Skin and Coat

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Introduction

The coat and skin are the most immediate and visual way to assess the general health of an animal. The skin, the largest organ in the body, and coat provide a protective layer between the environment and the rest of the body. The skin of a newborn puppy can represent up to 25% of its overall weight and up to 12% of the total weight of adult dogs *(1).* Skin serves many purposes and plays a key role in the animal's overall health (Table 1).

Table 1. The protective functions of skin in dogs and cats

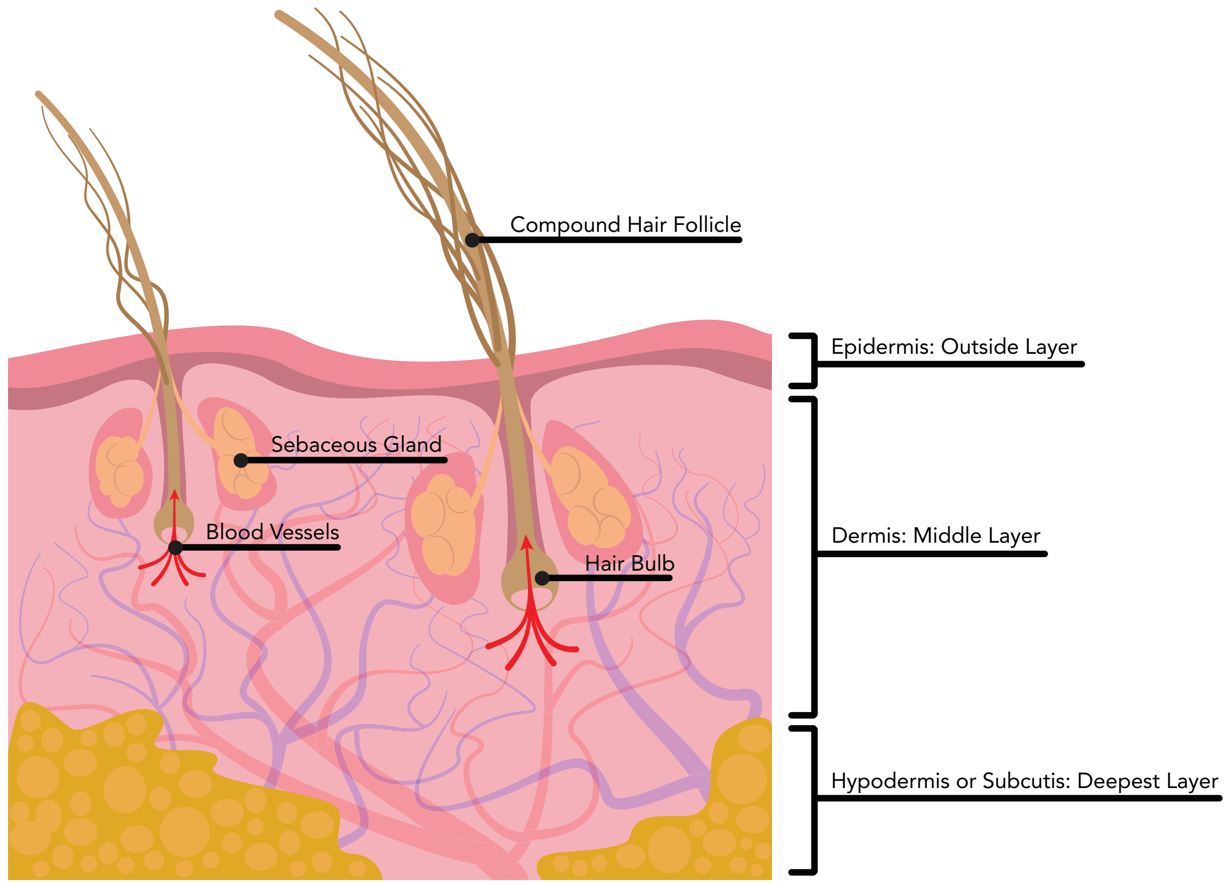
Skin Property	Function
Enclosing barrier	Effective barrier to prevent loss of electrolytes, macromolecules and water
Environmental protection	Prevents physical, chemical, microbiological, and solar agents from entering the body
Shape and motion	Flexible, elastic skin with appropriate membrane integrity influences body shape and motion
Temperature regulation	Manages temperature through coat, cutaneous blood supply and sweat gland function
Nutrient storage	Reserves of electrolytes, water, vitamins, fat, carbohydrates, proteins
Indicator	Signals physical and sexual identity, general health, potentially internal health
Immuno-regulation	Specialized cells provide an immuno-surveillance capability
Pigmentation	Skin processes determine color of skin and coat; pigmentation aids in solar protection
Anti-microbial action	Anti-microbial and anti-fungal process on skin surface help control local skin flora populations
Sensory perception	Primary contact for hot, cold, pain, itch, touch and pressure sensing
Secretion	Features sebaceous, epitrichial and ecocrine glands
Excretion	Excretion is limited in the skin of dogs and cats
Vitamin D production	Solar radiation on the skin surface stimulates conversion of pro-vitamin D to active vitamin D

