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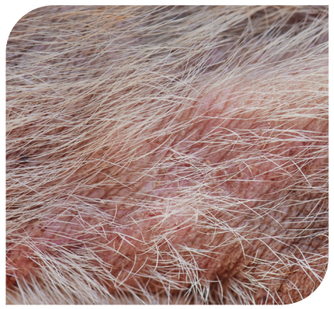
Atopivet® collar

Tell me more



SPECIALISTS IN DERMO-REPAIR

Bioiberica

Product Monograph

Atopivet® collar

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Bioiberica

Atopivet® collar

Bioibérica

Who we are

Bioiberica is a leader in the production of the active pharmaceutical ingredient heparin and is an expert in the **identification, extraction**, and **development of molecules from natural sources** into high-quality products for the pharmaceutical, nutraceutical, veterinary, food and agricultural industries.

Pets are an increasingly important part of our families. In recent decades they have been shown to contribute to people's physical and psychosocial health and well-being.

At Bioiberica we are aware of how important pets are and for this reason we are committed to improving their quality of life.

We are experts in offering innovative solutions for pet health based on scientific evidence. We do this through products that contain high-quality ingredients that are also safe and highly palatable. This is the vision that drives our research and development team. A vision that is embodied in our mission statement **"Taking life science further"**, in other words, contributing to the advancement of life sciences, a sector working to improve global health.

Bioibérica factory at Palafolls.

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Atopivet® collar

Atopic dermatitis

A. **Problems**

One of the most common visitors to veterinary clinics are dogs with skin problems. Some experts now put the prevalence of ailments such as atopic dermatitis in dogs at between 10% and 15% of the total canine population.

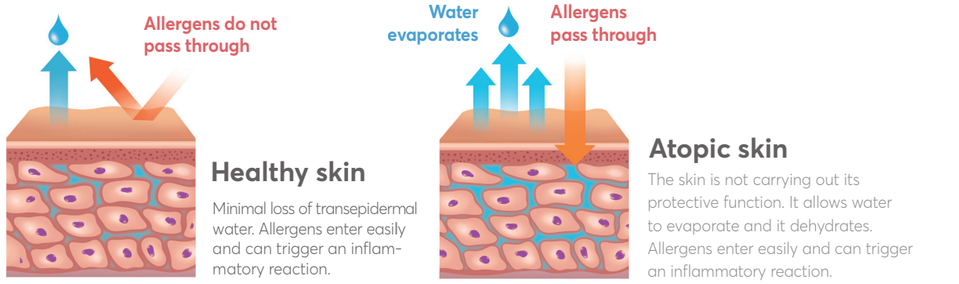
Canine atopic dermatitis is a skin disease that manifests as itching and inflammation. Its etiology is multifactorial as a result of the interaction between factors relating to the dog itself and environmental factors. Traditionally, the approach has always been to consider atopic dermatitis as an allergic reaction. However, there is increasing evidence that it is the epidermal barrier function that is impaired in canine atopic dermatitis (change in the proportion of ceramides in the stratum corneum, altered filaggrin and anti-microbial peptide expression), confirming the need to target the skin barrier with specific products that act at this level.

It is an uncomfortable disease, which causes the pet's owner and the veterinary professional to experience self-doubt. For the former, this may be affecting their relationship with the animal, leaving them feeling guilty in their role as caregiver and they need to find an external cause that will absolve their guilt. And as far as the veterinarian is concerned, they may experience a feeling that sometimes it is not the clinical criteria that set the course of the treatment, with time and cost being determining variables, and as a consequence it may be the pet's owner who makes the medical decision on treatment. The main objective is to control the itching in order to satisfy the pet's owner, to avoid further scratching injuries.

Referring back to the clinical aspect of the disease, dermal barrier function changes have been documented in both animals and humans with atopic dermatitis, including the presence of enzymes that degrade components of the stratum corneum of the skin, changes to the proportion of ceramides in the stratum corneum and increased transepidermal water loss.

