

## **Nutrition and Skin and the Role Fatty Acids Play**

The skin is the largest organ in the dog's body and holds many important roles such as sensing touch, thermoregulation, providing protection from the external environment and potential harmful pathogens, as well as keeping everything important on the inside! Pet owners often notice poor skin or coat quality as a sign of underlying problems, and the causes can be numerous including: hormonal imbalances, microorganisms, physical or chemical agents, immune reactions, and poor nutrition. As a Board Certified Veterinary Nutritionist® considering dermatologic conditions, I usually approach the problem looking at the dog's nutrition to see if there are alterations or improvements that can be made on that front.

It is important to note when evaluating skin or coat problems, that a full physical examination and history should be performed, and a thorough dermatological examination should include cytology. It may also include dermatohistopathology, cultures, and examination with specialty tools such as a Woods lamp<sup>1,2</sup>. Cytology is often the most cost effective, least invasive, and helpful diagnostic tool available in clinic and includes skin scrapings of varying depths, trichograms (hair plucking), and tape preparations<sup>1</sup>. A detailed diet history including supplements, treats, and dental care is also of great importance as this information can identify potential problems, or direct treatment options.

Many dog foods and supplements exist today that suggest inclusion of specific ingredients or nutrients that benefit skin, but how do we know if these statements are accurate, or the products are effective? Looking at some recent publications I will attempt to highlight features to better help identify what may be beneficial (and what may better be left on the shelf).

Nutrients known to influence skin health include protein, essential fatty acids (particularly linoleic acid, LA; eicosapentaenoic acid, EPA; docosahexaenoic acid, DHA), zinc, copper, vitamin A, vitamin E, and B vitamins<sup>3,4</sup>. Dietary fats and fatty acids have long been considered important to dogs, since some polyunsaturated fatty acids (PUFAs) serve as precursors of prostaglandins and other eicosanoids, which help regulate cell function<sup>4,5</sup> (Figure 1). Dietary fat can improve palatability and can facilitate fat-soluble vitamin absorption<sup>4</sup>. Numerous research articles have evaluated the influence of different fatty acids' effects on skin and coat quality in either healthy dogs or dogs with diagnosed skin disease<sup>6-10</sup>. Two reviews on the influence of dietary fats<sup>11</sup> and fish oil use<sup>12</sup> offer nutritional insight on this topic, but what does the newer research reveal?

A recent publication by Combarros et al.,<sup>6</sup> examined the effects of an n-3 fatty acid supplement on red blood cell membranes, hair shafts, and skin surface in dogs with poor quality coats. This prospective, randomized, double blind, placebo-controlled study examined the effect of supplementation of an EPA+DHA capsule compared to a placebo capsule containing microcrystalline cellulose on 24 healthy adult dogs with poor skin and hair coat. The dogs had no underlying disease (e.g., no parasites, no fungal or bacterial skin infections). Subjects were given 1 capsule per 10 kg of the EPA-DHA (Agepi® ω3) containing 160 mg EPA, 100 mg DHA, and 4.5 mg vitamin E, once daily in the morning with food for ninety days. All dogs were fed by the same person, housed in the same indoor-outdoor environment, and were monitored for any adverse events of which no diarrhea or vomiting were reported by the owner. Clinical assessment

of the dogs, including dermatologic assessments, were conducted by the same investigator once every thirty days for six months. Whole blood, hair samples, and skin surface samples were collected at various time points throughout the study (protocol outlined in Table 1). Fatty acids in the erythrocyte membranes, fatty acids on hair fibers, and neutral lipids in skin surface samples were evaluated in both EPA-DHA and placebo-supplemented dogs.

The results of this study were interesting and offer potential options for treatment of otherwise healthy dogs experiencing poor skin and coat. Clinical scores in both groups of dogs were similar at baseline (day 0) and remained steady in the placebo group throughout the study. Conversely a statistically significant reduction of seborrheic scoring index (SSI) was noted in the treatment group at day 60 and day 90. Most notable was after withdrawal of the EPA-DHA supplement at day 90, the SSI remained stable for one month then gradually increased to baseline levels (Figure 2).

