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Investigation of Effects of Combined Trichodoll® and Cutibacterium granulosum Administration on Total Oxidant Status and Total Antioxidant Status in Sheep with Dermatophytosis

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ABSTRACT

Dermatophytosis is a contagious zoonotic fungal disease affecting keratinized tissues in humans and animals, caused by dermatophytes of the species *Trichophyton* spp., *Microsporum* spp. and *Epidermophyton* spp. In this study, it was aimed to evaluate the effects of vaccination and immunomodulatory treatment protocols administered to sheep with dermatophytosis on serum total antioxidant status (TAS) and total oxidant status (TOS). The study material consisted of a total of 20 female Zom breed sheep, aged three years or over, with a history of dermatological lesions for at least one month and no prior treatment. Sheep diagnosed with dermatophytosis were randomly divided into two equal groups (n = 10). Blood samples were collected from all sheep at two different time (pre-administration and post-administration). Serum TAS and TOS levels were determined using a commercial ELISA kit. Only in the group that received the vaccine, a decrease in TAS levels was observed on day 7 (P = .059), while no significant change was detected in TOS levels (P = .910). In the combined treatment group, a significant increase in TAS levels was determined (P = .028), while no statistically significant difference was observed in TOS levels (P = .705). The results obtained reveal that Cutibacterium granulosum regulates the oxidative stress response and increases antioxidant capacity due to its immunomodulatory properties.

Keywords: Dermatophytosis, immudoll[CG], oxidative stress, sheep

INTRODUCTION

Dermatophytosis is an infection caused by keratinophilic fungi of the species *Trichophyton spp*., *Microsporum spp*., and *Epidermophyton spp*., which affect keratinized tissues. Dermatophyte infection is a contagious skin disease with zoonotic characteristics that has a significant impact on human health as well as domestic animals.[1-4] The clinical findings of the disease generally vary depending on the site of infection, the host's immunity, and the affected species.[5] The pathogenesis of dermatophytosis depends on the interaction between the pathogen and the host. The immune defense system of the affected animal is activated in response to fungal metabolic products.[4-7] The epidermal layer of the skin contains high concentrations of antioxidants, and antioxidant substances are distributed in increasing concentrations towards the deeper layers of the stratum corneum.[8] Therefore, keratinolytic fungal pathogens invade the stratum corneum by breaking down the keratin-protein complex through the keratinase enzyme they secrete, thereby causing inflammatory reactions.[9]

The body maintains redox balance through enzymatic and non-enzymatic antioxidant systems that limit excessive pro-oxidant production.[10-12] This defence mechanism plays an important role in host defence, but has limited capacity and is sensitive to free radicals.[11,13] In healthy animals, there is a balance between the antioxidant defence system and free radicals.[14-16] However, this balance is disrupted in favor of oxidants causes oxidative stress and leads to damage in cellular macromolecules.[14,17]

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Cutibacterium granulosum (C. granulosum) is an anaerobic diphtheroid bacterium found as a commensal on the skin surface of healthy individuals. It is considered among the Cutibacterium species involved in the pathogenesis of acne vulgaris and certain other dermatological conditions.[18,19] It has been reported that *Cutibacterium spp.* species possess immunomodulatory properties that can interact with host defence mechanisms and play a role in regulating non-specific antibacterial, antiviral and antitumour responses.[19] It is stated that propionic acid, one of the metabolites of *Cutibacterium acnes*, which has a similar genetic structure to *C. granulosum*, can stimulate lipid synthesis in keratinocytes and may contribute to supporting epidermal barrier function. Furthermore, it has been reported that this metabolite may contribute to limiting bacterial proliferation and maintaining skin homeostasis by affecting the antimicrobial activity of the epidermis.[20] TAS, reflects the cumulative effect of all antioxidant components and provides an overall assessment of the oxidant–antioxidant balance.[12,21] Measuring oxidant and antioxidant parameters associated with oxidative stress separately to assess the severity and prognosis of dermatophytosis can be time-consuming and limited in practice. Therefore, redox balance in the body is evaluated by measuring TAS and TOS levels.[22]

The aim of this study is to investigate the effects of vaccination and immunomodulatory treatment protocols applied to sheep with dermatophytosis on serum TAS and TOS levels. Additionally, the aim is to determine the potential contributions of the combined use of vaccines and immunomodulators on the clinical course of the disease and the body's oxidant-antioxidant balance.