What happens when a patient is affected by atopic dermatitis?

- The skin barrier loses its protective function and **becomes permeable: altered skin microbiome**
- Allergens enter easily and **can generate an inflammatory reaction and immune dysregulation**
- **Decrease in filaggrin and ceramides**
- **Lets water evaporates and the dog scratches**



For the skin barrier to work correctly, the stratum corneum must be well structured, with a healthy lipid barrier and adequate filaggrin expression.

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Atopic dermatitis

B. Treatments

As soon as the itching subsides, pet owners stop the treatment, due partly to the financial cost and also the difficulty of consistently applying the various treatments over the long term.

In situations of atopic dermatitis, the skin's barrier is deteriorated, so it is necessary to intervene using specific products that act at this level. For the skin barrier to work properly, the skin's structure must be restored, promoting an adequate, well-structured lipid barrier that prevents the entry of allergens and the loss of water from the skin.

"The approach has gone from being simplistic to something more multifaceted. Topical therapy has gained much relevance."
Cesar Yotti

"The long-term goal has to be a reduction in the frequency of outbreaks and less aggressive outbreaks."
Laura Ordeix

"The ideal treatment is a long-term treatment that will prevent new outbreaks, intended to improve the quality of the skin's structure."
Gustavo Machicote

Goals for patients in the outbreak phase
differ from the goals for patients in the maintenance phase:

- Eliminate infections
- Control inflammation /itching

- Infection control
- Avoid recurrences

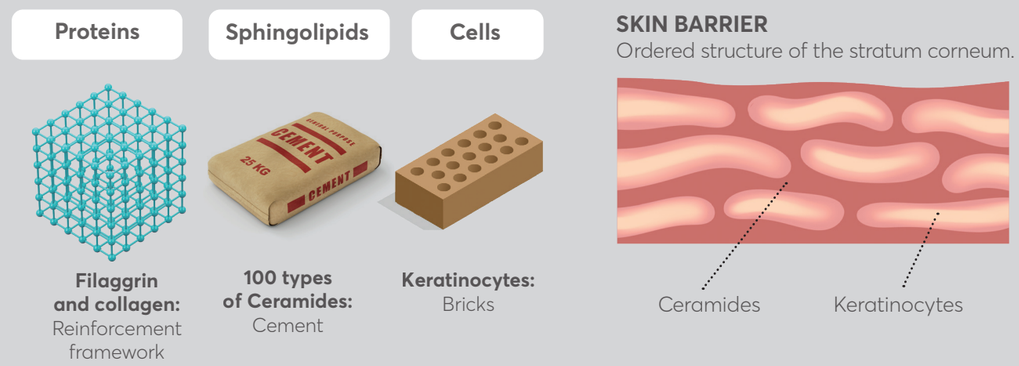
Dermal repair and skin barrier

"Dermo-repair decreases antigen penetration and the intensity of the outbreak is also reduced in the medium to long term." *Lluís Ferrer*

The internal and external repair of the skin acts on the dermis and epidermis levels. Covering this aspect is of vital importance to strengthen and repair the skin so that the skin barrier is more impermeable to allergens, and the animal has milder outbreaks, thus reducing the need for rescue treatments and maintaining a better quality of life for the animal for a longer period of time.

Filaggrin is one of the most important proteins in the epidermis and is involved in dermal barrier formation and stratum corneum hydration. A decrease in epidermal filaggrin expression has been described in dogs with atopic dermatitis. Such expression may be modulated by the atopic inflammatory response. On the other hand, improvements in skin health have been reported with the use of sphingolipids and glycosaminoglycans, as we will see below.

Sphingolipids perform both structural and biological functions in the epidermis, mainly related to the maintenance of the skin barrier. The most abundant in the epidermis are ceramides, and their levels decrease in both dogs and people with atopic dermatitis, altering the skin barrier and its functions.



