

# *Rehmanniae Radix*, an Effective Treatment for Patients with Various Inflammatory and Metabolic Diseases: Results from a Review of Korean Publications

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## Key Words

caltalpol, *Rehmannia Glutinosa*, *Rehmanniae Radix*, review

## Abstract

**Objectives:** This study was a review of the literature published on the efficacy of *Rehmanniae Radix* to obtain information to provide both a foundation for its clinical use and directions for future studies.

**Methods:** This study selected 30 publications registered to databases or published in Korea by March 13, 2017, by searching electronic journal databases, i.e., NDSL, OASIS, RISS, and KISS, in order to review the efficacy of *Rehmanniae Radix*. The search was conducted using the keywords ‘生地黃’, ‘鮮地黃’, ‘*Rehmannia Glutinosa*’, and ‘*Rehmanniae Radix*’, and the search results were compiled and analyzed.

**Results:** The selected publications included antioxidant effects (12 publications), data involving blood glucose reduction (4 publications), effects on the autonomic nervous system (3 publications), and effects on the human body (11 publications).

**Conclusion:** The results of this literature review indicate that *Rehmanniae Radix* is effective in treating patients with various inflammatory and metabolic diseases, such as high blood pressure and diabetes. Based on

these results, we believe that *Rehmanniae Radix* can be used effectively to treat patients with such diseases.

## 1. Introduction

*Rehmanniae Radix* is a perennial herb that belongs to the Scrophulariaceae family. It is the washed tuberous root of *Rehmannia Glutinosa* after removing the pyl-lorhiza and fine root. It is very cold, non-toxic, sweet, and a little bitter. The medicine channels its way to the heart, liver, and kidneys. Therefore, it reduces body temperature and cools the blood. It is used to remove extravasated blood, increase body fluid, and slake one’s thirst. It is also used for breaking fevers, cardiac stimulation, detoxification, and hemostasis [1-3]. *Rehmanniae Radix*, consequently, has been used as an important ingredient in diverse Oriental medicines (Gyeongokgo, Jihwangeumja, Saenghyeoryunbueum, and Samuransintang) [4]. Recently, many studies have evaluated its effects on antioxidants [5-16], blood sugar reduction [17-20], the autonomic nervous system [21-23], and the human body [24-34].

The majority of studies have focused on restorative herb medicines such as ginseng [35, 36], *Astragalus membranaceus* [37], and *Cynanchum wilfordii* [38]. Only a few studies have evaluated the herbal medicines highly useful for clinical applications. Thus, the objective of this study was to review Korean publications in the literature on the efficacy of *Rehmanniae Radix* so as to suggest a foundation for its clinical use and to discuss the directions of future studies.

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## 2. Methods

Papers or abstracts published in the literature or registered in a database until Mar 13, 2017, were the targets. Three researchers independently searched e-journals in NDSL, OASIS, RISS, and KISS. Publications published, but not registered, in these databases were added. The search was conducted with using the keywords '生地黃', '鮮地黃', '*Rehmannia Glutinosa*', and '*Rehmanniae Radix*', and the search results were compiled and analyzed.

Among the reports in the published literature, we selected clinical studies that evaluated the efficacy of *Rehmanniae Radix*. Studies not related to *Rehmanniae Radix* or studies on mixtures including *Rehmanniae Radix* were excluded. Moreover, the cultivation methods for *Rehmanniae Radix* were excluded as well. After three researchers had independently selected and excluded reports in the literature, their listed were compared. In cases of disagreement, all the authors discussed those reports and determined whether they should be included or not.

