

Alaptide Could Have Hasten Clinical Recovery Among Dogs with Atopic Dermatitis

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Abstract

Atopic dermatitis is a chronic inflammatory skin disease in dogs, characterized by intense pruritus and increased IgE production. The aim of this study was to evaluate the effects of a topical cream containing alaptide on skin pH and hydration levels, which are important indicators of skin health, in dogs with atopic dermatitis. A total of 24 dogs were included in the study, and the inclusion criteria were determined based on the Favrot criteria, clinical scoring, and allergic evaluations. Epidermal pH and hydration measurements were analyzed in lesional and non-lesional skin areas using a non-invasive device designed to assess skin health. Analyses were performed before treatment and at the end of the second week following the initiation of treatment with 1% alaptide. The obtained data were analyzed using the Wilcoxon test. After treatment, a statistically significant increase was detected in epidermal pH values (from 5.91 ± 1.34 to 7.16 ± 0.42 ; $p=0.02$), along with a marked increase in skin hydration levels (from 31.7 ± 8.35 to 56.7 ± 9.35 ; $p=0.01$). Evaluation of the findings indicated that alaptide significantly improved epidermal biophysical parameters and contributed to the regeneration of the skin barrier. In conclusion, topical application containing 1% alaptide may be considered a regenerative and supportive therapeutic option in the treatment of atopic dermatitis in dogs.

Keywords: Atopic dermatitis, alaptide, Dog, Immunglobuline E, skin disease

INTRODUCTION

Alaptide (spirocyclic synthetic dipeptide cyclo(1-amino-1-cyclopentanecarbonyl-1-alanyl) or 8(S)-methyl-6,9-diazaspiro[4,5] dekan-7,10-dion), has been explored as a unique compound previously in Prague (Šturc and Kasafirek, 1990). ALAPTID® (Bioveta, Czech Republic) has been postulated that the latter compound was a constituional analogue for hypothalamic factor, capable for inhibition of melanocyte-stimulating hormone (MIF) release, randomly explored to influence behaviour and cognitive features of rodents, selectively rats and mice (Hlišák and Krejčí, 1992, Hlišák et al 1996, Nedvídková et al 1994). Taking into account

veterinary dermatology, this unique compound has traditionally been used as topical agent (Rádl et al 1990) against ulcers abrasions, burns, frostbites, bedsores, etc. Pharmacological studies have proven that alaptitin promotes the migration of keratinocytes and supports the healing process by increasing the water-binding capacity of the tissue (Opatrilova et al., 2013; Bioveta, n.d.). Besides, the dermal penetration enhancing effect of nanonized forms of alaptitin provides an advantage in skin structure modification (Cernikova et al., 2015).

Atopic dermatitis (AD) in dogs is a chronic inflammatory skin condition marked by intense pruritus and the production of immunoglobulin

E (IgE) in genetically predisposed individuals in response to allergens (Ural et al., 2020; Erdogan et al., 2024). This pathology entails a multifaceted process leading to compromised skin barrier function, allergen infiltration through the stratum corneum, and immune system activation (Erdogan et al., 2024). Trans epidermal water loss, pH, and hydration level status are regarded as essential non-invasive biomarkers for evaluating skin barrier integrity (Erdogan et al., 2024). In atopic dogs, disruption of skin barrier homeostasis results in a more alkaline skin pH and reduced hydration levels relative to healthy dogs (Ural et al., 2020a; Ural et al., 2020b, Ural et al 2023, Erdogan et al., 2024).

The objective of this study is to assess the impact of alaptide-containing cream application on epidermal pH and hydration levels, which are critical indicators of skin barrier function, in dogs with atopic dermatitis, and to evaluate its restorative efficacy in this context.

