Review Article

Medicinal potential of *Panax ginseng* and its ginsenosides in atopic dermatitis treatment

Laura Rojas Lorz¹, Mi-Yeon Kim²,*, Jae Youl Cho¹,*

¹ Department of Integrative Biotechnology, Sungkyunkwan University, Suwon, Republic of Korea
² School of Systems Biomedical Science, Soongsil University, Seoul, Republic of Korea

**A R T I C L E  I N F O**

Article history:
Received 7 December 2018
Accepted 31 December 2018
Available online 7 January 2019

Keywords:
Alternative medicine
Atopic dermatitis
Filaggrin
Ginsenosides
*Panax ginseng*

**A B S T R A C T**

Atopic dermatitis (AD) is a chronic and relapsing inflammatory disease that affects 1%–20% of people worldwide. Despite affecting many people, AD current treatments, such as topical corticosteroids and calcineurin inhibitors, have not only harmful secondary effects but are also often ineffective. Therefore, natural nontoxic compounds are on high demand for developing new effective AD treatments. *Panax ginseng* Meyer has been used traditionally for its promising healing and restorative properties to treat many diseases including skin disorders, reason why in this review we want to explore the research performed with AD and *P. ginseng* as well as determining its potential for new drug development. Previous researches have shown that *P. ginseng* has positive effects in AD patients such as lower eczema area and severity index, transdermal water loss, and immunoglobulin E levels and better quality of sleep. In vivo animal models, as well, have shown positive results to *P. ginseng* and derived ginsenosides, such as the decrease of transdermal water loss, immunoglobulin E levels in serum, allergy-related cytokines, and downregulation of NF-κB, MAPK, and Ikaros pathways. All of these previous data suggest that *P. ginseng* and its derived ginsenosides are undoubtedly a nontoxic effective option to treat AD.

© 2019 The Korean Society of Ginseng. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Atopic dermatitis (AD) is a chronic and relapsing inflammatory skin disease characterized by pruritus, erythema, scaling, edema, and inflammatory eczematous eruptions that usually begin early in life [1]. AD is a major global public health problem, affecting 1%–20% of people worldwide, with a prevalence of about 1%–3% in adults and 10%–20% in children [2]. Instead of having one specific cause, AD is considered to be triggered by the interaction of many pathological mechanisms such as genetic background, impaired skin barrier function, impaired immunity, and environmental factors acting synergistically [3]. Despite affecting a great amount of people around the world, effective therapeutic strategies are yet to be established [4]. *Panax ginseng* has been extensively used in Asian traditional medicine because of its healing, restorative, and anti-inflammatory properties [5]. It has also been used in traditional Chinese medicine to treat skin disorders including atopic suppurative dermatitis, but the modern knowledge in this area continues to be lacking [6]. Nowadays, many studies focus on purified individual ginsenosides, which are ginseng’s most important constituents and study their specific mechanism of action, so diseases’ treatment can be more accurate [6]. Because of its traditional use in the treatment of skin disorders, in this review, we aim to examine the research performed with ginseng and determine its potential as a more natural nontoxic alternative for treating AD.

*Abbreviations: AD, atopic dermatitis; ATX, plasma autotaxin; CC, cultivated ginseng; CCL2, Chemokine ligand 2; COX-2, Cyclooxygenase-2; DNPB, 1-fluoro-2,4-dinitrobenzene; DFE, Dermatophagoides farinae body extract; EASY, eczema area and severity index; FLG, filaggrin; GDP, 20-O-β-d-glucopyranosyl-20(S)-proto-panaxadiol; GMCSF, granulocyte macrophage colony-stimulating factor; HMC-1, human mast cell line; IL, interleukin; IFN, interferon; KRG, Korean Red Ginseng; LPS, lipopolysaccharide; MCP-1, monocyte chemoattractant protein-1; MDC, macrophage-derived chemokine; MIP-1alpha, macrophage inflammatory protein-1alpha; MIP-1beta, macrophage inflammatory protein-1beta; NO, Nitric oxide; PMA, phorbol-myristate acetate; RANTES, regulated on activation normal T cell expressed and secreted; RGE, red ginseng extract; TARC, thymus and activation-regulated chemokine; TH cell, lymphocyte T helper cell; TEWL, trans epidermal water loss; TNB, 2,4,6-trinitro-1-chlorobenzene; TNCB, 2,4,6-trinitro-1-fluoro-2,4-dinitrobenzene; TSLP, thymic stromal lymphopoietin.