## 3. Results of the Literature Search

Six hundred sixty-nine publications were retrieved at the first step after merging separate search results and excluding duplicated publications. Next, 48 publications were selected by excluding publications that did not mention *Rehmanniae Radix* in the title or abstract, that studied mixtures containing *Rehmanniae Radix*, or that studied cultivation methods for *Rehmanniae Radix*. Thirty publications were found to satisfy the selection criteria by examining and analyzing the main text and were finally chosen for inclusion in this study [5-34] (Table 1). Of the 30 clinical studies, one was published in each of the following years: 1982, 1990, 1994, 1998, 2001, 2010, and 2015; two were published in 2000, 2005, 2007, 2009, and 2012, three in 2004, 2008, and 2011, and four in 2006. Fourteen studies were published between 2004 and 2008. These studies evaluated the anti-oxidation effects [5-16], blood sugar decrease [17-20], the autonomic nervous system [21-23], and other effects on the human body [24-34].

### 3.1. Anti-inflammation and Anti-oxidation

Studies evaluating the anti-inflammation and the anti-oxidation effects were divided into those addressing dermatitis, autoimmune disorders, and experimental antioxidant capability measures. In the case of dermatitis, studies were segmented into general dermatitis [5], allergic dermatitis [7], contact dermatitis [8], and atopic dermatitis [9]. Seo [5] evaluated the toxicity, as well as the anti-inflammation and the anti-oxidation effects, of Indigo Naturalis and *Rehmanniae Radix* in order to alleviate inflammatory dermatitis. Seo [5] reported that Indigo Naturalis and *Rehmanniae Radix* had no cytotoxicity, inhibited NO production, and exhibited high DPPH (1,1-diphenyl-2-picryl hydrazyl) radical scavenging ability, but these results did not achieve statistical significance. Kang and Kim [7] confirmed the

cytokine-expression inhibiting ability and the anti-allergic action of *Rehmannia Glutinosa* Pharmacopuncture when it was used to treat type-1 allergic dermatitis. Shin *et al* [8] confirmed that drinking *Rehmanniae Radix* extract was effective for treating the symptoms of contact dermatitis induced by dinitrochlorobenzene (DNCB) through mast cells, IL-2 receptors, and T-lymphocytes. Jo [9] reported that after the study subjects had been divided into a group treated with an anti-inflammatory agent, a group treated with a hydrodistillation-extracted *Rehmannia Glutinosa* pharmacopuncture, and a group treated with a methanol-extracted *Rehmannia Glutinosa* pharmacopuncture in order to compare the effects of the anti-inflammatory agent and the *Rehmannia Glutinosa* pharmacopuncture on the atopic dermatitis of NC/Nga mice, the groups being treated with the anti-inflammatory agent and the methanol extract of *Rehmannia Glutinosa* pharmacopuncture showed a strong anti-inflammatory response when skin observations and inflammatory factors were compared.

Chae and Yang [6] reported that methanol-extracted *Rehmanniae Radix* decreased IL-2, IFN- $\gamma$ , IL-6, IL-10, and TNF- $\alpha$  when they treated lupus mice with methanol-extracted *Rehmanniae Radix* to confirm the inflammatory cytokines associated with autoimmune disorders. They concluded that it had been effective for treating the immune disorder because it downregulated the productions of TNF- $\alpha$  and T-cell-dependent cytokines.

In a study related to the measurements of experimental anti-oxidation functions, Lee *et al* [10] observed the anti-apoptotic effect of catalpol, the main component of *Rehmanniae Radix*, by using the embryos of pigs and confirmed its anti-oxidant and anti-cancer effects. Jin *et al* [11] showed that ethyl-acetate extracts of *Rehmanniae Radix* inhibited the productions of nuclear factor (NF)- $\kappa$ B and reactive oxygen species (ROS) and were effective in treating inflammatory diseases such as rheumatoid arthritis. Lim *et al* [13] measured the antioxidant effects, antihypertensive effects, anti-arthritic effects, antimicrobial activity, whitening effects, wrinkle alleviation effects, and anti-inflammatory effects of *Rehmanniae Radix* extracts. The results of the study showed that it could be used as a functional health food owing to its excellent antioxidant and antihypertensive functions. Moreover, they suggested that it could be commercialized as a raw ingredient in multifunctional cosmetics because it effectively inhibited skin flora and whitening and reduced skin wrinkling.