MATERIALS AND METHODS

Animal Selection Criteria

The study included 20 female Zom breed sheep aged ≥ 3 years from the sheep farm of Dicle University's Faculty of Veterinary Medicine. All animals had dermatological lesions and had not received any topical or systemic treatment prior to the study. Dermatophytosis was diagnosed in all animals based on clinical and microbiological examinations. The affected sheep were randomly divided into two equal groups (n = 10). Sheep in Group 1 received the Trichodoll® vaccine on day 0. Sheep in Group 2 were administered to the Trichodoll® vaccine (Dollvet, Şanlıurfa, Türkiye) and inactivated Immudoll^{CG} containing Cutibacterium granulosum on day 0. Animal welfare was prioritized throughout the study, and all procedures were performed in accordance with relevant ethical guidelines and principles governing for the use of experimental animals. This study was conducted in accordance with the decision of the Dicle University Health Sciences Research and Application Center Local Animal Experimentation Ethics Committee (DÜHADEK) dated September 25, 2025 (decision no: 07, meeting no: 10).

Clinical Examination

All sheep included in the study underwent a detailed clinical examination. During the dermatological examination, the location, extent, diameter, crusting, and presence of alopecia of the lesions were recorded, along with the degree of itching. Samples were collected from the lesions for parasitological and microbiological examination. During the treatment process, clinical checks were repeated on specified days to monitor the healing status of lesions, the formation of new lesions, and overall health.

Microbiological and Parasitological Examination

During dermatological examination, lesions were mostly located on the head and face, and less frequently on the body and back. The affected areas were cleaned with 70% ethyl alcohol and allowed to dry. Hair and skin scrapings were then collected from lesion margins using a sterile scalpel. Swab samples were obtained with sterile swabs. All samples were submitted to the Department of Microbiology at the Dicle University, Faculty of Veterinary Medicine for mycological and bacteriological examination. Cases in which no growth was detected in bacteriological cultures but dermatophyte growth was identified in mycological examinations were included in the evaluation. Additionally, To exclude ectoparasitic infestations with similar clinical signs, skin scrapings were examined microscopically using 10% potassium hydroxide (KOH). Animals with *Demodex* spp. or *Sarcoptes* spp. were excluded.

Collection of Blood Samples and Laboratory Analysis

Blood samples were taken from all sheep via the jugular vein into containing clot activator tubes at before treatment (day 0) and after treatment (day 7). After collection, blood samples were allowed to clot at room temperature for approximately 30 minutes and then centrifuged at 3000 rpm for 10 minutes. The separated serum samples were transferred to eppendorf tubes and stored at −86 °C until ELISA analysis was performed. Serum TAS and TOS levels were measured using commercial kits (Rel Assay Diagnostics, Türkiye).

Statistical Analyses

Statistical evaluation of the data was performed using the SPSS 24.0 software package (IBM SPSS Corp., Armonk, NY, USA). Since the data did not conform to a normal distribution, non-parametric tests were employed. The Wilcoxon signed-rank test was used for intra-group comparisons of TAS and TOS values between day 0 and day 7, while the Mann-Whitney U test was applied for inter-

group comparisons. The results were presented in table 1 format as mean values, and a $P < .05$ was considered statistically significant.

Table 1. Mean values of total oxidant capacity and total antioxidant capacity in sheep

Group	Day	n	Mean	Asymp. Sig.(p)
TAS – Vaccination Group	0. day	10	13.00	0.059
	7. day	10	8.00	
TOS – Vaccination Group	0. day	10	10.35	0.910
	7. day	10	10.65	
TAS – Vaccination + Immudoll Group	0. day	10	7.60	0.028*
	7. day	10	13.40	
TOS – Vaccination + Immudoll Group	0. day	10	10.00	0.705
	7. day	10	11.00	

*$P < .05$, Total Antioxidant Status (TAS), Total Oxidant Status (TOS)

RESULTS

Clinical examination of the affected sheep revealed dermatological findings characteristic of dermatophytosis. The main lesions observed were scaling, lichenification, keratinised crust formation and alopecia. Lesions were most commonly localised on the forehead, ears and dorsal region; less frequently, they were localised on the lower abdomen, chest and elbows. However, loss of appetite, noticeable itching and a coarse appearance of the coat were among the findings accompanying the clinical picture in some animals. The clinical appearance of dermatophytosis lesions in the dorsal region of sheep before and after administration of the Trichodoll® vaccine is presented in figure 1 clinical appearance of lesions on the dorsal region of sheep before and after application of Immudoll^{CG} in figure 2.