* Corresponding author. Department of Integrative Biotechnology, Sungkyunkwan University, 2066 Seobu-ro, Suwon 16419, Republic of Korea.

** Corresponding author. School of Systems Biomedical Science, Soongsil University, 369 Sangdo-ro, Seoul 06978, Republic of Korea.

E-mail addresses: kimmy@ssu.ac.kr (M.-Y. Kim), jaecho@skku.edu (J.Y. Cho).

https://doi.org/10.1016/j.jgr.2018.12.012
p1226-8453 e2093-4947/$ – see front matter © 2019 The Korean Society of Ginseng. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
2. AD pathology and mechanism of action

Atopy is defined as an inherited tendency to produce immunoglobulin E (IgE) antibodies in response to minute amounts of common environmental proteins such as pollen, house dust mites, and food allergens [7]. Dermatitis derives from the Greek word ‘derma,’ which means skin and ‘itis,’ which means inflammation, therefore skin inflammation [3]. The occurrence of AD has been associated with two anomalies: the first one corresponding to an imbalance of the adaptive immune system [8] and the second one being the presence of a defective skin barrier [9]. Because AD is strongly correlated to inflammation, several arguments support that AD is primarily an immune disease [8].

The theory of immunological imbalance argues that AD results from an imbalance of T cells, particularly T helper cell types 1 and 2, the latest being the predominant type in AD’s acute phase and the second one predominating in an inflammatory chronic phase [3] (Fig. 1). Antigen-activated TH2 cells cause an increased production of interleukins (ILs), primarily IL-4, IL-5, IL-13, IL-31, and tumor necrosis factor-alpha (TNF-α) [10]. IL-5 induces eosinophil recruitment [11], whereas IL-31 is related to pruritus development [12] and IL-4 enhances B cells to start producing IgE antibodies. When IgE antibodies interact with the specific receptor FcεRI on mast cells, it activates a signaling cascade that ends up with an increase in the intracellular Ca²⁺, mast cell degranulation, and the release of allergic mediators (histamine, prostaglandins, β-hexosaminidase, and leukotrienes) [13]. Mast cell activation is also associated with an increase in Th17-associated cytokines (IL-17A, IL-6, IL-23) [14] and the production of proinflammatory cytokines (IL-1β, IL-6, IL-8) [15,16], and chemokines (macrophage inflammatory protein [MIP]-1α, MIP-1β, regulated on activation normal T cell expressed and secreted, monocyte chemoattractant protein-1) [15], which together with TH1-derived mediators (IL-1β, IL-6, IL-8, IL-10, interferon [IFN]-γ) induce the chronic inflammatory phase of AD (Fig. 1).

The allergic inflammatory response has been associated mainly with the activation of the mitogen-activated protein kinases (MAPKs), which include the extracellular signal-regulated kinase, c-Jun N-terminal kinase, and p38 MAPK [17]. MAPKs are involved in the activation of NF-κB pathway, whose translocation into the nucleus initiates the transcription of inflammatory and allergy-related mediators, reason why regulation of MAPK and NF-κB pathways is considered vital for AD prevention [15]. Another transcription factor involved in the allergic reaction is Ikaros, which has been related to Th2 activation and IL-4 production, therefore playing an important role in AD progression [17].