Kang and Kim [16] evaluated the effects of *Rehmanniae Radix* on angiogenesis, cell survival, and inflammation-related protein expression. Based on the fact that *Rehmanniae Radix* extracts caused angiogenesis inhibition, the expressions of inflammation-associated materials, which increase in the process of proliferation, were confirmed. The results suggested that *Rehmanniae Radix* inhibited angiogenesis by decreasing the expression of the VEGF protein through a decrease in the expression of HIF-1 $\alpha$ , which is one of the angiogenesis factors. The study also revealed that *Rehmanniae Radix* extracts inhibited neovascularization by regulating cell survival and the expressions of inflammation-related proteins.

Chae and Shin [15] evaluated the effects of methanol-extracted *Rehmanniae Radix* on the cytokine production

**Table 1** Selected Studies

Author year	Category	Subject	Remarks
Seo 2008 [5]		The Experimental Study on Anti-inflammation and Anti-oxidation of Indigo Naturalis and <i>Rehmanniae Radix</i>	Dermatitis
Chae and Yang 2007 [6]		Regulatory effect of fresh <i>rehmanniae radix</i> extract on the <i>in vitro</i> production of proinflammatory cytokines in pristane-induced lupus mice	Autoimmune Disease
Kang and Kim 2011 [7]		Inhibitory Effect of Rehmannia Glutinosa Pharmacopuncture Solution on $\beta$ -hexosaminidase Release and Cytokine Production via Fc $\epsilon$ RI signaling in RBL-2H3 Cells	Allergic Disease
Shin <i>et al</i> 2000 [8]		The effect of <i>Rehmanniae Radix</i> extract on allergic contact dermatitis on Mice induced by DNCB	Contact Dermatitis
JO 2012 [9]		Characterization of Biological Activities of Rehmannia glutinosa Extracts	Atopic dermatitis
Lee <i>et al</i> 2015 [10]	Anti-inflammation and Anti-oxidation	Anti-Apoptotic Effects of Catalpol on Preimplantation Porcine Embryos	Anti-Apoptotic Effects
Jin <i>et al</i> 2009 [11]		Anti-inflammatory Activities of Ethylacetate Extract of Rehmannia glutinosa in LPS-induced RAW 264.7 Cells	RAW 264.7 Cells
Moon <i>et al</i> 2004 [12]		Antioxidant enzyme responses against abiotic and biotic stresses in <i>Rehmanniae Radix</i> and Glycine max L.	Antioxidant enzyme responses
Lim <i>et al</i> 2005 [13]		Biological activities of resveratrol-3-O- $\beta$ -D-giucoside in transgenic <i>Rehmanniae Radix</i>	resveratrol-3-O- $\beta$ -D-giucoside
Kang <i>et al</i> 2012 [14]		Rehmannia Glutinosa Pharmacopuncture Solution Regulates Functional Activation, Fc $\epsilon$ RI Expression, and Signaling Events in Mast Cells	Mast Cells
Chae and Shin 2006 [15]		Effect of Fresh <i>Rehmanniae Radix</i> Methanol Extracts on the Production of Cytokines	Methanol Extracts
Kim and Kim 2006 [16]		The Effects of Rehmannia glutinosa on the Protein Expression Related to the Angiogenesis, Cell Survival and Inflammation	Cell Survival and Inflammation
Kim 2008 [17]		Antidiabetic, antioxidative and renoprotective effects of <i>Rehmanniae Radix</i> preparata extract in streptozotocin-induced diabetic rats	Antidiabetic Effect
Kim and Na 2004 [18]	Reducing Blood Glucose Level	Effect of <i>Rehmanniae Radix</i> and Pear Phenolic Compound on the STZ-Treated Mice for Induction of Diabetes	Antidiabetic Effect
Kim 2004 [19]		Effect of <i>Rehmanniae Radix</i> on Hyperglycemic Mice Induced with Streptozotocin	Antidiabetic Effect
Jeong and Kim 1990 [20]		The Effects of Rehmanniae Radices Extracts on Streptozotocin-Induced Hyperglycemia in Rats	Antidiabetic Effect
Yook <i>et al</i> 2009 [21]	Effect on Autonomic Nervous System	Comparing the effects of distilled Rehmannia glutinosa, Wild Ginseng and Astragali Radix pharmacopuncture with heart rate variability (HRV): a randomized, sham-controlled and double-blind clinical trial	HRV