EPADHA treated dogs showed increasing EPADHA content of the erythrocyte membranes and then a gradual return to baseline after supplementation was stopped (Figure 3). Considering the average lifespan of red blood cells in dogs is ~120 days, and that supplementation of EPA-DHA was only for 90 days in the study, it would have been interesting to see what longer term supplementation showed. The study did not continue blood sampling post day 120, but both EPA+ DHA decreased once supplementation stopped.

Evaluation of total lipids and EPA+DHA content on hairs did not demonstrate significant findings; neither EPA nor DHA were detected on any hair samples. Evaluation of squalene, cholesterol, cholesterol esters and total neutral lipids from skin surface sampling revealed no significant differences between treatment and placebo groups, except squalene content was decreased on skin surface samples at day 90 compared to day 0, (Figure 4). Skin samples were only taken on day 0 and 90, so it is unclear if squalene would have increased to baseline following cessation of the supplement, or what the significance of the decrease in squalene might be.

Skin surface lipids result from the blending of sebaceous and epidermal lipids, which derive from the sebaceous gland secretion and the permeability barrier of the stratum corneum respectively<sup>13</sup>. Figure 5 presents a schematic of the various layers of the skin (brief refresher!) Sebum is an oily to waxy mixture of mainly triglycerides, wax esters, free fatty acids, and squalene as well as minor components of cholesterol and cholesterol esters. The epidermal lipid compartment localized in the stratum corneum contains ceramides, free fatty acids, cholesterol, and cholesterol sulfate<sup>14</sup>. The authors mentioned that it would have been valuable to measure ceramide contents as well as add more time points in the study but left that for future work. This paper provides evidence that the supplementation of an n-3 EPA+DHA capsule shows an effect in dogs, with results being noted upon supplementation and then returning to baseline when supplementation was withdrawn. It was useful to see this trial conducted over 3 months, since many studies are for shorter (6-10 week) periods.

Supplementary materials included information on the base diet, such as some ingredient details, a guaranteed analysis, and other essential nutrients (Table 2). It would have been ideal to report the concentrations of specific fatty acids in the diet, since only fat content on a whole was

reported. The benefit of knowing individual n-3 and n-6 fatty acid content is relevant to skin health. Multiple studies have demonstrated improved skin and coat quality with the addition of linoleic acid above what is found in a complete and balanced diet<sup>10</sup>, as well as supplementation with flaxseed oil and various marine sources of EPA-DHA<sup>8,9</sup>. Considering the pathways of the omega 3 and 6 fatty acids in Figure 1, it is important to note that various sources provide different essential fatty acids. Marine sources provide EPA and DHA - precursors to the beneficial eicosanoids and prostaglandins, while plant sources provide more of the shorter chain PUFAs. Dogs do not convert alpha-linolenic acid (ALA) into long-chain n-3 EPA and DHA to any great extent. Thus, many products that purport a high omega-3 diet for benefits of skin should clearly have marine sources since ALA will not provide the reported benefit; this was demonstrated in another recent publication<sup>7</sup>. In comparison to the Combarros study, Dominguez et al., studied supplementation of an astaxanthin krill oil versus flaxseed oil in 10 adult Alaskan Huskies. Their results showed that erythrocyte membrane EPA-DHA fatty acid composition increased with krill oil, and interestingly showed no EPA-DHA content with flaxseed oil supplementation<sup>7</sup>. Considering trends of consumers reaching for alternative oils, a potential future study could include sources of fatty acids such as walnut oil, extra virgin olive oil, or coconut oil. Having evidence to show that supplementation of certain fatty acids can help improve coat quality is essential, and Combarros et al. showed that EPA & DHA supplementation can improve skin and coat quality.

