

Redonyl® Ultra

(Ultra-micronized Palmitoylethanolamide)

An ultra-small ingredient that offers ultra-big support for skin health.

When skin health is compromised, the exact cause can often be difficult to determine. Supporting the skin, regardless of the cause, is essential in keeping your canine patients and their owners happy and comfortable.



What is PEA?

PEA (palmitoylethanolamide) is a naturally-occurring lipid compound, endogenously present in both animals and plants. Soybean is one of the natural food sources with the highest content of PEA (7 µg per gram of fresh weight).1 However, PEA intake through food consumption is inadequate to reach a level necessary for skin health support ($\geq 5 \text{ mg/kg}$). To reach a daily PEA intake of $\geq 5 \text{ mg/kg}$, a dog would need to eat almost 70% of its weight in soybeans daily. (An 11 lb [5 kg] dog would need more than 7.7 lb [3.5 kg] of soybeans daily.) Redonyl[®] Ultra Soft Chew provides a concentrated source of PEA for dogs in a palatable, easy-to-administer soft chew.



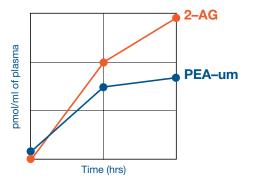


3.7 kg of soybean = 5 mg/kg of PEA for a 5 kg dog

How does PEA help support skin health in the dog?

PEA is an endogenous substance locally produced on demand in response to tissue injury and stress.² When a dog's skin becomes unhealthy, the endogenous level of PEA is 30x higher than normal canine skin.³ PEA is the parent molecule of aliamides, a class of compounds able to rebalance tissue homeostasis by controlling mast cell function.⁴⁻⁶ It has been shown that PEA has an effect on canine skin mast cell degranulation⁷ and thus the release of several biological mediators involved in the development of unhealthy skin. Immunogenically challenged mast cells, previously isolated from healthy canine skin, release less histamine, PGD_α, and TNF-α in the presence of ultra-micronized PEA (PEA-um).⁷ Although mast cells are its main cellular target, PEA also affects the homeostasis of both keratinocytes⁸ and macrophages.^{9,10}

When orally administered to dogs, PEA-um enhances the plasma level of one of the most extensively investigated endocannabinoids, 2-AG (2-arachidonoylglycerol),¹¹ thus confirming the hypothesis that PEA behaves as an "indirect endocannabinoid".¹² Endocannabinoids make up an endogenous system that helps maintain tissue homeostasis, and they share metabolic and functional pathways with PEA.13-19 Cannabinoid receptors (CB1 and CB2) are expressed in the skin of healthy dogs, and their expression significantly increases in dogs with unhealthy skin.20





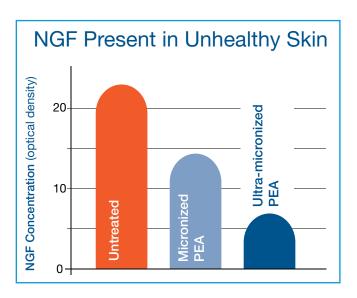
In an 8-week study of 160 dogs, oral PEA-um was beneficial for skin health.

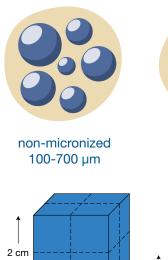
Has Ultra-micronized PEA been studied in dogs?

In an 8-week study of 160 client-owned dogs, oral PEA-um was shown to be beneficial for skin health.²¹ 75% of the clinicians rated the overall response to be at least "sufficient", "good" or "excellent". Tolerability in this study was good-to-excellent with only four dogs experiencing associated reversible side effects.

Why is it important to use Ultra-micronized PEA?

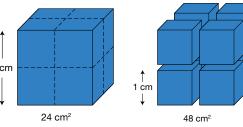
Thanks to a patented technological process, called jet milling, the raw material for the PEA in Redonyl Ultra is composed of much smaller particles than other sources of PEA. In fact, 99.9% of the particles are smaller than 6 μ m and 60% of PEA-um particles are smaller than 2 μ m. As particle size is reduced, surface area increases, thus improving water solubility of PEA powder. This feature improves both the distribution and diffusion of PEA in the body.^{22,23}







ultra-micronized 99.9% < 6 µm



The surface area of a solid increases as its size decreases

Ultra-micronized PEA is more effective than micronized PEA, especially in controlling the release of NGF (nerve growth factor),²⁴ a mast cell mediator frequently found in unhealthy skin.²⁵⁻²⁷



Redonyl® is a patented product by Innovet Italia S.r.I. Redonyl Ultra is protected by the following US patents: 6,548,550, US 8,470,373, and US 8,663,701. Dechra is a registered trademark of Dechra Pharmaceuticals PLC. © Dechra

How do I use Redonyl® Ultra?

