



Preventive effects of skullcap (*Scutellaria baicalensis*) extract in a mouse model of food allergy



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ABSTRACT

Ethnopharmacological relevance: Food allergy, which accompanies acute symptoms such as pruritus, vomiting, diarrhea, and lethal anaphylactic shock is an increasing clinical problem. Skullcap (*Scutellaria baicalensis* Georgi) has been widely used as a traditional herbal medicine to treat inflammation, cancer, and allergy, but its effects in treating food allergy are not yet known.

Materials and methods: To examine the effect of skullcap on food allergy, female BALB/c mice were sensitized with 20 µg OVA and 2 mg alum by intraperitoneal injection on day 0. From day 17, mice were orally challenged with OVA (50 mg) in saline every 3 days, for a total of six times. To investigate the preventive effect, skullcap (25 mg/kg) was orally administered every day from day 17 to 34.

Results: Food allergy symptoms were evaluated by the criteria for diarrhea, anaphylactic response, and rectal temperature. Severe symptoms of food allergy were observed in the sham group (diarrhea, 3 points; anaphylactic response, 2.6 points; rectal temperature, −8.36 °C. In contrast, the skullcap treatment group had a significantly suppressed OVA-induced anaphylactic response (1.3 points) and rectal temperature (−4.76 °C). Moreover, both OVA-specific IgE, Th17 cytokine (IL-17), and Th2-related cytokines (IL-4, IL-5, IL-10, and IL-13), which increased with food allergy, were significantly inhibited by skullcap treatment.

Conclusion: We demonstrate that the administration of skullcap attenuates OVA-induced food allergy symptoms through regulating systemic immune responses of Th cells. These results indicate that skullcap may be a potential candidate as a preventive agent for food allergy.

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1. Introduction

Food allergy, a hypersensitivity disorder caused by substances derived from foods, occurs when the immune system reacts to food allergens after ingestion. In other words, food allergy is defined as abnormal immune responses resulting from breakdown of natural oral tolerance. Food allergy accompanies acute symptoms such as pruritus, abdominal pain, vomiting, diarrhea, urticaria, hypotension, and, in severe cases, lethal anaphylactic shock (Ben-Shoshan and Clarke, 2011; Benhamou et al., 2010). Food allergy is an increasing clinical problem and has been estimated to

affect 5–6% of the pediatric and 3–4% of the adult population (Sampson, 1976; Venter et al., 2008).

Common well-known food allergens are ovalbumin (OVA) and ovomucoid from eggs, caseins and beta-lactoglobulin from milk, gliadin from wheat, peanut agglutinin from peanuts, and tropomyosins from shrimp (Tanabe, 2007). These orally ingested food allergens trigger and generate allergic responses through various cellular interactions and molecular mechanisms. Initially, allergens are permeated into the gastrointestinal tract via the paracellular diffusion pathway (Kaminogawa et al., 1999). Permeated allergens are attacked and presented as small peptide fragments to CD4⁺ T cells by antigen presenting cells. The interaction between APCs and CD4⁺ T cells leads to T cell proliferation and T-helper 2 (Th2) cytokine secretion. Subsequently, Th2 cells produce cytokines such as IL-4, IL-5, and IL-13 and induce the production of antigen-specific immunoglobulin E (IgE) from B cells. The IgE thus produced binds to the IgE surface receptor FcεRI on mast cells. Finally, mast cells are exposed to re-permeated allergens and activated through cross-linking between IgE and allergens. Allergen-provoked mast cells trigger their degranulation; thereafter, allergic inflammatory mediators such as histamine, prostaglandin, and leukotriene are released, which cause allergic symptoms (Galli et al., 2008; Bischoff and Crowe, 2005).

Abbreviations: APC, antigen presenting cell; D-PBS, Dulbecco's phosphate-buffered saline; Foxp3, forkhead box P3; IFN, interferon; Ig, immunoglobulin; IL, interleukin; MLN, mesenteric lymph node; OVA, ovalbumin; TGF, transforming growth factor; Th, T helper; Treg, regulatory T

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Recently, several studies have demonstrated that natural products, foods, microbiota, and chemicals can regulate food allergy symptoms in experimental mouse models (Wang et al., 2013; Bae et al., 2013; Noval Rivas et al., 2013; Yamaki and Yoshino, 2012). For instance, resveratrol, a polyphenol from red wine, has been shown to prevent food allergy symptoms (loss of body temperature, increase of IgE, and over-expression of IL-13); this preventive effect of resveratrol was derived by inhibiting dendritic cell maturation and T cell activation (Okada et al., 2012). These studies have shown the potential of certain agents to treat and/or prevent food allergy.

