
Allergy to fenugreek (*Trigonella foenum graecum*)

Sangita P Patil, PhD*; Pramod V Niphadkar, MD†; and Mrinal M Bapat, PhD*

Background: Allergic reactions after consumption of spices are well-known. In Asia, fenugreek seeds are consumed as spices and also as medicines. Literature survey carried out does not reveal reports of allergic reactions to fenugreek. In our survey carried out on patients with food allergy, we found two cases of severe allergy to fenugreek.

Methods: We report here two cases of immediate allergy following ingestion, inhalation, and external application of fenugreek seed powder. In the first case, inhalation of the fenugreek seed powder resulted in rhinorrhea, wheezing, and fainting. The second case was of a patient with chronic asthma who developed numbness of head, facial angioedema, and wheezing after application of fenugreek paste to her scalp as a treatment for dandruff. Skin scratch test was performed with fenugreek and other members of the Leguminosae family as fenugreek also belongs to Leguminosae. Objective evidence of the reaction was obtained by conducting double-blind placebo-controlled challenges (DBPCFC). For detecting IgE binding by immunoblotting method, the proteins of the fenugreek extract were resolved using sodium dodecyl sulphate polyacrylamide gel electrophoresis.

Results: Skin scratch tests for the patients revealed strong sensitivity to fenugreek and chickpeas. None of the controls showed such response with fenugreek extract. During DBPCFC, both patients showed >20% drop in peak flow rate after consumption of fenugreek and chickpea. Immunoblots demonstrated binding of specific IgE from the patients' sera with the protein from extracts between 20 kD to 70 kD bands.

Conclusion: This case report has enlarged the list of food allergens with the addition of fenugreek.

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INTRODUCTION

Fenugreek (*Trigonella foenum graecum*), one of many condiments known to mankind, has been cultivated for a very long time. It has been popularly used as a food and as a medicine in the Mediterranean region, western Asia, northern India, and Africa. In India, fenugreek seeds are consumed with jaggery during the postpartum period, which is supposed to facilitate lactation. Also, its seed powder is considered an antiseptic and employed towards improving skin texture. The foliage of fenugreek is also a com-

monly consumed leafy vegetable in many parts of India. Fenugreek seeds contain 26.2 g% protein, 5.8 g% fat, and 44.1 g% carbohydrate. One hundred grams of seeds provides 333 Kcal (ie, 1399 kJ).¹

Spiced food has been reported to cause immediate allergy symptoms in the mouth, nasopharynx, the gastrointestinal tract, and the skin. In the process, it sometimes leads to serious complications like generalized urticaria and anaphylactic shock. Immediate allergy to spices such as coriander, caraway, cayenne, paprika, and mustard have been reported.² No allergic reaction has been reported to the aromatic seeds of fenugreek.

IgE-mediated reactions in two cases of immediate allergy caused by inhalation, ingestion, and external applica-

tion of fenugreek seed powder are reported here.

CASE REPORT 1

A 36-year-old housewife, experienced sneezing, rhinorrhea, and excessive tearing after opening a jar containing fenugreek powder and smelling it for identification. This was followed by persistent coughing, wheezing, and fainting. Her family doctor immediately referred her to our hospital where she was admitted in a state of shock.

There was profuse sweating, the pulse was 140/min and the blood pressure was 100/80 mm Hg. Antishock treatment was immediately administered with epinephrine, intravenous aminophylline, and hydrocortisone, supplemental oxygen and hydration. Her condition stabilized after three hours. Complete blood count and chemistries were normal except for eosinophilia (1500/mm²). Electrocardiograph and chest radiographs were normal. Her pulmonary function test disclosed moderate obstruction. The past history revealed allergy to chickpeas and occasional mild asthma. On the day this incident took place she had not consumed chickpeas.

CASE REPORT 2

A 45-year-old woman with a history of allergic rhinitis and asthma since childhood recently developed pruritus and dandruff. On advice from a relative, she applied fenugreek seed paste to her scalp to get rid of dandruff. Within minutes, she developed nasal congestion and hoarseness. Later, she experienced facial angioedema, wheezing, and numbness of the head. She was rushed to our hospital casualty ward where her pulse rate was 110/min and blood pressure 130/80 mm Hg. There was acute rhinitis with angioedema of

* The Institute of Science, Bombay, India.

† Sir Harkisondas Nurrotumdas Medical Research Society, Bombay, India.

