**Table 1** Niacin graded challenge protocol administration record.

| Time (h) | Dose (mg) | Therapeutic dose (%) | Cumulative dose (mg) | Symptoms |
|---|---|---|---|---|
| 0.0 | 25 | 5 | 25 | None |
| 0.5 | 50 | 10 | 75 | None |
| 1.0 | 100 | 20 | 175 | None |
| 1.5 | 250 | 50 | 425 | Flushing |

Flushing, a well-known side effect, was mild and resolved completely within 5 min. After the final dose, the patient was observed for an hour and 15 min without incident.

cessation, ACE inhibitors should always be considered in the differential for angio-oedema, particularly if recently stopped.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this investigation.

**Patients' data protection.** The authors declare that they have followed the protocols of their work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study.

**Right to privacy and informed consent.** The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

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http://dx.doi.org/10.1016/j.aller.2014.02.001

# Contact urticaria to *Cannabis sativa* due to a lipid transfer protein (LTP)

*Cannabis sativa*, which belongs to the Cannabaceae family, contains about sixty compounds named cannabinoids which are involved in its psychoactive effects, as well as antiemetic and anti-inflammatory properties. Hypersensitivity reactions to *C. sativa* are uncommon (or not recorded) probably because its consumption is illegal in most countries and patients do not address the physician for this reason. The possible involvement of LTP in *C. sativa* allergy has been pointed out[1] and recently several new putative *C. sativa* allergens have been described.[2,3]

A 30-year-old man without atopy history began to work in *C. sativa* harvesting for therapeutic use. After two months he developed several episodes of wheals and pruritus immediately after the contact of the skin with the leaves while collecting the plant. The symptoms disappeared spontaneously in less than an hour.

He previously consumed *C. sativa* recreationally (smoked) with good tolerance. He never experienced other allergies.

After obtaining informed consent and approval from the Hospital Ethics Committee, prick-by-prick test was carried out with dried and fresh *C. sativa* leaf obtaining positive results (mean wheal diameter of 6 mm and mean flare 10 mm). Positive (histamine dihydrochoride 10 mg/mL; Alk-Abelló, Madrid, Spain) and negative controls (saline) were

used. Five control subjects were also tested, with negative results.

Skin prick tests to commercial extracts from common inhaled allergenic sources and panallergens: purified profilin from date palm pollen (Pho d 2), peach extract enriched with Pru p3 (as a Lipid Transfer Protein [LTP]) and a polcalcin-enriched extract from date palm pollen (ALK-Abelló, Madrid, Spain) were performed and they turned out to be positive against pollens from *Lolium perenne*, *Phleum pratense*, *Olea europaea* and *Cupressus arizonica* and negative with the three tested panallergens.

We also tested patch tests (PT) with dry and fresh leaf with readings at day 2 (D2) and day 4 (D4) with negative result. The test was negative in five control subjects.

Patient serum was obtained for further studies. Serum total IgE was 241 kU/L (CAP system FEIA; Phadia, Uppsala, Sweden).

Protein extract from *C. sativa* leaves was prepared by homogenisation in phosphate-buffered saline, followed by dialysation and lyophilisation.

Serum specific IgE was determined against pollen extract from *P. pratense* 5.5 kU/L, *O. europaea* 3.4 kU/L and *C. arizonica* 1.12 kU/L (CAP system FEIA; Phadia, Uppsala, Sweden). Specific IgE by Enzyme AllergoSorbent test (EAST) technique (Specific IgE EIA kit; HYTEC, HYCOR Biomedical Ltd.) to *C. sativa* extract and Pru p 3 (peach LTP) was 3.3 kU/L and <0.35 kU/L, respectively.

The *C. sativa* leaves extract was electrophoresed by SDS-PAGE according to the Laemmli method in non-reducing conditions.[4] Separated protein was electrophoretically transferred to polyvinylene difluoride (PVDF) essentially as described by Towin et al.[5] and incubated with patient serum as well as with an anti-Pru p 3 rabbit serum. Both revealed two antibody-binding bands with the same molecular mass, approximately 14 kDa and 12 kDa, respectively.

We present a case of *C. sativa* allergy in which the in vivo and in vitro results confirmed a type I-IgE contact urticaria to this plant. Other cases of contact urticaria due to a type I-IgE mechanism have been reported.[6–8] Gamboa et al.[1] isolated a protein which belongs to Lipid Transfer Proteins (LTP) family called Can s 3 and it was considered as a relevant allergen of *C. sativa*. Other recent studies confirmed this hypothesis.[2]

LTPs are proteins with a molecular weight of around 8–9 kDa with high stability to thermal processing and to proteolysis. Cross-reactivity between LTP from plant foods (fruits frequently) and LTP from *C. sativa* has been described; De Larramendi et al.[2] reported a series of patients with cross-reactivity between *C. sativa* and tomato due to a sensitisation to LTP, and Ebo et al.[9] suggested the possibility that the plant-food allergy detected in some non-Mediterranean regions could be caused by a previous sensitisation to the *C. sativa* LTP. However, the homology between LTP sequences from botanically unrelated vegetable varies from 35% to 95%[10]; this broad range of possible homology among LTPs explains the non-cross-reactivity found in some cases between LTPs from different sources. This fact explains the negative Pru p 3 specific IgE value detected in the sera of our patient. Anyhow this sensitisation to LTP of *C. sativa* surely increases the risk to develop hypersensitivity to vegetable foods in the future, as has been suggested by Ebo et al.[9]

