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Evaluation of Pyunkang-tang® Administration on Hematological, Biochemical, and Protein and Lipid Profiles in Dogs

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Abstract : Pyunkang-tang® is a kind of herbal medicine and has been used for the treatment of atopy and allergic disease in humans over forty years. The purpose of this study was to evaluate the hematological, biochemical, and protein and lipid electrophoresis profiles after the oral administration of Pyunkang-tang® in healthy dogs. Fifteen clinically healthy beagle dogs were selected and orally administered either 33 ml of Pyunkang-tang® (group I, n = 5), 16.5 ml of Pyunkang-tang® (group II, n = 5), or 33 ml of distilled water (group III, n = 5) 3 times a day for 4 weeks. The results of the hematological, serum biochemical, and urine analysis did not differ significantly among the 3 groups. The oral administration of Pyunkang-tang® for 4 weeks was associated with significant changes in the serum globulin levels and an elevation in the high-density lipoprotein (HDL) concentrations in groups I and II ($p < 0.05$), compared to group III. The α1-globulin and γ-globulin levels were significantly increased in group I, and the α1-globulin and β-globulin levels were significantly increased in group II. The α2-globulin levels were significantly decreased in both groups. During the short-term evaluation of Pyunkang-tang® administration, we did not detect any specific adverse effects in the dogs. However, further evaluation of the safety and efficacy of Pyunkang-tang® for the treatment of atopic disease in dogs is needed.

Key words **:** lipoprotein electrophoresis, Pyunkang-tang®, safety, serum protein electrophoresis.

Introduction

Herbal medicines have a long history of being used in human medicine for the prevention and treatment of disease, and the use of these medicines has increased substantially in recent decades (6). With this, concerns about the efficacy and safety of herbal medicines have been raised because of the lack of scientific evidence (3,16).

The use of herbal medicines in animals has also increased, and several studies of veterinary herbal medicine have recently been undertaken (9,19-21). The effect of the Chinese herbal formula, Hai Zao Yu Hu Tang, was compared with that of methimazole for the treatment of feline hyperthyroidism (21). The herbal compound improved the general condition and quality of life, but the circulating serum tetraiodothyronine levels were not changed. When Yin Chen Hu Gan San (a hepatoprotective powder derived from capillaris plants) was used to treat horses with acute parenchymatous hepatitis, there was an improvement in the clinical signs and liver test parameters (19). In a long-term follow-up of canine mammary gland neoplasia treated with surgery and a Chinese herbal formula, the survival rates were significantly improved compared to the survival rates in dogs treated with surgical excision and conventional chemotherapy (20).

Atopic dermatitis is recognized as a characteristic skin disease associated with environmental allergens, alterations of skin barrier function, microbial colonization, and abnormal cutaneous immunity in dogs and humans (13). The treatment of this disease involves a combination of trigger avoidance, restoration of impaired skin barrier function, and anti-inflammatory medication. However, in recent years, the clinical application of other therapeutic methods has increased in both humans and animals because of the high recurrence rate associated with these conventional therapies (8,15). Pyunkang-tang® is a commercialized herbal medicine used for the treatment of atopic disease, including asthma, atopic dermatitis, and allergic rhinitis, since the early 2000s in Korea. However, there is no scientific evidence of its efficacy and safety in animals.

The purpose of this study was to evaluate the hematological, biochemical, and protein and lipid electrophoresis profiles in healthy dogs undergoing a 4-week oral administration of Pyunkang-tang®.

Materials and Methods

Study designs and Animals

The Pyunkang-tang® formulation used in this study consisted of more than 10 herbal compounds, including *Liriope platyphylla, Platycodon grandiflorum, Lonicera japonica flowers, Xanthium sibiricum, and Radix adenophorae.*

Fifteen 6-month-old clinically healthy beagle dogs (6 were intact females and 9 were intact males) with a mean body weight of 4.56 ± 1.36 kg (range, 2.6-7.1 kg) were selected for this study. All the dogs were screened for underlying disease

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and considered healthy based on a physical examination, complete blood count (CBC), serum chemistry profiles, and urinalysis. The dogs were individually housed in experimental facilities (constant temperature [24-27°C] and humidity level [50-55%] on a 12-hour cycle) and fed commercial dry dog food (Natural Balance®; Dick Van Patten's Natural Balance Pet Foods, Inc., Burbank, CA, USA). The dogs had at least a 7-day adaptation period before the study commenced, and were treated in accordance with the animal care and use guidelines set out by the Institutional Animal Care and Use Committee.