(Continued)

Shin <i>et al</i> 2008 [22]		The Effects of distilled <i>Rehmannia glutinosa</i> Herbal Acupuncture on Heart Rate Variability (HRV)	HRV
Lee <i>et al</i> 2007 [23]	Effect on Autonomic Nervous System	The Effects of Distilled <i>Astragali Radix</i> Herbal Acupuncture, Wild Ginseng Herbal Acupuncture and <i>Rehmannia Glutinosa</i> Herbal Acupuncture on Vital Signs: A Randomized, Placebo-controlled, Double-blind Clinical Trial	Vital Signs
Lee <i>et al</i> 2011 [24]		<i>Rehmannia glutinosa</i> Ameliorates Scopolamine-Induced Learning and Memory Impairment in Rats	Cognitive Function
Park and Lee 2010 [25]		Effects of <i>Rehmanniae Radix</i> on the HPA Axis System and the Catecholaminergic System in FST	Antidepressant
Heo and Yook 2011 [26]		The Study on the Composition of <i>Rehmanniae Radix</i> Extracts by Supercritical Carbon Dioxide Extraction and by Hydrodistillation Extraction	Component Comparison by Extraction Method
Shin <i>et al</i> 2001 [27]		The Effects of <i>Rehmanniae Radix</i> on the Propulsive Peristalsis of the Rat's Gastrointestine	Intestinal Peristalsis
Kim <i>et al</i> 2006 [28]		Rhizoma <i>Rehmanniae</i> induced Apoptosis in Human Cervical Carcinoma HeLa Cells	Cervical Cancer
Park and Kim 1994 [29]	Miscellaneous	Effects of <i>Rehmannia glutinosa</i> Aqua-acupuncture at the Meridian Points BL 23 on the Renal Function in Two-Kidney One Clip Goldblatt Hypertensive Rats	Nephrotic Hypertension
Lee <i>et al</i> 2006 [30]		Comparison of Immune Promotion Effects of Water-extracted <i>Angelicae Gigantis</i> , <i>Rehmanniae Radix</i> , <i>Paeoniae Japonica</i> and <i>Polygoni multiflori Radix</i>	Immune Response
Kwon and Song 1998 [31]		Effects of Rhizoma <i>rehmanniae</i> administration on the Innate and Adaptive Responses in the Mouse	Immune Response
Kim <i>et al</i> 2005 [32]		Studies on the Stability of Catalpol Components, and Genotoxic Safety of $\gamma$ -Irradiated <i>Rehmanniae Radix</i> Crude	Toxicity
Ki <i>et al</i> 2000 [33]		Effects of <i>Rehmanniae Radix</i> on the Rat Liver Damaged with $\text{CCl}_4$	Liver Damage
Kwon <i>et al</i> 1982 [34]		An Experimental Study of the Effects of <i>Rehmanniae Radix</i> and <i>Cirsii Herba</i> Extract Administration to the Serum Prothrombin Time in Mouse	Prothrombin Time

of abdominal cavity macrophages and splenocytes. They found that methanol *Rehmanniae Radix* extracts inhibited the production of  $\text{TNF-}\alpha$ , had an anti-inflammatory effect by increasing the production of IL-10, and was effective for leucocyte immune response by promoting the productions of IL-2 and  $\text{IFN-}\gamma$ . However, they also reported that a high dose could enhance inflammatory response and decrease cellular immunity immune response. Additionally, Moon *et al* [12] and Kang *et al* [14] measured the antioxidant efficacy of *Rehmanniae Radix* for RAW 264.7 cells and mast cells, respectively, and showed that *Rehmanniae Radix* effectively inhibited degranulation and inflammation.