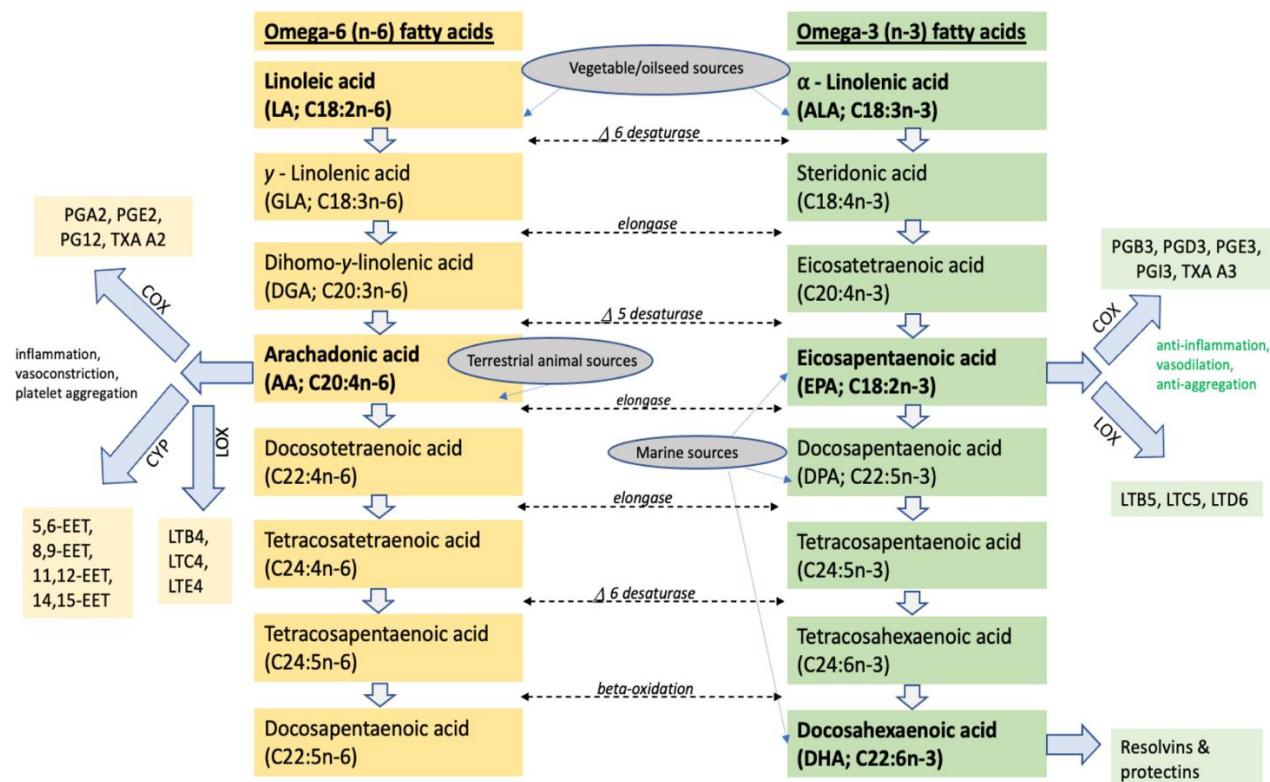
It is important to note that the reported doses of EPA and DHA in the study (160 mg EPA & 100 mg DHA per capsule), and current online product doses (110 mg EPA & 68 mg DHA per capsule) differ, as do the dosing recommendations (1 capsule/ 10 kg/ day in study; 1 capsule/ 20 kg/ day online). This brings to light the final point: when considering supplementation with an EPA-DHA product or food - it is important to evaluate each source, how they are obtained, what the calorie content is, how the product will be shipped and stored, and whether or not the animal will have 'fish breath', which can be offensive to some pet owners.