Following the adaptation period, the 15 dogs were randomly divided into 3 groups. Pyunkang-tang® was orally administered to groups I and II, at doses of 33 ml/dog and 16.5 ml/dog, respectively, 3 times a day for 4 weeks (the dosage was extrapolated from treatment dosage for human patients). Group III received distilled water at a dose of 33 ml/dog, 3 times a day for 4 weeks. The dogs were evaluated at 0 and at 4 weeks after the first administration. Clinical observations were recorded daily throughout the entire study period, including the monitoring of feed, water consumption, periodic weighing, and clinical signs (general appearance, consciousness/attitude, activity, vomiting, and diarrhea).

Blood sampling and laboratory examination

Five milliliters of venous blood was withdrawn from the jugular vein after a 15 h overnight fast at weeks 0 and 4. The blood was transferred to an EDTA coated tube and a lithium-heparinized collecting tube. The CBC was determined with an automated hematology analyzer (Vetscan® HM2 Hematology system, Abaxis, Inc., Union City, CA, USA) and a manual differential count was also performed. The serum chemistry (Cobas C III instrument, Roche Diagnostics, San Francisco, CA, USA) and electrolyte levels (9180 Electrolyte Analyzer, Roche Diagnostics) were also analyzed to evaluate the effects of Pyunkang-tang® in dogs. We measured the levels of blood urea nitrogen (BUN), creatinine (CREA), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total cholesterol (T. chol), triglyceride (TG), lipase (Lipa), total protein (TP), albumin (Alb), calcium (Ca), phosphate (P), sodium (Na), and potassium (K). The remaining blood sample was transferred into a serum separation tube. After clotting, the serum was separated and frozen at −20°C for the serum protein electrophoresis (SPE). The samples were analyzed within 2 weeks. For lipoprotein electrophoresis (LPE), the serum was stored at 4°C and tested within 72 hours of collection.

Urinalysis

Urinalysis was performed before and after the Pyunkang-tang® administration (at weeks 0 and 4) to evaluate the effects on renal function. The urine samples were collected by cystocentesis and the pH and protein levels were measured with a dip-stick test (Comber M, Roche, Germany). The specific gravity of the urine was measured using a refractometer (Reichert VET 360, Reichert Technologies, NY, USA).

Serum protein electrophoresis (SPE) and Lipoprotein electrophoresis (LPE)

The protein and lipoprotein electrophoresis of the serum were performed using a semi-automated Hydrasys® agarose gel electrophoresis system (Sebia, Norcross, GA, USA), according to the manufacturer's instructions. The gels were imaged and analyzed using a Gel Scan densitometer and the Phoresis software (Sebia Phoresis Imaging System) in the Neodin Veterinary Science Institute (Seoul, South Korea). The serum proteins were separated into the albumin, α1- and α2-globulins, β-globulins, and γ-globulins in order of highest to lowest mobility. The individual fraction concentrations (g/dl) were calculated using the percentage of the optical absorbance of each fraction and the total serum protein concentrations. The albumin to globulin ratios (A/G ratio) were also determined. The individual fraction concentrations of the lipoprotein fractions (α-, pre β-, and β-lipoproteins) were also estimated in percentages using the densitometric scans.

Statistical Analysis

All data are presented as mean ± standard deviation (SD). The statistical analysis was performed using the commercial software, SPSS version 20 (IBM, Chicago, IL, USA) and Excel 2010 (Microsoft, Redmond, WA, USA). Statistical comparisons between the two groups were carried out with using the *F*-test, followed by a Student's *t*-test. A one-way analysis of variance test was used to test the hypothesis of differing test values among groups. The Paired *t*-test was used to compare the results before and after the Pyunkang-tang® administration in each group. A value of $p < 0.05$ indicated statistical significance.

Results

Clinical assessment and laboratory examinations

None of the dogs exhibited noticeable clinical signs during the study period. The results of the CBC among the 3 groups before and after 4 weeks of the administration of Pyunkang-tang® are presented in Table 1. During the 4-week experiment, the results of the white blood cell (WBC) with differentials, hematocrit (HCT), and platelet counts in all the groups were within the normal ranges and did not show significant changes.