Skin

On the trunk, or body, skin is generally thickest dorsally (on the upper side) with a decrease in thickness ventrally (on the underside). On the limbs, the skin is thickest proximally (near the point of attachment) and decreases distally (away from the point of attachment) except for specialized areas like the footpads. Skin is thickest on the forehead, dorsal neck, thorax, rump, and base of the tail. Skin is thinnest on the ears, axillary (armpit), inguinal (groin), and perianal (around the anus) areas *(1).* In dogs, skin thickness ranges from 2.6 to 5.2 mm *(1) (2).* Breed and gender both affect skin thickness in dogs *(2).* In cats, skin thickness ranges from 0.4 to 3.6 mm *(1) (3).* Adult male cats have thicker skin than female cats regardless of reproductive status *(4).*The pH of dog skin is generally more basic than that of cat skin, ranging from 5.5 to 8.8 *(2) (5).* Skin pH is variable in dogs and depends on site of observation, day, stress level, sex, gonadal status, coat color, and breed *(1) (2) (4).* Skin pH is higher in older cats when compared to young cats and higher in female cats compared to male cats *(4).*

The skin is composed of three layers: the epidermis, dermis and subcutis or hypodermis. Each layer protects the body, but the layers specific roles differ (Figure 1).

Figure 1. The skin of dogs and cats has three distinct layers, and most dogs and cats have multiple hairs per follicle.



Epidermis

The epidermis is the most metabolically active layer of the skin. The epidermal layer is a stratified, continuously renewing set of primarily keratinocytes that progressively differentiate from the dermis in a superficial direction *(6).* The epidermis is fairly thin in dogs; however, areas of thin hair cover have a thicker epidermal layer. Epidermal cells in dogs and cats have a lifespan of approximately 22 days, which is shorter than the human epidermal cell lifespan of 28 days *(1) (6).*

Dermis

The dermis is the middle layer of the skin and its thickness varies depending on the hair cover and epidermal thickness of the region of the body. This layer is primarily responsible for tensile strength and elasticity. Other functions of the dermis include regulation of cell growth and proliferation, adhesion, migration and differentiation of cells, and wound healing *(1).* Although sparsely populated with cells, the dermis contains significant amounts of fibers and ground substance.

Subcutis (Hypodermis)

The subcutis is the thickest and deepest layer of the skin. This layer contains a network of fibrous bands that are connected to the dermis and the underlying fascial sheets. These fibers divide the adipocytes (fat cells) into many lobules. Not surprisingly, the subcutis is 80% triglyceride *(1).* The degree of vascularization in the hypodermis is inversely proportional to its thickness. More hypodermis equates to slower blood flow and increased lipogenesis (fat production), and less hypodermis means more blood flow and lipolysis (fat breakdown). Therefore, animals with thicker hypodermis tend to preserve fat stores whereas animals with thin hypodermis are more likely to use skin fat stores.