Redonyl Ultra is available as a tasty, soft chew treat for dogs in a hypoallergenic base. The hypoallergenic formula contains no wheat, beef, or chicken and uses a hydrolyzed soy protein for flavoring. The vast majority of the protein molecules are hydrolyzed to a size smaller than 1000 daltons.

Two strengths of Redonyl Ultra are available, 100 mg and 200 mg, for dogs of all sizes. The soft chews have been tested for content uniformity so the tiniest dogs can accurately receive their ultra-micronized PEA by cutting a 100 mg chew in half. The soft chews for dogs are designed for easy administration. Additionally, the ultra-micronized PEA in Redonyl Ultra allows for better absorption than non-micronized PEA.

The length of support needed for each dog should be determined by patient history, follow-up veterinary examinations, and other diagnostic work. At home, dog owners can watch for a response in their pet's attitude, comfort, and activity level.

Redonyl Ultra has no known serious side effects.

Dosing

Optimized Dosing Body Weight Chart

Dog – Pounds	100 mg	200 mg	Frequency
Less than 7	1/2 chew		Every other day
7 – 14	1/2 chew		Once daily
15 – 24	1 chew		Once daily
25 – 35	1 1/2 chews		Once daily
36 – 49		1 chew	Once daily
50 – 73		1 1/2 chews	Once daily
74– 100		2 chews	Once daily

TRIZCHLOR

Concurrent use of Redonyl Ultra Soft Chews and topical therapies for the skin, including shampoos, mousse, conditioners, sprays, and wipes, can help maintain the health of your canine patients' skin. For skin issues with wide ranging causes, a multimodal approach is often recommended. Add Redonyl Ultra Soft Chews to your current dermatology protocol for additional skin support.

To order or schedule a lunch and learn, call your Dechra representative or call (866) 683-0660. For Technical Support Contact Dechra Veterinary Products at: 866-933-2472, www.dechra-us.com, support@dechra.com.

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REFERENCES

- 1. Kilaru A et al. Chem Biodivers. 2007; 4(8):1933-55.
- 2. Pistis M, Melis M. Curr Med Chem. 2010;17(14):1450-67.
- 3. Abramo F et al. BMC Vet Res. 2014;10(1):21.
- 4. Noli C, Miolo Veterinaria. 2012;26(3):9-19.
- 5. Abramo F. Mastociti, Proceedings SkinALIA2012, Verona, Italy. 30th-31st March 2012: pp 3-8.
- 6. Miolo A et al. J Vet Pharmacol Ther. 2006; 29 Suppl 1:204-5.
- 7. Cerrato S et al. Vet Immunol Immunopathol. 2010;133(1): 9-15.
- 8. Petrosino S et al. Allergy. 2010;65(6):698-711.
- 9. Ross RA et al. Eur J Pharmacol. 2000;401(2):121-30.
- 10. Bisogno T et al. J Biol Chem. 1997; 272(6):3315-23.
- 11. Petrosino S et al. Proceedings 69° Congr Internaz SCIVAC 2011. Rimini, Italy.
- 12. Di Marzo V. Proceedings SkinALIA2012, Verona, Italy: pp 9-12.
- 13. Re G et al. Vet J. 2007; 173(1):23-32.
- 14. De Filippis D et al. Pharmacol Res. 2010; 61(4):321-8.

- 15. Biro T et al. Trends Pharmacol Sci. 2009; 30(8):411-20.
- 16. Sugawara K et al. J Allergy Clin Immunol. 2012;129(3):726-738.e8.
- Ständer S. Proceedings SkinALIA2012, Verona, Italy. pp 51-55.
- 18. Petrosino S et al. Curr Opin Chem Biol. 2009; 13(3):309-20.
- 19. Di Marzo V. Pharmacol Res. 2009;60(2):77-84.
- 20. Campora L et al. Am J Vet Res. 2012:73(7):988-95.
- 21. Noli, C et al. Vet Dermatol. 2015;26(6):432-440.
- 22. Kim MS et al. Chem Pharm Bull (Tokyo). 2010;58(2):230-3.
- 23. Rasenack N, Müller BW. Pharm Dev Technol. 2004;9(1):1-13.
- 24. Luvone T et al. Data on file (brevetto PCT W02011/027373A1)
- 25. Ikoma A et al. Arch Dermatol. 2003;139(11):1475-8.
- 26. Arck P, Paus R. Neuroimmunomodulation. 2006;13(5-6):347-56.
- 27. Metz M, Stander S. Vet Dermatol. 2011;22(2):121-131.