

Anaphylaxis to saffron

SAFFRON (German: *Safran*; French: *safran cultivé*; Italian: *zafferano*; Spanish: *azafrán*) is the most expensive of all spices (1). It is produced from the dry stigma of the flower *Crocus sativa* L., which belongs to the Iridaceae family (*Iris*) and has a dark-yellow/orange to dark-red color. It is used as a spice, but often as a coloring in soups, bouillabaisse, sauces, rice dishes (paella, "risotto milanese"), cakes, cheese, and liqueurs. The following pigments and components are present in saffron: carthamine, saffron yellow A and B (safflor yellow), saffloamine A, ethereal oils (safranal, pinen, cineol),

glycosides (picrocrocin), and pectins (1). To our knowledge, allergy reactions to saffron have not yet been described in the literature. We report on a patient who experienced a severe anaphylactic reaction a few minutes after eating "risotto ai funghi", a yellow rice dish prepared

This case of a life-threatening reaction after a risotto meal illustrates the risk of "hidden allergens" in restaurant meals and fast food.

with saffron and mushrooms. The skin test and RAST were positive for saffron.

A 21-year-old atopic farmer with mild atopic dermatitis since the age of 10 years; oral allergy syndrome to apple, nuts, and spinach; and perennial allergic asthma for 1 year was referred for allergologic investigations because he developed a severe anaphylactic reaction with violent abdominal cramps, laryngeal edema, and generalized urticaria a few minutes after a meal of saffron rice and mushrooms. He was taken to a nearby hospital, where he collapsed at the entrance. The emergency doctor found a cyanotic patient, without pulse, and with wide, but reacting pupils. He was resuscitated with cardiac massage, intubation, application of oxygen-respirator, and e.v. epinephrine, steroids, antihistamines, and theophylline.

The skin prick tests (SPT) for routine inhalant allergens (Alyostal, Stallergènes Laboratoires) demonstrated polyvalent sensitization to various pollens, house-dust and storage mites, mammal epithelia, and *Cladosporium*. Prick-to-prick tests with fresh apple, carrot, potato, celeriac, and celery (raw and cooked) were strongly positive (+ +) (wheal > 5 mm).

Scratch tests were also performed with the ingredients of the risotto meal; they were negative for

rice, two kinds of mushrooms (*Boletus* and *Agaricus*), garlic, and onion, but strongly positive for saffron (+ +; wheal > 5 mm).

The total serum IgE was 2440 kU/l, and CAP results (FEIA, Pharmacia Diagnostics, Uppsala, Sweden) showed polyvalent sensitization to house-dust mite *Dermatophagoides pteronyssinus* (> 100 kU/l), birch pollen (52.9 kU/l), cow epithelia (13.0 kU/l), mugwort pollen (10.2 kU/l), and various spices and foods listed in Table 1, but were negative for the mushrooms *Boletus*, *Agaricus*, and *Coprinus*.

The patient's serum was tested in the RAST system against disks prepared from two saffron preparations (one bought in Sweden in a grocery store and one pure preparation kindly supplied by McCormick, Regensdorf, Switzerland). Both gave a positive result: 3.5 and 4.3 PRU/ml (class 3), respectively.

RAST inhibition of saffron using the patient's serum, McCormick disks, and another commercially available saffron preparation showed that the latter preparation gave complete inhibition (approx. 90% with an extract 1:1), and that 50% inhibition was obtained at a dilution of approx. 1:140.

With the McCormick preparation, SDS-PAGE and immunoblotting showed five IgE-binding bands with molecular weights between 40 and 90 kDa.

In conclusion, these results strongly suggest that saffron was the cause of the life-threatening anaphylactic reaction after the risotto meal in this asthmatic patient. The sudden start of urticaria excludes intoxication; allergy to mushrooms (3) and other