Hair

The coat of dogs and cats serves many functions (Figure 2).

Figure 2. The functions of the coat in dogs and cats.

Dogs have two types of hair: the primary or outer coat and the secondary or undercoat. Cats have three types of hair: guard hairs awn hairs, and down hair *(1).* Guard hairs are primary hairs (outer coat), and both down and awn hairs are secondary hairs (undercoat).

Hair shape is determined by follicle shape. Straight follicles produce straight hairs (for example, greyhounds), whereas curly follicles produce curly hairs (for example, poodles). Dog coats come in many varieties, but, on average, dogs produce 60 to 180 g hair/kg of body weight per year. In contrast, the average domestic shorthair cat grows about 32.7g of hair/kg of body weight *(1).* All hair growth is generated from follicles that are present at birth. Dogs and cats cannot replace or add hair follicles after the neonatal period. Therefore, puppies do not "lose" their puppy coat; instead they gain an adult coat.

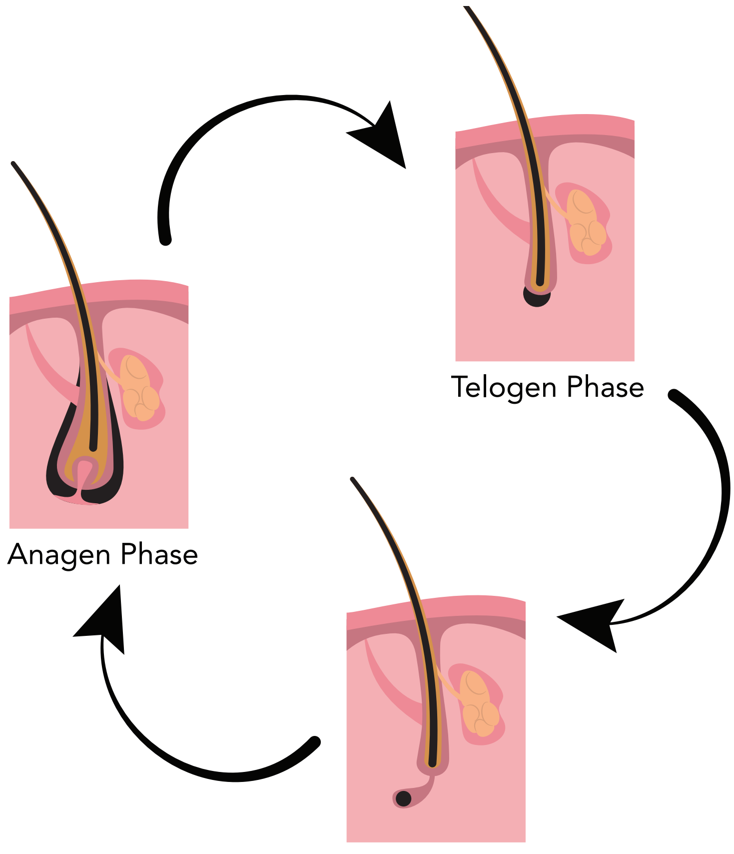
When puppies are born, they have simple hair follicles - like humans - with mostly secondary hairs exiting the follicle. As puppies mature, the hair follicle becomes more complex, and the dog acquires an outer coat of primary hairs rather than losing its the puppy coat. Changes in hair follicles as dogs mature result in compound hair follicles, which mean that multiple hairs exit the skin from the same opening or follicular os (Figure 1).

The hair follicle consists of an outer and inner root sheath with the hair shaft in the middle. At the base of the shaft is the hair bulb. Within the hair bulb are the tissues that regulate growth, involution (recession of follicle) and senescence (cellular aging).