### 3.2. Reducing Blood Glucose Level

Kim [17] studied the hypoglycemic effects of *Rehmanniae Radix* and evaluated the changes in diet efficiency, blood sugar, kidney function, antioxidant enzyme in kidney tissue, serum, glucose, insulin, blood urea nitrogen (BUN), creatinine concentration, organ weight, and the activity of harmful oxygen metabolism enzyme in kidney tissues after administrating *Rehmanniae Radix* in order to confirm its effects on diabetic improvement and renal protection in the streptozotocin (STZ)-injected insulin-dependent

diabetes experimental model. The results showed that *Rehmanniae Radix* improved saccharometabolism, prevented weight loss due to diabetes, and positively affected the renal anti-oxidation system, resulting in a decrease in the blood sugar level. Moreover, it was effective in diabetes improvement and kidney protection by decreasing albuminuria. Kim and Na [18] and Kim [19] investigated the effects of a phenol compound (PC) extracted from *Rehmanniae Radix* and the skin of pears on STZ-induced hyperglycemic mice. These studies administrated *Rehmanniae Radix* and PC orally and conducted blood sugar and glucose tolerance tests. Their results showed that *Rehmanniae Radix* extracts and PC were significantly effective in blood sugar and glucose tolerance control.

Jeong and Kim [20] evaluated water and methanol extracts of dried *Rehmanniae Radix*, *Rehmanniae Radix* (not dried), and *Rehmanniae Radix Preparata* on STZ-induced hyperglycemia in order to compare the hypoglycemic effects of *Rehmanniae Radices*. They measured the blood sugar, total cholesterol in serum, and triglycerides in serum. Results showed that the water extracts of dried *Rehmanniae Radix* and of *Rehmanniae Radix Preparata* had significant hypoglycemic effects. Moreover, the water extracts of *Rehmanniae Radix* and of dried *Rehmanniae Radix* significantly decreased cholesterol. Methanol extracts of *Rehmanniae Radix* and of *Rehmanniae Radix Preparata* significantly inhibited triglycerides.

### 3.3. Effect on the Autonomic Nervous System

Studies [21, 22] on the autonomic nervous system evaluated the heart rate variability by using a heart rate variability (HRV) test after having injected *Rehmannia Glutinosa* Pharmacopuncture into a healthy person's Gyeonjeong (GB21) acupoint. Yook *et al* [21] showed that *Rehmannia Glutinosa* Pharmacopuncture activated the sympathetic nervous system among the autonomic nervous systems. On the other hand, Shin *et al* [22] revealed that it tended to activate the parasympathetic nervous system more. Lee *et al* [23] analyzed the changes in the vital signs after treatment with *Astragalus membranaceus* Pharmacopuncture, *Panax ginseng* Pharmacopuncture, and *Rehmannia Glutinosa* Pharmacopuncture by using a randomized, double-blind, experimental design. The results showed no significant differences in systolic blood pressure, diastolic blood pressure, pulse rate, and respiratory rate.

