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Comparison of Therapeutic Efficacy of Spa Mud and Bath Applications in the Treatment of Experimentally Induced Psoriasis and Eczema in Rats

ELITOK Bülent[1], ULUSOY Yavuz[2], KİLİNC Bahadir[2]

1. Afyon Kocatepe University, Faculty of Veterinary Medicine,
2. Ministry of Agriculture and Forestry, Veterinary Control Central Research Institute, Pathology Laboratory, Ankara/ Turkey

Corresponding author: **ELITOK Bülent, Email: elitok1969@hotmail.com**

ORCID: https:/ /orcid. org/ 0000-0003-3336-4479

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Abstract

Psoriasis and eczema are most common diseses of human and seen some animals. In this research project, a total of 49 Albino rats, 25 of which were psoriasis and 24 of eczema, were used. The back of all the animals were shaved 3 cm x 2 cm in size, and were deepilated using a 50% barium sulfate solution and deepillation tape. Then, 5% imiquimod was applied to the area for 5-6 days in the rats in psoriasis group, whereas 2%, 4-dinitrochlorobenzene was performed 2 times per day for one week in eczema group animals along with 150 µg of mite extract (*Dermatophagoides farinae*). After diseases formation in both groups, animals were divided into control and study groups, and then treatment period was started. In the rats with psoriasis and eczema, clinical, hematological, blood biochemical and histopathological findings were determined. In the light of the data obtained; it was concluded that a 21-day spa treatment in rats with psoriasis and eczema was very successful and could be considered as an option in the treatment of these diseases or it would increase the success of the treatment when combinated with classical medical treatments.

Key words: *Afyonkarahisar, balneotherapy, eczema, psoriasis, rat,*

Introduction

Psoriasis is a skin disease mainly developed in humans, although it is also seen in monkeys and dogs (Rodriquez-Martinez et al., 2017). The disease is the most common autoimmune disease in humans, characterized by continuous squamation and the combination of variable erythema and increased cutaneous plaques, which can be seen at any age, life-long, negatively affecting the quality of life by affecting physical and psycho-social health (2,3). It is a disease that can occur at any age, with a rate of 1.5-3% in the society. Although the age groups in which the incidence is peaked are 16-22 and 57-60, the first findings begin before the age of 15 in 30% of the cases (2,4). Today, psoriasis, which has a 2-3% incidence worldwide, is considered to be limited only to the skin in the past, today it is considered as a chronic systemic inflammatory disease accompanied by many comorbidities (5,6).

Similarly, eczema is also a common, chronic, non-infectious skin condition. The main symptom of this inflammatory disease is a very itchy rashcan be seen in human and the animals (7). In human beings, the disease is mostly seen in children (8). About 15% of children have eczema, but this only occurs in 2-4% of adults (9). Eczema pathogenesis is quite complex due to metabolic abnormalities, endocrine dyscrasias, diseases of the digestive system, viruses and bacteria in the external environment, temperature and humidity and foreign body allergen and stress (10,11).

Hot waters with rich mineral content have also been used successfully in the treatment of skin diseases such as eczema for thousands of years (12-14). Chemical components of thermal water known to have beneficial effects on the skin include minerals such as sulfur, magnesium and selenium (15,16). Thermal stimulation causes vasodilation, increases blood circulation and decreases blood pressure (16). Bathing with hot spring waters has a moisturizing effect on the stratum corneum and enhancing keratinocyte activity (17,18). In addition, minerals directly related to skin structure such as magnesium, sulfur, selenium, calcium and zinc are abundant in spa mud (19). In addition, the psychological effects of balneotherapy should not be overlooked (20).

Unfortunately, we have not been able to find a direct study on the healing effects of balneotherapy on psoriasis and eczema in human and animal species. This study was carried out with scientific data to determine the effectiveness of Süreyya I hot spring spring water and mud in psoriasis and eczema treatment, which is within the borders of Afyonkarahisar Province, and is very rich in content.

Materials and Methods

The experimental part of this study was carried out in Afyon Kocatepe University Experimental Animals Application and Research Center and was carried out with the reference number of AKUHADYEK 124-18 within the framework of the ethical rules determined by Afyon Kocatepe University Experimental Animals Ethics Committee (AKUHADYEK) and also supported by Şuayp Demirel within the scope of the Research Project.

Animal Material

In this research project, a total of 49 Albino rats were used to form 25 psoriasis and 24 eczema groups. The animals were kept in placitic cages in Afyon Kocatepe University Experimental Animals Application and Research Center in a stable environment with equal humidity and temperature conditions, 12 hours night and 12 hours day. During the study, animals were provided to receive *ad libitum* mouse food.

a) Psoriasis Group:

After shaving a 3 cm x 2 cm area in the back region of all rats, the area was deepened using 50 % barium sulfate solution and deepilation tape (Epiten® Veet), then to the deepile region for 5–6 days, daily 62.5 mg. Psoriasis was created (Figure 1) by applying %5 imiquimod (IMQ) (Aldara krem®Meda) (21). Following psoriasis formation, 2 rats exed for blood and histopathological examinations. Remaning 23 rats were divided into control (CG, n=11) and study group (SG, n=12).