The hair cycle is divided into three distinctive phases: anagen, catogen and telogen *(7)* (Figure 3).

The hair cycle helps dogs adapt to seasonal or environmental changes. This cycle is clearly regulated by photoperiod through the hypothalamus, hypophysis and pineal gland *(1).* In general, hair follicle activity, or shedding, is maximal in the spring and autumn and minimal in the winter. One study showed all primary and up to 50% of secondary hair follicles were in telogen (the resting phase) during the winter *(1) (8).* However, dogs that are kept primarily indoors and exposed to many hours of artificial light tend to shed continuously throughout the year. In addition to photoperiod, hormonal status, environmental temperature, nutrition and stress affect the length of the telogen *(8) (1).* Hair replacement tends to be mosaic in pattern, with hairs growing in different phases. Work by two

Figure 3. The hair cycle of dogs and cats.



Anagen: the active period of hair growth. The hair bulb is connected to the dermis, and the inner root sheath is intact.

Telogen: the resting phase. The inner sheath is completely replaced with cornified cells, and the length of the follicle from the follicular os downward shrinks by two-thirds in length. Hairs in telogen are easily epilated. However if the hair is not shed, the telogenic hair is pushed out of the follicle during the beginning of anagen (7).

Catagen: the transition phase. During this time, the hair bulb recedes, the connection to the dermis disintegrates, and the inner sheath is partially replaced by cornified cells, and melanogenesis stops.

different researchers examined hair regrowth rates in growing labrador retrievers and reported hair growth rates of 5.5 to 17 mm/30 days depending on the season *(3) (7).* Stress, either from a disease state, environment or nutritional imbalance, can cause synchronized telogen onset that results in a generalized thinning of the coat. Oftentimes this hair loss does not occur until several weeks after the stressful event *(9).* Needless to say, this makes identifying of the stressor more difficult.

The dog hair cycle is primarily telogen-based, which means hairs are maintained in a state of senescence for long periods. However, hair cycles vary among dog breeds. Some Nordic breeds, such as Siberian huskies, hold hair in the telogen phase for years *(7) (9).* Poodles and breeds with similar coat types have anagen-based hair cycles, which are more similar to humans. These breeds require more grooming because their hair is constantly growing.

The coat and skin can vary based on age, breed, gender, the individual, and anatomic location *(1).* A wide range of different coat and skin combinations can be observed at any dog show or veterinary practice. Healthy dogs and cats will have breed-appropriate hair growth, thickness and shininess, whereas unhealthy skin and coat appears as dry, brittle or greasy hair and flaky, dry skin or oily skin with overly active sebaceous glands and perhaps malodor.

Functional Supplements for Skin and Hair Coat

Supplementing the diet with a combination of skin-targeted nutrients will help strengthen the skin barrier and provide a positive environment for optimal hair growth. Prudence Skin and Coat formula contains a proprietary blend of ingredients, which are synergistically combined to improve skin and coat health. Figure 4 outlines the ingredients in Prudence Skin and Coat and their specific functions.

Figure 4. Prudence Skin and Coat supplement has several ingredients with multiple functions.

Complete Skin and Coat

Omega 3-6-9 Advanced with Krill

Body

Krill Oil
48x more effective antioxidant than fish oil
May decrease the rate of aging
Easily absorbed by the body

Astaxanthin from Krill Oil
Acts as a Sunscreen

Biotin
Helps maintain skin thickness and nail integriy

Fish Oil
Prevents inflammation

Gamma linoleic acid
Has anti-inflammatory properties

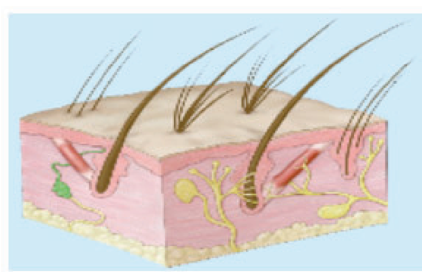
Lycopene from Fish Oil
Potent antioxidant