Skullcap (*Scutellaria baicalensis* Georgi), especially its root, has been widely used as both a dietary ingredient and traditional herbal medicine in Korea, Japan, and China to treat inflammation, cancer, and bacterial and viral infections of the respiratory tract and gastrointestinal tract (Lu et al., 2011; Yoon et al., 2009; Ye et al., 2002; Kim et al., 2009). Furthermore, anti-allergic effects of skullcap in allergic disorders such as asthma and atopic dermatitis have been documented (Kim et al., 2013; Jang et al., 2012). For example, in a previous study, the skullcap extract significantly suppressed IgE levels and IL-5 production in the NC/Nga mice model of atopic dermatitis (Kim et al., 2010). However, the effect of skullcap in food allergy is not yet known.

The aim of the present study was to evaluate whether skullcap extract can improve allergic symptoms, including diarrhea, anaphylactic response, and rectal temperature, in an OVA-induced food allergy model. We also investigated the anti-allergic effects of skullcap through measuring IgE and cytokine levels in food allergy.

2. Material and methods

2.1. Materials

RPMI 1640 medium, fetal bovine serum, penicillin–streptomycin, and Dulbecco's phosphate-buffered saline (D-PBS) were purchased from WelGENE (Daegu, Korea). OVA (grade VI) and red blood cell lysis buffer were purchased from Sigma-Aldrich (St. Louis, MO, USA).

2.2. Sample preparation

The skullcap used in this study was purchased from Kyeong-dong Oriental Pharmacy (Seoul, Korea) and identified by Professor Y. Bu, Department of Herbal Pharmacology, Kyung Hee University. The specimen (KFRI-SL-101) has been stored at the Functional Materials Research Group, Korea Food Research Institute. Skullcap sample was obtained by reflux extraction twice in 70% ethanol using a Soxhlet apparatus. The ethanol extract was dried under a vacuum in a rotary evaporator. Lastly, the concentrated extract was lyophilized to yield a dried powder that was stored at 4 °C until needed. The dried ethanol extract was dissolved in saline prior to use.

2.3. Animals

Female BALB/c mice, weighing approximately 18–20 g, were purchased from OrientBio Inc. (Kyeonggi, Korea). BALB/c mice (6 weeks old) were housed in an air-conditioned room (23 °C ± 2 °C) with a 12-h light/dark cycle. Mice were allowed free access to food and water. All animal experiments were performed in accordance with the guidelines for animal use and care of the Korea Food Research Institute.

2.4. Induction of anaphylactic response by oral administration of OVA

Mice were divided into naïve ($n=5$), sham ($n=9$), and skullcap ($n=9$) groups. To induce an allergic response, mice were sensitized with 20 µg OVA adsorbed in 2 mg/mL Imject Alum (Pierce, Rockford,

IL, USA) by intraperitoneal (i.p.) injection on day 0. From day 17, mice were orally challenged with 50 mg OVA in saline every 3 days, for a total of six times. To investigate the preventive effect of skullcap, the skullcap (25 mg/kg) was orally administered every day, from day 17 to 34 (Fig. 1). Diarrhea, anaphylaxis, and rectal temperature were measured as an index of food allergy symptoms. Diarrhea and anaphylaxis were observed by visually monitoring mice for 60 min after challenge. Diarrhea was scored as follows: 0, normal stools; 1, a few wet and unformed stools; 2, a number of wet and unformed stools with moderate perianal staining of the coat; and 3, severe and watery stool with severe perianal staining of the coat. Anaphylactic response was also scored as follows: 0, no symptom; 1, reduced activity, trembling of limbs; 2, loss of consciousness, no activity upon prodding; 3, convulsions; and 4, death. Rectal temperature was measured using a Thermalert TH5 monitoring thermometer (Physi-temp, Clifton, NJ, USA).

2.5. Measurement of immunoglobulins (IgE/IgG1/IgG2a) from mouse serum

To measure immunoglobulin levels, serum samples from each group were obtained by collecting blood from the orbital venous plexus. An ELISA protocol was used to determine the total and OVA-specific IgE/IgG1/IgG2a antibody levels in the samples. Aliquots (200 µL/well) of IgE/IgG1/IgG2a capture antibody (BD Pharmingen, San Diego, CA, USA) or OVA (10 µg/mL dissolved in 0.1 mol/L NaHCO₃, pH 8.2; Wako Pure Chemical Industries) were coated on 96-microwell plates (Nunc, Thermo Fisher Scientific, Roskilde, Denmark). The plates were incubated overnight at 4 °C and then carefully washed 3 times with washing buffer (0.5 g/L Tween 20 in PBS). Serum samples were diluted 1:5 for total and specific IgE/IgG1/IgG2a determinations. Aliquots (100 µL) of diluted serum samples were added to the wells. Total and OVA-specific IgE/IgG1/IgG2a levels were determined using biotin-conjugated rat anti-mouse IgE/IgG1/IgG2a (BD Pharmingen) according to the manufacturer's protocols. The plates were read using an ELISA plate reader (Molecular Devices, Inc.) at 450 nm.