In SG, all the rats were bathing for 10-15 minutes in bathtubs with fresh Süreyya I hot spring water set at 35 ± 2 °C, for 2 times for 21 day. Before bathing (Figure 4) in Süreyya I hot spring water thermal mud obtained from Süreyya I Spa source was applied to back area of animals where psoriasis was formed for 30 minutes 2 times a week (Figure 3). In CG, only bath applications were made under the same conditions with tap water. These applications were repeated for 21 days at the specified times.

b) Eczema Group:

A total of 24 rats were used in the eczema group. Following eczema formation, 2 rats exed for blood and histopathological examinations. Remaning 22 rats were divided into control (CG, n=11) and study group (SG, n=11).

After shaving an area of 3 cm x 2 cm in the back region in all rats, the area was deepened using 50% barium sulfate solution and deepilation band (Epithen, Veet), 2.4% dinitrochlorobenzene (DNCB) on the first day to the deepile region Sigma Aldrich, St Louis, MO, USA) was repeated 6 times, once a week. 3 days after this application, 150 µg of mite extract (*Dermatophagoides farinae*) was dissolved in PBS containing 0.5% tween 20 and eczema was created (Figure 2) (22).

Following the eczema formation, thermal mud obtained from Süreyya I hot spring source was applied to the area where eczema was created in 11 SG animals, twice a week, and before bathing. The baths were made for 10-15 minutes in the bath tubs with hot spring water set at 35 ± 2 ° C, 2 times at the same time, every 12 hours. These applications were repeated for 21 days at the specified times.

Preparation of Hot Spring Mud:

For this purpose, mineral accumulation in the place where Süreyya I hot spring water is flowing collected and sterilized in a oven set at 300 °C for 1.5 hours. Then, it mixed with mineral water comes from Süreyya I hot spring source, and mud was obtained.

Collecting Blood and Tissue Samples:

Randomly selected few animals from each groups were euthanized under ketamine (100 mg/kg)/ xylazine (10 mg/kg) anesthesia (23) on days of 1st, 7th, 14th and 21st after treatment period. Blood samples taken from intracadiac route, and tissue samples were stored at 10% formol and + 4 °C, and sent to the Etlik Veterinary Research and Application Institute Pathology Laboratory for histopathological eamnnation.

Süreyya I Well Spring Water used in the treatment of study group animals was in the class of thermomineral water with sodium bicarbonate, carbon dioxide, calcium, magnesium, fluoride and silicon, and its total mineralization was 4046.8 g / L.

Methods

Clinical Examinations

In all the animals, body temperatures (T), heart (P) and respiratory frequencies (R) were measured.

Hematological Examinations

In blood samples with EDTA; erythrocyte (RBC), total leukocyte (WBC), hematocrit (HCT), hemoglobin (HB), mean corpusculer volume (MCV), mean corpusculer hemoglobin (MHC), mean corpusculer hemoglobin concentration (MCHC), lymphocyte (LENF), neutrophil (Hematological examinations such as NOTR), eosinophil (EOS), monocyte (MON) and basophil (BAS) were measured using Chemray Brand blood count device using commercial test kits.

Blood Biochemical Examinations

In blood biochemical examinations; Immune globulin E (IgE) and C-reactive protein (CRP) measurements in ELISA reader device (ChemWell Chromate 4300 Elisa Reader, Awareness Technology, Inc. Martin Hwy. Palm City, USA) Elisa kits (Sunred Biological Technology Company Co., Shangai/Using China), measurements of Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Gamma-glutamyl transferase (GGT), Total Protein (TP), Albumin (ALB) and Glucose (GLU) levels are Cobas Integra 400 Plus Roche Brand (Roche Diagnostics GmbH, Germany) on the analyzer.

Histopathology Examinations

For histopathological examinations, 5 micron thick sections were taken and stained with hematoxylin eosin, then examined histopathologically in the light microscope.

Statistical Analysis

Statistical calculations of the groups were made according to the variance analysis (ANOVA) method. Duncan test was used to reveal the importance of intra-group differences in the study group. Statistical analyzes were made using Windows compatible SPSS 18.1 (Inc., Chicago, II, USA) package program. The data were given as mean ± standard error and $p < 0.05$ was considered significant.

Results

In the current study, following the formation of psoriasis, the animals were weighed one by one and the mean of body weight (bw) was found to be 283.7 g, and it was observed that there was a decrease in terms of bw average after psoriasis formation and the difference was statistically significant ($p < 0.05$). In weighing performed on the 21st day after treatment, it was determined that mean bw of CG rats (284.6 g) was higher than that of SG rats (280.2 g) ($p < 0.05$).

