

Occupational allergic contact dermatitis in a chemist

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We report the first case of allergic contact dermatitis to 6,8-dibromo imidazo[1,2-a]pyrazine.

A 34-year-old non-atopic female chemist working in a cancer research

laboratory was referred with a history of three episodes of an acute eczematous rash over her neck, spreading to her face with eyelid involvement. Before each episode, she had been working with diazines (an imidazo[1,2-a]pyrazine and halogenated pyridazines). The acute eruptions were treated with topical steroids, but she required systemic steroids on one occasion.

She was patch tested to an extended European baseline series of contact allergens [(Trolab™; Almirall Hermal, Reinbek, Germany) in Finn™ Chambers (Epitest Oy Ltd, Tuusula, Finland) on Scanpor Tape], carbamates, fragrances, and a local face series and to the diazines she had been using: 6,8-dibromoimidazo[1,2-a]pyrazine (1%, 0.1%, and 0.01% in ethanol), ethyl 6-chloroimidazo[1,2-b]pyridazine-2-carboxylate (0.5% in ethanol), and 6-chloropyridazin-3-amine (0.5% in ethanol). Occlusion was 2 days with readings at D2 and D4 (International Contact Dermatitis Research criteria).

She produced a strongly positive reaction (++) on D2 and D4) to 6,8-dibromoimidazo[1,2-a]pyrazine at 1%, 0.1%, and 0.01% in ethanol. She also showed a positive reaction (+ on D2 and D4) to ethyl 6-chloroimidazo[1,2-b]pyridazine-2-carboxylate and 6-chloropyridazin-3-amine at 0.5% in ethanol. After informed consent, 20 normal control volunteers were patch tested with 6,8-dibromoimidazo[1,2-a]pyrazine at 0.01% in ethanol; there were no reactions.

The fume cupboards that she used were checked to ensure adequate ventilation, and appropriate occupational hygiene advice was reinforced. She has remained symptom free.

Discussion

Diazines are organic compounds containing a benzene ring in which two of the carbon atoms have been replaced by nitrogen. There are three isomers: pyrazine (1,4-diazine), pyrimidine (1,3-diazine), and pyridazine (1,2-diazine).

6,8-dibromoimidazo[1,2-a]pyrazine (CAS number 63744-22-9) is a pyrazine (Fig. 1). Many derivatives of pyrazines have been investigated for their pharmacological profile, ranging from antidepressant to inotropic or anti-ulcer activity (1).

Ethyl 6-chloroimidazo[1,2-b]pyridazine-2-carboxylate (CAS number 64067-99-8) and 6-chloropyridazin-3-amine (CAS number 5469-69-2) are halogenated pyridazines and are known to cause skin, eye, gastrointestinal (if ingested), and respiratory tract irritation. The pyridazine ring has demonstrated many synthetic and several biological uses (2) including herbicides (3) and pharmaceutical drugs such as cadralazine (4).

It is probable that our patient's eruption was an allergic contact dermatitis to 6,8-dibromoimidazo[1,2-a]pyrazine and possibly also to the halogenated pyridazines, although cross-reactivity is a possibility. She showed a consistently strongly positive reaction across a range of dilutions (0.01–1% in ethanol) of 6,8-

dibromoimidazo[1,2-a]pyrazine, and none of the control group showed a positive reaction to this chemical at the lowest concentration.

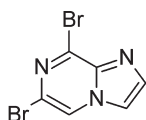
This case highlights the importance of stringent occupational hygiene in chemistry laboratories to prevent sensitization while handling potential allergens.

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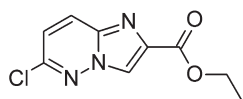
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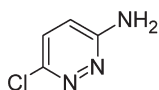
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6,8-Dibromoimidazo[1,2-a]pyrazine



Ethyl 6-chloroimidazo[1,2-b]pyridazine-2-carboxylate



6-Chloropyridazin-3-amine

Fig. 1. Structural formulae of the halogenated pyrazine/pyridazine derivatives.