Table 1. Results of specific IgE determinations (RAST) against food

Allergen	Class, PRU/ml
Celeriac	5 (>52)
Celery	3 (7.4)
Celery (mix) (f85)	3 (4.7)
Black pepper (f280)	5 (>52)
Chili (f279)	3 (10.9)
Dill (f289)	3 (7.3)
Lovage (f275)	3 (6.2)
Estragon (f272)	3 (4.1)
Oregano (f283)	3 (3.7)
Ginger (f270)	2 (2.7)
Fennel, fresh (f276)	2 (2.1)
Basil (f269)	2 (2.0)
Cardamom (f267)	2 (1.8)
Fennel seed (f219)	2 (1.0)
Green pepper (f263)	2 (0.83)
Marjoram (f274)	2 (0.78)
Clove (f268)	1 (0.49)
Thyme (f273)	1 (0.42)
Cinnamon (f220)	0
Bay leaf (f278)	0
<i>Boletus edulis</i>	0
<i>Agaricus bisporum</i>	0
<i>Coprinus</i>	0

ingredients of the meal could not be demonstrated by skin and serologic examinations. A concomitant role of celery salt – which is often used in soup and bouillon – cannot be completely excluded due to the strong skin positivity in the prick-prick testing also with cooked celeriac and celery and the high RAST sensitization.

Because of the life-threatening anaphylactic reaction, oral challenge tests were not performed. Obviously, saffron is an allergenic spice and must be considered in cases of food anaphylaxis (2, 4, 5).

Key words: anaphylaxis; food allergy; immunoblot; RAST inhibition; saffron; scratch test.

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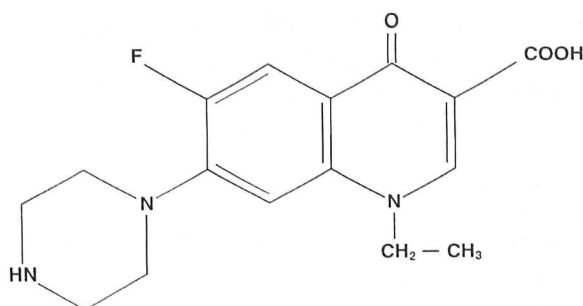
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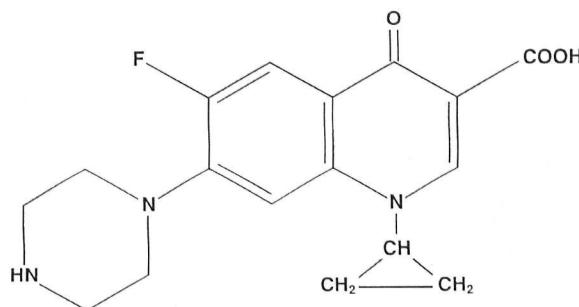
Fixed drug eruption (FDE) caused by norfloxacin

NORFLOXACIN is a fluorinated 4-quinolone with an excellent safety record, mainly used in urinary tract infections (1). We report a patient with fixed drug eruption (FDE) induced by norfloxacin. To the best of our knowledge, there is only one previous report of FDE to this drug (2).

In the previous 8 months, a 73-year-old woman had presented three episodes of pruritic erythematous-violaceous macular lesions. They appeared always on limbs, at the same sites, in a number lower than 10. The three episodes started on the first or second day of intake of norfloxacin 400 mg twice daily, a drug given for urinary tract infections. The lesions resolved in 4–6 days, but local hyperpigmentation remained.



NORFLOXACIN



CIPROFLOXACIN

FIGURE 1 Structural formulas of norfloxacin and ciprofloxacin.

Patch tests performed on residual pigmented and normal skin with norfloxacin 10% in white petrolatum were negative. Patch tests on unaffected skin with nalidixic, oxolinic, and pipemidic acids and ciprofloxacin, all of them at a concentration of 10% in petrolatum, were negative. After giving written informed consent, the

A provocation and biopsy confirmed case of FDE probably due to drug metabolites.

patient was challenged with norfloxacin. Six hours after the intake of norfloxacin 400 mg, she developed several sharply demarcated erythematous pruritic lesions: one on the right pretibial region (3 × 2.8 cm), another one on the back of the right hand (4.3 × 4 cm), two on the back of the left hand (1 × 1 cm each), and three on the right arm (1 × 1 cm each). A skin biopsy of the lesion on the right hand taken 24 h after challenge showed a lymphocyte inflammatory infiltrate in dermis and epidermis and keratinocytic necrosis. Five weeks after the provocation with norfloxacin, the patient was challenged with ciprofloxacin 500 mg, which was well tolerated.

We present a case of FDE induced by norfloxacin, as confirmed by oral provocation and biopsy of the

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