Barrier function has long been known to be reduced in the skin of patients with AD [9]. Previous studies showed that AD patients had increased transepidermal water loss and that this was due to a loss of function of the filaggrin (FLG) protein [18]. FLG facilitates not only the terminal differentiation of the epidermis but also the formation of the skin barrier, thus having an important role in maintaining the epidermis structure and hydration [19]. Because a defective skin barrier allows allergens to penetrate the epidermis more easily, patients with FLG mutation are more prone to develop AD [20]. Keratinocytes, the main cells in the epidermis, also play an

---

**Fig. 1.** AD patients have a dysfunctional epidermis due to a mutation in the filaggrin gene (FLG) that allows transepidermal water loss (TEWL) and easy entrance of allergens in the skin. Allergens induce the production of the thymus and activation-regulated chemokine (TARC), macrophage-derived chemokine (MDC), and thymic stromal lymphopoietin (TSLP) in the keratinocytes. TSLP activates Langerhans cells (dendritic cells), which induce the differentiation of CD4⁺ T cells into Th2 helper cell type 2 cells (TH2), whose infiltration into tissue is mediated by TARC and MDC. TH2 cells produce IL-4, IL-5, IL-13, and IL-31, among others. IL-31 induces pruritus response in the epidermis, which causes the change into the inflammatory chronic phase. IL-5 is related to eosinophil recruitment to the damaged tissue, whereas IL-4 further induces TH2 polarization and IgE production by B cells. IgE crosslinks with specific receptor FcεRI on mast cells, causing mast cell degranulation and release of allergic mediators (histamine, prostaglandins, leukotrienes, MIP-α, MCP-1, IL-6, and IL-8), which in cooperation with Th helper cells type 1 (TH1) released mediators (IL-1-1, IL-6, IL-8, IL-10, TNF-α, and IFN-γ) enhance the inflammatory phase of AD. Recently, TH17 secreted mediators (IL-17A, IL-6, IL-23) have been shown to play a role in the development of AD. IL, interleukin; AD, atopic dermatitis; IFN, interferon; MCP-1, monocyte chemoattractant protein-1; TNF-α, tumor necrosis factor-alpha; MIP, macrophage inflammatory protein; IgE, immunoglobulin E.
important role in the progression of AD, because, when exposed to allergens or microbes, they are able to secrete Thymus and activation-regulated chemokine (TARC) and macrophage-derived chemokine (C-C motif chemokine ligand 2), which mediate the inflammatory tissue Th2 cells infiltration and thymic stromal lymphopoietin (TSLP), which activates Langerhans cells (dendritic cells) to induce TH2 differentiation [15] (Fig. 1).

3. Commonly used AD treatments

As previously mentioned, it has been generally established that AD patients suffer either a skin barrier dysfunction, skin inflammation, or both, reason why it is difficult to find an adequate treatment and a combined treatment is often recommended [21]. An important feature of AD treatment is the maintenance of skin function; thus, typical AD treatments have included the use of emollients for improving skin hydration and barrier repair [22,23], as well as the elimination of factors (including allergens, irritants, and emotional triggers) that might exacerbate the scratch-itch cycle [24].

Even though emollients are vital for maintaining skin hydration, they cannot be used, for example, against Staphylococcus aureus infection and there is also no definite evidence to prove that their use diminishes AD’s severity [23]. Because chronic and severe pruritus reduces the quality of life in patients and scratching damages the skin barrier and worsens inflammation of the skin, the regulation of both symptoms has become one of the most important aims for the treatment of AD [25]. Previous pruritus’ treatment has included the use of antihistamines and antiallergic drugs [26], which have been shown to help in the pruritus-related insomnia; however, further studies are needed to prove their true efficacy [27]. Previous treatments for managing AD-related inflammation include corticosteroids and calcineurin inhibitors. Corticosteroids act on a variety of immune cells, including T lymphocytes, monocytes, macrophages, and dendritic cells, interfering with antigen processing and suppressing the release of proinflammatory cytokines. However, if used for long terms, they can lead to skin atrophy or the development of rosacea, striae, and hypothalamic-pituitary-adrenal axis alteration, among other secondary effects [28]. Calcineurin inhibitors, even though less potent than steroids, are also used with anti-inflammatory purposes [29]. Calcineurin inhibitors’ common side effects include burning, redness, and pruritus that may appear depending on each patient [7].