Fish oils can be high in vitamin D and may contain mercury or other potentially harmful inclusions. So, choosing a company that does regular testing to ensure safe products, and one that verifies inclusion levels of desired nutrients, will benefit the pet and owner significantly. For example, ConsumerLab.com is an independent website that evaluates a myriad of human and pet supplements for potentially harmful inclusions as well as verifies reported concentrations of nutrients. Access to the information at ConsumerLab.com does require paying an annual subscription fee, but that fee can be worth it to veterinary health care teams wanting to find the best products for their patients.

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**Figure 1:** Predominant pathways of omega-3 & -6 fatty acid metabolism in mammals demonstrating enzymes involved in each pathway and highlighting sources of specific fatty acids as well as pathways of eicosanoid production. Adapted from<sup>4,5</sup>. COX, cyclooxygenase; CYP, cytochrome P450; EET, epoxyeicosatrienoic acid; LOX, lipoxygenase; LT, leukotriene; PG, prostaglandin; TXA, thromboxane.

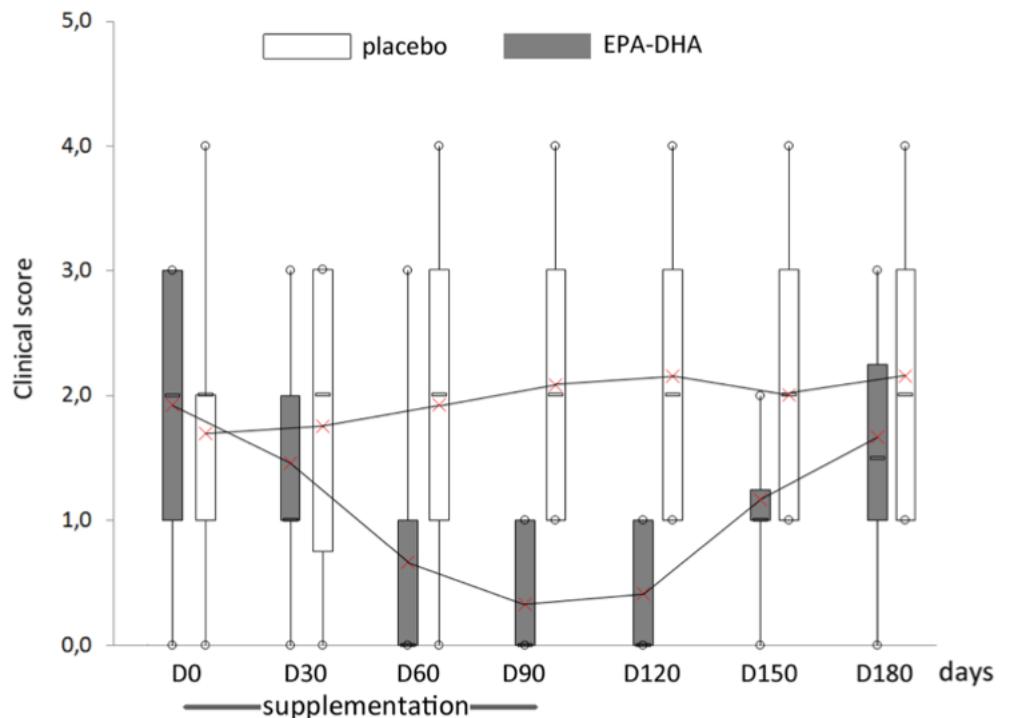


**Table 1:** Timeline of Combarros 2020 study protocol

|                     | D0  | D30 | D60 | D90 | D120 | D150 | D180 |
|---------------------|-----|-----|-----|-----|------|------|------|
| Supplementation     | Yes | Yes | Yes | Yes | No   | No   | No   |
| Clinical score      | X   | X   | X   | X   | X    | X    | X    |
| Blood sample        | X   | X   | X   | X   | X    |      |      |
| Hair sample         | X   | X   | X   | X   | X    | X    |      |
| Skin surface sample | X   |     |     | X   |      |      |      |