### 3.4. Other Effects

Various studies have evaluated the effects of *Rehmanniae Radix* on cognitive function, depression, intestinal motility, cervical cancer and hypoglycemia, renal hypertension, immune response, toxicity, inflammation and oxidation, liver damage recovery, and prothrombin time (PT). Lee *et al* [24] found that *Rehmanniae Radix* extracts were effective in nerve damage recovery, memory enhancement, and cognitive function improvement in mice with parasympathetic nerve induced by administering scopolamine

(SCO). Park and Lee [25] examined behavioral changes by evaluating the anti-depression effects of *Rehmanniae Radix* from Sihosogantang on the despair behavior observed during forced swimming tests (FSTs). They also measured the corticotropin-releasing factor (CRF) and the expression of tyrosine hydroxylase (TH) in the locus coeruleus (LC) and the ventral tegmental area (VTA). They showed that *Rhizoma Rehmanniae* had an anti-depressive effect; i.e., it inhibited the passivation behavior of an albino mouse by decreasing the expressions of CRF in the paraventricular nucleus (PVN) and TH in the ventral tegmental area (VTA). Shin *et al* [27] evaluated the effects of *Rehmanniae Radix* on propulsive peristalsis of the rat's gastrointestinal. They measured the movement of the gastrointestinal track by using barium gum. The study showed that *Rehmanniae Radix* decreased the rate of movement of barium gonads and decreased propulsive peristalsis of the gastrointestinal.

Kim *et al* [28] investigated cervical carcinoma HeLa cells after having administered *Rehmanniae Radix* to understand the effects of *Rehmanniae Radix* on cervical cancer. It induced HeLa cell necrosis, increased the activities of caspase-3 and caspase-8, segmented poly (ADP-Ribose) polymerase (PARP), and increased the expression of Fas/Fast. These results indicated that *Rehmanniae Radix* was effective in preventing and treating cervical cancer. Park and Kim [29] injected a water extract of *Rehmannia Glutinosa* pharmacopuncture at the Sinsu (BL23) acupoint and observed the kidney function and the blood pressure in order to understand its effects on the renal function of hypertensive rats. They showed that a water extract of *Rehmannia Glutinosa* pharmacopuncture was effective in lowering both blood pressure and serum rennin activity.

Lee *et al* [30] and Kwon and Song [31] intended to evaluate the effects of *Rehmanniae Radix* on the immune response. Kwon and Song [31] measured the effects of *Rehmanniae Radix* extracts on the innate immune response by using NK cells and macrophages. Moreover, they measured the leucocyte immune response through isoantigen and the DNFB-induced accessibility oversensitive response. Additionally, they measured its effects on the humoral immune response in order to evaluate the effects of *Rehmanniae Radix* extracts on the innate and the adaptive immune responses of a mouse. The production of antibodies was increased, and the isoantigen responses were significantly different. Furthermore, the accessibility oversensitive response was significantly inhibited, and the destruction of NK cancer cells was increased. Consequently, *Rehmanniae Radix* extracts increased the innate and the adaptive immune responses. Lee *et al* [30] compared the immune regulation effects of *Angelicae gigantis*, *Rehmanniae Radix*, *Paeonia japonica* and *Polygoni multiflori Radix*, which are blood-nourishing medicines. *Polygoni multiflori Radix* showed the most significant effects on biological immune responses such as cell proliferation, cytokine induction, recovery owing to methotrexate (MTX) treatment, and inhibition of S-180 multiple cancer-cell progression.

Ki *et al* [33] evaluated the effects of *Rehmanniae Radix* on rat liver damage induced by CCl<sub>4</sub>. *Rehmanniae Radix* extracts considerably decreased the activities of Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), and Alkaline Phosphatase (ALP) increased the activity of

ALP, did not directly affect the activities of enzymes, and aided in the recovery of damaged liver tissues. Kwon *et al* [34] evaluated the effects of *Rehmanniae Radix* and *Cirsii Herba* extracts on the serum prothrombin time. They measured the prothrombin times for groups treated with *Rehmanniae Radix*, *Cirsii Herba*, and warfarin and showed that claims of the anti-plasma effects of *Rehmanniae Radix* and *Cirsii Herba* were not valid.