The Pyunkang-tang®-related effects on serum chemistry, electrolyte levels, and urinalysis were also evaluated during the experimental period. The results of serum chemistry and electrolyte analysis in all the groups were within the normal reference ranges. The ALT and BUN values were slightly decreased, and the CREA and lipase values were slightly increased compared to baseline values at 4 weeks after Pyunkang-tang® administration in groups I and II, but the differences were not significant between and within groups (Table 2). The USG and urine pH values were slightly changed 4 weeks after Pyunkang-tang® administration in all groups, but they were all within normal reference ranges and there were no significant differences. None of the dogs had protein in their urine during the study period (Table 3).

Table 1. Evaluation of complete blood count parameters before and after administration of Pyunkang-tang® in beagle dogs

Variables	Weeks	Group I	Group II	Group III	p value	RI
WBC (10^3/μl)	0	8.3 ± 2.34	7.8 ± 0.65	11.7 ± 0.26	0.068	8.5-28
	4	9.5 ± 1.82	8.1 ± 1.50	9.8 ± 0.42	0.376	
HCT (%)	0	34.6 ± 3.94	32.2 ± 7.93	36.5 ± 5.44	0.326	22-55
	4	36.1 ± 4.53	37.1 ± 7.34	42.5 ± 3.81	0.093	
PLT (10^3/μl)	0	412.0 ± 58.36	363.8 ± 195.49	386.0 ± 202.23	0.223	200-500
	4	435.5 ± 22.16	379.8 ± 69.12	413.3 ± 93.99	0.312	
Neutrophils (10^3/μl)	0	6.1 ± 2.26	5.6 ± 0.76	6.6 ± 2.64	0.925	3.0-11.5
	4	6.3 ± 1.32	5.9 ± 1.22	6.7 ± 0.67	0.158	
Lymphocytes (10^3/μl)	0	2.4 ± 1.30	1.8 ± 0.49	2.6 ± 2.03	0.887	0.8-4.8
	4	1.7 ± 0.54	1.8 ± 0.91	2.7 ± 1.64	0.057	
Monocytes (10^3/μl)	0	0.6 ± 0.52	0.5 ± 0.35	0.5 ± 0.25	0.793	0.1-1.35
	4	0.9 ± 0.44	0.8 ± 0.28	0.6 ± 0.24	0.093	
Eosinophils (10^3/μl)	0	0.17 ± 0.12	0.17 ± 0.10	0.29 ± 0.19	0.403	0.01-1.3
	4	0.06 ± 0.10	0.06 ± 0.08	0.24 ± 0.20	0.117	

Group I: administered Pyunkang-tang® at a dosage of 33 ml/day, three times a day.
Group II: administered Pyunkang-tang® at a dosage of 16.5 ml/day, three times a day.
Group III: administered distilled water at a dosage of 33 ml/day, three times a day.
WBC, white blood cell; HCT, hematocrit; PLT, platelet; RI, reference interval.

Table 2. Evaluation of serum chemistry and electrolyte profiles before and after administration of Pyunkang-tang® in beagle dogs

