

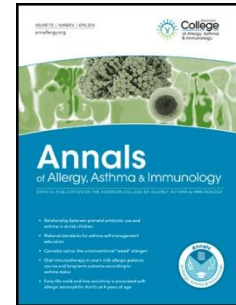
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Author: Prerana Bhatia, Meng Chen, Sandra Christiansen

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Marijuana and Stoned Fruit

Prerana Bhatia, MD¹; Meng Chen, MD¹; Sandra Christiansen, MD¹

1. Department of Medicine, University of California, San Diego

Corresponding Author:

Prerana M Bhatia

402 Dickinson Street, Suite 380

San Diego, CA 92103-8425

(Phone) 507-358-3312, (Fax) 619-543-6529

P3bhatia@ucsd.edu

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Abbreviations: nsLTP, Non-specific lipid transfer protein; SPT, Skin prick test

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The *Cannabis sativa* plant has various uses depending on the preparation. The flowering tops and leaves from *C. sativa*, called marijuana, are high in psychoactive compounds and typically smoked. Hemp is the fibrous component of the plant used in the clothing industry, while hemp seeds are a commercial food growing in popularity. *C. sativa* components can, reportedly, cause various allergic symptoms, including rhinoconjunctivitis, contact urticaria, and anaphylaxis.^{1-3,2} The mode of sensitization and role of cross-sensitivity remains unclear. We present here a patient with contact urticaria to *C. sativa* and anaphylaxis with hemp seed ingestion in the setting of numerous other allergies to stone fruits and nuts.

A 24 year old man who smokes marijuana daily presented to Allergy clinic two weeks following an anaphylactic reaction after eating yogurt with hemp seeds. This was his first known ingestion of hemp seeds. Immediately following consumption, he developed oral pruritus that progressed to shortness of breath, facial swelling, and pre-syncope. He took diphenhydramine 25mg without relief. He proceeded to the Emergency Department where he received intramuscular epinephrine with improvement. After this episode, he continued to smoke marijuana and eat yogurt without further episodes of anaphylaxis. He has since strictly avoided hemp seeds.

The patient's allergy history included cutaneous reactions to shellfish at age eight that prompted skin prick testing. This testing revealed sensitivity to foods, including stone fruits, nuts, crustaceans, and aeroallergens. He had stringently avoided stone fruits, including peach and cherry. He reported oral pruritus with the ingestion of these fruits in the raw form. He had chronic nasal congestion but no asthma dating to his childhood on the Eastern coast of the United States. He denied any rhinoconjunctivitis, dyspnea, or oral allergy symptoms when smoking

marijuana. He developed contact urticaria if the *C. sativa* leaves and flowers touched his forearms. Our workup included a positive skin prick test (SPT) to hemp, fresh marijuana, and multiple stone fruits (Table 1). Saline control was negative. Tryptase level was within normal limits. In vitro studies for aeroallergens demonstrated positive responses for grass, birch and mite with negative seafood testing.

This case demonstrates that allergy to *C. sativa* can range from contact urticaria to anaphylaxis in the same person depending on the mode of exposure. In this instance, the patient had known stone fruit allergies and mild contact reaction to marijuana until hemp ingestion resulted in anaphylaxis. He did not have any respiratory or anaphylaxis symptoms with prior or subsequent marijuana smoking. Skin prick testing confirmed reaction to the fresh marijuana sample provided by the patient; a limitation for this testing is the lack of standardized marijuana extracts. A commercial hemp seed sample also yielded a positive SPT result.

Sensitization to hemp can occur from prior marijuana handling, smoking, and ingestion. IgE reactivity to various *C. sativa* components has been previously described, including proteins involved in photosynthesis.^{3,4} This patient had significant exposure to *C. sativa* due to his recreational marijuana smoking, and it is possible that he became sensitized to *C. sativa* through marijuana smoking and handling.

Cross reactivity via non-specific lipid transfer proteins (nsLTPs) must also be considered given this patient's extensive food allergies. He had marked reactivity to stone fruits, nuts and *Cannabis* which are all known to contain nsLTPs. The phenomenon of cross-reactivity between

C. sativa and plant foods is known as ‘*Cannabis* fruit/vegetable syndrome’ or ‘LTP syndrome.’⁵ Numerous studies have analyzed the nsLTP mediated cross-reactivity between *C. sativa* and stone fruits, such as peaches, nectarines, and plums, as well as nuts, apples and tomatoes.⁵⁻⁸ The nsLTPs belong to the prolamin protein superfamily and provide protection against bacteria and fungi in plants. Given their important role in the plant defense system, these nsLTPs are highly conserved and as a result, often cause clinical reactivity to multiple different foods in sensitized patients.⁸ The nsLTPs are highly resistant to thermal stress and proteolysis, which may account for their ability to withstand digestion and cause more systemic reactions, although oral allergy syndrome has also been described.⁹

Prior studies have suggested that nsLTP mediated reactivity is geographic, mainly in Europe.^{5,8} Some reports have indicated sensitization to stone fruits in the wake of developing an allergy to marijuana.^{5,10} In our case, the history of stone fruit allergies preceded the development of anaphylaxis to *C. sativa* components. This raises the novel possibility that the reverse sequence for nsLTP cross-reactivity may be relevant as well.

In summary, gathering a thorough allergy and social history is essential for patients reporting allergic symptoms to *C. sativa*. Given the expanding medical and recreational use, we anticipate that marijuana hypersensitivity will be a topic of growing importance in the field of allergy. Our case raises the possibility that, in addition to marijuana smoking and handling, nsLTP mediated stone fruit cross-reactivity may be another ‘gateway’ to *C. sativa* sensitization.

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Table 1: Skin prick testing with a patient-provided marijuana and hemp samples among other foods. The results are reported as millimeter wheal/millimeter flare. * Stonefruits

Sample	Result	Sample	Result
Saline control	Negative	Histamine control	5/21
Almond	11/34	Hemp seeds	19/45+
Apple	4/24	Hops	7/22
Blackberry	11/31	Marijuana	24/45+
Blueberry	Negative	Nectarine*	7/27
Cherry*	11/43	Peach*	9/38
Hazel Nut	7/33	Raspberry	7/16