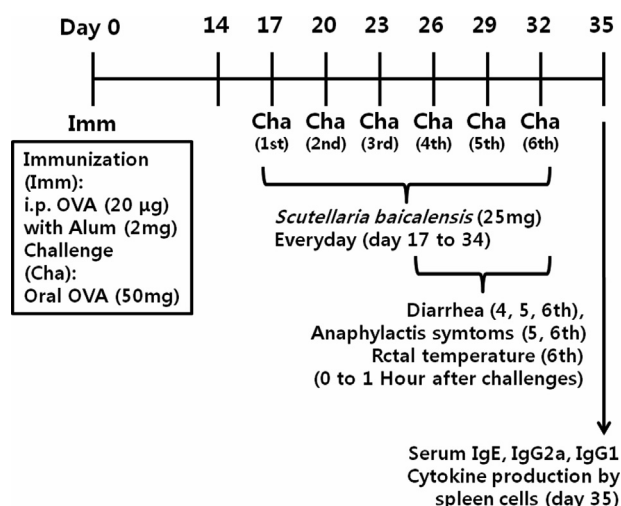


Fig. 1. Timeline of experimental procedures. Female BALB/c mice (6 weeks old) were divided into naïve ($n=5$), sham ($n=9$), and skullcap ($n=9$) groups. To induce food allergy, mice were immunized with 20 µg OVA and 2 mg Imject Alum by intraperitoneal (i.p.) injection on day 0. From day 17, mice were orally challenged with 50 mg OVA in saline every 3 days, for a total of six times. To investigate the preventive effect of skullcap, 25 mg/kg skullcap was administered orally every day from day 17 to 34. Diarrhea (4th, 5th, and 6th challenges), anaphylaxis (5th and 6th challenges), and rectal temperature (6th challenges) were measured for 1 h as an index of food allergy symptoms.

2.6. Measurement of cytokines from cultured splenocytes in mice

A cytokine assay kit (BD Pharmingen) was used to measure cytokine levels (interferon-gamma (IFN- γ), IL-12, IL-4, IL-5, IL-13, IL10, and IL-17) in the supernatant, according to the manufacturer's protocols. Briefly, recovered supernatants and standard solutions were transferred to 96-well plates pre-coated with the appropriate monoclonal antibodies raised against each of the target cytokines, and then incubated at room temperature for 2 h. After thorough washing with the wash buffer included in the kit, a horseradish peroxidase-conjugated secondary antibody was added to each well, and incubation was continued at room temperature for 2 h. After removal of the secondary antibody, the substrate solution for the enzymatic reaction was added, and samples were incubated for another 30 min in the dark. The reaction was terminated by addition of stop solution, and absorbance was measured at 450 nm using a microplate reader (Molecular Devices, Inc.).

2.7. Statistical analysis

Each result is expressed as the mean $\pm$ standard deviation (SD). Differences between the experimental data were assessed by 1-way analysis of variance (ANOVA) followed by F-protected Fisher's least significant difference test.

3. Theory/calculation

3.1. Theory

Skullcap extract is traditionally used for the treatment of allergic and inflammatory diseases such as bronchitis, jaundice, and stroke. However, the scientific proof for anti-allergic effects of skullcap extract is not clear, especially for food allergy. In this study, we examined the anti-allergenic effects of skullcap extract in a Th2-induced food allergy model.

3.2. Calculation

Th2 cells producing IL-4, IL-5, and IL-13 play a critical role in the initiation phase of food allergy progression. Skullcap administration attenuated Th2 cell-mediated allergic responses in an OVA-induced food allergy model. Moreover, our results strongly suggest that the mechanism underlying these effects on OVA-induced Th2-dominant immune responses promoted Th1 responses through the production of IFN- γ and IL-12. These results indicate that skullcap is a useful agent for preventing food allergic disorders.