- Reduce the entry of allergens and macromolecules.
- Prevent water escaping and consequently dehydration of the epidermis.

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Atopivet® collar

Atopivet® Collar: NEW PRODUCT

Atopivet® Collar is an innovative product for cats and dogs that helps maintain skin integrity for up to 2 months. Atopivet® Collar meets the needs of the veterinarian and the animal's owner, improving compliance by facilitating the administration of the product in a very comfortable way, thus optimizing monthly care costs, and contributing effectively to the multimodal approach to atopic dermatitis.

"Atopivet® Collar reinforces the multifactorial approach, the idea that care has to be prolonged, it is also designed from the owner's aspect, to make life easier for them."
Lluís Ferrer

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Atopivet® Collar is available in 2 sizes (35 and 75 cm)

Small dogs and cats
35 cm (< 10 kg)

Medium and large dogs
75 cm (> 10 kg)

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Atopivet® collar

Atopivet® Collar: NEW PRODUCT

A. How it works

Atopivet® Collar contains excipients that facilitate the release of the ingredient (Biosfeen®) onto the surface of the skin then through the lipids of the stratum corneum in the epidermis.

The Biosfeen® release system works through a concentration gradient, i.e. it works as an osmotic membrane that regulates the amount of ingredient that is released. When the dog or cat has enough of the ingredient, the collar stops releasing it until the concentration of Biosfeen® on the skin decreases and the release system is activated again.

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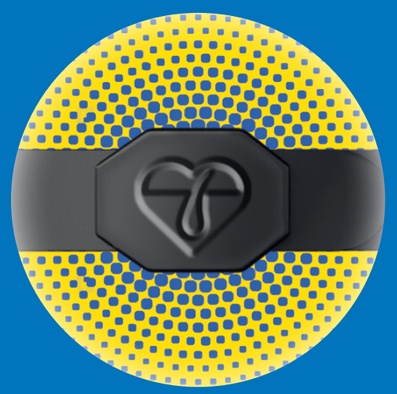
Atopivet® Collar can be used for up to 2 months

1 Put the collar on the animal leaving a space of 2 fingers between the collar and its neck.

2 Biosfeen® is incorporated into the collar's polymer matrix. It begins to be released when it comes into contact with the animal's skin.



3 Biosfeen® has a continuous and sustained homogeneous release all over the animal's skin.

4 Atopivet® Collar can be used for up to 2 months.

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Atopivet® Collar: **NEW PRODUCT**

The format for cats and small dogs incorporates a safety mechanism in the fastener. The collar also has a lavender scent. Atopivet® Collar releases Biosfeen® in a sustained and continuous manner for a period of up to 2 months.

Biosfeen®

Biosfeen® is a UNIQUE ingredient of animal origin, rich in sphingomyelins and ceramides, and developed by Bioiberica. Its diversity of ceramides, and especially its high content of bioactive sphingomyelin, is clearly superior to compounds of vegetable origin. Sphingomyelin is a precursor to skin ceramides, and the animal origin of Biosfeen® makes it more suitable for the endogenous synthesis of ceramides (page 16).

In one study, Biosfeen® was seen to increase 97 of the 99 ceramides that were quantified. The types of ceramides enhanced with Biosfeen® are those that are reported to be decreased in the stratum corneum of dogs with atopic dermatitis, namely CER[EOS] and CER[EOP] (page 16).

Biosfeen® promotes the expression of filaggrin and endogenous lipid synthesis, essential for the stratum corneum. All this helps to maintain the skin's cutaneous barrier.

Atopivet® collar

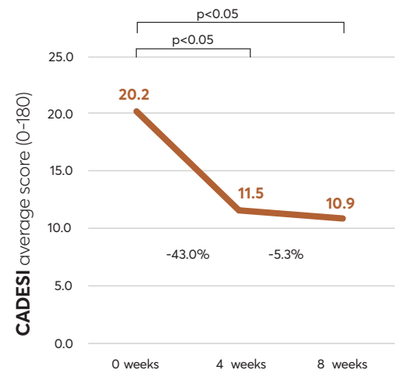
The effect of the Atopivet® Collar.

