

## Allergy to Beer and Wine Caused by *Saccharomyces cerevisiae* in a Patient Sensitized to Fungi

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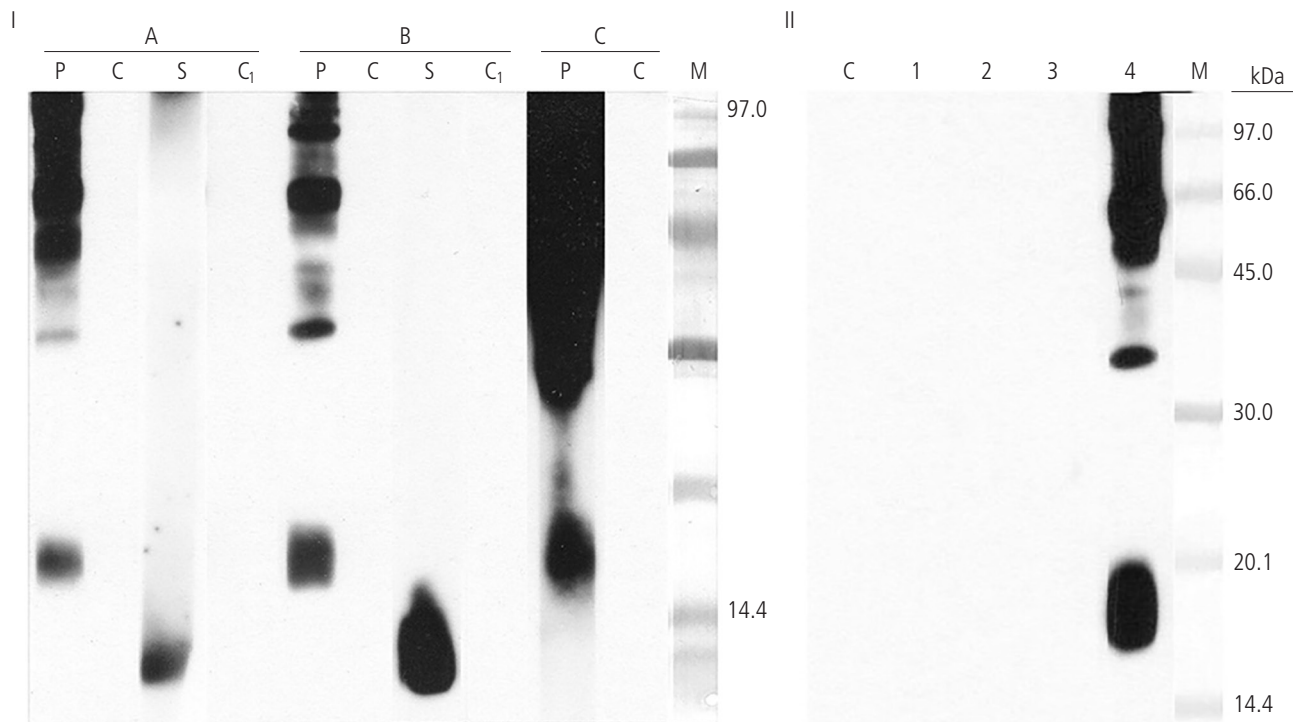
Beer and wine are the most widely consumed alcoholic beverages in the world. Wine is made from fermented grape juice and beer is brewed from fermented cereal grains (most commonly malted barley). Hops are also used to flavor beer. Both beverages are produced by fermentation with yeasts (*Saccharomyces cerevisiae* or *Saccharomyces carlsbergensis*). Hypersensitivity reactions to beer or wine are rare and have been attributed mainly to grains [1] and grapes. Proteins from barley are the most common cause of beer allergy [2].

The presence of potential barley allergens and proteins from *S cerevisiae* have been described in beer through proteomic studies (nonspecific lipid transfer protein [nsLTP], gliadins, glutelins, trypsin  $\alpha$ -amylase inhibitors, serpins) [3,4], and some have been shown to trigger allergic reactions, as follows: nsLTP (9 kDa), protein Z (45 kDa) [5], and protein Z-type serpin (20-25 kDa) [6]. Similarly, sensitization to yeast [7] has been described as the cause of allergy to beer, cider, and wine.

The patient was a 33-year-old woman with a personal history of allergic rhinoconjunctivitis and exercise-induced asthma who had been experiencing episodes of anaphylaxis (ocular pruritus, eyelid angioedema, globus sensation, dysphonia, diarrhea, urticaria, and dizziness) with no associated exercise over a period of 3 years. These reactions resolved with self-administered epinephrine. She related the episodes to ingestion of beer with chips or olives. Occasionally, she had experienced milder symptoms after drinking red and white wine. She tolerates other alcoholic beverages, cereals (including bread), grapes, nuts, and all kinds of food.

Protein extracts from various brands of beer (Heineken, San Miguel, Chimay, Franziskaner) were prepared by homogenization in phosphate-buffered saline (50% vol/vol) (50 mM phosphate buffer, 100 mM NaCl, pH 7.5), dialyzed against distilled water, and lyophilized. As some beers are produced with wheat, 1 of the beers studied was a wheat beer (Franziskaner).