On the other hand, several studies have shown that the narrowband UVB (311 nm) and high dose UVA1 (340–400 nm) can act as moderately potent topical steroids for acute, severe atopic eczema. However, special irradiation devices, which are only available in specialist centers, are needed for this type of treatment [30], and depending on the patient, unwanted side effects such as erythema, blistering, hyperpigmentation, and eczema, among others, might appear [31]. In addition, specific AD mediator’s inhibition treatments have been developed as cyclosporine A [32] and azathioprine [33] (Tecll inhibitors), infliximab [34] (TNF-α inhibitor), omalizumab [35] (IgE inhibitor), mepolizumab (IL-5 inhibitor) [11], and dupilumab (IL-4 and IL-13 inhibitors) [36]. Exempting dupilumab, which is currently on medical trial, all remaining treatments have proved to have either low efficacy on AD’s treatment or undesired secondary effects (Table 1).

4. Use of P. ginseng extract and ginsenosides in AD treatment

Ginseng refers to the root and rhizome of P. ginseng (Araliaceae), an herb extensively used in Asia because of its anti-inflammatory, anticancerous, antidiabetic, and antiallergic properties [37].
Ginsenosides, ginseng’s major active pharmacological components, are steroid-like saponins which can only be found in the ginseng species [37]. Besides being used in the treatment of many inflammatory diseases, *P. ginseng* and derived ginsenosides have shown to be effective in the treatment of many skin diseases [38]. Ginseng roots have been used in Chinese medicine to treat skin ailments such as wounds, psoriasis, skin inflammation, and supplicative AD. Nevertheless, relatively few studies have been performed regarding the use of *P. ginseng* in the treatment of AD [6].

*P. ginseng* has been proven to be a good candidate in the treatment of AD because Korean Red Ginseng (KRG) extract trials in AD patients resulted not only in a decrease of eczema area and severity index but also a decrease in the transepidermal water loss [39], IgE serum levels, and skin squamation, while improving the patients sleep disturbance and aiding the stratum corneum recovery [40].

In addition, KRG treatment in 1-fluoro-2,4-dinitrobenzene (DNFB)—induced NC/Nga showed a decrease in ear thickness, TEWL, IgE contents in serum, and AD-related cytokines such as TSLP, TNF-α, IL-4, IL-17, and IFN-γ [41], whereas, when induced with 2,4,6-trinitro-1-chlorobenzene, it not only showed decrease in ear thickness and IgE contents but also downregulated the expression of TSLP, TNF-α, IFN-γ, and IL-31 (Table 2) [42].

