Effect of Oral Administration of *Scutellaria Baicalensis* Root Extract on Atopic Dermatitis-like Skin Lesion Induced by Oxazolone in Hairless Mice

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**Abstract**

Effect of oral administration of methanolic extract from *Scutellaria baicalensis* root (SB) on the development of oxazolone-induced atopic dermatitis-like skin lesions in hairless mice was investigated. Mice were orally administered SB 250, 500 mg/kg/day, or dexamethasone 1 mg/kg/day for 33 days. Oral administration of SB inhibited the development of clinical symptoms, and reduced dermal mast cell infiltration, but did not show definite suppressive effect on elevation of serum total IgE level under experimental condition. Interleukin (IL)-6 level in serum and the mRNA expressions of IL-4, IL-13, IL-12, interferon-γ, transforming growth factor-β, and fork head box P3 in draining lymph nodes were not significantly affected by SB administration, indicating SB could alleviate atopic dermatitis via the inhibition of mast cell infiltration.

**Keywords**

atopic dermatitis · extract from *Scutellaria baicalensis* root · mast cells · oxazolone · immunoglobulin E

**Introduction**

Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disease, and its incidence has doubled or tripled in industrialized countries during the past three decades (Leung et al., 2004; Bieber, 2010). Though the lifetime prevalence of AD is estimated to be 15–30% in children and 2–10% in adults, AD can be problematic because it is often the first step in the atopic march preceding asthma and/or allergic rhinitis (Leung et al., 2004; Bieber, 2010).

AD is a complex disease involving gene-gene and gene-environment interactions (Bieber, 2010). The pathogenesis of AD is not fully understood. Patients with AD generally have peripheral blood eosinophilia and high levels of serum IgE due to the elevated production of interleukin (IL)-4 and IL-13 and suppression of IFN-γ production in acute lesional skin (Leung et al., 2004). IL-4 and IL-13 are T helper (Th) 2-type cytokines inducing isotype switching to IgE synthesis, and interferon (IFN)-γ and IL-12 are Th1-type cytokines (Leung et al., 2004; Kindt et al., 2007). Moreover, regulatory T cells (Treg cells) are key regulators of the immunologic processes associated with the development of peripheral tolerance to allergens, and they play a suppressive role on both Th1 and Th2 responses (Akdis et al., 2005). In addition, mast cells play a significant role in AD via IgE-mediated sensitization and the activation of mast cells localized in the skin by IgE (Cookson, 2004; Kawakami et al., 2009; Liu et al., 2011). The release of preformed mediators, such as histamine and leukotrienes, and various proinflammatory cytokines promote allergic inflammatory response (Kawakami et al., 2009).

Several murine models have been developed and characterized to display certain features of AD. They include NC/Nga, hapten-induced model, transgenic, and knockout mice (Shiohara et al., 2004). Among them, mice induced by the repeated application of haptens are used based on the advantages of their short period of induction and reproducibility (Shiohara et al., 2004; Tomimori et al., 2005). As characterized by Man et al. (2008), the oxazolone (Ox)-induced AD model resembles human AD in terms of clinical, physiological, and immunological features such as decreased barrier function, elevated IgE level, Th2-dominant infiltrates, and increased mast cells in skin lesions.

Recently, several studies have reported that oral administration...
of natural immune modulators derived from herbal extracts has preventive or therapeutic effects on AD, whereas oral glucocorticoid, which has been used for the treatment of AD, has adverse effects especially during long term use (Matsumoto et al., 2002; Lee et al., 2006; Park et al., 2007; Kim et al., 2009a; Lee et al., 2009; Bieber, 2010; Hokazono et al., 2010; Kim et al., 2011). To search for a useful food material for the treatment of AD, Ulmus davidiana, Opuntia humifusa, Xanthium strumarium, Dioscorea rhizome, Phellinus linteus, Scutellaria baicalensis, Lithospermum erythrorhiza, Taraxacum platycarpum, Saururus chinensis, fermented Panax ginseng, pine bark, silmarin, borage oil, docosahexaenoic acid, gamma amino butyric acid, baicalin, compound K, and Bifidobacterium bifidum BGN4, which are all known to have anti-allergic and anti-inflammatory effects, were examined.