As a result of laboratory investigations, *Trichophyton spp*. was identified as the dermatophyte causative agent in mycological cultures and evaluations. No significant growth was detected in the bacteriological analyses. In parasitological examinations, no findings related to scabies agents were detected as a result of the microscopic evaluation of skin scrapings. These data supported the finding that the lesions in the cases included in the study were caused by dermatophytes.

Serum TAS and TOS levels were measured by ELISA on days 0 and 7 in both groups (Table 1). In the vaccine group, mean TAS values decreased from 13.00 (day 0) to 8.00 (day 7). Mean TOS values were 10.35 on day 0 and 10.65 on day 7. The change in TAS was not found statistically significant ($P = .059$), and no significant difference was observed in TOS ($P = .910$). In the vaccine + Immudoll^{CG} group, mean TAS values increased from 7.60 (day 0) to 13.40 (day 7). Mean TOS values were 10.00 on day 0 and 11.00 on day 7. A statistically significant increase in TAS level was found. ($P = .028$), whereas no significant difference was found in TOS ($P = .705$).

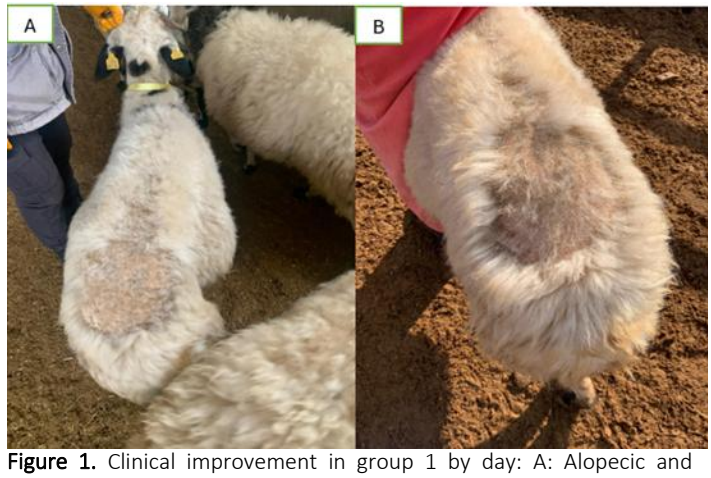

Figure 1. Clinical improvement in group 1 by day: A: Alopecic and crusted lesions observed on the dorsal region prior to treatment (day 0), B: After the Trichodoll® vaccine was administered (day 7), hair regrowth was observed and a reduction in the lesion area was noted.

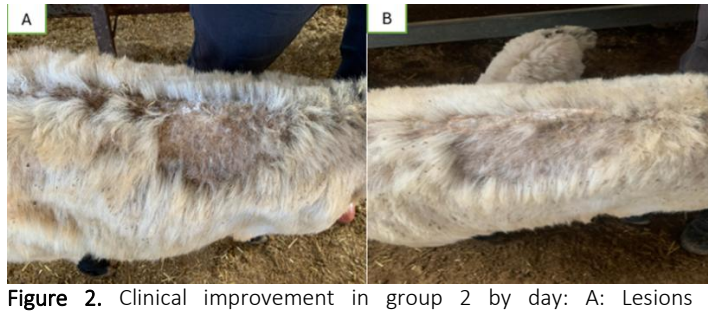

Figure 2. Clinical improvement in group 2 by day: A: Lesions characterized by alopecia, crusting, and hyperpigmentation prior to drug application (day 0), B: Partial clinical improvement observed after drug application, including hair regrowth and a reduction in lesion size (day 7).

DISCUSSION

Zoophilic dermatophytes in animals are not restricted to superficial cutaneous infections; rather, they are capable of inducing chronic and severe inflammatory responses, reflecting a complex host–pathogen interaction. During an infection, increased production of free radicals can disrupt the antioxidant-oxidant balance by overwhelming the body's antioxidant defenses.[5] Oxidative stress plays a significant role in the pathogenesis of dermatophytosis. Keratinase activity facilitates fungal invasion into the stratum corneum, triggering inflammation and reactive oxygen species production.[11,23] In this context, TAS and TOS provide practical and reliable indicators of redox balance, reflecting total antioxidant capacity and oxidant burden, respectively.[15] Clinical examination of sheep with dermatophytosis demonstrated the presence of scaly, well-demarcated circular lesions accompanied by alopecic areas