| Treatment       | Experimental model                  | Effects                                      | References |
|-----------------|-------------------------------------|----------------------------------------------|------------|
| KRG             | 41 AD patients (KRG consumption for 8 weeks) | (1) EASI, (1) TEWL, (1) pruritus (1) sleep disturbance | [39]       |
|                 | 30 AD patients (KRG consumption for 16 weeks) | (1) Skin squamation (1)TEWL (1) IgE in serum (1) Stratum corneum recovery | [40]       |
| TNCB-treated NC/Nga mice | (1) ear thickness (1)TEWL (1) IgE in serum (1) TSLP (1) TNF-α (1) IL-4, IL-17, IFN-γ | [41]       |
| Compound 48/80—induced anaphylactic shock and DNFB—induced skin lesion in Balb/c mice | (1) AD-like skin lesions and anaphylaxis (1) IL-1β, IL-6, and IL-8 (1) IgE in serum (1) MAPPK and NF-κB pathway | [15]       |
| TNF-α— and IFN-γ—induced HaCaT cells | (1) IL-1β, IL-6, and IL-8 (1) MAPK and NF-κB pathway (1) TARC, MDC | [15]       |
| PMA/A23187—induced HMC-1 cells | (1) MIP-1α, MIP-1β, RANTES, MCP-1 | [15]       |
| TNCB—induced NC/Nga mice | (1) ear thickness (1)TEWL (1) IgE in serum (1) TSLP (1) TNF-α (1) IL-4, IL-17, IFN-γ | [41]       |
| DNCB—induced Balb/c mice | (1) IL-4, IL-10 (1) scratching (1) IgE in serum (1) MAPK, NF-κB, Ikaraos | [17]       |
| DNFB—induced Wistar rats, Balb/c and ICR mice | (1) scratching (1) ear thickness (1) substance P (pruritus related) | [43]       |
| KRG, Rh2, Rg3 | TNBC—treated NC/Nga mice | (1) TNF-α, IL-4, IFN-γ scratching | [10]       |
| Gintonin        | DNFB—induced NC/Nga mice | (1) IgE in serum (1) ear thickness (1) IL-4, IFN-γ (1) ear thickness histamine (1) IgE in serum (1) plasma ATX | [45]       |
| CG              | DNBC—induced NC/Nga mice | (1) IgE in serum (1) IL-4, IL-5, IL-13, TNF-α, IFN-γ (1) ear thickness (1) immune cells infiltration | [44]       |
| GDP             | DFE—induced AD-like symptoms in NC/ Nga mice | (1) dermatitis score (1) ear thickness, (1) scratching (1) skin lesion (1) IL-12, IL-4, IL-5, IL-10, IFN-γ, GM-CSF (1) eosinophils and mast cell infiltration | [46]       |
| RGE, Rh1, Rg1, | IgE crossing linked—KU812 cells | (1) IFN-γ (1) CCL2 | [47]       |
| Rg3, and Rh1    | IFN-γ—induced human epidermal keratinocyte NBHEK (NB) | (1) β-hexosaminidase | [16]       |
| Rg3, Rh2        | IgE crossing linked—RBL-2H3 cells anti-DNP | (1) TFN-α, IL-1β, COX-2, IL-4, IFN-γ | [16]       |
| LPS             | induced RAW264.7 cells | (1) IgE, (1) ear thickness (1) COX-2 NO | [16]       |

KRG, Korean red ginseng; EASI, eczema area and severity index; TNCB, 2,4,6-trinitro-1-chlorobenzene; TEWL, transdermal water loss; TSLP, thymic stromal lymphopoietin; TNF-α, tumor necrosis factor; IL, interleukin; IFN, interferon; DNBC, N-fluoro-2,4-dinitrobenzene; TARC, thymus and activation-regulated chemokine; MDC, macrophage—derived chemokine; MCP-1, macrophage inflammatory protein-1α; MIP-1β, macrophage inflammatory protein-1b; RANTES, regulated on activation normal T cell expressed and secreted; MCP-1, macrophage chemotactic protein-1; PMA, phorbol-myristate acetate; HMC-1, human mast cell line; ATX, plasma autotaxin; CG, cultivated ginseng; GDP, 20-O-β-d-glucopyranosyl-20(S)-protopanaxadiol; DFE, *Dermatophagoides farinae* body extract; GM-CSF, granulocyte macrophage colony—stimulating factor; RGE, red ginseng extract; CCL2, chemokine ligand 2; LPS, lipopolysaccharide; COX-2, cyclooxygenase-2; NO, nitric oxide.
As per the research performed with *P. ginseng*, we can conclude that, besides its promising healing and restorative properties to treat many skin disorders, it has shown to be also a well-being promoter. Therefore, more research related with *P. ginseng* as well as its derived ginsenosides are further needed for new drug development.

**Conflicts of interest**

The authors report no conflicts of interest.

**Acknowledgments**

This study was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (2017R1A6A1A03015642) from South Korea.

**Appendix A. Supplementary data**

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jgr.2018.12.012.