Scutellaria baicalensis is a widely used traditional Chinese herbal medicine that is also officially listed in the Korea Pharmacopoeia (Li et al., 2004). The root of S. baicalensis contains flavonoids including baicalin, baicalein, wogonin, and oxoroxin A, and is reported to exhibit various beneficial bioactivities such as anti-inflammatory (Kim et al., 2009b; Yoon et al., 2011), anti-allergic (Kim et al., 2010a), antibacterial, and antiviral infection effects in the respiratory and the gastrointestinal tract (Isis, 1997; Li et al., 2004). Moreover, the immunomodulatory effect of Scutellariae radix on spontaneous AD in NC/Nga mice was recently studied (Kim et al., 2010b). In the present study, the effect of methanolic extract from S. baicalensis root (SB) in Ox-induced AD mice was evaluated for the first time. Among the above-mentioned twelve plant extracts and six compounds, SB was found to have significant potential to reduce total IgE level. For a better understanding of the mechanism involved, SB was orally administered daily for 33 days, and the effects on the clinical symptoms, the levels of IgE and IL-6 in serum, mast cell infiltration, and on the mRNA expressions of IL-4, IL-13, IFN-γ, IL-12, transforming growth factor (TGF)-β, and Foxp3 in draining lymph nodes (DLNs) in Ox-induced AD mice were examined.

**Materials and Methods**

**Animals.** Five-week-old female hairless mice were purchased from Orient Co. (Seongnam, Korea) and maintained for one week for acclimation. Animals were under specific pathogen-free conditions at 23±3°C with 50±10% humidity. The mice were provided with a rodent diet NIH-31 Open Formula Auto (Ziegler, Gardners, PA) and water ad libitum with a 12 h/12 h light/dark cycle. All animal experiments were approved by the Institutional Animal Care and Use Committee of Seoul National University.

**Induction of AD-like skin lesions.** Dermatitis was induced with oxazolone (Sigma, St. Louis, MO), and the schematic induction schedules are presented in Fig. 1. Briefly, after one week of acclimation, ear and dorsal skin of the mice were sensitized with 10 µL of 0.5% Ox dissolved in 100% ethanol (day 0). One week after sensitization, ear and dorsal skin were challenged with 20 and 40 µL of 0.1% Ox in ethanol, respectively, and repeated twice with one week interval. Mice were then divided into four groups (Table 1): control group (ox treated), two SB groups, 250 mg/kg (SB250) and 500 mg/kg (SB500), and Dex group (dexamethasone 1 mg/kg) considering both the clinical severity score of day 17 and serum total IgE level of day 20 (n=4). Ox at 0.1% was additionally applied twice and stopped application for 2 weeks. Application was performed again at day 49 and 4 h before sacrifice. Ethanol was applied to naïve group (n=3).

**Preparation of SB and oral administration.** Dried S. baicalensis root was purchased from the oriental drug store, Kyeoung-dong Market (Seoul, Korea). The extraction was performed twice at room temperature with 100% methanol for 24 h, then filtered through Whatman paper no. 2, evaporated, and freeze dried. The yield of SB was about 7%. Freeze-dried powder of SB was dissolved in phosphate buffer saline containing 3% Tween80 and orally administered at 250 and 500 mg/kg daily from day 21 to day 53. Dex was also dissolved in vehicle and orally administered at 1 mg/kg daily. Experimental groups are shown in Table 1.

**Evaluation of clinical severity scores.** Macroscopic severity score of dorsal skin lesion was evaluated with sum of two criteria: erosion/excoriation/hemorrhage and dryness/scaling. Each sign

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**Table 1** Experimental groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Oxazolone induction</th>
<th>Oral administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naïve</td>
<td>X (100% ethanol)</td>
<td>Vehicle (3% Tween80 in PBS)</td>
</tr>
<tr>
<td>Control</td>
<td>O</td>
<td>Vehicle (3% Tween80 in PBS)</td>
</tr>
<tr>
<td>SB250</td>
<td>O</td>
<td>S. baicalensis root extract 250 mg/kg/day</td>
</tr>
<tr>
<td>SB500</td>
<td>O</td>
<td>S. baicalensis root extract 500 mg/kg/day</td>
</tr>
<tr>
<td>Dex</td>
<td>O</td>
<td>Dexamethasone 1 mg/kg/day</td>
</tr>
</tbody>
</table>

**Fig. 1** Schematic representation of the experimental plan.