Skin prick tests (SPTs) with common aeroallergens (pollens, dust mites, molds, pet dander) were positive to



**Figure I.** SDS-PAGE Immunoblotting. A, Franziskaner beer extract. B, Chimay beer extract. C, *Saccharomyces cerevisiae* extract. Lane P, patient's serum; Lane C, control serum (pool of sera from nonatopic individuals); Lane S, anti-Pru p 3 rabbit serum; Lane C<sub>1</sub>, unimmunized rabbit serum; Lane M, molecular mass standard. **II.** SDS-PAGE immunoblotting-inhibition. Solid phase: Chimay beer extract. Lane C, control serum (pool of sera from nonatopic individuals); Lanes 1-4, patient serum preincubated with Chimay beer extract (lane 1), with Franziskaner beer extract (lane 2), with *S cerevisiae* extract (lane 3), and with lamb extract (lane 4).

*Dermatophagoides pteronyssinus* (3×3), *Lepidoglyphus destructor* (3×3), *Alternaria alternata* (3×3), and *Aspergillus fumigatus* (7×8). SPTs were positive with beer extracts, as follows: Heineken, 5×5; San Miguel, 4×4; Chimay, 6×5; Franziskaner (from wheat), 5×5; red wine, 7×7; white wine, 8×6; *S cerevisiae*, 7×6; raw *S cerevisiae*, 6×6; cooked *S cerevisiae* 6×6; *Penicillium nalgiovense*, 7×6; and mushrooms, 8×8. The results of SPTs performed with cereal extracts (wheat, barley, corn), fruits (apple, pear, peach, red and white grape), and Pru p 3 (peach nsLTP) were negative.

Total serum IgE (ImmunoCAP, Thermo Fisher) was 178 kU/L, and the results for specific IgE were as follows: 4.51 to *S cerevisiae*, 4.29 to *Penicillium chrysogenum* (*Penicillium notatum*), 3.93 to *A fumigatus*, 3.87 to *Candida albicans*, 1.93 to *Cladosporium herbarum*, 1.93 to *A alternata*, 4.24 to rPru p 3, and 3.96 to rMal d 3. Specific IgE <0.10 was recorded for cereals (barley, oat, maize, malt, hop, rye, wheat, rTri a 19, rTri a 14), rAlt a 1, rAsp f 2, rAsp f 4, and rAsp f 6.

SDS-PAGE immunoblotting was carried out under reducing conditions (with mercaptoethanol) as described by Lammeli [8], with Franziskaner and Chimay extracts, *S cerevisiae* extract, and the patient's serum (Figure). In order to study the possible involvement of the cereal nsLTP in the allergic reaction due to beer ingestion, the beer extracts were also incubated with rabbit serum against Pru p 3.

A similar profile of IgE-reactive bands was detected in both beer extracts, the main ones being bands of around 97 kDa, 80 kDa, 55 kDa, 40 kDa, 32 kDa, and 17 kDa. In the *S cerevisiae* extract, a high intensity IgE-binding zone was revealed between 100 kDa and 29 kDa, as was a band of around 17 kDa. The anti-Pru p 3 rabbit serum revealed a band with a molecular mass below 14 kDa in both beer extracts; no bands of this molecular mass were detected in beer extracts with the patient's serum.

In order to determine whether *S cerevisiae* was the allergenic source of the IgE-reactive proteins detected in beer extracts, an immunoblotting-inhibition assay was carried out with Chimay beer extract in the solid phase and beer extracts and *S cerevisiae* extract as inhibitors. Both beer extracts and *S cerevisiae* extract produced total inhibition of IgE-binding in Chimay beer extract.

Airola et al [9] reported a case of allergy to *S cerevisiae* in a patient who experienced anaphylactic reactions to beer, red wine, and sauces, suggesting that the reaction may have been due to cross-reactivity with antigens from fungi to which the patient was sensitized (*C herbarum*, *A alternata*, *A fumigatus*, *P notatum*, *Malassezia furfur*, and mushroom).

Proteins ranging from 5 to 100 kDa have been described in beer and include mainly albumins, globulins, serpin, amylase inhibitors, lipid-binding proteins, chaperones, and enzymes. During the manufacturing process, proteins can also be modified. The proteins most frequently found in beer are serpin-Z-4 (45 kDa) and LTP (9 kDa) [10]. The result of SDS-PAGE immunoblotting suggests that these proteins were not involved in the present case, as they were not recognized by the patient's serum. *S cerevisiae* proteins of 97 kDa, 80 kDa, 55 kDa, 40 kDa, 32 kDa, and 17 kDa, which have not been

previously reported, might be the responsible for the patient's condition.

We present a case of beer and wine allergy caused by allergy to *S cerevisiae*, which is used in the fermentation of both beverages. When this allergenic source is heated, it does not cause allergy symptoms. Given that the patient in the present report tolerates bread, we believe that some *S cerevisiae* allergens can be inactivated with heat. She had a previous history of respiratory allergy due to *A alternata* and subsequently developed anaphylactic reactions after drinking beer and wine. Therefore, we think that the primary sensitization could be due to environmental fungi. More research will be necessary to identify and characterize the allergenic proteins of *S cerevisiae*.

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#### Conflicts of Interest

The authors declare that they have no conflicts of interest.

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