in multiple body regions. These findings are consistent with the clinical lesions reported in previous studies.[24,25] Although *Trichophyton verrucosum* is a dermatophyte species well adapted to cattle, previous studies have shown that it can cause more severe inflammatory dermatological lesions in sheep.[5] In the vaccination-only group, TAS levels decreased by day 7, although this change was not statistically significant. This finding supports the idea that limited antioxidant response following vaccination. The absence of a significant change in TOS further indicates that short-term vaccination alone does not effectively reduce oxidative load. These results are consistent with previous studies reporting increased oxidative activity following immunostimulatory treatments. In contrast, the combination of vaccine and Immudoll^{CG} resulted in a significant increase in TAS levels. This finding indicates that the addition of an immunomodulator enhances antioxidant defense capacity. Similar studies have shown that immunomodulatory agents can influence oxidative balance by stimulating endogenous defense mechanisms.[26-28] The increase in TAS observed in this group suggests a synergistic effect between vaccination and immunomodulation.[28]

Despite this improvement in antioxidant capacity, TOS levels did not change significantly in either group. This suggests that the primary effect of the treatment protocols is not the direct suppression of oxidant production but rather the enhancement of antioxidant defenses. Therefore, oxidative stress in dermatophytosis may be more closely associated with insufficient antioxidant capacity than with excessive oxidant production.

As results, indicate that immunomodulatory support plays a critical role in regulating oxidative stress. Strengthening the antioxidant defense system appears to be a more effective strategy than targeting oxidant production alone. This approach may contribute to improved clinical outcomes in dermatophytosis and similar infectious conditions. The combined use of Trichodoll® and Immudoll^{CG} appears to improve antioxidant capacity in sheep with dermatophytosis. These results indicate that supportive immunomodulatory approaches may contribute to the management of dermatophytosis by strengthening host defense mechanisms.

Ethics Committee Approval: The study was conducted in accordance with the decision of the Dicle University Health Sciences Research and Application Center Local Animal Experimentation Ethics Committee (DÜHADEK) dated September 25, 2025 (decision no: 07, meeting no: 10).
Informed Consent: Informed consent was obtained from the relevant authorities at the sheep farm affiliated with the Faculty of Veterinary Medicine at Dicle University prior to the animals' inclusion in the study.
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REFERENCES

1. Perez-Laguna V, Rezusta A, Ramos JJ, et al. Daylight photodynamic therapy using methylene blue to treat sheep with dermatophytosis caused by Arthroderma vanbreuseghemii. *Small Rumin Res*. 2017;150:97-101.
2. Al-Duboon A-H, Farhan FJ. Dermatophytosis in sheep of al-safat show in Basrah, Iraq. *Basrah J Vet Res*. 2007;6(1):54-62.
3. Borman AM, Summerbell RC. Trichophyton, Microsporum, Epidermophyton, and agents of superficial mycoses. In: J.H. Jorgensen KCC, G. Funke, M.A. Pfaller, M.L Landry, S.S. Richter, D.W. Warnock, ed. Manual of clinical microbiology. 11th, ed. JohnWiley & Sons Ltd; 2015:p.2128-2152.
4. Gupta AK, Wang T, Piguet V, Chowdhary A. New insights into host–dermatophyte interactions: pathogenesis, host defense mechanisms, and emerging clinical challenges. *Curr Opin Microbiol*. 2026;(90):102711.
5. Saleh MA, Rateb M, Abd-Allah EA, Mohamed GA. Circulating redox status in sheep naturally infected with Trichophyton verrucosum. *Trop Anim Health Prod*. 2022;54(5):288.
6. Dubljanin E, Zunic J, Vujcic I, et al. Host-pathogen interaction and resistance mechanisms in dermatophytes. *Pathogens*. 2024;13(8):657.
7. Baek J, Lee M-G. Oxidative stress and antioxidant strategies in dermatology. *Redox Rep*. 2016;21(4):164-169.
8. Gnat S, Łagowski D, Nowakiewicz A, Zięba P. The host range of dermatophytes, it is at all possible? Phenotypic evaluation of the keratinolytic activity of Trichophyton verrucosum clinical isolates. *Mycoses*. 2019;62(3):274-283.
9. de Oliveira JM, Carnib BL, Destro ALF, et al. Non-