Similarly, after the eczema formation, it was observed that there was a decrease in bw mean (285.6 g) and the difference was statistically significant ($p < 0.05$). In the weighing performed on the last day of treatment, it was determined that mean bw of CG (287.8 g) was higher ($p < 0.05$) than the that of SG rats (283.3 g).

Clinical Findings

The clinical findings are shown in Table 1 and Table 2. When these tables are examined; no statistically significant differences were found in terms of T ($p > 0.05$), whereas, significant differences ($p < 0.05$) were formed in terms of P and R after the psoriasis and eczema procedure were applied, and the most significant ($p < 0.05$) changes occurred in SG animals.

Hematological Findings

The hematological examination findings of psoriasis and eczema rats are presented in Table 3 and Table 4. When these tables are examined; WBC, NOTR, MON, EOS and MCV levels increased statistically significantly ($p < 0.05$) after psoriasis and eczema formation, whereas RBC, HG, HCT, LENF, MCH and MCHC levels significantly ($p < 0.05$) decreased. With the start of the treatment period, WBC, NOTR, MON, EOS and MCV levels decreased in both disease groups, while significant ($p < 0.05$) increases were observed in RBC, HG, HCT, LENF, MCH and MCHC levels. However, it was observed that the most statistically significant changes occurred in SG animals in both groups, and on the last day of the study.

Blood Biochemical Findings

Blood biochemical findings are shown in Table 5 and Table 6. When these tables are examined; ALT, AST, GGT, CRP and IgE levels increased significantly ($p < 0.05$) in the period following psoriasis and eczema formation, whereas TP, ALB and GLU levels decreased significantly ($p < 0.05$). After treatment, TP, ALB and GLU levels increased in both disease groups ($p < 0.05$), whereas ALT, AST, GGT, CRP and IgE levels decreased ($p < 0.05$), and the most important changes in terms of increasing and decreasing parameters were determined in SG animals on 21st day of the study in both groups.

Histopathological Exam Results

In the tissue sections taken from the animals with psoriasis, severe destruction in the epithelium and propriosa mucosa exposure were observed, whereas in the tissue samples taken after eczema formation, severe inflammation in the propriotic mucosa and degeneration in the epithelium were detected (Figures 5,8). In the last day of treatment, it was seen that histopathological findings of psoriasis and eczema were significantly improved in SG groups which treated with hot spring water (Figure 6.9), whereas severe epithelial destructions still continued in CG of psoriasis and eczema which treated with tap water (Figure 7.10).

Discussion

Although, psoriasis and eczema are most common disese of human and more less in animals, we can not find any literatures about balneotherapy in

domestic animals with psoriasis or eczema as well as directly studies in human beings. Therefore, as far as we know the present study will be at first in this area.

There are many studies reporting that balneotherapeutic applications increase fat burning by increasing the metabolic rate and thus lead to weight loss (24,25). Fioravanti et al. (26) reported this rate in body weight loss as 7% after spa treatment. In our study, similar findings were obtained, and determined a statistically significant ($p < 0.05$) bw loss in SG animals compared to CG animals in psoriasis and eczema groups.

In our study, it was observed that mean P and R were higher in SG animals when compared with CG group in both groups, although significant changes were not formed in terms of T measured after bath in animals with psoriasis and eczema ($p > 0.05$). These findings was found to be consistent with findings previously obtained by researchers (27,28), who claimed that balneotherapy increased cardiac output, causes vasodilation in peripheral vessels, and caused an increase in the frequency of the heart and, accordingly, respiration. Our findings was also found to be consistent with findings reported by the other researchers (29,30), who notified that balneotherapy caused increases in blood pressure, heart and respiratory frequency.

Psoriasis and eczema is an immune-mediated chronic inflammatory skin disease that is characterized by hyperproliferative keratinocytes, T cells immune deficiency, infiltration of macrophages and neutrophils and eosinophilia (31). Similar to other inflammatory diseases, white cell cells frequently increase in psoriasis patients (32). In addition, it has been reported that the neutrophils increase and neutrophil activation products increase in the blood of psoriasis patients (33). Similarly, it has been reported that the body provides homeostasis, the number of WBCs increase, and only collateral damage occurs in normal tissues during this process against inflammation developing in chronic cases such as eczema (34). In our study, after the formation of psoriasis and eczema, WBC, NOTR, MON, EOS and MCV levels increased statistically significantly ($p < 0.05$), whereas RBC, HG, HCT, LENF, MCH and MCHC levels were significantly ($p < 0.05$) decreased. However, when the treatment period was initiated, WBC, NOTR, MON, EOS and MCV levels decreased in CG and SG rats in both groups, while RBC, HG, HCT, LENF, MCH and MCHC levels increased. However, it was observed that the changes shaped after treatment occurred in SG rats in both disease groups and on the last day of the study.

