

# Can Atopic Dermatitis in Dogs Be Associated with Intestinal Inflammation?

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## ABSTRACT

The aim of this study is to investigate the relationship between atopic dermatitis and intestinal inflammation in dogs, highlighting the potential role of mucosal epithelial barrier damage in the development of the disease.

The study reviews the current literature on atopic dermatitis in dogs, focusing on the role of environmental and food allergens, as well as the potential contribution of intestinal inflammation and damage to the development of the disease. Biomarkers such as Intestinal Trafoil Factor 3 (ITFF-3), Intestinal Alkaline Phosphatase (IAP), Immunoglobulin E (IgE), Interleukin-4 (IL-4), and Interleukin-13 (IL-13) are discussed in relation to their potential use in diagnosing and managing atopic dermatitis.

The study highlights the significant correlation between atopic dermatitis and intestinal inflammation in dogs. Elevated levels of ITFF-3 and IAP biomarkers are associated with epithelial damage in the intestine and may indicate the presence of leaky gut syndrome. The study suggests that correcting intestinal microbiota and repairing intestinal damage through treatments such as oral faecal microbiota transplantation may be beneficial in managing atopic dermatitis.

In conclusion, the study emphasizes the importance of considering the role of intestinal inflammation and damage in the development of atopic dermatitis in dogs. The use of biomarkers such as ITFF-3 and IAP can help diagnose and monitor the disease. Additionally, the study suggests that incorporating treatments that correct intestinal microbiota and repair intestinal damage into the standard treatment plan may be beneficial in managing atopic dermatitis. Further comprehensive studies are needed to fully understand the relationship between atopic dermatitis and intestinal inflammation in dogs.

**Keywords:** Atopic dermatitis; Intestinal inflammation; Leaky gut syndrome; Biomarkers (ITFF-3, IAP, IgE, IL-4, IL-13); Intestinal microbiota.

## INTRODUCTION

Atopic dermatitis is one of the most important immunological skin diseases in dogs, which occurs with severe itching as a result of hypersensitivity reactions of the body to environmental antigens. In the last 10 years, it has been demonstrated that primary disease and secondary cofactors play a role in the pathogenesis of atopic dermatitis. Cofactors contribute significantly to the progression and aggravation of the disease. The body immune system, IgE produced against allergens binds to mast cells in the skin and stimulates the release of histamine, leading to the formation of skin lesions. Environmental and

food allergens play an important role in the development of the disease. In particular, mucosal epithelial barrier damage (leaky gut) that cannot heal in previous intestinal inflammation may be effective in the substructure of atopic dermatitis. Therefore, it is useful to evaluate intestinal damage biomarkers in these patients. In this article, a possible relationship between atopic dermatitis and intestinal inflammation is discussed. Allergic diseases are very common in the veterinary field as well as in human medicine. Allergy is the hypersensitivity of some organisms to substances that are harmless in the same amount and conditions.

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## LITERATURE REVIEW

In allergic conditions, some organisms overreact to substances that are not normally harmful to the body [1,2]. Atopic dermatitis is a type-1 hypersensitivity reaction of the organism against common environmental antigens [3,4]. Although environmental allergens such as indoor allergens, harmful dust, pollen, mould mite and grass and meadow grass play an important role in the etiology of atopic dermatitis, it has been reported that allergenic foods consumed predispose to the disease [4-6]. A consequence of the organism's type 1 hypersensitivity response to environmental allergens such as house dust mites, mould mites, wheat dust, grass or spring grass allergens, pollens, epidermal antigens, insect antigens and feathers causes a significant increase in serum IgE levels [7,8]. The estimated prevalence of atopic dermatitis in dogs is 10%-15% [5].

The primary clinical sign in canine atopic dermatitis is pruritus. Depending on the causative allergen, itching may be seasonal (pollen) or non-seasonal (mites in dust or food). In cases of atopic dermatitis in dogs, the face, the concave surface of the auricle, the lower abdomen, axilla, inguinal region, perineal region and distal extremities are most commonly affected [4,8]. There is no single diagnostic test that can reliably diagnose atopic dermatitis in dogs. The diagnosis is based on a comprehensive anamnesis, clinical symptoms and differential diagnosis. Important diagnostic tests are required for the diagnosis of the disease. Allergen and serological tests are mostly used in the diagnosis of the disease. Allergic tests can be performed as Intradermal Test (IDT) or Allergen-Specific IgE Serology (ASIS) [4,8]. The management of atopy in cats and dogs is long-term and life-long. In addition to the application of many treatment procedures for this disease, it is necessary to make arrangements for the patient's life. Usually, depending on the severity of the disease, a treatment plan is designed on an individual basis for the compliance of the owners as well as the health of the patient. In the treatment or management of atopic dermatitis, most dermatologists agree that a multimodal approach is the most appropriate option. Therefore, treatment is based on (1) keeping patients away from allergens as much as possible, (2) immunotherapy, (3) control of possible infections, (4) treatment of skin lesions, (5) control of inflammation and itching [9,10].