4. Results

4.1. Effect of skullcap on OVA-induced food allergy symptoms (diarrhea, anaphylactic response, and rectal temperature)

Food allergy symptoms induced by OVA were evaluated and scored by the criteria for diarrhea (4th, 5th, and 6th challenges), anaphylactic response (5th and 6th challenges), and rectal temperature (6th challenge). Severe symptoms of OVA-induced food allergy were observed in the sham-treated group (diarrhea, 3 points; anaphylactic response, 2.6 points). In contrast, the skullcap-treated group showed a significant suppression of the oral OVA challenge-induced anaphylactic response (1.3 points), although skullcap administration did not affect diarrhea symptoms (Fig. 2). We also measured rectal temperature for 1 h after

the 6th challenge with OVA. Rectal temperature in the sham group was decreased to -8.36°C compared to the normal group. However, skullcap treatment in our food allergy model significantly ameliorated the decrease in the rectal temperature by OVA to -4.76°C (Fig. 3). These results demonstrate that skullcap administration can attenuate food allergy through inhibition of the anaphylactic response.

4.2. Inhibitory effects of skullcap on IgE levels in serum of OVA-induced mouse model of food allergy

As demonstrated, we have verified the anti-allergic effects of skullcap on food allergy symptoms, for the first time. Next, we investigated immunoglobulin levels (IgE, IgG1, and IgG2a) in our food allergy mouse model. Both total and OVA-specific IgEs (Th2-related Ig and allergic mediator) were increased with food allergy in response to OVA, whereas skullcap administration suppressed total and OVA-specific IgEs (Table 1). Specifically, OVA-specific IgE was significantly reduced by skullcap treatment compared to the sham group. Furthermore, total and OVA-specific IgG1 (Th2-related Ig) levels that were increased by OVA administration in the sham group were unaffected by skullcap administration. However, total and OVA-specific IgG2a (Th1-related Ig) serum levels showed a tendency of increasing following skullcap treatment. These results indicate that the administration of skullcap promotes an anti-allergic effect by regulating T cell-mediated response.

4.3. Immunomodulatory effect of skullcap on cytokine patterns in splenocytes of OVA-induced mouse model of food allergy

We next investigated the cytokine patterns in splenocytes isolated from mice with OVA-induced food allergy. IL-4, IL-5, IL-10, and IL-13 were taken as a measure of Th2-related cytokines. All of the Th2-related cytokines (IL-4, IL-5, IL-10, and IL-13) showed increased patterns following food allergy and were significantly inhibited by treatment with skullcap (Fig. 4A–D). Th1-related cytokines such as IFN- γ and IL-12 decreased in the sham group, but their levels increased with skullcap treatment (Fig. 4E and F). We also investigated IL-17 as a Th17-related cytokine for food allergy. IL-17 production was observed to increase in food allergy and was significantly suppressed by skullcap treatment (Fig. 4G). These results indicate that the administration of skullcap regulates the Th1 and Th2 balance by enhancing the Th1 response and suppressing the Th2 response from abnormal Th2 dominance from allergic responses to food.

4.4. Effect of skullcap on mortality by anaphylactic shock in OVA-induced mouse model of food allergy

We next investigated the effect of skullcap on mortality by anaphylactic shock in OVA-induced food allergy. Mice were immunized twice with 20 μg OVA and then orally challenged six times with 50 mg OVA (Fig. 5A). A severe anaphylactic response was observed from the 4th oral challenge of OVA in the sham group, with a final survival rate of 20%. In contrast, the skullcap treatment group had reduced mortality by anaphylactic shock with a survival rate of 60%. Our results indicate that the administration of skullcap could be used to prevent anaphylactic response and shock occurring with food allergy.

5. Discussion

In the present study, we revealed that the administration of skullcap attenuated symptoms (anaphylactic response and rectal