Evening Primrose Oil
Decreases inflammation

Skin

Krill Oil
Source of anti-inflammatory omega-3 fatty acids

Astaxanthin from Krill Oil
Similar to B-carotene, a strong antioxidant



Vitamin E
Keeps skin supple and hair shiny

Fish Oil
Maintains skin elasticity
Helps maintain skin moisture

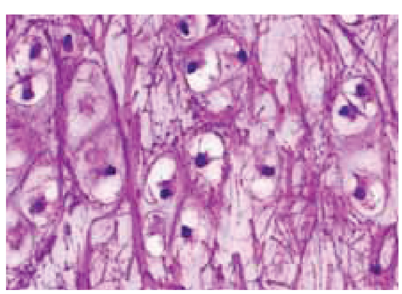
Gamma linoleic acid
Only Omega 6 fatty acid to have anti-inflammatory properties

Lycopene from Fish Oil
Potent antioxidant

Biotin
Maintains skin and hair condition

Cellular

Krill Oil
Decreases free radical production



Astaxanthin from Krill Oil
Helps prevent free radical production in cells

Biotin
Catalyst for fatty acid metabolism in cells

Lycopene from Fish Oil
Prevents cellular damage

Evening Primrose Oil
Provides essential fatty acids for skin cell membranes

Vitamin A
Maintains appropriate cell turnover rates

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Omega-3 and Omega-6 Fatty Acids from Krill Oil, Fish Oil and Evening Primrose Oil

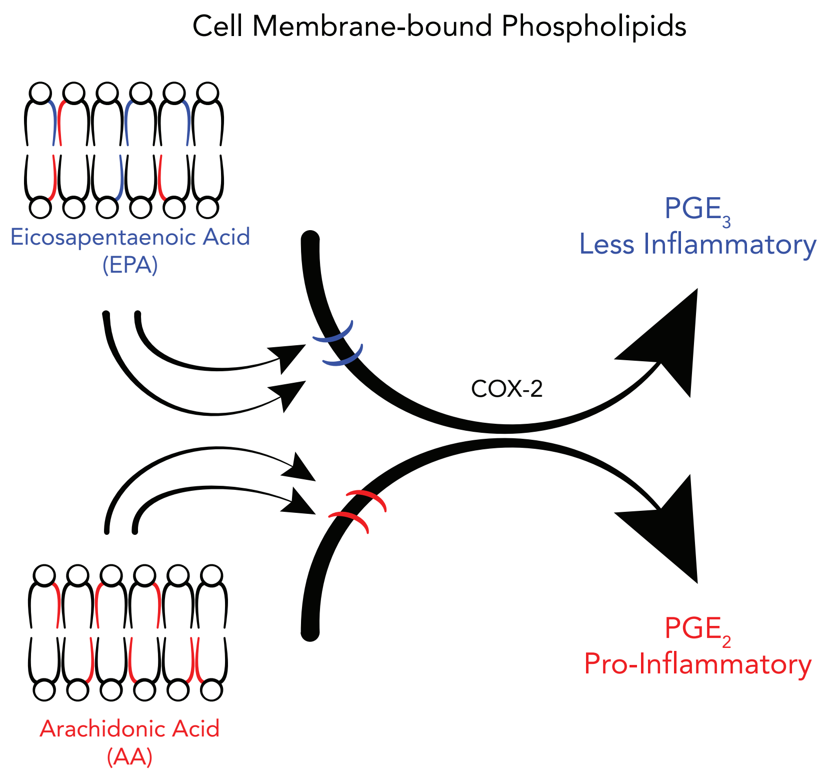
Fatty acids are identified by the number of carbon atoms in the molecule, as well as by the presence and location of double (unsaturated) bonds between the carbons. For example, omega-6 fatty acids have a double bond between the 6th and 7th, carbon, and omega 3-fatty acids have a bond between the 3rd and 4th carbon. Polyunsaturated fatty acids (PUFAs) are those fatty acids with more than one double bond. Fatty acids in the omega-6 and omega-3 families serve important physiologic functions and are considered essential or conditionally essential nutrients for most mammals *(10).*