Material and methods

Demographic data

In a total of 34 dogs that met a diagnostic criteria of atopic dermatitis were enrolled based on both exclusion and inclusion criteria (Favrot Criteria, Canine Atopic Dermatitis Extent and Severity Index, epidermal corneometry and skin bioresonance). In an attempt to diagnose atopic dermatitis a) breed, age, sex of dogs were recorded, b) Canine Atopic Dermatitis Extent and Severity Index itinerary 04 along with relevant clinical signs [erythema, alopecia, excoriation, lichenification, alopecia recorded at 12 different bodily sites were scored at 0 to 3, c) Favrot Criteria, c) Polycheck in vitro allergen specific Ig E concentrations (by use of rapid diagnostic test cassette) e) excluding external parasitic etiology by use of deep skin scraping, acetate tape impression, f) dermatoscopic examination [DermLite DL4 dermatoscope] were all performed. Aydin Adnan Menderes University, local Research Ethics Committee (ADÜ- HADYEK) report (21.12.2023; 64583101/2023/165)

Measurement of Biophysical Skin Parameters (pH and Hydration)

Epidermal pH and hydration levels were measured in the determined lesional and non-lesional areas of atopic dogs for objective assessment of skin barrier function. Measurements were performed as described in previous studies, and the averages of the measurement areas were taken as a single result (Erdogan et al. 2024). Dermatological measurements

were performed using the Callegari Soft Plus (Parma, Italy, RDA Group, Turkey), a non-invasive skin analysis system.

Treatment Protocol and Application

In dogs with a confirmed diagnosis of atopic dermatitis, for accelerating local skin repair and normalize deviations in biophysical parameters, topical application of alaptide (spirocyclic synthetic dipeptide) was performed for 2 weeks. Specifically, this veterinary ointment containing 1% alaptide (Alaptid®, Bioveta, Czech Republic; Turkish side distributor İnterhas Hayvan Sağlığı, Ankara, Türkiye) was applied in a thin layer to the lesioned skin areas. Application of 2gr. Per lesional sites were carried out regularly twice daily (morning and evening) throughout the treatment process.

Statistical analyses

pH and hydration-related data were recorded for each case before and after treatment and tabulated as mean and standard deviation. Since the data did not show a normal distribution, the Wilcoxon test was used for pre- and post-treatment comparisons. In all analyses, p-values less than 0.05 were considered statistically significant. The Graphpad (Prism, 9.0.2, USA) program was used to perform the analyses.

Results

Epidermal corneometric analytes were shown in table 1 and fig. 1 below. The findings regarding skin pH and hydration levels evaluated before and after Alaptid cream application are presented in Table X. pH value was determined to 5.91 ± 1.34 before application, while increased to 7.16 ± 0.42 after application, and this increase was found to be statistically significant ($p = 0.02$). Similarly, the skin hydration level was measured as 31.7 ± 8.35 before application and 56.7 ± 9.35 after application, and this increase was also found to be statistically significant ($p = 0.01$). Dermatological improvements observed in the dogs are shown in Figures 2 and 3.

Table 1. Epidermal corneometric analytes were shown comparatively, prior to and thereafter Alaptid Veterinary Ointment.

| | Before Treatment | After Treatment | P value |
|-----------|------------------|-----------------|---------|
| pH | 5.91 ± 1.34 | 7.16 ± 0.42 | 0.02 |
| Hydration | 31.7 ± 8.35 | 56.7 ± 9.35 | 0.01 |

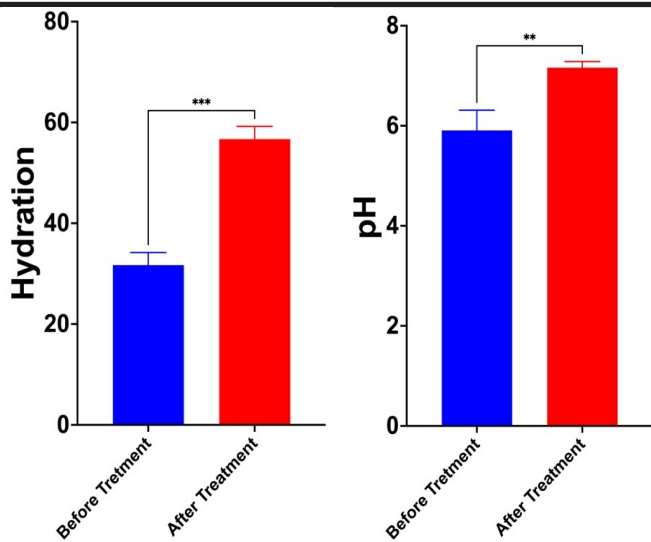


Figure 1. Boxplot analyses of epidermal corneometric analyses.



Figure 2. Clinical improvement of a dog.



Figure 3. Clinical alterations of a dog.