In addition, the average platelet volume was found to be correlated with disease severity in psoriasis patients (35). Ünal M et al. (36) reported that leukocyte, neutrophil and PLT values increased in psoriasis patients and showed a positive correlation with C-reactive protein (CRP). As a matter of fact, it was found in our study that similarly high WBC, NOTR, PLT and CRP levels were accompanied by increased CRP levels. Similarly, in our current study, the high IgE levels that we detected after eczema formation were accompanied by an eosinophilia, increased IgE response observed in patients with eczema. Similar findings previously reported by some researchers (37). Obtaining the lowest IgE levels in SG animals on the 21st day of treatment can be interpreted as the most important improvement was in this group.

In addition, Mg deficiency has been reported to cause clinical inflammation syndrome, resulting in leukocyte and macrophage activation and overproduction of free radicals, showing a pro-inflammatory effect (38). Sureyya I hot spring water that we use in our current study is a water rich in magnesium. The detection of lower inflammation processes in SG rats which treated by this water supports these researchers.

In our study, ALT, AST, GGT, CRP and IgE levels increased significantly ($p < 0.05$) from the blood biochemical parameters in the period following the disease formation in the groups with psoriasis and eczema, whereas TP, ALB and GLU levels were significantly ($p < 0.05$). decreased. With the transition to the treatment period, a reverse course was observed in both disease groups, so, the levels for TP, ALB and GLU increased, whereas ALT, AST, GGT, CRP and IgE levels decreased. It was observed that the most important changes detected in SG rats in both disease groups on the 21st day of the study. It well known that ALT and AST are liver enzymes, and their increase after the formation of psoriasis and eczema show that these diseases affect the liver (39). Rich mineral water applications have been reported to contribute to a decrease in liver damage indices with high AST and ALT levels (40). In addition, hot spring mineral water therapy have been reported to decrease lipid peroxidation and related hepatic malondialdehyde (MDA) content in the liver and decrease hepatic damage, increase antioxidant capacity against oxidative stress through

boron and Mg, and cause a significant reduction in glucose (GLU) levels (24). In our current study, ALT, AST, ALP enzyme levels, which were found to be higher, and GLU concentrations lower when compared to pre-study measurements, which were found to be high, by the transition to the treatment period, a reverse situation is shaped in both disease groups. Indeed, minerals such as bicarbonate and magnesium have been reported to affect glucose metabolism and reduce the increased dietary acid load associated with the development of insulin resistance (41).

In our study, unlike CG in psoriasis and eczema groups, histopathological findings of psoriasis and eczema almost completely recovered after performed treatment in SG which treated by Süreyya I hot spring water. However, animals treated with tap water still had severe inflammation, epithelium destruction continued. These data we obtained were compatible with a study (14) that balneotherapy was very successful in the treatment of skin diseases.

Conclussion

Consequently, the clinical, hematological, blood biochemical parameters and histopathological examination findings obtained from this study showed that Sureyya I hot spring water was very successful in the treatment of psoriasis and eczema. It can be evaluated it-self or along with classical medical therapy.

Declaration of conflict of interests/Conflict of Interest Statement

The authors declare that there is no conflict of interest regarding the publication of this article.

Informed consent

Informed consent was obtained from all patients included in this study.

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Table 1. Statistical comparison of body temperature, pulse and respiratory in the animals with psoriasis

Measurement Time/Parameters		T (°C)	P (frequence/min)	R (frequence/min)
		X±SD	X±SD	X±SD
	Groups			
BS (n=25)	-	37.20±0.20	316.44±38.12^{e}	107.11±28.41^{e}
APF (n=23)	-	37.30±0.30	356.24±57.62^{a}	138.24±32.14^{a}
AT 1st Day	CG (n=11)	37.30±0.20	355.18±53.21^{a}	139.27±34.32^{a}
	SG (n=12)	37.20±0.10	355.09±52.12^{a}	138.26±35.22^{a}
AT 7th Day	CG (n=9)	37.30±0.10	328.24±37.43^{d}	125.34±26.43^{d}
	SG (n=10)	37.20±0.10	345.28±35.28^{b}	132.12±18.33^{b}
AT 14th Day	CG (n=7)	37.20±0.10	320.56±22.14^{e}	117.23±11.22^{d}
	SG (n=8)	37.20±0.00	337.11±16.43^{bc}	126.33±10.21^{c}
AT 21th Day	CG (n=4)	37.10±0.10	316.33±9.43^{e}	111.23±7.43^{e}
	SG (n=4)	37.30±0.10	328.24±8.23^{d}	118.18±6.44^{d}

a-e : Different letters in the same column are statistically significant ($p < 0.05$). BS: Before study, APF: After psoriasis formation, AT: After treatment, CG: Control group, SG: Study group

