gentian violet and methyl green for chronic leg ulcers. Patch tests with these solutions revealed positive reactions. Test concentrations were not mentioned and no further tests were conducted. In 1981, Epstein (8) suspected sensitivity to gentian violet in 3 patients with stasis dermatitis. All patients gave a positive intradermal test, but only 1 positive patch test to gentian violet 1% was observed.

Bielicky & Novak (9) reported on 11 patients with eczema localized mainly on the legs and sensitization to brilliant green. As 8 positive patch tests to gentian violet 2% in water were found, the possibility of cross-sensitization between brilliant green and gentian violet was raised. The authors found that the determinant groups of sensitization were $-N(CH_3)_2$ or $-N(C_2H_5)_2$ in the para-position of the benzene ring structure. Cross-reactions between triphenylmethane dyes could only be expected in cases of strong sensitization and were limited to substances with amino-groups with at least 2 alkyls.

In 1981, Lawrence & Smith (10) reported a female patient with a leg ulcer who showed a clearly positive patch test result to a 0.25% gentian violet solution in addition to several other contact allergies. In 1986, Bajaj & Gupta (11) patch tested 390 patients who were suspected of having contact sensitivity to

topical antibacterial agents. Among these patients, they found 9 positive patch test results to gentian violet 1% aqueous solution (1). In 1989, Cox et al. (12) reported on a contact allergy to marker solution, which among other substances contained gentian violet. A patch test with the ingredients was performed with negative result. Finally, Hausen (13) in 1992 described 3 patients with positive patch test results to a 1% gentian violet solution.

With the exception of Lawrence & Smith (8), all other aforementioned authors tested pyoctanin at a concentration higher than our therapeutically recommended pyoctanin concentration of 0.25–0.5%. Even though pyoctanin at a concentration of 1 or 2% applied to healthy skin will generally not cause a toxic reaction, the concentrations used in most patch tests appear to be too high. Although cutaneous effects of irritants depend on the type, physico-chemical properties, concentration and mode and area of application of the irritant, one can surely exclude the chance of an irritant reaction at test concentrations of 0.0025% and 0.05% aq., as in our patients.

Because our 2nd patient had an additional contact allergy to solutio Castellani, we suspected cross-reaction between the 2 triphenylmethane dyes pyoctanin and fuchsin (=rosalinine or magenta dye II). In testing the ingredients of solutio Castellani, we discovered that, instead of a positive reaction to fuchsin, resorcinol proved to be the causative agent. Although cross-reactions between pyoctanin and other triphenylmethane dyes like malachite green have been reported (2), cross-reactions between pyoctanin and fuchsin have not so far been observed.

In summary, there are just a very few reports of actual pyoctanin contact allergy. To prove an allergy against pyoctanin, a patch test has to be performed with a pyoctanin concentration that excludes irritant reactions. As pyoctanin is widely used and contact allergy to pyoctanin is extremely rare, it appears to be a very weak sensitizer. It seems that contact allergy to pyoctanin only occurs after long-term application to damaged skin. As topical corticosteroids are often applied simultaneously and the skin remains coloured after the use of pyoctanin, allergic reactions might not always be recognized. If pyoctanin contact allergy is suspected, one should not hesitate to perform a patch test as described.

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