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Table 1. Comparison of Skin, Provocation, and Immunoblot Results Among Patients and Controls

Food	Patient	Controls' No	Skin Test	Provocation	Immunoblot
Fenugreek		2	1+	—	—
		3	1+	—	—
		17	1+	—	—
	1		4+	+	+
	2		3+	+	+
Chickpea		1	1+	—	—
		25	1+	—	—
	1*		3+	+	+
	2*		3+	+	+

* Immunoblots not shown here.

the face and wheezing. She received an antihistamine and epinephrine. Within five hours her condition stabilized. A retrospective analysis of her history revealed that she had experienced wheezing after ingestion of fenugreek seeds. Pulmonary function testing disclosed moderately severe obstruction.

MATERIAL AND METHODS

Clean seeds of fenugreek (*Trigonella foenum graecum*), chickpea (*Cicer arietinum*), red gram (*Cajanus cajan*), lentil (*Lens esculenta*), black gram (*Phaseolus mungo*), green gram (*Phaseolus aureus*), field bean (*Dolichos lablab*), and peanut (*Arachis hypogaea*) were finely powdered. The dessiccated, defatted (using diethyl ether in Soxhlet apparatus) powders were used for extract preparation (Fig 1).

Twenty-four hours prior to any of the tests, the patient was kept off medication such as antihistamines and steroids. The control group consisted of ten volunteers each from (1) atopic patients with food allergies other than fenugreek and chickpea (controls 1 to 10) (2) atopic patients without food allergies (controls 11 to 20), and (3) nonatopic persons (21 to 30).

A skin test was carried out by the scratch method. For this test, 10 μ L of legume extract each containing approximately 22 to 25 μ g protein, was used. Histamine (1 mg/mL) served as positive control and glycerinated saline was used as negative control. The results were read 20 minutes after the application of the test material.³ The

net wheal diameter of 3 mm was graded as 1+, 4 to 7 mm as 2+, and 8 to 10 mm as 3+.⁴ A reaction greater than this with pseudopodia was graded as 4+.^{3,4} The net wheal diameter was calculated as the wheal response obtained with test extract minus wheal response from saline control. A reac-

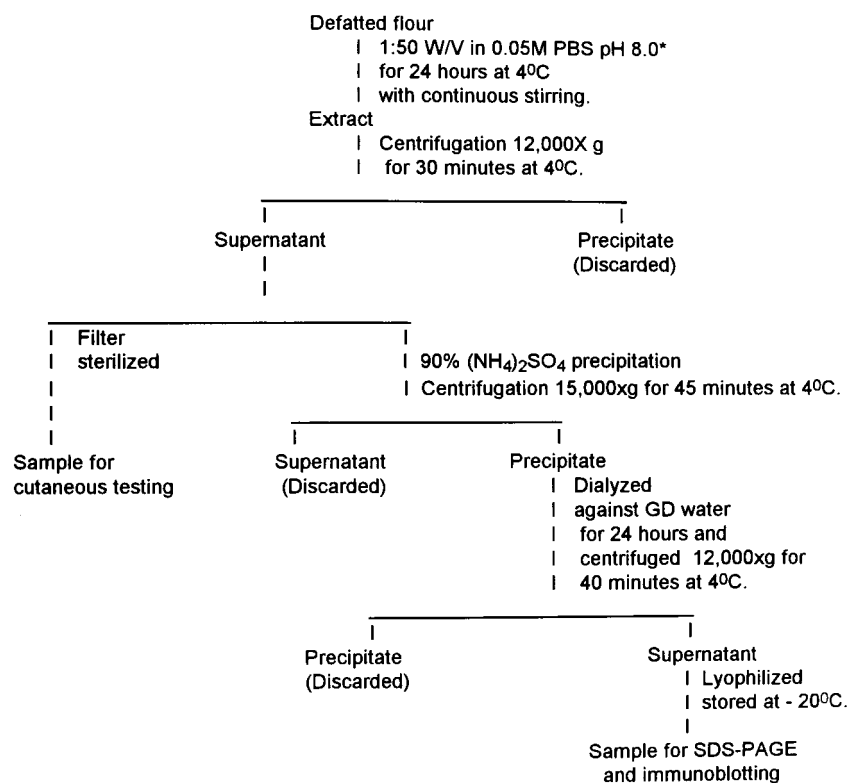
tion was graded as negative if it was not different from the control.

