ATOPIS

A moisturizing and soothing sprayable emulsion for the itchy, dry skin

ΑΤΟΡΙΑ (Α-ΤΟ-ΡΊ-Α)

The name is inspired by the Greek word «ἀτοπία » which means «the abnormal course of things»

Liddell HG, Scott R. An Intermediate Greek-English Lexicon. Oxford: Clarendon Press; 1889.

Allergy-related dermatoses such as atopic dermatitis, flea allergy and food adverse skin reaction are very common in companion animals^{1,2}. Although there is a variety of conditions and triggers which may cause clinical signs such as pruritus, erythema, skin thinning, hair loss and excoriation, two factors have been identified as crucial in the management of symptoms. Firstly, the skin barrier, especially for atopic dermatitis and the propensity to epicutaneous sensitization to allergens. Secondly, the microbiome and the importance of restoring biodiversity. Dysbiosis (i.e., disruption of the normal microbiome) can contribute to the development of allergic and inflammatory diseases. Topical products which not only soothe and address inflammation but also help rebalance the microbiome and reconstruct the skin barrier are bound to be helpful in managing symptoms in allergy-related dermatoses.

Ceramide complex

Ceramides are the most important structural elements of the lipid barrier. They are orderly arranged in lamellar form to act as a membrane and fill the intercellular space in the stratum corneum (SC). Apart from the important barrier function, this membrane also controls cohesion of dead cells, the corneocytes. In dry and fissured skin this lipid barrier is largely destroyed and the skin suffers increased desquamation of corneocytes and high transepidermal water loss.

Canine atopic skin has shown alterations in SC lipid properties, similar to the changes observed in atopic dermatitis in humans, that correlated with a disruption of the skin barrier³. The deficiency of ceramides observed in canine atopic skin has been found to occur in part secondary to inflammation⁴.

In a study in dogs with atopic dermatitis⁵, a topical formulation containing sphingomyelin-rich sphingolipids plus extracts attenuated the clinical worsening induced by house dust mite, supporting its use in atopic patients.

It has been reported that specific lipids exogenously applied to the skin may be taken up by keratinocytes and incorporated into newly formed lamellar bodies⁶. However, to promote normal barrier repair, the lipid mixture should be as close as possible to the normal composition of skin lipids⁷.

Ceramide Complex is a plant-derived lipid mixture which consists of 2% lipids in lamellar, liquid crystalline form, of which 10% at least is sphingolipids. The lipids contained in Ceramide Complex are present in a membranous and thus active structure.

Peony extract

Studies of the genus *Paeonia* have identified polyphenols as their main constituents, with various biological activities, such as antioxidant and anti-inflammatory⁸. *P. officinalis* in particular is a rich source of polyphenolic compounds with high antioxidant potential⁹.Comparably strong phenolic profile has been demonstrated from *Paeonia* species growing wild in Attica (Greece)¹⁰ as well as in Serbia¹¹.

Oat extract

Oat extracts, such as oat kernel extracts, colloidal oatmeal and oat plantlet extracts, are present in cosmetic formulations as emollient, moisturizing and soothing ingredients and have been shown to achieve particular benefits on damaged skin, especially in patients suffering from eczema.

In a study on human subjects, it was demonstrated that colloidal oatmeal is able to modulate sodium lauryl sulfate induced skin irritation, confirming their preventive effects on alteration of the cutaneous barrier function and microvasculature¹². In another study on atopic human subjects¹³, the use of a 1% colloidal oat eczema cream improved microbiome composition and significantly repaired skin barrier defects.

Almond oil

Sweet almond oil is widely used in traditional medicine in order to protect the skin against external factors such as wounds, superficial lacerations, eczema, and psoriasis. It is suggested that it participates in increasing skin resistance, repairing the upper layer of epidermis, stimulating collagen production, and protecting the skin against the damaging effects of free radicals^{14,15}. In addition, almond oil is a nontoxic substance that has anti-inflammatory and antiallergenic properties and it can be topically applied.

Triethyl citrate

Triethyl citrate is hydrolyzed on skin surface to the diethyl ester and monoethyl ester of citric acid and to citric acid itself, thus regulating skin pH. It is perfectly compatible with the skin, has antimicrobial action and blocks skin malodor by deactivating the enzymes responsible for decomposing secretions^{16,17}.

Leuconostoc kimchii - derived peptide

Skin barrier dysfunction and host-microbiome interactions are emerging as primary alterations in canine AD, leading to the need for development of therapies able to restore the skin barrier and increase the natural defenses against pathogenic organisms¹⁸.

The aforementioned peptide is derived from the lactic acid bacteria *Leuconostoc kimchii*. The probiotic *L. kimchii* is capable of restricting the growth of other microorganisms by acidifying its environment and produces a novel antimicrobial peptide, which has been studied for its antimicrobial and moisturizing action.

In vitro evaluations of antimicrobial efficacy of the *Leuconostoc kimchii* - derived peptide in various pharmaceutical forms and different concentrations were performed and confirmed its ability to prevent the growth of test microorganisms in tested formulations¹⁹.