Table 2. Statistical comparison of body temperature, pulse and respiratory in the animals with eczema

Measurement Time/Parameters		T (°C)	P (frequence/min)	R (frequence/min)
		X±SD	X±SD	X±SD
	Groups			
BS (n=24)	-	37.10±0.10	313.28±44.22^{d}	105.42±31.14^{d}
AEF (n=22)	-	37.20±0.20	347.16±48.14^{a}	126.32±36.24^{a}
AT 1st Day	CG (n=11)	37.20±0.20	346.24±44.15^{a}	127.21±35.47^{a}
	SG (n=11)	37.30±0.20	345.18±43.23^{a}	128.13±33.23^{a}
AT 7th Day	CG (n=10)	37.20±0.10	323.12±28.32^{c}	121.21±18.33^{b}
	SG (n=10)	37.30±0.20	335.16±24.11^{b}	120.44±16.15^{b}
AT 14th Day	CG (n=7)	37.20±0.20	321.24±23.08^{c}	114.43±12.14^{bc}
	SG (n=7)	37.30±0.10	334.20±14.12^{b}	119.28±11.42^{b}
AT 21th Day	CG (n=4)	37.10±0.10	322.28±10.24^{c}	111.17±9.45^{c}
	SG (n=4)	37.30±0.10	333.16±9.08^{b}	119.23±8.34^{b}

a-d : Different letters in the same column are statistically significant ($p < 0.05$). BS: Before study, AEF: After eczemaformation, AT: After treatment, CG: Control group, SG: Study group

Table 3. Hematological examination findings of animals with psoriasis.

Measurement Time/Parameters		WBC (10^3/mm3)	RBC (10^6/mm3)	HB (g/dl)	HCT (%)	MCV (fl)	MCH (pg)	MCHC (g/dl)
	Groups	**X±SD**	**X±SD**	**X±SD**	**X±SD**	**X±SD**	**X±SD**	**X±SD**
BS (n=25)	-	13.51 ±3.43^{c}	8.51 ± 2.13^{ab}	13.37 ± 3.11^{a}	42.38 ± 3.26^{b}	49.19± 3.21^{c}	15.57±3.19^{a}	31.43± 3.27^{a}
APF (n=23)	-	11.39 ± 3.20^{ab}	7.59 ± 2.18^{b}	13.75 ± 3.43^{b}	44.81 ± 3.29^{b}	58.24± 3.46^{a}	17.71± 3.32^{a}	30.66± 3.36^{b}
AT 1st Day	CG (n=11)	12.11 ± 3.18^{a}	7.72 ± 1.57^{b}	13.65 ± 3.18^{b}	45.12 ± 3.16^{ab}	57.51± 3.21^{b}	17.25± 3.18^{a}	30.17± 2.44^{b}
	SG (n=12)	11.41 ± 3.14^{ab}	8.07 ± 1.47^{ab}	14.08 ± 2.45^{a}	44.63 ± 3.08^{b}	55.04± 2.48^{c}	17.46± 2.23^{a}	31.53± 2.45^{a}
AT 7th Day	CG (n=9)	12.14 ± 2.16^{a}	8.03 ± 1.46^{ab}	13.81 ± 2.23^{b}	45.39 ± 2.34^{a}	56.68± 2.46^{a}	17.10± 2.31^{a}	30.50± 1.55^{b}
	SG (n=10)	11.21 ± 2.32^{ab}	8.13 ± 1.42^{ab}	14.19 ± 2.16^{a}	45.13 ± 2.57^{ab}	55.50± 2.34^{c}	17.38± 1.56^{a}	31.27± 1.53^{ab}
AT 14th Day	CG (n=7)	11.87 ± 1.63^{ab}	7.93 ± 1.42^{b}	14.05 ± 1.45^{a}	44.83 ± 1.56^{b}	54.58± 1.43^{c}	17.53± 1.19^{a}	31.23± 1.43^{a}
	SG (n=8)	9.56±1.57^{b}	8.31± 1.27^{a}	14.21 ± 1.38^{a}	45.19 ± 1.47^{ab}	54.88± 1.19^{c}	17.19± 1.51^{a}	31.39± 1.28^{a}
AT 21th Day	CG (n=4)	11.13 ± 1.46^{ab}	8.06 ± 1.24^{ab}	13.87 ± 1.46^{b}	45.51± 1.33^{a}	56.50± 1.36^{ab}	17.15± 1.42^{a}	30.31± 1.31^{b}
	SG (n=4)	8.71 ± 1.43^{c}	8.43 ± 1.21^{a}	14.10 ± 1.28^{a}	45.83 ± 1.57^{a}	54.69± 1.18^{c}	16.68± 1.41^{b}	30.62± 1.24^{b}