Provocation

The food challenge test was carried out by the double-blind placebo-controlled food challenge (DBPCFC) method.⁵ Three sets of capsules were prepared, two containing placebo and one with the test sample. Dextrose was used as placebo. The DBPCFC was carried out on separate days for each test sample; namely fenugreek, chickpea, or placebo.

SDS-PAGE

Sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS-PAGE) was used to resolve the protein pattern of the fenugreek powder extract using 12.5% running gel and tris-glycine buffer of pH 8.3. After the electrophoretic run, the gels were



* 50% glycerol PBS pH 7.4 was used for the preparation of extract to be used for skin test.

Figure 1. Flow chart for preparation of antigen extract.

stained by Coomassie blue⁶ to determine the protein pattern. Molecular weights of these proteins were determined by simultaneously running standard molecular weight proteins.

Immunoblotting

SDS-PAGE resolved protein bands were transferred electrophoretically (LKB Novablot) from the gel to the nitrocellulose paper (Millipore). This paper was then treated with 1% BSA in 0.1 M PBS, pH 7.4 for one hour at 37 °C to block the unoccupied sites. Excess BSA was washed off with 0.05% Tween 20 in PBS and incubated overnight with previously diluted test sera (1:5 vol/vol with PBS-Tween buffer containing 0.02% NaN₃). After incubation, the excess serum was washed off and the strip was incubated with goat anti-human IgE-horse radish peroxidase conjugate for three hours. The washing step was repeated and the strips were developed with 0.2 mg/mL DAB (Diamino benzidine) and 0.015% H₂O₂ in 0.05 M Na-acetate buffer pH 5 for seven to eight minutes, rinsed in distilled water, and the paper was then air dried.⁷

RESULTS

Scratch testing of patient 1 elicited a severe 4+ reaction to fenugreek and 3+ reaction to chickpea, while in patient 2 there were 3+ reactions to both test samples. Patient 1 also was found to be moderately allergic to house dust mite and patient 2 to *Amaranthus* and *Curvularia*.

Two patients from the first group of controls and one patient from the second group of controls, who did not have any previous history of fenugreek allergy, had 1+ reactions to fenugreek by scratch testing (Table 1). These patients did not have any adverse reaction in the open food challenge test even after consumption of 20 g of fenugreek powder; immunoblots with their sera were also negative. Two other patients, one from the first group of controls and one from the third group of controls, had 1+ reactions to chickpea extract but did not have any adverse reactions even after consump-

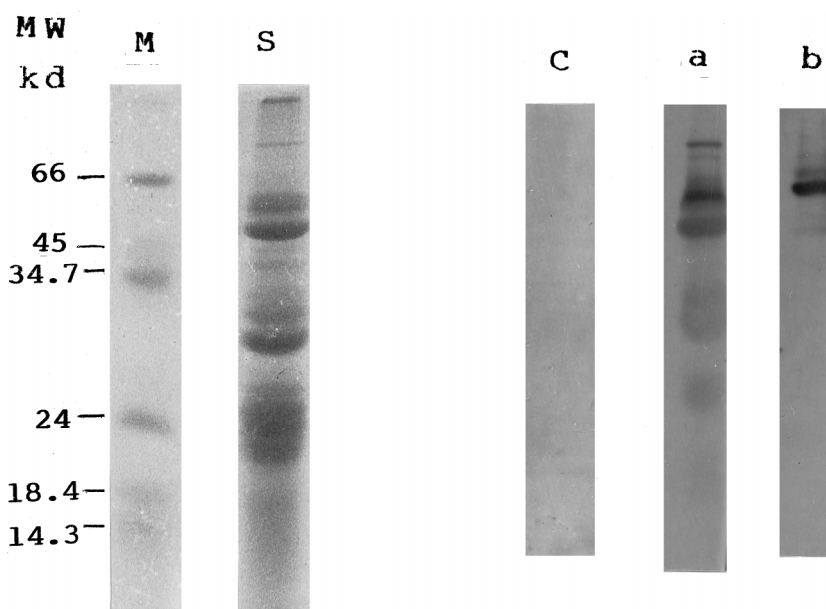


Figure 2. SDS-PAGE of molecular weight markers (M) and fenugreek protein (S) stained with Coomassie blue and immunoblots of fenugreek protein with serum from a control subject (c), patient-1 (a) and patient 2 (b).

tion of 20 g of chickpea powder in the open challenge test. Their immunoblots were also negative.