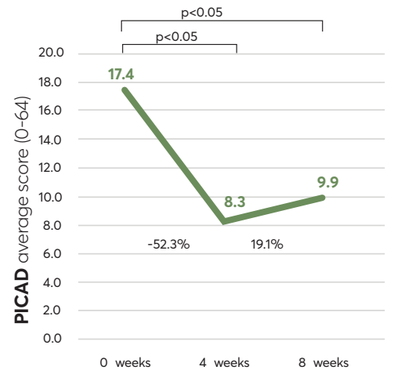
Atopivet® Collar in vivo study

Purpose: to determine the effects of applying the Atopivet® Collar for the management of canine patients with atopic dermatitis.
Description: for a period of 8 weeks the Atopivet® Collar was applied to 12 dogs of different breeds with a confirmed diagnosis of non-seasonal atopic dermatitis

RESULTS

Good feedback from owners and veterinarians on the benefits of the Atopivet® Collar.
Safety: no safety problems were detected.
Efficiency: statistically significant improvements in CADESI, PICAD and PVAS





54c11 0 weeks

54c11 4 weeks

54c11 8 weeks

The efficacy, ease of use and convenience of Atopivet® Collar makes it the ideal format for anyone to use

Other ingredients in the Atopivet® range

A. **Nucleoforce®**

Nucleoforce® is a balanced concentrate of free nucleotides and active precursors and is present in Atopivet® Capsules and Oral Suspension.

Nucleotides are semi-essential nutrients notable as being the structural unit of nucleic acids in cells. Their molecular composition is one sugar, one base and one to three phosphate groups. Nucleotides are molecules with a great deal of energy stored in the bonds of these phosphate groups, so they are widely used in all types of cells for energy transfer in metabolic processes. Cells possess enzymes whose function is specifically to hydrolyze nucleotides to extract the energy potential stored in their bonds.

For this reason nucleotides are the most used source of energy in cells and therefore cells with a high demand for cellular repair and proliferation benefit from their administration.

Dietary ingredients are generally low in nucleotides. However, endogenous synthesis is possible, although very costly in terms of energy. In certain situations, and in certain tissues with high rates of cell proliferation, such as the immune system or the intestine, when the demand for nucleotides increases and endogenous de novo synthesis is insufficient, it becomes necessary to supplement them using a diet that is able to meet these needs. *(Matthew, C.D.; Stein, H.H. Nucleotides and young animal health: can we enhance intestinal tract development and immune function? Nutritional Biotechnology in the Feed and Food industries. Nottingham University Press, UK, p.159-170, 2004)*

For years, various applications of oral nucleotides have been investigated, given they have the capacity to modulate immune response. One of them is in the field of dermatology, since it has been observed that a combination of nucleotides can promote wound repair as well as fibroblast proliferation.

The addition of nucleotides to a combination of glycosaminoglycans and EPA significantly improves the ability to induce fibroblast proliferation (page 20). This combination, as found in Atopivet® Capsules and Atopivet® Oral Solution, could therefore provide a useful application.

Fibroblast proliferation is an important part of the healing process for diseases involving changes to the dermal barrier, such as atopic dermatitis, or where there are skin lesions, or in wound repair processes. Glycosaminoglycans such as hyaluronic acid and dermatan sulfate are involved in these processes.

B. **Dermial®**

Dermial® is a natural ingredient particularly rich in hyaluronic acid developed by Bioiberica (page 20), present in the Atopivet® range. Hyaluronic acid is a glycosaminoglycan that is highly abundant in the skin. Various in vitro tests carried out by Bioiberica R&D show that Dermial® promotes the proliferation and migration of dermal fibroblasts and stimulates the endogenous production of hyaluronic acid, which is associated with increased skin hydration and reduced itching.