Continuing Tablo 3

Measurement Time/Parameters		LENF %	NOTR %	EOS %	MON %	BAS %
	Groups	**X±SD**	**X±SD**	**X±SD**	**X±SD**	**X±SD**
BS (n=25)	-	70.25 ± 6.48^{d}	27.08 ± 5.22^{ab}	3.34 ± 1.46^{d}	3.54 ± 1.48^{b}	ÖD
APF (n=23)	-	61.91 ± 7.28^{a}	38.43 ± 6.46^{c}	6.34 ± 1.37^{a}	4.09 ± 2.24^{a}	ÖD
AT 1st Day	CG (n=11)	56.09 ± 6.23^{c}	38.76 ± 6.12^{c}	6.41 ± 1.36^{a}	4.08 ± 2.16^{a}	ÖD
	SG (n=12)	56.10 ± 5.18^{c}	36.38 ± 5.21^{d}	5.23 ± 1.34^{b}	3.84 ± 2.12^{ab}	ÖD
AT 7th Day	CG (n=9)	51.36 ±4.44^{d}	43.27 ± 3.18^{b}	5.29 ± 1.32^{b}	4.07 ± 1.56^{ab}	ÖD
	SG (n=10)	45.11 ± 4.27^{f}	47.16 ± 3.33^{a}	4.07 ± 1.37^{c}	3.63 ± 1.46^{b}	ÖD
AT 14th Day	CG (n=7)	53.19 ± 3.44^{de}	45.43 ± 3.24^{ab}	4.19 ± 1.34^{c}	4.03± 1.38^{ab}	ÖD
	SG (n=8)	50.15 ± 3.28^{d}	45.39 ± 2.18^{ab}	2.79 ± 1.22^{d}	3.01 ± 1.41^{c}	ÖD
AT 21th Day	CG (n=4)	51.31 ± 1.66^{d}	43.32 ± 1.54^{b}	4.06 ± 1.32^{c}	3.94 ± 1.25^{ab}	ÖD
	SG (n=4)	48.91 ± 1.57^{e}	46.37 ± 1.48^{a}	2.45 ± 1.28^{d}	2.79 ± 1.18^{d}	ÖD

a-f: Different letters in the same column are statistically significant ($p < 0.05$). BS: Before study,
APF: After psoriasis formation, AT: After treatment, CG: Control group, SG: Study group

Table 4. Hematological examination findings of animals with eczema.

Measurement Time/Parameters		WBC (10^3/mm3)	RBC (10^6/mm3)	HB (g/dl)	HCT (%)	MCV (fl)	MCH (pg)	MCHC (g/dl)
	Groups	**X±SD**	**X±SD**	**X±SD**	**X±SD**	**X±SD**	**X±SD**	**X±SD**
BS (n=24)	-	13.58 ±4.32^{c}	8.54 ± 4.22^{ab}	13.44 ± 4.37^{a}	42.45 ± 4.37^{b}	49.21± 3.32^{c}	15.60±3.27^{a}	31.47± 3.17^{a}
AEF (n=22)	-	11.42 ± 4.13^{ab}	7.61 ± 4.34^{b}	13.81 ± 5.65^{b}	44.93 ± 5.63^{b}	58.26± 4.23^{a}	17.75± 4.48^{a}	30.68±4.24^{b}
AT 1st Day	CG (n=11)	12.14 ± 3.21^{a}	7.79 ± 3.45^{b}	13.70 ± 4.45^{b}	45.17 ± 4.35^{ab}	57.58± 3.31^{b}	17.28± 4.23^{a}	30.20± 3.13^{b}
	SG (n=11)	11.43 ± 3.36^{ab}	8.11 ± 2.52^{ab}	14.13 ± 3.52^{a}	44.70 ± 4.44^{b}	55.07± 3.41^{c}	17.47± 3.31^{a}	31.56± 3.41^{a}
AT 7th Day	CG (n=10)	12.21 ± 3.24^{a}	8.08 ± 2.43^{ab}	13.93 ± 3.39^{b}	45.42 ± 3.18^{a}	56.70± 3.36^{a}	17.12± 3.43^{a}	30.53± 2.34^{b}
	SG (n=10)	11.25 ± 3.17^{ab}	8.17 ± 2.31^{ab}	14.22 ± 3.27^{a}	45.16 ± 3.09^{ab}	55.53± 2.19^{c}	17.41± 2.38^{a}	31.29± 246
AT 14th Day	CG (n=7)	11.92 ± 2.33^{ab}	7.98 ± 1.63^{b}	14.11 ± 2.38^{a}	44.87 ± 2.36^{b}	54.61± 2.07^{c}	17.55± 2.24^{a}	31.26± 2.25^{a}
	SG (n=7)	9.62±1.48^{b}	8.36± 1.57^{a}	14.25 ± 2.34^{a}	45.22 ± 2.34^{ab}	54.92± 2.09^{c}	17.21± 2.37^{a}	31.41± 2.31^{a}
AT 21th Day	CG (n=4)	11.16 ± 1.41^{ab}	8.10 ± 1.38^{ab}	13.91 ± 1.53^{b}	45.56± 1.48^{a}	56.53± 1.52^{ab}	17.16± 1.38^{a}	30.33± 1.59^{b}
	SG (n=4)	8.78 ± 1.39^{c}	8.49 ± 1.24^{a}	14.13 ± 1.48^{a}	45.85 ± 1.54^{a}	54.72± 1.43^{c}	16.71± 1.35^{b}	30.66± 1.48^{b}