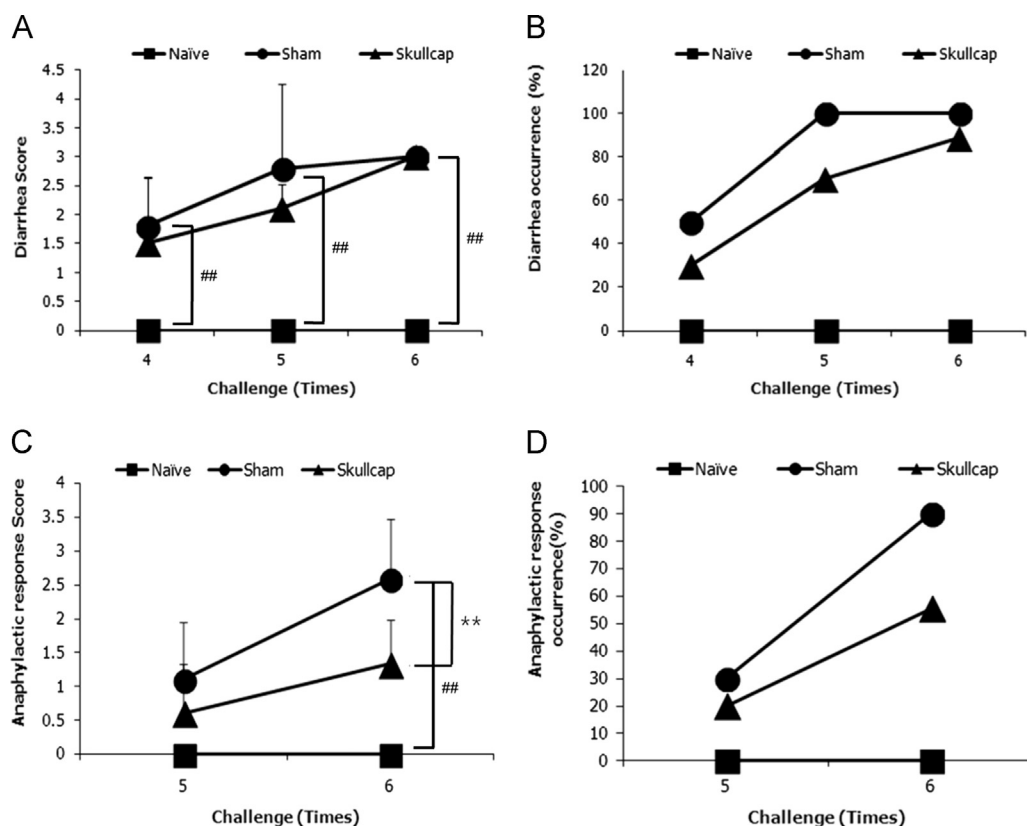


Fig. 2. Effect of skullcap on OVA-induced diarrhea and anaphylactic response. Food allergy symptoms induced by OVA were evaluated and scored by criteria for diarrhea symptoms and anaphylactic response for 1 h after challenge with OVA. Diarrhea score (A) and diarrhea occurrence (% score ≥ 2) (B) were evaluated on the 4th, 5th, and 6th challenges. Anaphylactic response score (C) and anaphylactic response occurrence (% score ≥ 2) were also evaluated on the 5th and 6th challenges. Each value is presented as mean $\pm$ SD (naïve, $n=5$; sham and skullcap, $n=9$). Bars represent significant difference from the naïve group at $^{\#}P < 0.05$ and $^{\#\#}P < 0.01$ and the sham group at $^{\ast}P < 0.05$ and $^{\ast\ast}P < 0.01$. Data were analyzed using ANOVA followed by F-protected Fisher's least significant difference test.

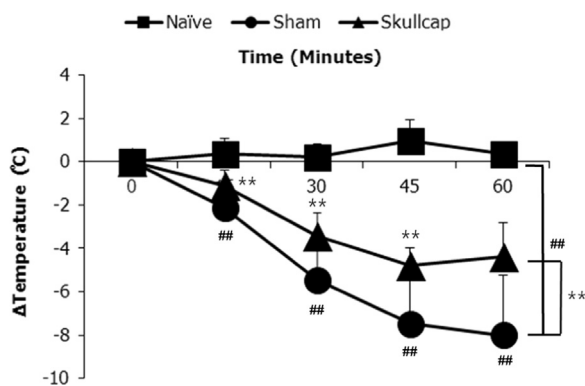


Fig. 3. Effect of skullcap in attenuating OVA-induced rectal temperature changes. Rectal temperature was measured every 15 min for 1 h after the 6th challenge of OVA. Each value is presented as mean $\pm$ SD (naïve, $n=5$; sham and skullcap, $n=9$). Bars represent significant difference from the naïve group at $^{\ast}P < 0.05$ and $^{\#\#}P < 0.01$ and the sham group at $^{\ast}P < 0.05$ and $^{\ast\ast}P < 0.01$. Data was analyzed using ANOVA followed by F-protected Fisher's least significant difference test.

Table 1

Effect of skullcap on immunoglobulin levels in serum.