Heo and Yook [26] compared the compositions of *Rehmanniae Radix* hydrodistillation-extract and *Rehmanniae Radix* supercritical carbon-dioxide extract. They found nine types of essential oils from the *Rehmanniae Radix* supercritical carbon dioxide extract. No active ingredients were found in the *Rehmanniae Radix* hydrodistillation-extract. Kim *et al* [32] compared the active ingredients, High Performance Liquid Chromatography (HPLC) results, and toxicological results between the  $\gamma$ -irradiation and the control groups in order to evaluate the stability and the genotoxic safety of the catalpol component in *Rehmanniae Radix*. They found that the active ingredients in *Rehmanniae Radix* remained active after  $\gamma$ -irradiation and that the compositions of the active ingredients did not change.

#### 4. Discussion

This study selected 30 publications [5-34] registered in databases or published in Korea by March 13, 2017, by searching electronic journal databases (i.e., NDSL, OASIS, RISS, and KISS) in order to review the efficacy of *Rehmanniae Radix*. The selected publications included information on antioxidant effects [5-16] (12 publications), blood glucose reduction [17-20] (4 publications), the autonomic nervous system [21-23] (3 publications), and the effects of *Rehmanniae Radix* on the human body [24-34] (11 publications).

Studies on the anti-inflammatory and the antioxidant effects of *Rehmanniae Radix* proved it to be effective in treating not only general dermatitis but also allergic dermatitis [7], contact dermatitis [8], and atopic dermatitis [9]. The effect of methanol extracts of *Rehmanniae Radix* in treating atopic dermatitis was similar to that of anti-inflammatory ointment. Such results indicate the possibility of developing a natural anti-inflammatory ointment for the treatment of dermatitis. Moreover, as Lim *et al* [13] showed, possibilities exist to commercialize *Rehmanniae Radix* in the form of a functional health food to prevent lifestyle-related disease and as a raw material for use in multi-functional cosmetics. In studies on the reduction of blood glucose, *Rehmanniae Radix* was found to increase the rate of recovery from pancreatic islet damage induced by STZ. Moreover, methanol extracts of *Rehmanniae Radix* effectively inhibited triglycerides. Such results imply that *Rehmanniae Radix* could be used for the treatment of metabolic syndrome.

Studies on the autonomic nervous system by Yook *et al* [21] and Shin *et al* [22] showed that *Rehmanniae Radix* activated the autonomic nervous system. However, Yook *et al* [21] showed that it activated the sympathetic nervous system whereas Shin *et al* [22] showed that it activated the parasympathetic nervous system. Such results indicate

that further studies are needed. Additionally, many other studies were conducted. The data that they contained on the recovery from nerve damage [24], improvement of memory capability [24], improvement of cognitive function [24], anti-depressive efficacy [25], treatment effects on cervical cancer [28] and renal hypertension [29], immune response [30, 31], and recovery from liver-tissue damage [33] show future research directions and have implications for the development of natural medicines.

#### 5. Conclusion

Thirty publications on the efficacy of *Rehmanniae Radix* were selected from publications registered to databases or published before March 13, 2017. Those publications were reviewed, and the contents were analyzed, producing the following results:

1. *Rehmanniae Radix* is effective in treating various types of dermatitis, such as allergic dermatitis, contact dermatitis, and atopic dermatitis, and has antioxidative effects. However, a high dose can induce an inflammation reaction and decrease cellular immunity.

2. *Rehmanniae Radix* is effective in reducing blood sugar and in restoring STZ-induced pancreatic islet damage.

3. *Rehmanniae Radix* is effective in activating the autonomic nervous system, but effectively affects vital signs.

4. *Rehmanniae Radix* is effective for improving cognitive function, antidepressant action, and immunity control, for treating cervical cancer and nephrotic hypertension, and for repairing damaged liver tissue. It can also reduce intestinal peristalsis.

These results indicate that *Rehmanniae Radix* is an effective treatment for various inflammatory diseases and metabolic diseases, such as blood pressure and diabetes.

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#### Conflict of interest

The authors declare that they have no conflicts of interest.

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