Variables	Weeks	Group I	Group II	Group III	p value	RI
ALT (U/L)	0	47.7 ± 22.12	43.8 ± 16.05	46.8 ± 15.79	0.962	16-70
	4	45.3 ± 8.33	40.0 ± 9.30	42.6 ± 19.92	0.878	
AST (U/L)	0	41.2 ± 4.38	33.0 ± 10.37	50.0 ± 17.42	0.119	4-50
	4	42.0 ± 16.49	32.4 ± 8.20	30.0 ± 12.43	0.062	
ALP (U/L)	0	70.2 ± 12.19	56.5 ± 9.33	83.8 ± 37.32	0.163	15-127
	4	74.2 ± 23.53	60.8 ± 15.71	79.8 ± 33.71	0.690	
BUN (mg/dl)	0	20.0 ± 4.53	22.0 ± 7.62	21.4 ± 5.98	0.376	5-29
	4	19.0 ± 4.62	19.5 ± 5.32	19.3 ± 4.27	0.967	
CREA (mg/dl)	0	0.5 ± 0.15	0.5 ± 0.07	0.7 ± 0.13	0.997	0.1-1.6
	4	0.7 ± 0.15	0.7 ± 0.10	0.9 ± 0.23	0.962	
BUN : Crea ratio	0	17.9 ± 5.13	18.5 ± 2.78	20.5 ± 3.28	0.138	4-27
	4	19.0 ± 4.26	18.5 ± 4.23	18.1 ± 4.00	0.312	
Lipase (U/L)	0	29.6 ± 13.99	20.6 ± 6.50	24.2 ± 6.65	0.569	0~500
	4	38.2 ± 13.77	30.2 ± 13.74	32.6 ± 14.24	0.650	
Ca (mg/dl)	0	10.9 ± 0.83	11.9 ± 0.67	13.2 ± 0.57	0.060	7-15
	4	10.6 ± 0.58	11.8 ± 1.78	11.7 ± 1.17	0.961	
P (mg/dl)	0	5.4 ± 0.72	6.1 ± 0.38	7.3 ± 0.71	0.058	4.2-10
	4	7.2 ± 0.76	6.3 ± 0.49	6.0 ± 0.96	0.523	
Na (mmol/L)	0	144.0 ± 3.39	146.0 ± 2.35	145.4 ± 2.70	0.689	141-152
	4	142.8 ± 1.10	145.2 ± 1.79	145.4 ± 3.78	0.095	
K (mmol/L)	0	4.0 ± 0.15	4.1 ± 0.12	4.2 ± 0.15	0.124	3.8-5
	4	4.7 ± 0.40	4.2 ± 0.16	4.3 ± 0.13	0.093	

Group I: administered Pyunkang-tang® at a dosage of 33 ml/day, three times a day.
Group II: administered Pyunkang-tang® at a dosage of 16.5 ml/day, three times a day.
Group III: administered distilled water at a dosage of 33 ml/day, three times a day.
ALT, alanine transferase; AST, asparate transferase; ALP, alkaline phosphatase; BUN, blood urea nitrogen; CREA, creatinine; Ca, calcium; P, phosphorus; Na, sodium; K, potassium; RI, reference interval.

Table 3. Evaluation of urinalysis before and after administration of Pyunkang-tang® in beagle dogs

Variables	Weeks	Group I	Group II	Group III	p value	RI
USG	0	1.041 ± 0.01	1.041 ± 0.01	1.047 ± 0.01	0.122	1.015-1.045
	4	1.031 ± 0.01	1.039 ± 0.02	1.035 ± 0.01	0.368	
pH	0	6.1 ± 1.03	6.5 ± 0.71	5.7 ± 0.45	0.102	5-7.5
	4	5.0 ± 0.00	5.2 ± 0.45	5.0 ± 0.00	0.138	
Urine Protein	0	Negative to trace	Negative to trace	Negative to trace	-	Negative or trace
	4	Negative to trace	Negative to trace	Negative to trace	-	

Group I: administered Pyunkang-tang® at a dosage of 33 ml/day, three times a day.
Group II: administered Pyunkang-tang® at a dosage of 16.5 ml/day, three times a day.
Group III: administered distilled water at a dosage of 33 ml/day, three times a day.
USG, Urine specific gravity; RI, reference interval.

Table 4. Evaluation of Serum protein EP before and after administration of Pyunkang-tang® in beagle dogs

Variables	Weeks	Group I	Group II	Group III	p value	RI
TP (g/dl)	0	6.1 ± 0.60	6.6 ± 0.52	7.0 ± 0.82	0.180	5.0-7.4
	4	6.2 ± 0.61	6.8 ± 0.91	7.2 ± 1.12	0.498	
Albumin (g/dl)	0	3.5 ± 0.36	3.9 ± 0.17	4.0 ± 0.35	0.083	2.7-4.4
	4	3.3 ± 0.17	3.6 ± 0.60	3.8 ± 0.26	0.599	
A/G ratio (g/dl)	0	1.4 ± 0.35	1.5 ± 0.04	1.5 ± 0.20	0.138	0.8-2.0
	4	1.1 ± 0.13	1.2 ± 0.25	1.3 ± 0.27	0.312	