	Immunoglobulins		
	Naïve	Sham	Skullcap
Total (ng/mL)			
IgE	562.95 $\pm$ 137.25	4811.8 $\pm$ 1820.8 $^{\#\#}$	4551.8 $\pm$ 1197.8
IgG1	238.68 $\pm$ 111.05	3330.86 $\pm$ 1373.67 $^{\#\#}$	3333.07 $\pm$ 1262.88
IgG2a	870.1 $\pm$ 67.98	592.65 $\pm$ 258.32 $^{\#}$	618.83 $\pm$ 113.57
OVA-specific (O.D. value at 450 nm)			
IgE	N.D.	0.0948 $\pm$ 0.0293	0.05 $\pm$ 0.0294 **
IgG1	N.D.	0.6627 $\pm$ 0.054	0.6773 $\pm$ 0.0606
IgG2a	0.0822 $\pm$ 0.0313	0.5726 $\pm$ 0.3265 $^{\#}$	0.6954 $\pm$ 0.4506

To measure immunoglobulin levels, serum samples from each group were obtained by collecting blood from the orbital venous plexus. Serum samples were diluted 1:5 for total and specific IgE/IgG1/IgG2a determinations, and levels determined by ELISA. Each value is presented as mean $\pm$ SD (naïve, $n=5$; sham and skullcap, $n=8$). Bars represent significant difference from the naïve group at $^{\ast}P < 0.05$ and $^{\#\#}P < 0.01$ and the sham group at $^{\ast\ast}P < 0.01$. Data were analyzed using ANOVA followed by F-protected Fisher's least significant difference test.

temperature) of food allergy (Figs. 2 and 3). Skullcap also inhibited IgE levels and Th2-related cytokine production (IL-4, IL-5, IL-10, and IL-13), which were increased with food allergy, as well as suppressed IL-17 production (Table 1 and Fig. 4). Herein, we have demonstrated the inhibitory effect of skullcap in an OVA-induced food allergy model for the first time; these results provide a scientific rationale for the use of skullcap as an anti-allergic agent.

Food allergy symptoms such as diarrhea and anaphylaxis were immediate and appeared in the first hour following challenge. Our results also showed severe diarrhea and anaphylaxis in the sham

treatment group. Interestingly, skullcap treatment resulted in a mild anaphylactic response and severe diarrhea (Fig. 2). This result indicated that skullcap regulates a systemic immune response, but not an intestinal immune response. We also investigated cytokine patterns in the mesenteric lymph node (MLN) isolated from the small intestine. Administration of skullcap did not exert an influence on cytokine levels (IL-4, IL-5, IL-13, IL-10, IFN- γ , and IL-12) in MLN (data not shown). Therefore, we have demonstrated that skullcap treatment could attenuate food allergy symptoms such as anaphylactic response by regulating the systemic immune response.