In vivo efficacy evaluations of the *Leuconostoc kimchii* - derived peptide on human subjects were conducted to determine moisturization, Transepidermal Water Loss (TEWL) and skin density and the results were strongly positive on all parameters with increase in moisture levels, enhancement of barrier function through reduction in Transepidermal Water Loss and improvement of skin density¹⁹.

References

- 1. Gedon, N.K.Y., Mueller, R.S. Atopic dermatitis in cats and dogs: a difficult disease for animals and owners. *Clin Transl Allergy* 8, 41 2018.
- Marsella, R. Atopic Dermatitis in Domestic Animals: What Our Current Understanding Is and How This Applies to Clinical Practice. *Vet. Sci.* 2021, 8, 124.
- 3. Chermprapai S, Broere F, Gooris G, Schlotter YM, Rutten VPMG, Bouwstra JA. Altered lipid properties of the stratum corneum in Canine Atopic Dermatitis. *Biochim Biophys Acta Biomembr.* 2018 ;1860(2):526-533.
- Stahl J, Paps J, Bäumer W, Olivry T. *Dermatophagoides farinae* house dust mite allergen challenges reduce stratum corneum ceramides in an experimental dog model of acute atopic dermatitis. *Vet Dermatol.* 2012 ;23(6):497-e97.
- 5. Marsella, R., Segarra, S., Ahrens, K. et al. Topical treatment with SPHINGOLIPIDS and GLYCOSAMINOGLYCANS for canine atopic dermatitis. *BMC Vet Res.* 16, 92 2020.
- Mao-Qiang M, Brown BE, Wu-Pong S, Feingold KR, Elias PM. Exogenous nonphysiologic vs physiologic lipids. Divergent mechanisms for correction of permeability barrier dysfunction. *Arch Dermatol.* 1995;131(7):809-16.

- Man MQ, Feingold KR, Elias PM. Exogenous lipids influence permeability barrier recovery in acetone-treated murine skin. *Arch Dermatol.* 1993 ;129(6):728-38.
- 8. He, C.; Peng, Y.; Zhang, Y.; Xu, L.; Gu, J.; Xiao, P. Phytochemical and Biological Studies of Paeoniaceae. *Chem. Biodivers.* 2010, 7, 805–838.
- Dienaitė, L.; Pukalskienė, M.; Pukalskas, A.; Pereira, C.V.; Matias, A.A.; Venskutonis, P.R. Isolation of Strong Antioxidants from *Paeonia Officinalis* Roots and Leaves and Evaluation of Their Bioactivities. *Antioxidants* 2019, 8, 249.
- Letsiou, S., Bakea, A., Holefors, A. et al. In vitro protective effects of *Paeonia* officinalis var. mascula callus extract on human keratinocytes. Sci Rep 10, 19213 (2020)
- Čutović, N.; Marković, T.; Kostić, M.; Gašić, U.; Prijić, Ž.; Ren, X.; Lukić, M.; Bugarski, B. Chemical Profile and Skin-Beneficial Activities of the Petal Extracts of *Paeonia tenuifolia* L. from Serbia. *Pharmaceuticals* 2022, 15, 1537.
- 12. Vié K, Cours-Darne S, Vienne MP, Boyer F, Fabre B, Dupuy P. Modulating effects of oatmeal extracts in the sodium lauryl sulfate skin irritancy model. *Skin Pharmacol Appl Skin Physiol.* 2002 ;15(2):120-4.
- Capone K, Kirchner F, Klein SL, Tierney NK. Effects of Colloidal Oatmeal Topical Atopic Dermatitis Cream on Skin Microbiome and Skin Barrier Properties. J Drugs Dermatol. 2020 1;19(5):524-531.
- 14. Lin TK, Zhong L, Santiago JL. Anti-Inflammatory and Skin Barrier Repair Effects of Topical Application of Some Plant Oils. *Int J Mol Sci.* 2017 27;19(1):70.
- 15. Ahmad Z. The uses and properties of almond oil. *Complement Ther Clin Pract.* 2010 ;16(1):10-2.
- 16. Charakida A, Charakida M, Chu AC. Double-blind, randomized, placebocontrolled study of a lotion containing triethyl citrate and ethyl linoleate in the treatment of acne vulgaris. *Br J Dermatol*. 2007 ;157(3):569-74. *Erratum* in: *Br J Dermatol*. 2010 Aug;163(2):437.
- 17. Supplier info (www.jungbunzlauer.com/en/products/specialties/citrofol-ai)
- Santoro D, Marsella R, Pucheu-Haston CM, Eisenschenk MN, Nuttall T, Bizikova P. Review: Pathogenesis of canine atopic dermatitis: skin barrier and host-micro-organism interaction. *Vet Dermatol.* 2015;26(2):84-e25.
- 19. Supplier info (<u>www.activemicrotechnologies.com/product/leucidal-liquid/</u>)