Glycosaminoglycans are essential components of skin. Of these, hyaluronic acid is involved in important functions such as the re-epithelialization process. Hyaluronic acid supports the hydration of the extracellular matrix in normal skin, providing resilience, viscoelasticity and an environment conducive to cell function and development.

In normal skin, hyaluronic acid is found in relatively high concentrations in the basal layer of the epidermis, where the proliferative keratinocytes are found. Its role is important in the re-epithelialization processes through its effect on fibroblasts, which are implicated in the skin's capacity to regenerate.

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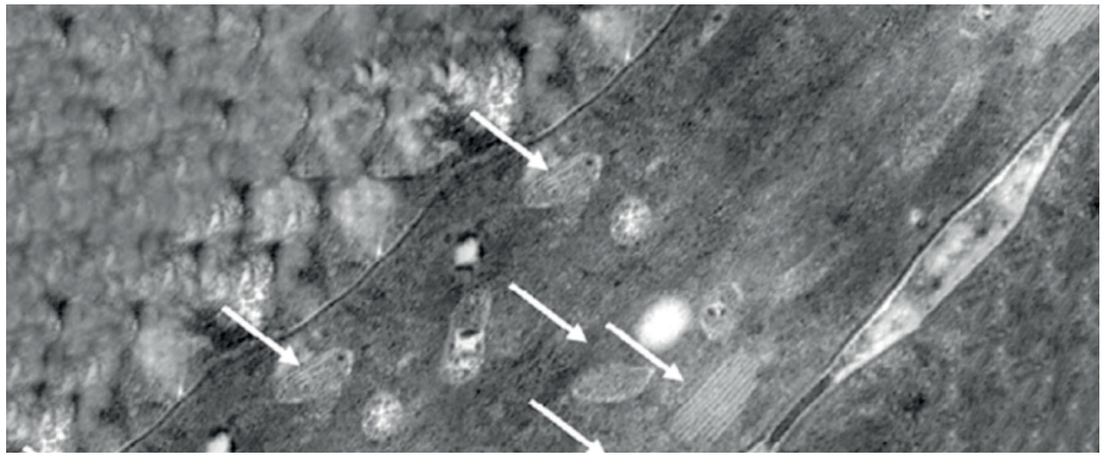
Atopivet® collar

Scientific evidence

Cerrato S, Ramió-Lluch, Brazís P, Fondevila D, Segarra S, Puigdemont A, Effects of sphingolipid extracts on the morphological structure and lipid profile in an in vitro model of canine skin. The Veterinary Journal 2016; 212:58-64.

Although stratum corneum ceramides were known to be essential for proper epidermal barrier function, it was not known whether the addition of these complex lipids, or their precursors, to the epidermis would increase their quantity and improve the structure and function of the skin barrier. In this study, using a sophisticated model of in vitro canine skin (skin equivalent), it was shown that the addition of sphingolipid mixtures (ceramide precursors) to the culture medium triggered an increase in ceramide production in the epidermis. In addition, when sphingolipid-treated skin samples were examined by electron microscopy, an increase in the lipid lamellar structures of the stratum corneum was observed. In other words, this enrichment of the medium induced the formation of a well-structured stratum corneum rich in ceramides, both characteristics associated with good skin barrier function.



Electron microscope image showing numerous lamellar bodies (white arrows) in the stratum granulosum

Biosfeen® elicits an increase in 97 out of the 99 ceramides that were quantified. The increases in ceramide levels are not simply due to the fact that the ceramides applied are deposited on the skin, but also because endogenous ceramide production is stimulated due to the high sphingomyelin content of the sphingolipid extract. This is confirmed by observing an increase in lamellar bodies under electron microscopy.