Variables	Group I			Group II			Group III		
	0 week	4 weeks	p	0 week	4 weeks	p	0 week	4 weeks	p
α 1-globulines (g/dl)	0.20 ± 0.01	0.27 ± 0.02	0.042*	0.21 ± 0.01	0.26 ± 0.01	0.042*	0.17 ± 0.01	0.14 ± 0.02	0.066
α 2-globulines (g/dl)	1.33 ± 0.03	0.72 ± 0.17	0.043*	1.14 ± 0.04	0.80 ± 0.11	0.041*	1.24 ± 0.05	1.23 ± 0.14	0.686
β-globulins (g/dl)	0.33 ± 0.07	0.36 ± 0.01	0.500	0.19 ± 0.03	0.37 ± 0.02	0.039*	0.20 ± 0.01	0.22 ± 0.02	0.066
γ-globulins (g/dl)	0.69 ± 0.07	0.83 ± 0.03	0.043*	0.61 ± 0.03	0.68 ± 0.07	0.138	0.64 ± 0.02	0.64 ± 0.02	0.357

Group I: administered Pyunkang-tang® at a dosage of 33 ml/day, three times a day.
Group II: administered Pyunkang-tang® at a dosage of 16.5 ml/day, three times a day.
Group III: administered distilled water at a dosage of 33 ml/day, three times a day.
TP, Total protein; A/G ratio, albumin/globulin ratio; RI, reference interval.
*The value of $p < 0.05$ was considered significant.

Table 5. Evaluation of lipid and lipoprotein EP before and after administration of Pyunkang-tang® in beagle dogs

Variables	Weeks	Group I	Group II	Group III	p value	RI
T. chol (mg/dl)	0	260.7 ± 41.19	252.6 ± 12.68	242.8 ± 26.58	0.393	92-324
	4	217.5 ± 81.50	199.4 ± 38.10	207.4 ± 20.16	0.322	
TG (mg/dl)	0	37.4 ± 6.26	41.0 ± 13.55	54.4 ± 18.37	0.058	29-291
	4	60.6 ± 10.31	53.2 ± 13.94	60.3 ± 18.23	0.542	

Variables	Group I			Group II			Group III		
	0 week	4 weeks	p	0 week	4 weeks	p	0 week	4 weeks	p
a-lipoproteins (%) (HDL)	71.40 ± 2.51	78.00 ± 4.00	0042*	74.60 ± 0.55	78.40 ± 1.82	0.042*	69.80 ± 2.59	70.00 ± 2.45	1.000
Pre- β-lipoprotein (%) (VLDL)	12.40 ± 2.07	7.0 ± 2.83	0.068	9.00 ± 2.00	6.40 ± 2.70	0.080	14.80 ± 3.56	13.00 ± 3.81	0.465
β-lipoproteins (%) (LDL)	16.20 ± 0.84	16.40 ± 5.90	0.786	16.40 ± 1.67	16.40 ± 2.70	1.000	15.40 ± 2.51	16.60 ± 3.21	0.786

Group I: administered Pyunkang-tang® at a dosage of 33 ml/day, three times a day.
Group II: administered Pyunkang-tang® at a dosage of 16.5 ml/day, three times a day.
Group III: administered distilled water at a dosage of 33 ml/day, three times a day.
T.chol, Total cholesterol; TG, Triglyceride, HDL, high-density lipoprotein; VLDL, very low-density lipoprotein; LDL, low-density lipoprotein; RI, reference interval.
*The value of $p < 0.05$ was considered significant.

Results of serum protein electrophoresis (SPE)

Four weeks after Pyunkang-tang® administration, the TP values had slightly increased and the albumin values had slightly decreased. Thus, the albumin to globulin (A/G) ratio had also slightly decreased in all the groups, which means that the serum globulin levels were relatively elevated (Table 4). The serum globulins were separated into four fractions, the α1- and α2-globulins, β-globulins, and γ-globulins, and measured. In group I, the α1-globulin and γ-globulin levels were significantly increased ($p = 0.042$ and $p = 0.043$, respectively), and the α2-globulin levels were significantly decreased ($p = 0.043$) 4 weeks after Pyunkang-tang® administration. In group II, the α1-globulin and β-globulin levels were significantly increased ($p = 0.042$ and $p = 0.039$, respectively), and the α2-globulin levels were significantly decreased ($p = 0.041$) 4 weeks after Pyunkang-tang® administration. There was no significant change in the serum protein levels in group III (the control group) during the study period.