Among the functions served by these fatty acids are normal growth, preservation of cellular membranes and functions, normal skin structure and function, renal function, reproduction, immune function, blood clotting, nerve structure and more. The omega-3 and omega-6 families of long-chain fatty acids are similar in many ways and can serve similar physiologic functions and may work in a complementary or synergistic manner in the body.

Within the skin, the omega-6 and omega-3 fatty acids serve three main functions *(10).* First, they serve as a structural component of the phospholipids of cellular membranes, where they maintain fluidity and normal permeability. If tissue permeability is disrupted, it can lead to nutrient and water loss. Second, fatty acids maintain the epidermal water barrier. And finally, they serve as precursors for the production of pro- and anti-inflammatory eicosanoids. It is this latter function where omega-3 fatty acids can play a major role in managing inflammation.

PUFAs in both the omega-6 and omega-3 families can have immunomodulatory effects. The primary omega-6 fatty acid in cell membranes is arachidonic acid, which serves as the precursor for the production of such potent inflammatory mediators such as prostaglandin E2, ,PGE_2, (Figure 5). Omega-3 fatty acids, eicospentaenoic acid (EPA) and docosahexaenoic acid (DHA) are also in cell membranes, but they are at a lower level. If the diet is enriched with long-chain omega-3 fatty acids, EPA and DHA, part of the arachidonic in cell membranes can be replaced by EPA and DHA (Figure 5).

Figure 5. Polyunsaturated fatty acids, omega-6 and omega-3 are incorporated into cell membranes. EPA and arachidonic acid compete as substrates for the cyclooxygenase, or cyclooxygenase-2 (COX-2) pathways.



When arachidonic acid is used by cyclooxygenase-2 (COX-2), more pro-inflammatory mediators (PGE2) are produced, but EPA yields less inflammatory mediators (PGE3).

EPA may then be used instead of arachidonic acid for the production of eicosanoids, resulting in a different and less inflammatory set of compounds, including PGE3 instead of PGE2. Thus, the substitution of omega-3 for part of the omega-6 fatty acids in the cell membrane should reduce inflammation.

Studies during the last decade have indicated that omega-3 fatty acid effects on skin are not limited to the manipulation of PGE production. Omega-3 fatty acids play a role in modulation of cell signaling, gene expression, pro-inflammatory mediation, immune function, oxidative stress and apoptosis or programmed cell death (Table 2) *(11).*

Table 2. Omega-3 fatty acids influence multiple biological processes

Omega 3 Fatty Acids Influences on Biological Processes
Alter PGE synthesis
Alter signaling in membranes
Influence inflammatory cell activation
Directly decrease pro-inflammatory activating factors
Alter gene expression of COX-2 enzyme
Alter expression of NFkB, which influences epidermal homeostasis, inflammation and carcinogens
Positively influence lymphocyte activity and downregulate T cell response in chronic inflammation
Act as a free radical buffer by modulating reactive oxygen species and nitric oxide in macrophages
Regulate apoptosis and decreasing tumor cell proliferation
Alter the expression of cell adhesion molecules

Krill Oil: A Unique Omega-3 Source with Extra Benefits

Krill oil comes from the arctic crustacean, Euphasia superba, and is considered by many researchers to be a more effective source of omega-3 fatty acids than common marine sources. Krill oil is unique because it contains not only omega-3 fatty acids but significant amounts of endogenous fat-soluble vitamins, antioxidants, folate and vitamin B_{12} (Table 3).

