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Hydrolysate of highly digestible phosphorylated buckwheat major allergen Fag e 2 attenuates allergic reactions in Fag e 2-sensitized mice

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Abstract

Fag e 2 is a 16 kDa major buckwheat allergen that is highly resistant to pepsin digestion. We previously reported that phosphorylation reduced the IgE-binding activity of Fag e 2 and oral administration of phosphorylated Fag e 2 (P-Fag e 2) attenuated allergic reactions in mice. In this study, we investigated the effects of phosphorylation on the digestibility of Fag e 2 and assessed whether digested P-Fag e 2 (DP-Fag e 2) can attenuate allergic reactions in Fag e 2-sensitized mice. Recombinant Fag e 2, obtained using the *Pichia* expression system, was phosphorylated via dry-heating in the presence of pyrophosphate. The peptic digestibility of Fag e 2 was enhanced by phosphorylation. Mice orally administered DP-Fag e 2 for 6 weeks after Fag e 2 sensitization exhibited reduced allergic symptom scores compared to those of sham-treated mice. Furthermore, decreased total and specific IgE, decreased specific IgG_1, and increased total IgA were observed in the serum of the DP-Fag e 2-fed group. These results suggest that P-Fag e 2 is easily digested in the stomach and induces the attenuation of the IgE-mediated allergic reaction.

Keywords : buckwheat, Fag e 2, allergy, phosphorylation, digestibility

I Introduction

Buckwheat (*Fagopyrum esculentum*) is a pseudocereal with rich nutritive benefits that originated in Asia and spread throughout the northern hemisphere[1, 2]. Buckwheat allergy is a typical IgE-mediated type I hypersensitivity and is considered a major inducer of anaphylaxis[3]. Buckwheat contains a variety of allergens with molecular weights of 9, 16, 19, and 24 kDa[4]. The 16 kDa protein is a major buckwheat allergen, also known as Fag e 2, belonging to the 2S albumin family, which shares a conserved motif of 8 cysteine residues that form disulfide bonds[5, 6]. In general, buckwheat allergens with molecular weights higher than 16 kDa are more susceptible to pepsin digestion, In contrast, owing to its high resistance to proteolysis, Fag e 2 plays an important role in buckwheat allergy[7].

Specific immunotherapy (SIT) is a promising treatment for food allergy; however, the use of crude allergen extracts can result in serious side effects[8, 9]. In our previous study, the allergenicity of Fag e 2 was attenuated by phosphorylation and the oral administration of phosphorylated Fag e 2 (P-Fag e 2) exhibited decreases in both allergic score and Fag e 2-specific IgE levels with attenuation of the Th2-dominated reaction in Fag e 2-sensitized mice[10]. We also found that phosphorylation of buckwheat allergen Fag e 1 resulted in the attenuation of allergic reactions in Fag e 1-sensitized mice[11]. Thus, phosphorylated hypoallergenic proteins appear to be good candidates for immunotherapeutic food allergy treatments. On the contrary, enzymatic digestion can also alter allergenicity by cutting the epitope region. The gastric digestion of bovine milk proteins reduced allergenicity; the digestibility and antigenicity of β-lactoglobulin were affected by several factors, such as heat, pH, and applied shear[12, 13]. Therefore, we hypothesized that the combination of phosphorylation and enzymatic digestion would provide a safer and more effective method. In this work, we first investigated the effects of

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