"Epidermal barrier dysfunction is one of the main pathogenic mechanisms of atopic dermatitis in both humans and dogs. The present study opens the door to the application of sphingolipids on the epidermis to contribute to the maintenance of skin barrier integrity." *Lluís Ferrer*

UF UNIVERSITY of FLORIDA

Marsella R, Segarra S, Ahrens K, Alonso C and Ferrer L. Topical treatment with sphingolipids and glycosaminoglycans for canine atopic dermatitis. BMC Veterinary Research 2020, 16:92.

This study demonstrates that the topical application of a formulation containing sphingolipids and glycosaminoglycans to an in vivo experimental model of canine atopic dermatitis, reduces the clinical severity (itching and broken skin) of atopic dermatitis. In the study, the product was administered topically twice a week and after 8 weeks the treated group had a significantly lower clinical score and a significantly lower level of itching than the control group.

This study provides a solid basis for recommending the use of this formulation for the care of canine atopic dermatitis, alone or as an adjuvant to treatment.

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Atopivet® collar

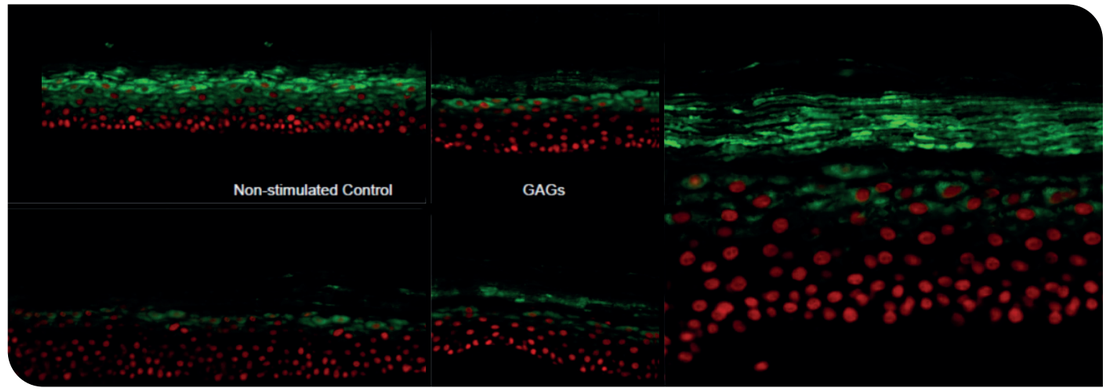
Scientific evidence

Control dog and Atopivet® Spot-On after 8 weeks from the beginning of the study.

"Although atopic dermatitis is a complex disease with multiple pathogenic mechanisms, it seems logical to think that the beneficial effect observed in this study is due, at least in part, to the effect on the epidermal barrier."
Lluís Ferrer

Segarra S, Bernard F-X, Flores J, Naiken T, Effects of sphingolipids, glycosaminoglycans, and their combination on in vitro filaggrin expression using reconstructed human epidermis. In: Abstracts of the 30th Annual Congress of the ECVO-ESVD, Dubrounik, Croatia. Vet Dermatol. 2018;29(5):372.u

This in vitro study demonstrates that a combination of sphingolipids and glycosaminoglycans significantly increases filaggrin expression in a model of reconstructed human epidermis that reproduces atopic dermatitis. This finding is very interesting in that it suggests the usefulness of topical applications of a formulation based on sphingolipids and glycosaminoglycans to contribute to the maintenance of impaired epidermal barrier function in human atopic dermatitis.