Approximately 65% of omega-3 fatty acids from Krill are incorporated into phospholipids, whereas fish oil fats are incorporated mainly into triglycerides. It has been hypothesized that omega-3 fatty acids attached to phospholipids are more bioavailable than fatty acids incorporated into triglycerides, according to studies that compared fatty acid uptake in humans supplemented with Krill oil or fish oil *(13) (14) (15) (16).* An additional study reported that essential fatty acids in phospholipid form are superior to essential fatty acids in triacylglycerol form in increasing bioavailability of EPA and DHA *(17*). Phospholipids play additional roles as building blocks for cell membrane stability and synthesis *(18)* and as a protector of cell membranes from toxic injury *(19).*

Astaxanthin is also bound primarily to phospholipids in Krill oil. Krill contains approximately 1.5 to 2.0 mg astaxanthin/100 g of Krill, indicating that it is a rich source of this carotenoid *(20).* Astaxanthin is a powerful carotenoid but does not have any vitamin A activity. It has been shown to protect against ultra violet (UV) light damage in vitro and in vivo *(21).* Astaxanthin inhibits the production of PGE2 and tumor necrosis factor (TNF) in human and animal models *(22).* Two studies in dogs reported that astaxanthin has a direct positive effect on oxidative stress and immune modulation *(22).* Dogs fed up

Table 3. Fat and vitamin content of marine sources of fatty acids. (Adapted from Tau et al) (12)

	Krill	Shrimp	Trout	Salmon
PUFA (%)	48.5	38.7	35.8	33.6
Linoleic acid (18:2) omega-6	3.3	1.6	6.9	6.5
Alpha-linoleic acid (18:3) omega-3	1.1	0.8	3.4	2.6
Arachidonic acid (20:4) omega-6	0.5	5.0	3.2	2.2
Eicosapentaenoic acid (20:5) omega-3	17.4	14.9	4.8	7.2
Docosahexaenoic acid (22:6) omega-3	12.4	12.8	12.1	11.1
Fat-soluble antioxidants (g)				
Vitamin A (IU/100g)	380	180	62	100
Vitamin E (mg/100g)	15	1.10	ND	0.65
Water-soluble antioxidants (g)				
Folate (µg/ 100g)	60	3	12	9
Vitamin B_{12} (µg/ 100g)	16	1.16	4.45	4.17

to 40 mg astaxanthin daily had heightened cell-mediated and humoral response and reduced DNA damage and inflammation *(23).*

Astaxanthin's potent antioxidant properties are exhibited at the cell membrane level rather than systemically in most cases *(24).* This is an important observation because the skin is the second largest immune organ after the gastrointestinal tract. The function of the skin associated lymphoid system, or SALT, is to protect the body from environmental threats. Krill oil has been determined to be approximately 50 times more effective as an antioxidant when compared to fish oil, primarily due to the high levels of astaxanthin *(25).*

Krill is considered less likely to oxidize when compared to other sources of omega-3 fatty acids, like flaxseed oil. This attribute is associated not only with the high levels of astaxanthin in Krill but also the significant amount of vitamin E also found in Krill *(12).* Marine-specific tocopherols have enhanced antioxidant effects on cellular lipids *(26)* and may contribute to the increased production of endogenous antioxidants (catalase, glutathione peroxidase and super oxide dismutase) in the tissues of animals fed 10 % Krill oil compared to animals fed corn oil *(27).*

Krill oil can contribute to skin and coat health by:

1) Providing omega 6 and omega 3 fatty acids for membrane stability and local immune response

2) Providing a source of phospholipids for cell membrane replenishment

3) Providing both fat-soluble and water-soluble vitamins to contribute to normal skin metabolism

4) Providing a significant source of astaxanthin, a powerful antioxidant shown to inhibit damage from UVA and UVB rays and modulate immune response

Fish Oil: A Marine Source of Omega-3 Fatty Acids

Fish oil has long been reported to benefit cat and dog skin health. Omega-3 fatty acids, in this case from fish oil, increase PGE_3 produced via the COX pathway in lieu of PGE_2. Dogs respond best to marine sources of Omega 3 fatty acids rather than vegetable sources, like flaxseed or linseed, because of their limited ability to convert γ-linoleic acid to EPA *(28)*. Dogs fed diets high in fish oil omega-3 fatty acids had decreased concentrations of pro-inflammatory leukotriene in skin and blood measurements *(29)*, which indicates that EPA from fish oil also affects lysyl oxidase, or LOX metabolites.

