

# Occupational allergic contact dermatitis caused by thebaine and oripavine

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Cases of allergic contact dermatitis caused by alkaloids derived from *Papaver somniferum* have been reported. We describe a case of occupational allergic contact dermatitis caused by thebaine and oripavine, precursors in the synthesis of morphine and codeine, and also various semisynthetic opioids.

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## Case Report

A 35-year-old male was referred because of eczema on the arms and lips that occurred episodically. He worked in a drug-manufacturing plant, and noticed that the episodes of eczema coincided with the production cycles of thebaine (CAS no. 115-37-7) and oripavine (CAS no. 467-04-9), but not with the production cycles of morphine (CAS no. 57-27-2) and noscapine (CAS no. 128-62-1). The eczema started in the third production cycle, and was severely exacerbated during the fourth production cycle. In between every production cycle, the

**Table 1.** Patch test results

|      | Morphine<br>Vehicle 1% | Thebaine<br>5% | Oripavine<br>5% | Codeine<br>5% | Noscapine<br>5% |
|------|------------------------|----------------|-----------------|---------------|-----------------|
| pet. | –                      | +              | –               | –             | –               |
| aq.  | –                      | ++             | +               | +             | –               |
| eth. | –                      | ++             | +               | +             | –               |

+, ++, +++, positive patch test reaction.

chemicals were not produced in the plant, and the patient was free of eczema.

The patient was patch tested with the European baseline series and Belgian supplements, cosmetics and pharmaceutical series, obtained from Chemotechnique (Vellinge, Sweden). Thebaine, oripavine, codeine and noscapine were tested at 5% pet., ethanol (eth.), and aq., and morphine was tested in the same vehicles but at 1% concentration (1) (Table 1). The chemicals were kindly provided by the employer of the patient, and the preparations were made by the hospital pharmacy.

The patch tests were applied on the upper back, and occluded for 2 days with van der Bend square chambers (van der Bend, Brielle, The Netherlands) and fixed with Hypafix (BSN Medical, Hamburg, Germany). Readings were performed on day (D) 2 and D4 according to ICDRG guidelines (2). Patch test results were positive at D4 for oripavine, thebaine, and codeine (Table 1; Fig. 1).

## Discussion

*P. somniferum* is a medicinal plant that contains many pharmaceutically important benzyloisoquinoline alkaloids, such as the narcotic analgesics morphine and codeine, and the cough suppressant noscapine (3). Contact dermatitis caused by several opiates, such as morphine, codeine, and heroin, has been described in patients using this medication, and in an occupational setting (4).

Thebaine is a precursor in the production of both morphine and codeine. Demethylation of thebaine results in oripavine, an intermediate in the production of morphine (3). Because the chemical structures of thebaine and oripavine are very similar, it is not surprising that the patient reacted to both molecules. Waclawski et al. described contact dermatitis caused by thebaine in a laboratory worker. Like our case, their patient cross-reacted to codeine but not to morphine or noscapine (4). Thebaine and noscapine share a common precursor, but noscapine is then produced through

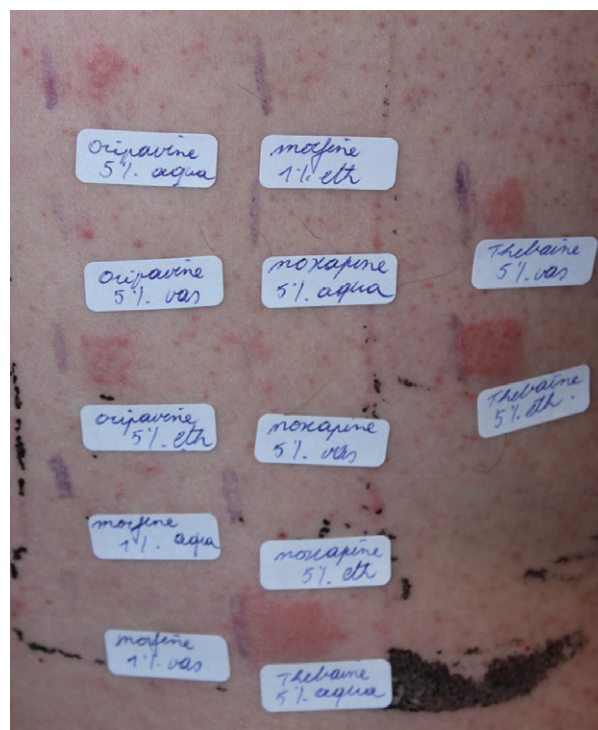


**Fig. 1.** Positive patch test reactions to oripavine 5% aq. and eth., and thebaine 5% aq., eth., and pet.

a different pathway, resulting in a chemical structure that shows little resemblance to that of thebaine (3).

The concentrations and vehicles used for patch testing vary among different publications, with aqueous and alcoholic solutions being most commonly used (4). In our case, the aqueous and alcoholic solutions performed better than petrolatum.

In conclusion, contact dermatitis caused by opiates in general is well known, whereas contact dermatitis caused by thebaine seems to be rare, but should not be overlooked in patients with occupational exposure. There seems to be no cross-reactivity with morphine; however, patch testing of a larger group of patients is necessary to confirm this. Several authors (1, 5) have suggested testing morphine at 1% in aq., eth., or pet., and we followed this recommendation. However, testing at higher concentrations could be indicated. More research is necessary to establish the optimal patch test concentration.

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