**References**

[1] Lee JH, Son SW, Cho SH. A comprehensive review of the treatment of atopic eczema. Allergy Asthma Immunol Res 2016;8:181–90.

[2] Odhiambo JA, Williams HC, Clayton TO, Robertson CF, Asher MI. Global variations in prevalence of eczema symptoms in children from ISAAC Phase three. J Allergy Clin Immunol 2009;124:1251–1258.e1223.

[3] Thomsen SF. Atopic dermatitis: natural history, diagnosis, and treatment. ISRN Allergy 2014;2014:354250–354250.

[4] Boguniewicz M, Alexis AF, Beck LA. Block J, Eichenfield LF, Fonacier L, Guttman-Yassky E, Pallar AS, Pariser D, Silverberg JI, et al. Expert perspectives on management of moderate-to-severe atopic dermatitis: a multidisciplinary consensus addressing current and emerging therapies. J Allergy Clin Immunol 2017;139:1519–31.

[5] Park HJ, Kim DH, Park SJ, Kim JM, Ryu JH. Ginseng in traditional herbal prescriptions. J Ginseng Res 2012;36:225–41.

[6] Kimura Y, Sumiyoshi M, Sakakura M. Effects of ginsenoside Rb1 on skin changes. J Biomed Biotechnol 2012;2012:946242-946242.

[7] Nowicki R, Nowicki R, Trzeciak M, Wilkowska A, sokolowska-wojdylo M, ługowska-Umer H, Baranska-Rybak W, Kaczmarzski M, Kowalewski C, Kruszewski J, et al. Special paper atopic dermatitis: current treatment guidelines. Statement of the experts of the Dermatological Section, Polish Society of Allergology, and the Allergology Section, Polish Society of Dermatology; 2015.

[8] Eyerich K, Novak N. Immunology of atopic eczema: overcoming the Th1/Th2 paradigm. Allergy 2013;68:974–82.

[9] Egawa G, Kabashima K. Barrier dysfunction in the skin allergy. Allergol Int 2018;67:3–11.

[10] Brandt EB, Swarupas U. Th2 cytokines and atopic dermatitis. J Clin Cell Immunol 2011;2:110.

[11] Oldhoff JM, Darsow U, Weerel T, Katzer K, Wulf A, Laiouafi J, Hijnen DJ, Plotz S, Knol EF, Kapp A, et al. Anti-IL-5 recombiant humanized monoclonal antibody (Praliczumab) for the treatment of atopic dermatitis. Allergy 2005;60:693–6.

[12] Furue M, Yamamura K, Kido-Nakahara M, Nakahara T, Fukuji Y. Emerging role of interleukin-31 and interleukin-31 receptor in pruritus in atopic dermatitis. Allergy 2016;71:295–302.

[13] Cesare AD, Meglio PD, Nester FO. A role for Th17 cells in the immunopathogenesis of atopic dermatitis? J Invest Dermatol 2008;128:2569–71.

[14] Kwee J-Y, Jeon Y-D, Kim D-S, Han Y-H, Park J, Youn D-H, Kim S-J, Ahn KS, Um J-Y, Hong S-H. Korean red ginseng improves atopic dermatitis-like skin lesions by suppressing expression of proinflammatory cytokines and chemokines in vivo and in vitro. J Ginseng Res 2017;13:41–43.

[15] Bae E-A, Han MJ, Shin Y-W, Kim D-H. Inhibitory effects of Korean red ginseng and its genuine constituents ginsenosides Rg3, Rf, and Rh2 in mouse passive cutaneous anaphylaxis reaction and contact dermatitis models. Biol Pharmaceut Bull 2006;29:1862–7.

[16] Link AJ, Tang A, Kugler JA, Smith SE, et al. Effects of Korean red ginseng for the treatment of atopic dermatitis. J Prev Med Public Health 2011;44:359–65.