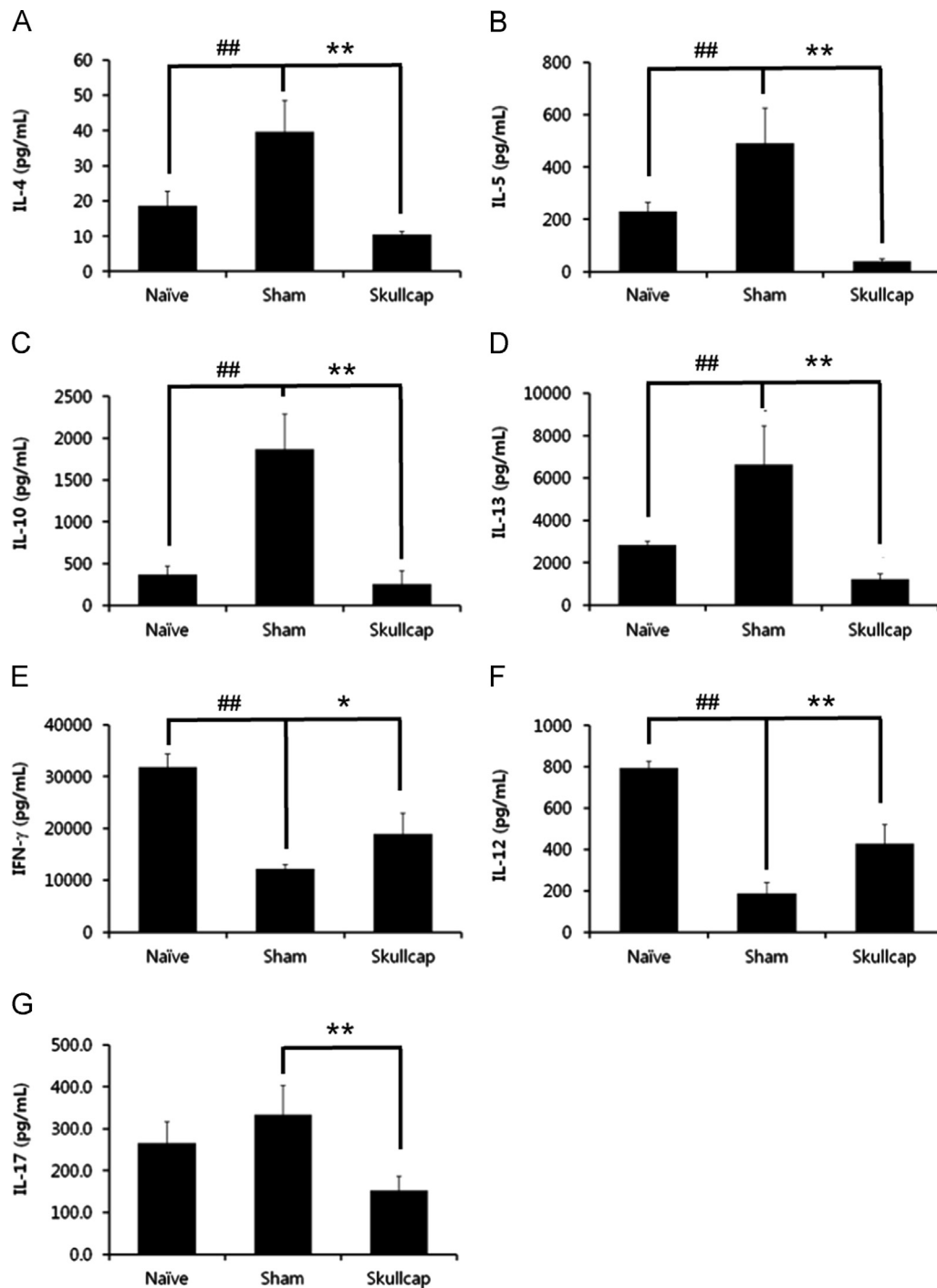


Fig. 4. Immunomodulatory effects of skullcap on cytokine patterns in splenocytes. Mice were sacrificed by cervical dislocation on day 35, and spleens were removed. Splenocytes were isolated from the spleen and cultured in RPMI medium containing 10% FBS for 72 h. Cytokines secreted from splenocytes were measured by ELISA. IL-4 (A), IL-5 (B), IL-10 (C), and IL-13 (D) were measured as Th2 cytokines. IFN- γ (E), IL-12 (F) were measured as Th1 cytokines and IL-17 (G) as a Th17 cytokine. Each value is presented as mean $\pm$ SD ($n=3$). Bars represent significant difference from the naïve group at $^*P < 0.05$ and $^{##}P < 0.01$ and the sham group at $^*P < 0.05$ and $^{**}P < 0.01$. Data were analyzed using ANOVA followed by F-protected Fisher's least significant difference test.

In our food allergy model, mice were administered skullcap orally at 25 mg/kg body weight for 18 days. The dosages of skullcap for treatment of many diseases such as inflammation (50–100 mg/kg), nausea (0.3–3 mg/kg), cancer (75 mg/kg), allergic diseases (25 mg/kg), and diabetes (400 mg/kg) reported by studies were various (Jeong et al., 2011; Aung et al., 2005; Zhang et al., 2003; Shin et al., 2014; Waisundara et al., 2008). To determine the correct concentration of skullcap, we examined 25, 100, or 250 mg/kg body weight treatments of skullcap in

in vivo experiments. We also monitored body weight changes every day and measured cytotoxicity in splenocytes by using the MTT assay. Neither changes in body weight nor cytotoxicity were apparent, even at the highest concentrations of skullcap evaluated (250 mg/kg). Interestingly, the anti-allergic effects of skullcap were similar at all three concentrations (data not shown). We hypothesize that anti-allergic effects of skullcap are not enhanced above the fixed dose of skullcap (25 mg/kg) as reported herein.