## DISCUSSION

In recent years, it has been suggested in human medicine that chronic intestinal diseases (irritable colon syndrome, Crohn's disease, celiac disease, etc.) predispose to dysbiosis (imbalance between the types of organisms found in the intestine) as a result of disruption of the intestinal microbiota or leaky gut by causing damage to the intestinal wall, and this situation creates a substructure for atopic dermatitis [11-13]. It is thought that toxins and allergens easily pass into the organism and contribute to atopic dermatitis as a result of disruption of the mucosal barrier in the leaky gut, especially regarding the disintegration of the tight junctions of epithelial cells [14-16]. Therefore, mixed probiotics were given to correct the intestinal microbiota in children with atopic dermatitis and were found to contribute

significantly to the improvement of atopic dermatitis [17]. Dysbiotic microbiota crossing the damaged intestinal barrier may play a role in the development of allergies and autoimmune diseases [18]. Sugita K, et al. [19], reported that gut microbiota plays an important role in the pathogenesis of canine atopic dermatitis and that oral faecal microbiota transplantation may be a novel treatment modality for atopic dermatitis. Similarly Ural [20], reported that transplantation capsules of faecal microbiota were useful in the treatment of atopic dermatitis in dogs.

Serum Intestinal Trefoil Factor 3 (ITFF-3), Intestinal Alkaline Phosphatase (IAP), Immunoglobulin E (IgE), Interleukin-4 (IL-4) and Interleukin-13 (IL-13) levels were significantly increased in dogs with atopic dermatitis (Table 1). The elevated levels of ITFF-3 and IAP biomarkers may be related to epithelial damage in the intestine and the intensive release of these markers from the intestine to repair this damage. This is probably related to chronic intestinal epithelial damage (leaky gut) and may be related to the entry of allergens and toxic substances into the organism from the damage sites formed in the intestines in the formation of atopic dermatitis [6].

Parameters	Healthy dogs (n: 10)	Dogs with atopic dermatitis (n: 26)	p-value
IAP (ng/mL)	9.56 ± 1.40	19.67 ± 1.50	0.001
I-FABP (ng/mL)	9.08 ± 0.46	10.77 ± 0.79	0.074
TFF-3 (ng/mL)	12.49 ± 0.67	17.50 ± 1.70	0.012
IgE (µg/mL)	1.74 ± 0.09	2.18 ± 0.14	0.015
IL-4 (pg/mL)	58.06 ± 2.70	78.3 ± 4.80	0.001
IL-13 (pg/mL)	131.50 ± 7.30	176.00 ± 9.10	0.001

**Table 1:** Means and significance of parameters in healthy and atopic dermatitis dogs (mean ± SEM). **Note:** IAP: Intestinal Alkaline Phosphatase; IFABP: Intestinal Fatty Acid Binding Protein; ITFF3: Intestinal Trefoil Factor 3; IgE: Immunoglobulin E; IL-4: Interleukin-4; IL-13: Interleukin-4 [6].

Environmental allergens are very effective in the development of atopic dermatitis in dogs. Home cooked food with unknown ingredients and prolonged and recurrent intestinal inflammation may predispose to the development of the disease. The clinician should investigate whether there is a history of enteritis in dogs with atopic dermatitis. In dogs with a history of enteritis, damage to the intestines due to various agents (leaky gut) that cannot heal sufficiently may be effective in the development of atopic dermatitis. This is because it is easier for allergens and toxic substances to enter the organism through the damaged areas. There may be a significant correlation between atopic dermatitis and intestinal inflammation in dogs. Serum ITFF3 and IAP levels should be evaluated to determine intestinal damage in dogs with atopic dermatitis (Table 1). Increases in these values indicate intestinal damage. Considering

the intestinal damage in canine atopic dermatitis, it may be beneficial to add a treatment that corrects intestinal microbiota and repairs intestinal damage to the standard treatment. Because we observed that the additional treatment was effective in our new trials. When the study is finalized, we will share our results with the scientific world.

## CONCLUSION

In conclusion, although environmental and food allergens play an important role in the formation of atopic dermatitis in dogs, the entry of allergens and toxic substances into the organism through the mucosal epithelial barrier damage areas in the intestines as a result of intestinal inflammation may have prepared the ground for atopic dermatitis. In order to clearly demonstrate this situation, new and comprehensive studies with a large number of subjects, a large number of intestinal damage biomarker measurements and histopathological evaluation by taking biopsy samples from the intestine accompanied by colonoscopy are needed.

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