[17] Horimukai K, Morita K, Narita M, Kondo M, Kitazawa H, Nozaki M, Shimematsu Y, Yoshida H, Asa K, Nizelki H, Motomura K, et al. Application of moisturizer to neonates prevents development of atopic dermatitis. J Allergy Clin Immunol 2013;144:769–79.

[18] McPherson T. Current understanding in pathogenesis of atopic dermatitis. Indian J Dermatol 2016;61:649–55.

[19] Watanuki H, Kuba A, Shin Y, Anagah M. Loss-of-function mutations within the Filaggrin gene and atopic dermatitis. J Allergy Clin Immunol 2013;131:113–20.

[20] Osawa R, Akiyama M, Shimizu H. Filaggrin gene defects and the risk of developing allergic disorders. Allergol Int 2011;60:1–9.

[21] Leung DYM, Guttman-Yassky E. Deciphering the complexities of atopic dermatitis: shifting paradigms in treatment approaches. J Allergy Clin Immunol 2014;134:769–79.

[22] Mooney E, Rademaker M, Dailey R, Daniel BS, Drummond C, Fischer G, Foster R, Grills C, Halbert L, Hill S, et al. Adverse effects of topical corticosteroids in paediatric eczema: australasian consensus statement. Australas J Dermatol 2015;56:241–9.

[23] Strohal K, Michaelis S, Vierling N. Topical crystal corticosteroids. Part 1: characteristics and efficacy of topical corticosteroids. J Dermatolog Treat 2013;25:421–30.

[24] Suárez AL, Feramisco JD, Koo J, Steinhoff M. Psychoneuroimmunology of dermatitis: shifting paradigms in treatment approaches. J Allergy Clin Immunol 2014;134:769–79.

[25] Suárez FL, Fonacier L, Gutierrez-León JM, Thomas KS, Cork MJ, McLean WH, Brown SJ, Chen Z, Chen Y, Williams HC. Emollient enhancement of the skin barrier from birth offers effective atopic dermatitis prevention. J Allergy Clin Immunol 2014;134:818–23.

[26] Kiwio H, Kurokawa A, Fujisaki T, Otsuka T, Nakanishi M. Filaggrin gene mutations and atopic dermatitis: a disease caused by innate immune defects? J Invest Dermatol 2013;68:135–40.

[27] Kinjoh S, Burmester G-R, Sterry W, et al. Cutaneous side-effects in patients with tumour necrosis factor-α inhibitors in atopic dermatitis: a systematic review and meta-analysis. J Dermatolog Treat 2001;357:2012–2018.

[28] McPherson T. Current understanding in pathogenesis of atopic dermatitis. Indian J Dermatol 2016;61:649–55.

[29] Suzuki AL, Feramisco JD, Koo J, Steinhoff M. Psychoneuroimmunology of dermatitis: shifting paradigms in treatment approaches. J Allergy Clin Immunol 2014;134:769–79.

[30] Taylor K, Swan DJ, Affleck A, Flodr C, Reynolds NJ. Dermatology UKTRN, the UKTRN. Treatment of moderate-to-severe atopic eczema in adults within the UK: results of a national survey of dermatologists. Br J Dermatol 2017;176:1617–23.

[31] Reynolds NJ, Franklin V, Gray JC, Diffey BL, Farr PM. Narrow-band ultraviolet B and broadband ultraviolet A phototherapy in adult atopic eczema: a randomised controlled trial. Lancet 2001;357:212–6.

[32] Goujon C, Viguier M, Staumont-Sallé D, Bernier C, Guillet G, Lahfa M, Ferrière Le Naour R. Atopic dermatitis: shifting paradigms in treatment approaches. J Allergy Clin Immunol 2014;134:769–79.

[33] Strohal K, Michaelis S, Vierling N. Topical crystal corticosteroids. Part 1: characteristics and efficacy of topical corticosteroids in paediatric eczema: australasian consensus statement. Australas J Dermatol 2015;56:241–9.