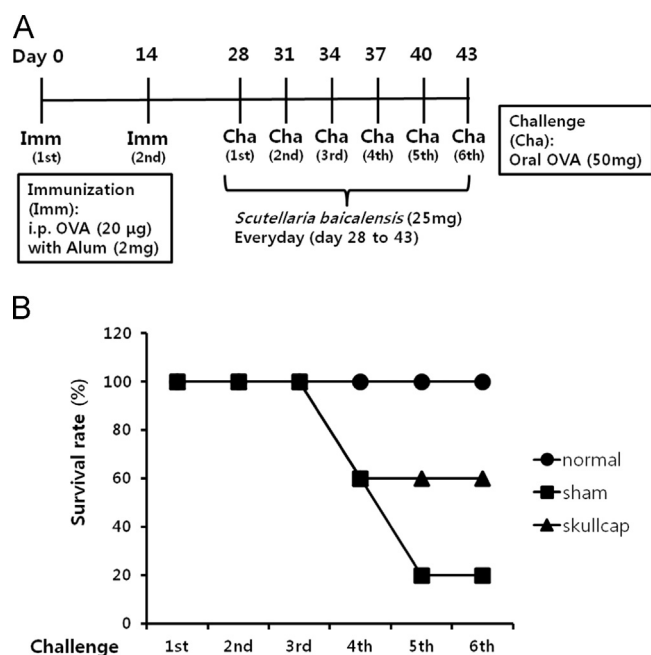


Fig. 5. Effect of skullcap on mortality by anaphylactic shock following OVA-induced food allergy. Female BALB/c mice (6 weeks old) were divided into naïve ($n=5$), sham ($n=5$), and skullcap ($n=5$) groups. (A) To investigate mortality by anaphylactic shock following food allergy, mice were immunized twice with 20 µg OVA and 2 mg Imject Alum by intraperitoneal (i.p.) injection on days 0 and 14. From day 28, mice were orally challenged with 50 mg OVA in saline every 3 days, for a total of six times. Skullcap (25 mg/kg) was orally administered every day from days 28 to 43. (B) Mortality was observed with food allergy symptoms (diarrhea, anaphylaxis, and rectal temperature) and shown as survival rate (%).

Our results showed that the administration of skullcap regulates systemic immune responses by enhancing Th1 from the Th2-dominant allergic response following food allergy (Fig. 4). Previous reports have indicated that IL-17 production is increased with food allergy (Yamaki and Yoshino, 2012). We have also investigated the regulatory effects of skullcap treatment on IL-17 (Th17-related cytokine) production. Skullcap treatment was shown to significantly inhibit IL-17 production following food allergy (Fig. 4G). In general, IL-17 is mainly produced by Th17 cells, which are activated and play a key role in inflammatory diseases and autoimmune disorders such as rheumatoid arthritis, systemic lupus erythematosus, and inflammatory bowel disease (Li et al., 2013; Robak et al., 2013; Maddur et al., 2012). Under normal immune conditions, Th17 cells maintain a balance with regulatory T cells (Treg) (Hanidziar and Koulmanda, 2010). Tregs also suppress other T cell subsets such as Th1 and Th2 cells through the induction of immune tolerance or immune suppression in addition to Th17 cells (Stummvoll et al., 2008). Furthermore, recently one of components in skullcap, baicalin, was reported to induce Tregs through expression of forkhead box3 (Foxp3) (Yang et al., 2012). To prove whether skullcap treatment induces Tregs, we measured transforming growth factor beta (TGF- β) production using ELISA and Foxp3 expression by using FACS analysis. We observed both TGF- β production and Foxp3 expression were not significantly augmented by skullcap treatment (data not shown). Thus, the inhibitory effect of skullcap on food allergy may result from the suppression of Th2 cells or Th17-induced allergy response by skewing Th1 differentiation, but it is not likely via the induction of Treg differentiation.

Skullcap contains many components, and more than 60 structures have been identified (Li et al., 2004). Among these components, the major compounds of skullcap have been well known, such as baicalein, baicalin, and wogonin. In particular, the

baicalein and baicalin were reported; their anti-allergy effects in allergic disorders such as atopic dermatitis and asthma although anti-allergic effect of them were not revealed (Huang et al., 2009; Yun et al., 2010). However, we recently revealed that the baicalein as an active component enhanced intestinal barrier function through increasing expression of tight junction proteins, but not baicalin (Shin et al., 2013). The enhancing of intestinal barrier function may contribute to prevention of food allergic responses through inhibiting allergen permeation (Ventura et al., 2006). Therefore, we suggest as a possible hypothesis that baicalein as an active component of skullcap may prevent the food allergy.

6. Conclusion

In the present study, we have demonstrated that administration of skullcap attenuates OVA-induced food allergy symptoms by enhancing a systemic immune response via augmentation of the Th1 response and inhibition of the Th2 and Th17 responses. Our results demonstrate the efficacy of skullcap as an anti-allergic agent for food allergy in a murine model for the first time and elucidate the anti-allergic mechanism of skullcap following food allergy. These results provide evidence that oral administration of skullcap can contribute to the prevention of food allergy disorder in an ethnopharmacological therapy.

Acknowledgments

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