Discussion

The present study has been focused on clinical efficacy of the original Czech compound (Turkish side distributor İnterhas Hayvan Sağlığı, Ankara, TÜRKİYE), a skin/mucosa tissue health promoter with well recognized regenerative effects. The latter compound internationally well recognized trade name as “Alaptid,” exhibited local usage against disased tissue (i.e. in an attempt to cure or regenerate injured cutaneous tissue). Technological modifications influencing the permeation of alaptide against membranes (Opatrilova et al 2013)

Previous studies on the dermatological use of alaptidum highlight its properties of promoting epithelialization, increasing keratinocyte migration, and improving the water-binding capacity of tissues (Rádl et al., 1990; Sklenář et al., 2012). Furthermore, micro and nano formulations developed with alaptidum have been shown to have significant enhancing effects on skin permeability (Opatrilova et al., 2013; Cernikova et al., 2015). Nano-formulated alaptidum has been reported to modify the lipid structure of the s. corneum, facilitating transdermal passage and increasing penetration into deeper layers (Cernikova et al., 2015).

In our study, it was determined that the topical formulation containing 1% Alaptid (Alaptidum, İnterhas, Turkey), used, significantly increased hydration and pH levels in epidermal biophysical parameters after treatment, approaching the values found in healthy dogs by Erdoğan et al. (2024). These characteristics show that alaptidum not only has positive effects on epithelialization but is also an important molecule that actively contributes to the modulation of the biophysical structure of the skin. In particular, the significant changes in pH and hydration seem consistent with the hydrophilic and regenerative effects of alaptide (Rádl et al., 1990; Sklenář et al., 2012). Atopic dermatitis is a significant chronic inflammatory disease affecting the epidermal barrier in dogs (Ural et al., 2020a; Ural et al 2020b, Ural et al 2023, Erdoğan et al., 2024). The pH of healthy skin and the lipid structure of the stratum corneum are critically important for antimicrobial defense. In cases of atopic dermatitis, increases in pH and decreased hydration lead to transepidermal water loss and facilitate the penetration of allergens into the skin (Ural et al., 2020a; Erdoğan et al., 2024). While the increase in pH observed in our study contradicts the expectation of restoring the acidic environment in atopic dermatitis, this situation can be attributed to alaptidum’s modulation of tissue

metabolism and cellular activity, not only to barrier acidification but also to epidermal renewal and cellular-level reorganization processes (Jampilek & Dohnal, 2015). This suggests a dynamic adaptation process that occurs alongside inflammatory processes.

As brief explanation the recovery based on corneometric analytes obtained at this study suggested that alaptidum, through its local effects on the immune response regulated within the gut-skin axis, may provide a synergistic effect on therapeutic processes. Furthermore, although not investigated in our study, this synergistic effect may be related to alaptidum's effects on the neuroendocrine system. Due to its structural similarities to hypothalamic factors, alaptidum's multifaceted effects on melanotropin release (Nedvídková et al., 1994; Hlišák & Krejčí, 1992) may explain the improvements and synergistic effects in these biophysical parameters. The absence of a control group in our study is a limitation, and the inability to measure other biophysical parameters may shed light on future research. Despite the limitations mentioned, the use of non-invasive measurement techniques and the fact that the agent can be easily used in clinical practice enhances the translational impact of the study.

Conclusion

Epidermal corneometric analytes were shown in table 1 and fig. 1 indicated that Alaptid Veterinary Ointment application altered mean pH values [5.91 ± 1.34 vs. 7.16 ± 0.42 , prior to and thereafter treatment] ($p = 0.02$). Moreover skin hydration levels were also increased from 31.7 ± 8.35 to 56.7 ± 9.35 , before and after application ($p = 0.01$). In conclusion, it was determined that the application of 1% alaptide (Alaptid® Veterinary Ointment, Bioveta, Czech Republic; Turkish side distributor İnterhas Hayvan Sağlığı, Ankara, Türkiye) in addition to short-term alternating probiotic therapy in dogs with atopic dermatitis significantly altered the biophysical parameters of the skin, namely pH and hydration. It was suggested that the application of 1% alaptide to lesioned areas in treatment applications for dogs with atopic dermatitis could contribute to the reconstruction of the skin barrier, thus serving as a regenerative and modulatory agent.

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