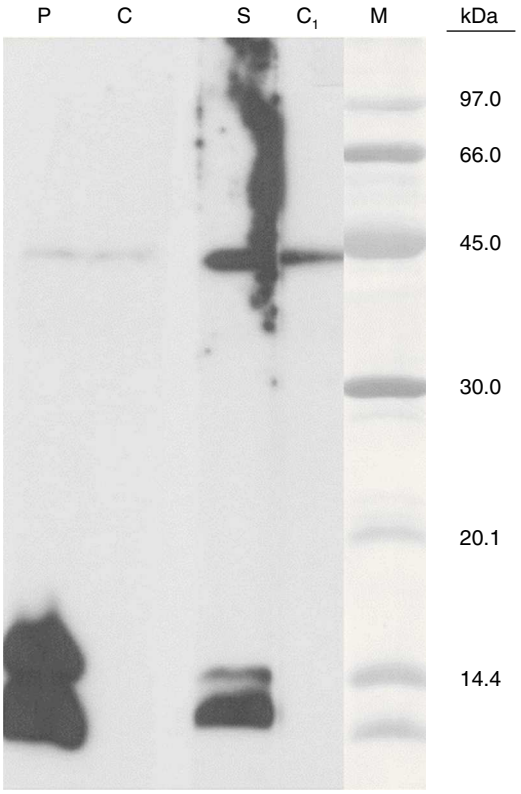


**Figure 1** SDS-PAGE immunoblotting results. *Cannabis sativa* leaves extract. Lane P: patient serum. Lane C: control serum (pool of sera from non-atopic subjects). Lane S: Anti-Pru p 3 rabbit serum. Lane C1: control serum (non-immunised rabbit serum).

In this setting, in our study in spite of the negative serum specific IgE levels detected against Pru p 3 (<0.35 kU/L), the immunoblotting results support the implication of *C. sativa* LTP as the relevant allergen.

In our patient it seems that there is a skin primary sensitisation to pollens without clinical relevance and that it was not due to LTP or other panallergens, as demonstrated by positive skin tests to the first ones and negative to the second ones, confirmed also by in vitro tests.

In this patient, sensitisation to *C. sativa* occurred by contact and was probably favoured by previous consumption of marihuana recreationally (smoking), but LTP also could produce sensitisation by ingestion pathway because of its thermostability and its resistance to proteolysis.

In conclusion, we report a case of contact urticaria to *C. sativa* plant due to a type I hypersensitivity mechanism. This plant should be considered as a possible source of occupational allergen in cases of *C. sativa* plantation workers (Fig. 1).

## Conflicts of interest

The authors declare that they have no conflicts of interest in the subject matter or materials discussed in this manuscript.

## Source of funding

Bial Aristegui Laboratories funded the study conducted in vitro. The other resources used in this work belong to the Spanish Health System.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that the procedures followed were in accordance with the regulations of the responsible Clinical Research Ethics Committee and in accordance with those of the World Medical Association and the Helsinki Declaration.

**Confidentiality of data.** The authors declare that they have followed the protocols of their work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in the study.

**Right to privacy and informed consent.** The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

## Acknowledgements

The author specially thanks doctors Cortés, de la Cueva, Echenagusía, Franco, Gómez, Iglesias, Montero, Ortega, Rodríguez-Bernal and Salvatierra for their expert view and helpful discussion of the case.

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http://dx.doi.org/10.1016/j.aller.2013.10.002

## DRESS syndrome induced by meropenem

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is just one of the several synonymous terms used to describe a severe, idiosyncratic reaction to a drug, presenting clinically as an extensive cutaneous rash, accompanied by fever, lymphoadenopathy, hepatitis, haematological abnormalities with eosinophilia and atypical lymphocytes, and may involve other organs with eosinophilic infiltration, especially the kidneys, heart, lungs and pancreas. This syndrome has been described to be mainly induced by anticonvulsants, allopurinol, sulphonamides, antiretroviral therapy and some antibiotics.[1] Anticonvulsants and allopurinol were the drugs most commonly associated with DRESS, and almost 20% of the patients had DRESS associated with antibiotics. Recognition of this syndrome is of paramount importance, since the mortality rate is about 10–20% and specific therapy may be necessary.[2]

We describe a case of DRESS syndrome induced by meropenem, with a tolerance to other beta-lactam agents, where epicutaneous test and lymphocyte activation test (LAT) have proved useful as a diagnostic method.

A 53-year-old female, without toxic habits or relevant medical history, was hospitalised 45 days previously due to serious traumatic injuries resulting from a road traffic