Enzymatic Antioxidants and the Regulation of Redox Balance in Health: *Mechanisms and Therapeutic Implications*. 2026.
10.El-Motaily NM, Farag HS, Abdou OM, Saber M, Ahmed KA. The relationship between antioxidant trace elements (Zn-Cu and Se) and oxidative stress in dogs affected with dermatophytosis. 2022.
11.Silvestrini A, Meucci E, Ricerca BM, Mancini A. Total antioxidant capacity: biochemical aspects and clinical significance. *Int J Mol Sci*. 2023;24(13):10978.
12.Gutteridge JM, Halliwell B. Mini-Review: Oxidative stress, redox stress or redox success? *Biochem Biophys Res Commun*. 2018;502(2):183-186.
13.Aktas M, Kandemir F, Kirbas A, Hanedan B, Aydin M. Evaluation of oxidative stress in sheep infected with Psoroptes ovis using total antioxidant capacity, total oxidant status, and malondialdehyde level. *J Vet Res*. 2017;61(2):197.
14.Ulaş N, Aktaş MS, Yanar KE, Aydın Ö, Eroğlu MS, Eren E. Evaluation of Oxidative Stress in Sheep with Toxoplasma gondii by Malondialdehyde, Glutathione Levels, Total Oxidant Status, Total Antioxidant Capacity and Oxidative Stress Index Markers. *Erciyes Univ Vet Faki Derg*. 2022;19(3):182-188.
15.Chandimali N, Bak SG, Park EH, et al. Free radicals and their impact on health and antioxidant defenses: A review. *Cell Death Discov*. 2025;11(1):19.
16.Camkerten I, Sahin T, Borazan G, Gokcen A, Erel O, Das A. Evaluation of blood oxidant/antioxidant balance in dogs with sarcoptic mange. *Vet Parasitol*. 2009;161(1-2):106-109.
17.Chen P, Wang S, Li H, Qi X, Hou Y, Ma T. Comparative genomic analyses of Cutibacterium granulosum provide insights into genomic diversity. *Front Microbiol*. 2024;15:1343227.
18.Corvec S. Clinical and biological features of Cutibacterium (formerly Propionibacterium) avidum, an underrecognized microorganism. *Clin Microbiol Rev*. 2018;31(3):10.1128.
19.Almoughrabie S, Cau L, Cavagnero K, et al. Commensal Cutibacterium acnes induce epidermal lipid synthesis important for skin barrier function. *Sci Adv*. 2023;9(33):13.
20.Cuevas-Budhart MA, Sánchez-Garre M, Sánchez-Bermúdez A, et al. Oxidative stress and postoperative outcomes: an umbrella review of systematic reviews and meta-analyses. *Antioxidants*. 2025;14(11):1349.
21.Erel O. A new automated colorimetric method for measuring total oxidant status. *Clin Biochem*. 2005;38(12):1103-1111.
22.Heinen M-P, Cambier L, Fievez L, Mignon B. Are Th17 cells playing a role in immunity to dermatophytosis? *Mycopathologia*. 2017;182(1):251-261.
23.Bölükbaşı L, Merhan O. Lipid peroxidation and thiol/disulfide homeostasis in cattle with trichophytosis. *Dicle Univ Vet Fak Derg*. 2024;17(2):161-164.
24.Özkanlar Y, Aktaş MS, Kireçci E. Mycozoonosis associated with ringworm of calves in Erzurum Province, Turkey. *Kafkas Univ Vet Fak Derg*. 2009;15(1):141-144.
25.Çiftci G, Çiftci A. The assessment of the protein profiles and oxidant/antioxidat status in conjunctival Brucella melitensis Rev1 vaccinated sheep. *Etlik Vet Microbiol*. 2021;32(2):101-106.
26.Kart A, Uzlu E, Karapehlivan M, Öğün M, Merhan O. Effect of Immunomodulator Zylexis on Blood Glutathione, Malondialdehyde, Nitric Oxide, Total and Lipid Bound Sialic Acids Levels in Calves. *Atatürk Univ Vet Bil Derg*. 2010;5(2):43-48.
27.Parray OR, Bhat RA, Malik HU, et al. Evaluation of ameliorative potential of antioxidants and/or immunomodulators in contagious caprine pleuropneumonia affected Himalayan Pashmina goats. *Indian J Anim Sci*. 2023;93(9):871-877.
28.Engler P, Desguerets C, Benarbia MEA, Mallem Y. Supplementing young cattle with a rumen-protected grape extract around vaccination increases humoral response and antioxidant defenses. *Vet Anim Sci*. 2022;15:100232.