[34] Di Banyak MM, Bossola MAW, Mashaly HM, Hafez VSGA. Topical calcineurin inhibitors in atopic dermatitis: a systematic review and meta-analysis. J Dermatol Sci 2009;54:76–87.

[35] Eyerich K, Novak N. Immunology of atopic eczema: overcoming the Th1/Th2 paradigm. Allergy 2013;68:974–82.
Simpson EL, Bieber T, Guttman-Yassky E, Beck LA, Blauvelt A, Cork MJ, Silverberg JL, Deleuran M, Kataoka Y, Lacour J-P, et al. Two phase 3 trials of Dupilumab versus placebo in atopic dermatitis. N Engl J Med 2016;375:2335–48.

Kim EH, Kim W. An insight into ginsenoside metabolite compound K as a potential tool for skin disorder. Evidence-based complementary and alternative medicine. eCAM 2018;2018. 8075870-8075870.

Kim EH, Kim W. An insight into ginsenoside metabolite compound K as a potential tool for skin disorder. Evidence-based complementary and alternative medicine. eCAM 2018;2018. 8075870-8075870.

Sarvenaz S-R, Sara S-R, Amirhossein S, Zahra T-N. Ginseng in dermatology: a review. Curr Pharmaceut Des 2017;23:1649–66.

Kim H, Park CW, Cho SH. The beneficial effect of Korean red ginseng extract on atopic dermatitis patients: an 8 weeks open, noncomparative clinical study. Ann Dermatol 2018;30:304–8.

Lee KG, Son SW. Efficacy of korean red ginseng in the treatment of atopic dermatitis. J Ginseng Res 2011;35:149–54.

Cho E, Cho SH. Effects of Korean red ginseng extract on the prevention of atopic dermatitis and its mechanism on early lesions in a murine model. J Ethnopharmacol 2013;145:294–302.

Lee HJ, Cho SH. Therapeutic effects of Korean red ginseng extract in a murine model of atopic dermatitis: anti-pruritic and anti-inflammatory mechanism. J Kor Med Sci 2017;32:879–87.

Samukawa K, Izumi Y, Shiotra M, Nakao T, Osada-Oka M, Miura K, Iwao H. Red ginseng inhibits scratching behavior associated with atopic dermatitis in experimental animal models. J Pharmacol Sci 2012;118:391–400.

Choi JH, Jin SW, Park BH, Kim HG, Khanal T, Han HJ, Hwang YP, Choi JM, Chung YC, Hwang SK, et al. Cultivated ginseng inhibits 2,4-dinitrochlorobenzene-induced atopic dermatitis-like skin lesions in NC/Nga mice and TNF-α/IFN-γ-induced TARC activation in HaCaT cells. Food Chem Toxicol 2013;56:195–203.

Lee B-H, Kim H-K, Jang M, Kim H-J, Choi S-H, Hwang S-H, Kim H-C, Rhim H, Cho I-H, Nah S-Y. Effects of gintonin-enriched fraction in an atopic dermatitis animal model: involvement of autotaxin regulation. Biol Pharmaceut Bull 2017;40:1063–70.

Kim JR, Choi J, Kim J, Kim H, Kang H, Kim EH, Chang J-H, Kim Y-E, Choi YJ, Lee KW, et al. 20-O-β-D-glucopyranosyl-20(S)-protopanaxadiol-fortified ginseng extract attenuates the development of atopic dermatitis-like symptoms in NC/Nga mice. J Ethnopharmacol 2014;151:365–71.

Osada-Oka M, Hirai S, Izumi Y, Misumi K, Samakawa K, Tomita S, Miura K, Minamyama Y, Iwao H. Red ginseng extracts attenuate skin inflammation in atopic dermatitis through p70 ribosomal protein S6 kinase activation. J Pharmacoecol Sci 2018;136:9–15.

Wang H-H, Li Y-C, Huang Y-C. Efficacy of omalizumab in patients with atopic dermatitis: a systematic review and meta-analysis. J Allergy Clin Immunol 2016;138. 1719-1722.e1711.