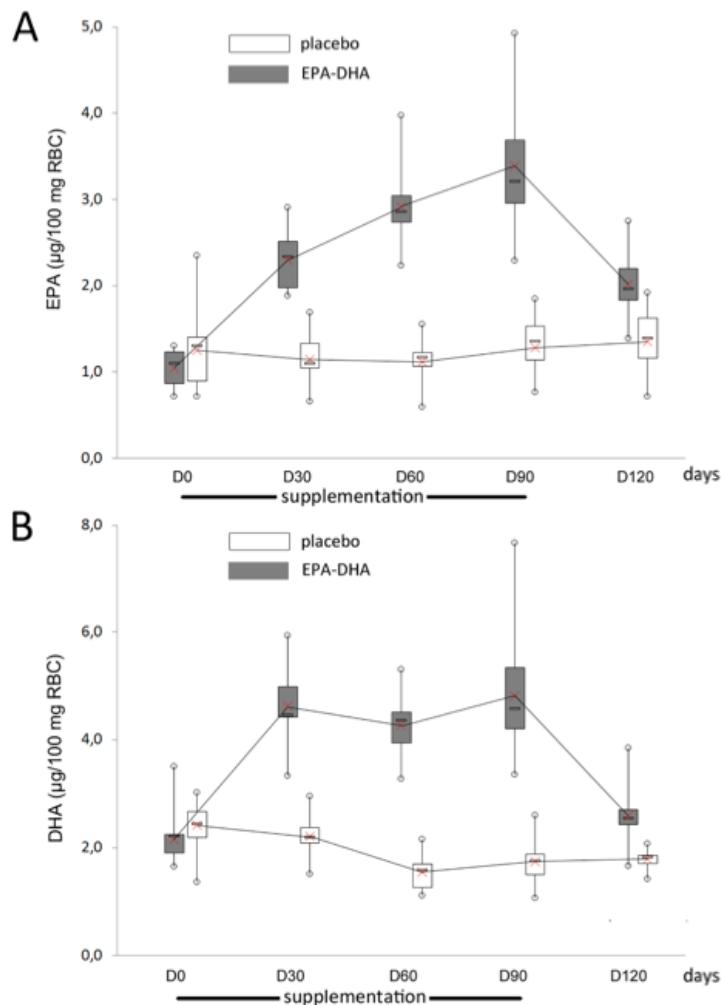
**Figure 2:** Kinetics of clinical scores (SSI) in dogs with poor coat condition that received either EPA-DHA (gray boxes) or placebo (white boxes) supplementation once daily for three consecutive months (from D0 to D90) at different time points during the study. Box and whiskers plot interpretation: Top of the box is the upper quartile, the line in the middle is the median, the bottom of the box is the lower quartile, and the upper and lower whiskers represent minimum and maximum scores. **X** represents the mean and the line connecting the dates represents the mean line.

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**Figure 3:** Kinetics of EPA (A) and DHA (B) levels on erythrocyte membranes in dogs with poor coat condition that received either EPA-DHA (gray boxes) or placebo (white boxes) supplementation once daily for three consecutive months (from D0 to D90) at different time points during the study. Box and whiskers plot interpretation: Top of box is the upper quartile, the line in the middle is the median, the bottom of the box is the lower quartile and the upper and lower whiskers represent minimum and maximum scores. **X** represents the mean and the line connecting the dates represents the mean line.

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**Figure 4:** Kinetics of squalene (A) and cholesterol (B) contents on skin surface in dogs with poor coat condition that received either EPA-DHA (gray boxes) or placebo (white boxes) supplementation once daily for three consecutive months (from D0 to D90) at different time points during the study. Box and whiskers plot interpretation: Top of box is the upper quartile and the upper and lower whiskers represent minimum and maximum scores. **X** represents the mean.