Results of lipoprotein electrophoresis (LPE)

The LPE values in all the groups at baseline and at 4 weeks after Pyunkang-tang® administration are shown in Table 5. No significant difference was observed in the levels of T. chol, TG, pre β- (very low-density lipoprotein, VLDL), and β-lipoprotein (low-density lipoprotein, LDL) between the groups, and between baseline and 4 weeks within each group (between and within groups, $p > 0.05$). The elevation in α-lipoprotein levels (high-density lipoprotein, HDL) after 4 weeks of Pyunkang-tang® administration was significant in group I ($p = 0.042$) and group II ($p = 0.042$), while no significant change was found in group III.

Discussion

Herbal medicines have been widely prescribed throughout the world in both human and veterinary medicine (6,19,20). The typical adverse effects of herbal medicines include liver and kidney injury. Herbal medicines known to cause liver injury include Ma-huang (ephedra) (12), Polygonum multiflorum (2), and Jin Bu Huan (22). Kidney injury has been reported to be associated with medicines such as Aristolochia manshuriensis (5) and aristolochic acid (4).

Pyunkang-tang® has been used in many patients with atopic diseases such as rhinitis, asthma, and atopic dermatitis in Korea. However, no clinical data are available on the safety and efficacy of this medicine. In this study, short-term adverse outcomes such as dermatologic problems and gastrointestinal disturbances (e.g., decreased appetite, weight loss, and fecal change) were not observed in any of the groups. In addition, the results of the hematological, serum biochemical, and urine analysis did not differ significantly between the treatment groups and the control group.

In this study, the albumin levels and A/G ratio were slightly decreased 4 weeks after Pyunkang-tang® administration. We performed SPE for the quantification of serum albumin and globulin levels. The oral administration of Pyunkang-tang® was associated with changes in serum globulin levels in groups I and II, in contrast to group III (the control group). In groups I and II, α2-globulin levels (which were elevated in all the groups at the start of the experiment) were decreased to a normal level ($p < 0.05$), but not in group III (control group). Changes in the levels of other proteins, such as an increase in α1-globulin levels in groups I and II, an increase in β-globulin in group II, and an increase in γ-globulin in group I, were subtle and the results were within normal ranges. Thus, the elevation of these globulins could be interpreted as normal variations, the dose dependent differences or non-specific.

Acute phase proteins (APPs), such as α1-lipoprotein, α2-macroglobulin, and haptoglobin, are serum proteins that can be used to assess the immune system's innate systemic response to infection, inflammation, or trauma (17). The serum concentration of these proteins changes by more than 25% in response to the pro-inflammatory cytokines produced during the disease process (11). According to previous studies (1,17), increases or decreases of these protein fractions occurred in animals with various inflammatory conditions. Even though, α2-globulin levels were decreased in this study, all dogs in the study group were healthy. Therefore, the effect of reducing the inflammation associated with α2-globulin after administration of Pyunkang-tang® was re-evaluated with the dogs in inflammatory status.

We used LPE to assess the influence of Pyunkang-tang® on lipid metabolism in dogs. After 4 weeks of administration of Pyunkang-tang®, a significant increase in HDL levels was observed in groups I and II ($p < 0.05$), while no change was observed in the control group (group III). Serum lipoproteins are divided into 4 major classes: chylomicrons, VLDL, LDL, and HDL (18). Among these, HDL is one of the major carriers of cholesterol in the blood. In humans, the modulation of HDL function and its serum concentrations significantly affects the management of cardiovascular diseases, cancers, and neurodegenerative and neurovascular diseases (10). Allergic sensitization has also been shown to be directly related to higher LDL and lower HDL levels in Chinese men (14). Thus, Pyunkang-tang® administration may also be useful for the prevention of the occurrence and aggravation of allergic conditions.

In conclusion, this study only focused on the short-term evaluation of the effects of oral administration of Pyunkang-tang® in dogs. During the 4-week study period, we did not observe any hematologic abnormalities or specific adverse effects. The dogs showed decreased α2-globulin levels and elevated HDL levels associated with the oral administration of this herbal medicine. However, controlled, randomized clinical trials and long-term evaluations still need to be conducted to fully evaluate the safety and efficacy of Pyunkang-tang® for the treatment of atopic disease in dogs. The scientific data and evidence obtained from our study might provide useful information about the traditionally used herbal medicine, Pyunkang-tang®, which would form the foundation for further research in dogs with atopic dermatitis.

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