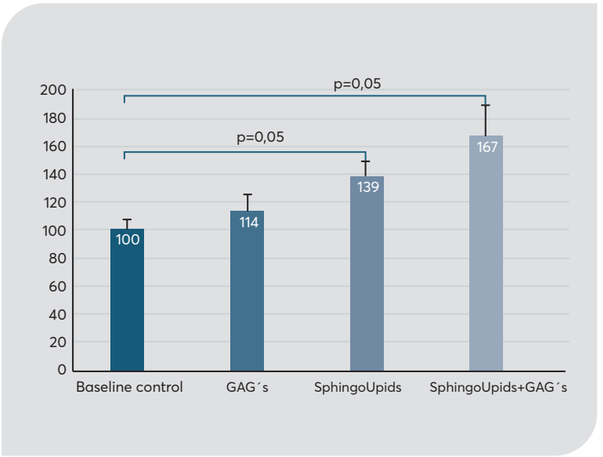


Microscope image showing the effect of the combination of Biosfeen® and Dermial® on filaggrin expression (in green).

"Bearing in mind that dogs are a suitable animal model of human atopic dermatitis and that a decrease in epidermal filaggrin expression in the dog's atopic skin has been described, these results may suggest the usefulness of such a product in atopic dogs"
Laura Ordeix

Segarra S, Bernard F-X, Naiken T Sphingolipids and glycosaminoglycans modulate the expression of antimicrobial peptides in keratinocytes under basal conditions. In: Abstracts of the XII South European Veterinary Conference (SEVC), Madrid; Spain, 2018.

This work shows that both sphingolipids alone as well as a combination of sphingolipids and glycosaminoglycans significantly increase the expression of human β defensin 2 (hBD-2) in normal human epidermal keratinocytes. The initial observation is very interesting given that hBD-2 is an antimicrobial peptide with cutaneous antimicrobial and immunomodulatory properties, the expression of which is shown to be reduced in canine atopic dermatitis.



A significant increase in the production of hBD-2 in the Biosfeen® group (+39% compared to the Control and in the Biosfeen®+ Dermial® group (+67% compared to the Control).

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Atopivet® collar

Scientific evidence

"For this reason, the beneficial use of sphingolipid and glycosaminoglycan-based formulations could be beneficial in increasing the expression of antimicrobial peptides"
Laura Ordeix

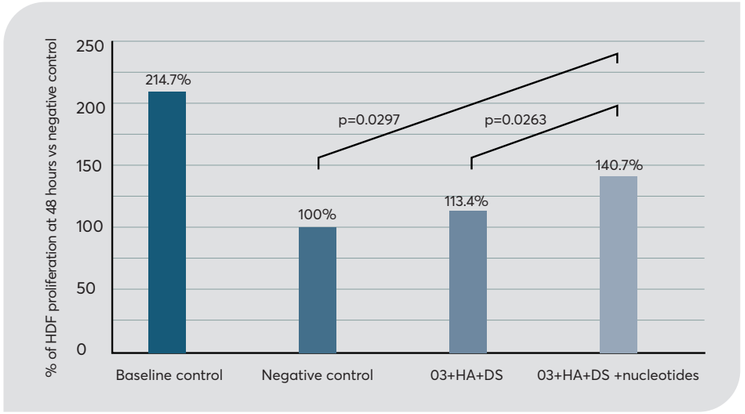
Torrent A, Montell E, Vergés J, et al. Dermial®: A new natural ingredient with anti-aging and regenerative properties for skin. The FASEB Journal 2013; 27: 633-2.

Dermal fibroblast cultures were used in this study. One of the objectives of the study was to analyze the effect of Dermial® on the skin's hydration capacity by measuring endogenous hyaluronic acid synthesis. The effects on the proliferation and migration capacity of these fibroblasts induced by Dermial®, as well as elastin production, were also studied as an indicator of increased skin elasticity. The results show that Dermial® significantly increased fibroblast proliferation and dermal migration. Dermial® stimulates an increase in the skin's moisturizing capacity due to an increase in hyaluronic acid production and its ability to increase elastin production.

Segarra S, Lendínez L, Rodríguez A, Gombau L, Romero J. Increased fibroblast proliferation stimulation by adding nucleotides to a combination of glycosaminoglycan and omega-3. XXXV AMVAC Congress.