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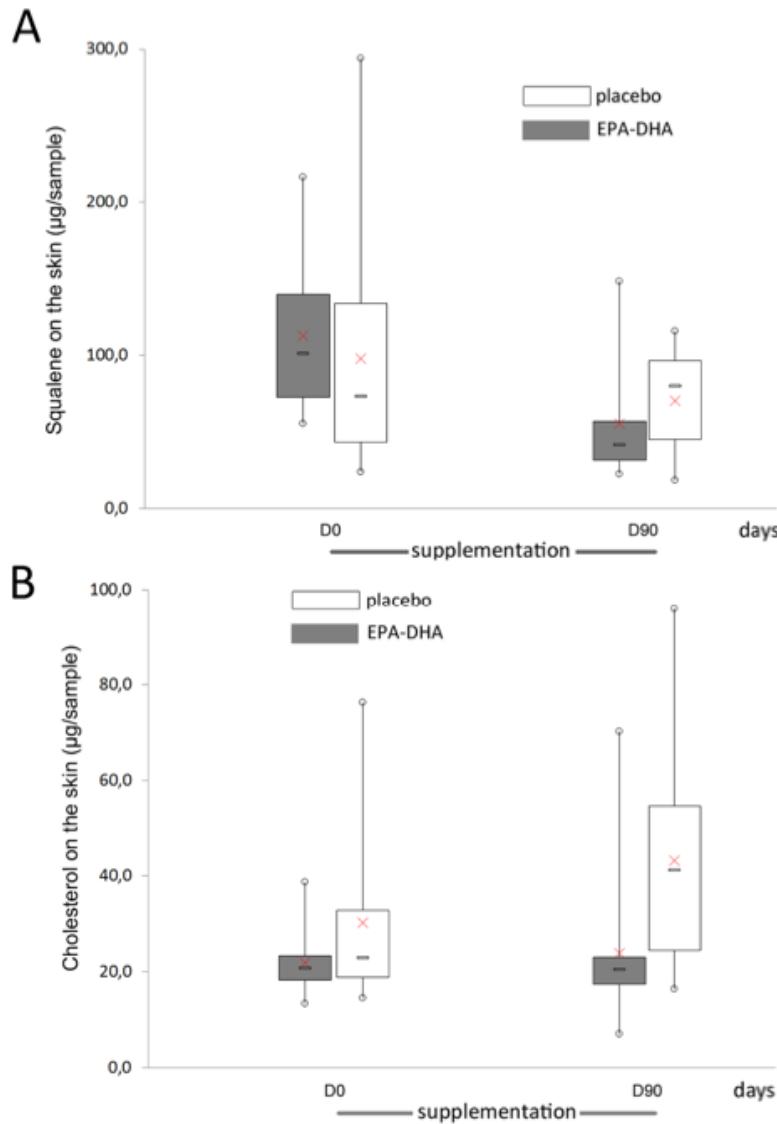


Figure 5: Structure of the skin and various layers of epidermis.