In patient 1, 0.5 g of fenugreek powder was found sufficient to cause a 40% drop in peak expiratory flow rate within 45 minutes during DBPCFC, while itching and urticaria resulted within two and one-half hours of consumption of 2 g of chickpea powder.

During DBPCFC, a 32% drop in the peak expiratory flow rate of patient 2 was observed three hours after the ingestion of 8 g of fenugreek; in contrast, 15 to 16 g of chickpea powder could trigger mild airway obstruction with a 20% drop in PFR five hours after ingestion.

Placebo caused no symptoms in either patient.

The Coomassie blue stained gels showed 16 prominent protein bands in the 70 to 20 kD molecular weight range. The protein bands at 55, 52, 48, 34, 32, 30, 29, 25, 24, 23, 22, and 20 kD molecular weight were stronger as compared with other protein bands. Immunoblotting carried out with the serum of patient 1 showed a binding of specific IgE with the 70, 68, 60, 55, 52, 48, 40, 34, 30, 29, 24, and 22 kD bands. The immunoblot with the sera of patient 2 showed specific IgE binding with 70, 60, 52, 48, 45, 40, and 30 kD bands (Fig 2).

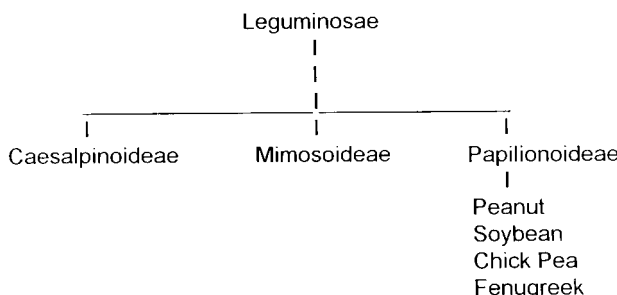


Figure 3. Botanical classification of fenugreek.

DISCUSSION

The spices known to cause allergic reactions belong to the Umbelliferae family (eg, coriander and caraway) and to the Solanaceae family (eg, cayenne and paprika). Fenugreek which is categorized as a 'spice', belongs to the Leguminosae family. Other members of the Leguminosae family, namely soybean, peanut and green pea, are proven food allergens (Fig 3).

The data presented here are a part of a study of the food allergy pattern in the Indian subcontinent, where the chickpea (Leguminosae) was found to be the predominant allergenic food substance. Severe reactions, including anaphylaxis, were observed after the ingestion of chickpea (unpublished data).

Robert Bush et al⁸ had shown that there is a possibility of cross-reactivity between members of the same plant family. In the present study, both patients had allergy to chickpeas. The severity, however, of the reactions caused by the ingestion of fenugreek seeds was much higher in comparison to their reactions to the chickpea. It would be interesting to find out whether IgE binding to fenugreek proteins is inhibited by the chickpea extract. This would help in understanding the possible cross-reactivity between these two legumes.

The essential oils from spices such as coriander, ginger, and paprika could be a part of the IgE binding structures.⁹ In the case of patient 1, this could be one of the possibilities since the symptoms were caused by the inhalation of fenugreek dust. Allergic reactions against the extract of defatted seed powder, were observed, however, in both patients, indicating that the defatted portion of fenugreek powder also contained the allergen(s). This was further proved by specific IgE binding

with the fenugreek proteins in immunoblotting.

The reported cases of spice allergy are mainly cases of occupational exposure to the spices.^{1,2} The allergenic load confronted by individuals in such cases is high. In the present study, however, exposure of patients to fenugreek was limited to its utilization for household purposes. This indicates that exposure even to small amounts was sufficient for sensitization.

With the increasing use of natural foods for their nutritive value as well as for their medicinal use, the need to determine whether the patient is allergic to such foods has gained importance. Fenugreek is generally utilized in very small quantities in Indian food preparation. Detecting an offending food substance present in very small quantities in food items is rather difficult for patients.

These are the first reported cases of fenugreek allergy. Severe reactions to fenugreek seeds, as seen in these patients, has added a new allergen to the long list of food allergens. The presence of IgE-mediated allergy to fenugreek seeds was confirmed in these patients by scratch testing, DBPCFC, and immunoblotting. Further immunoblotting studies with more patients could lead to identification of major allergens of fenugreek and eventually standard diagnostic reagents.

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Request for reprints should be addressed to:
Pramod V Niphadkar, MD
Sir Harkisondas Nurrotumdas Medical
Research Society
Raja Rammohan Roy Rd
Bombay 400 004
India