Continuing Table 4

Measurement Time/Parameters		LENF %	NOTR %	EOS %	MON %	BAS %
	Groups	**X±SD**	**X±SD**	**X±SD**	**X±SD**	**X±SD**
BS (n=24)	-	70.37 ± 5.45^{d}	27.12 ± 4.66^{ab}	3.35 ± 1.56^{d}	3.55 ± 0.66^{b}	ÖD
AEF (n=22)	-	61.83 ± 5.44^{a}	38.45 ± 5.39^{c}	6.35 ± 2.48^{a}	4.05 ± 2.48^{a}	ÖD
AT 1st Day	CG (n=11)	56.11 ± 5.43^{c}	38.81 ± 4.23^{c}	6.43 ± 2.54^{a}	4.05 ± 2.27^{a}	ÖD
	SG (n=11)	56.12 ± 4.24^{c}	36.44 ± 4.09^{d}	5.25 ± 2.41^{b}	3.81 ± 1.36^{ab}	ÖD
AT 7th Day	CG (n=10)	51.33 ±3.37^{d}	43.31 ± 3.37^{b}	5.31 ± 2.38^{b}	4.04 ± 1.48^{ab}	ÖD
	SG (n=10)	45.09 ± 3.27^{f}	47.18 ± 3.39^{a}	4.08 ± 1.54^{c}	3.61 ± 1.29^{b}	ÖD
AT 14th Day	CG (n=7)	53.18 ± 2.17^{de}	45.44 ± 2.39^{ab}	4.20 ± 1.49^{c}	4.02± 1.04^{ab}	ÖD
	SG (n=7)	50.3 ± 2.13^{d}	45.41 ± 2.36^{ab}	2.80 ± 1.41^{d}	3.00 ± 1.12^{c}	ÖD
AT 21th Day	CG (n=4)	51.29 ± 1.44^{d}	43.33 ± 1.57^{b}	4.08 ± 1.37^{c}	3.91 ± 0.47^{ab}	ÖD
	SG (n=4)	48.87 ± 1.39^{e}	46.39 ± 1.53^{a}	2.46 ± 1.34^{d}	2.76 ± 1.10^{d}	ÖD

a-f: Different letters in the same column are statistically significant (p <0.05). BS: Before study, AEF: After eczemaformation, AT: After treatment, CG: Control group, SG: Study group

Table 5. Blood biochemical findings of animals with psoriasis.

Measurement Time/Parameters		ALT (IU/L)	AST (IU/L)	GGT (IU/L)	CRP (mcg/ml)	TP (g/dl)	ALB (g/dl)	GLU (g/dl)	IgE (ng/ml)
	Groups	**X±SD**	**X±SD**	**X±SD**	**X±SD**	**X±SD**	**X±SD**	**X±SD**	**X±SD**
BS (n=25)	-	75.47±23.28^{e}	154.21±45.20^{e}	13.27±4.42^{b}	407.46±83.44^{e}	65.72±25.57^{a}	39.19±9.16^{a}	119.27±34.22^{a}	0.43 ±0.08^{g}
APF (n=23)	-	113.72±44.13^{a}	183.12±48.24^{a}	15.58±5.43^{a}	948.25±212.25^{a}	51.09±12.41^{d}	23.12±5.42^{g}	101.12±12.53^{d}	4.86 ±1.45^{a}
AT 1st Day	CG (n=11)	112.21±37.32^{a}	182.27±46.31^{a}	14.96±4.24^{ab}	942.15±283.41^{a}	52.26±11.13^{d}	23.65±4.13^{e}	96.13±12.34^{e}	5.03±1.17^{a}
	SG (n=12)	111.08±33.11^{a}	179.25±46.18^{a}	14.26±4.21^{b}	938.13±278.25^{a}	52.14±11.28^{d}	23.69±4.57^{e}	96.43±9.37^{e}	5.06 ±1.23^{a}
AT 7th Day	CG (n=9)	104.23±25.44^{b}	174.15±33.45^{b}	14.30±3.42^{b}	939.17±154.33^{a}	53.17±8.36^{c}	24.32±3.13^{e}	94.23±7.35^{e}	4.85 ±1.12^{b}
	SG (n=10)	96.18±23.25^{c}	165.34±31.42^{c}	13.78±2.18^{c}	905.14±148.13^{a}	55.08±7.14^{c}	25.28±3.48^{dc}	113.12±5.36^{b}	3.56±1.21^{d}
AT 14th Day	CG (n=7)	101.18±13.22^{bc}	169.17±19.32^{bc}	13.01±1.23^{d}	701.05±113.15^{b}	55.17±5.18^{c}	25.32±2.2^{de}	106.18±4.45^{e}	4.03±1.19^{e}
	SG (n=8)	81.19±9.16^{d}	160.34±18.23^{d}	13.32±1.34^{b}	521.16±76.32^{d}	57.16±4.09^{bc}	29.48±1.36^{c}	119.42±3.13^{a}	2.09±0.67^{e}
AT 21th Day	CG (n=4)	96.09±6.54^{c}	161.23±6.44^{d}	13.89±0.57^{b}	613.22±66.34^{c}	56.28±3.41^{bc}	27.04±118^{d}	112.44±3.14^{b}	3.83±0.78^{cd}
	SG (n=4)	76.27±4.23^{e}	153.22±5.48^{e}	12.84±0.48^{c}	412.43±59.73^{e}	61.18±2.16^{b}	35.44±1.27^{b}	121.33±3.15^{a}	0.78±0.34^{f}