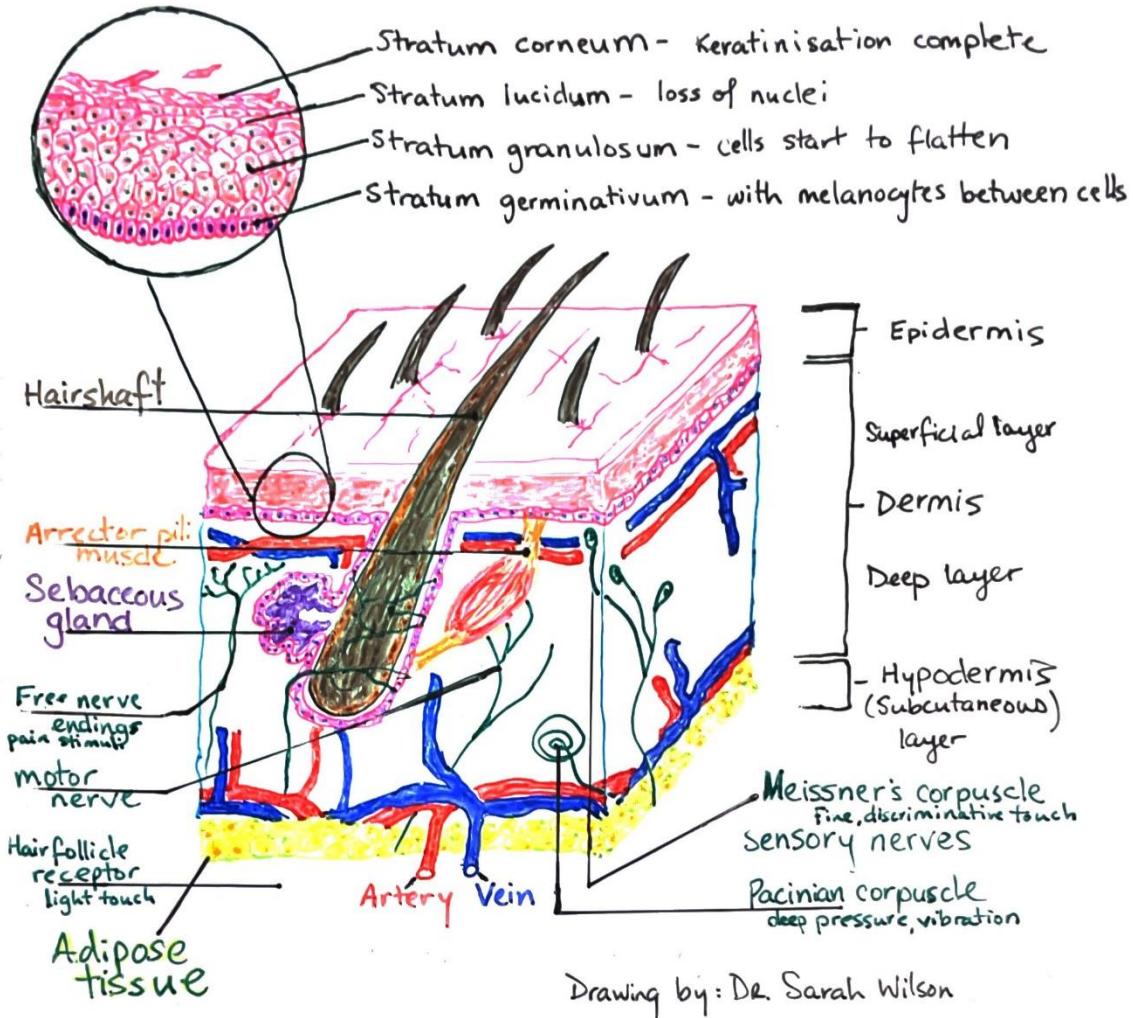


Table 2: Composition of baseline diet used in Combarros 2020 study (Pasqui Energi, agriPasquier, Les Cerqueux, France)

|                                |   |
|--------------------------------|---|
| <b>COMPOSITION</b>             | poultry dehydrated proteins (min 10%), cereals (rice min 8%), vegetables, derivative products of vegetable origin, oils and fats, yeast and mineral substances  |
| <b>ANALYTICAL CONSTITUANTS</b> | Proteins: 30%, fat content: 14%, crude ash: 10,5%, crude fibers: 2,5%, humidity: 10%, calcium: 2,4%, phosphore: 1,6%.   |
| <b>ADDITIVES</b>               | Vitamin A: 16000 UI/kg, Vitamin D3: 1200 UI/kg, Vitamin E: 85 mg/kg, E1 (iron): 105mg/kg, E5 (manganese): 45 mg/kg, E2 (iodine): 2 mg/kg, E4 (copper): 13 mg/kg, E6 (zinc): 75mg/kg, E8 (selenium): 0,2 mg/kg |