In this study, the stimulatory activity on human dermal fibroblast (HDF) proliferation exerted by a combination of EPA, hyaluronic acid and dermatan sulfate (combination 1) compared to the same combination with nucleotides (combination 2) was determined. With respect to the negative control, a significant level of proliferation stimulation was only observed with combination 2 (mean=140.7%, SD=13.19, p=0.0297). Combination 1 showed a non-significant increase (mean=113.4%, SD=6.86, p=0.2797). When comparing between groups, combination 2 proved to be significantly better than combination 1, achieving a significantly higher percentage of HDF proliferation (p=0.0263).

This in vitro study demonstrates how the addition of nucleotides to a combination of hyaluronic acid and EPA results in an increased proliferation-inducing effect on dermal fibroblasts. Consequently, a combination of EPA, glycosaminoglycans and nucleotides such as found in Atopivet® capsules could be useful for use in skin conditions in small animals and would also be indicated as an adjunct to therapies aimed at restoring skin integrity.



Percentage of HDF proliferation after 48 hours in each group.

"These results indicate that this combination could contribute to skin maintenance in patients with erosive lesions such as those occurring in pruritus-induced episodes of self-mutilation." *Cesar Yotti*

The Atopivet® range

B. Types of pet owners

It is essential that the veterinarian identifies the type of pet owner and their attitude towards atopic dermatitis in order to recommend the Atopivet® product that best suits the pet's problems and the owner's lifestyle.

In a market study conducted by Bioiberica among pet owners affected by atopic dermatitis, the following profiles were identified:

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Committed

- Very concerned about the welfare of the animal.
- They take on board the chronic nature of atopic dermatitis.
- Their pet has suffered severe outbreaks.
- They show more involvement with the problem and with the treatments.
- They try to comply with treatment instructions.
- More open to coadjuvant treatments.
- They can understand that they need to invest in treatment.

Very responsive.

Pragmatic

• Their pet has already suffered from several outbreaks of atopic dermatitis. They are not surprised.
• Very responsible in the treatment when the outbreak appears, but their concern ceases when the symptoms subside.
• They do not want to live with the disease.
• Very pragmatic attitude. The symptoms subside but they do not invest in expensive treatments just for prevention.
• Self-prescribing.
• Not consistent with treatment instructions because they do not want to live with the disease.
• Sensitive to the cost of treatments.

They must be educated and made aware of their role as a responsible pet owner.

Nonchalant

• Try to play down the problem with excuses: it's seasonal, it's not serious, it's just a few days.
• Mild, uncomplicated atopic dermatitis.
• The pet does not scratch too much. It does not appear to be suffering.
• They attribute it more to allergies. Therefore, it does not seem worrying.
• Looking to resolve the problem with the minimum effort: feeding, antiparasitic (allergies to insects), ointments.
• Not consistent with hygienic and treatment instructions because they do not no consider the animal has a problem.
• Sensitive to the cost of treatments.

Very distanced. Difficult to change their attitude.

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FAQ

My patient wears a deworming collar. Can they wear an Atopivet® Collar at the same time?

Yes, there is no contraindication in this regard.

If the patient is given a bath, can we be sure that the efficacy will last up to 2 months?

Bathing does not affect the efficacy of Atopivet® Collar, as Biosfeen® is integrated into the polymeric matrix of the collar itself.

What do we do if we put an Atopivet® Collar on a cat and it starts scratching?

If the cat is not used to wearing a collar, it may cause mild discomfort such as itching. This reaction usually occurs when the collar is first fitted and tends to disappear after a short time without needing to remove it, as the cat gets used to wearing it.

Does the collar have any scent?

Biosfeen® is an ingredient of animal origin, with an odor very similar to that of a dog's skin. Atopivet® Collar contains 1.5% lavender scent, providing a pleasant, low intensity odor. After 1-2 days, the odor of the collar will disappear.

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