a-g: Different letters in the same column are statistically significant (p <0.05). BS: Before study, APF: After psoriasis formation, AT: After treatment, CG: Control group, SG: Study group

Table 6. Blood biochemical findings of animals with eczema.

Measurement Time/Parameters		ALT (IU/L)	AST (IU/L)	GGT (IU/L)	CRP (mcg/ml)	TP (g/dl)	ALB (g/dl)	GLU (g/dl)	IgE (ng/ml)
	Groups	**X±SD**	**X±SD**	**X±SD**	**X±SD**	**X±SD**	**X±SD**	**X±SD**	**X±SD**
BS (n=24)	-	75.56±24.31^{e}	153.34±47.18^{e}	13.23±3.57^{b}	405.24±112.21^{e}	65.09±1934	39.37±8.24^{a}	122.32±28.14^{ab}	0.45 ±0.10^{g}
AEF (n=22)	-	113.87±43.24^{a}	182.34±44.12^{a}	15.31±4.32^{a}	932.14±323.04^{a}	51.34±13.26^{d}	23.56±7.23^{g}	103.24±32.16^{f}	4.78 ±2.08^{a}
AT 1st Day	CG (n=11)	112.28±36.48^{a}	183.13±37.38^{a}	14.78±3.11^{b}	932.23±287.17^{a}	52.48±12.24^{d}	23.57±5.42^{e}	104.18±24.21^{a}	5.01±2.07^{a}
	SG (n=11)	112.11±32.16^{a}	178.08±35.22^{a}	14.33±3.48^{b}	930.26±269.11^{a}	52.36±12.64^{d}	23.63±5.37^{e}	105.23±18.46^{f}	5.03 ±2.11^{a}
AT 7th Day	CG (n=10)	105.37±23.22^{b}	175.24±32.36^{b}	14.27±3.35^{b}	859.34±211.22^{a}	53.42±9.22^{c}	24.65±4.27^{e}	108.09±9.32^{e}	4.82 ±1.34^{b}
	SG (n=10)	97.15±25.32^{c}	164.23±28.14^{c}	13.56±2.43^{b}	804.28±202.23^{a}	55.13±8.27^{c}	25.38±3.57^{de}	111.27±7.18^{d}	3.63±1.45^{d}
AT 14th Day	CG (n=7)	102.27±15.09^{bc}	167.23±21.54^{bc}	13.14±1.34^{b}	705.14±156.41^{b}	55.08±6.09^{c}	25.28±2.44^{de}	111.36±6.31^{d}	4.17±1.09^{e}
	SG (n=7)	82.43±10.12^{d}	161.14±17.43^{d}	13.28±1.54^{b}	534.37±101.18^{d}	57.56±5.21^{bc}	31.59±2.31^{c}	120.13±4.42^{b}	2.43±0.75^{e}
AT 21th Day	CG (n=4)	97.16±8.24^{c}	160.18±9.32^{d}	13.04±0.66^{bc}	626.13±88.41^{c}	56.03±4.02^{bc}	27.13±1.57^{d}	116.25±2.32^{c}	3.78±0.57^{cd}
	SG (n=4)	77.29±7.36^{e}	154.09±7.16^{e}	12.82±0.59^{d}	403.29±61.48^{e}	63.41±3.46^{b}	37.51±1.48^{b}	124.08±2.56^{a}	0.86±0.49^{f}

a-g: Different letters in the same column are statistically significant (p <0.05). BS: Before study, AEF: After eczemaformation, AT: After treatment, CG: Control group, SG: Study group