Fish oils also contain carotenoids, like lutein, as well as small amounts of fat-soluble antioxidant vitamins (Table 3). Lutein resides in the dermis and epidermis of supplemented mice and humans, and it is likely that this is true in dogs and cats as well *(30)*. Lutein is a potent antioxidant that is easily absorbed by dogs and cats *(23)*. Lutein has cell-mediated immunomodulary characteristics and is known to reduce UV radiation-induced inflammation and immunosuppression in mice and humans. It also may contribute to the defense against deleterious effects of solar radiation *(30) (31)*.

Fish oil contributes to skin and coat health by providing omega-3 fatty acids to modulate inflammation and other cellular-signaling mechanisms, as well as providing an endogenous source of carotenoids that act as antioxidants.

Evening Primrose Oil: A Unique Omega-6 Fatty Acid that Decreases Inflammation

Evening primrose oil has been reported to restore a defective epidermal skin barrier, normalize excessive skin surface water loss and improve the smoothness of skin in both healthy and eczematous humans and other species *(32)*.

These skin-improving effects have been ascribed to gamma linolenic acid (GLA) of which evening primrose oil is a rich source. Many reports strongly suggest that the skin may have an inherent requirement for GLA, and because the skin is unable to synthesize this fatty acid, it relies on supply of preformed GLA for optimal structure and function *(32)*. Several small studies in dogs indicate a potential benefit of supplementing evening primrose oil or GLA on clinical symptoms of pruritus and atopy *(1) (33) (34)*. The skin is particularly sensitive to suboptimal GLA supply as it lacks the necessary delta-6-desaturase enzyme with which to form it in situ. This could have profound effects on skin barrier function and on dermal immune-inflammation. GLA, in vitro at least, suppresses the formation and release of interleukin 1β and TNFα, both important inflammatory mediators. GLA also provides required omega-6 fatty acids for optimal skin cell membrane integrity. Without sufficient omega-6 fatty acids in cell membranes, there is an increase in membrane fragility *(1)*.

Evening primrose oil is a plant-based source of GLA, which is unique in that it is both an omega-6 fatty acid and has anti-inflammatory properties instead of the typical pro-inflammatory properties found in other omega- 6 fatty acids. Evening primrose oil appears to work synergistically with fish oil and has proven effects in dogs *(33) (35)*.

Summary

The skin is a primary defense mechanism for dogs and cats and plays an integral role in communication between conspecifics, immune function, environmental protection, thermoregulation, etc. Omega-3 and omega-6 fatty acids modulate inflammation in a variety of ways and provides checks and balances for skin health. Prudence Skin and Coat combines Krill, fish and evening primrose oils for a synergistic approach to improving and maintaining overall skin and coat health by providing omega- 3 and omega-6 fatty acids and antioxidants. Krill oil is a concentrated source of EPA and DHA bound to phospholipids, which most likely contributes to its increased bioavailability when compared with other marine sources of omega-3 fatty acids. In addition, Krill contains astaxanthin, a very strong carotenoid that helps prevent sun damage and has immunomodulary effects. Krill is approximately 50 times more potent as an antioxidant than most other antioxidants measured *(12)*. Fish oil also contains omega-3 fatty acids and endogenous sources of lutein. Lutein is known to reside in the epidermis and dermis, having a potential effect on oxidative stress on the skin. Finally, evening primrose oil provides omega-6 fatty acids for skin cell membrane stability and GLA, which decreases inflammation.

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