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Role of Omega-3 Fatty Acids in Canine Health: A Review

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A B S T R A C T

Fats are regarded as crucial component of a balanced diet in dog as they help to maintain healthy skin coat, cell structure and function, including vision and learning abilities in addition to enhance taste and palatability of food. Omega-3 fatty acids are polyunsaturated fatty acids which are considered as essential fatty acids in dogs because they cannot be synthesized in the body and hence must be provided in the diet. This paper reviews the potential benefits of omega-3 fatty acids in dogs with osteoarthritis, cardiovascular disorders and renal diseases, atopy, or other inflammatory conditions. In addition, the role of omega fatty acids on neurologic development, behavioral disorders, and reproductive health is summarized along with potential adverse effects like immune function impairment, platelet dysfunction, and altered glucose and lipid metabolism.

Introduction

Fats and oils are a fundamental part of a balanced diet for dogs. Fats are a concentrated source of energy providing more than double the measure of energy as carbohydrates and proteins do. Fats are comprised of building blocks called fatty acids. Fatty acids are named by their chemical structure and how they are bonded together. There are certain fatty acids that dogs require in their eating regimen in light of the fact that the body can't make them. These are known as essential fatty acids. These essential fatty acids are divided into two groups called the omega-3 and omega-6 fatty acids (Stice, 2019). Fatty acids in both these groups must be given in a specifically adjusted proportion in the daily diet.

Omega-3 FAs are polyunsaturated fatty acids (PUFAs) responsible for numerous cellular functions including the maintenance of the cell membrane structure, fluidity, signaling, and cell-to-cell interaction. They primarily include EPA (eicosapentaenoic acid, C20:5n-3), DHA (docosahexaenoic acid, C22:6n-3), and ALA (alpha-linolenic acid, C18:3n-3).

Both EPA and DHA are found in high concentrations in fish oils, whereas ALA is predominantly present in flaxseeds, canola (rapeseed) oil, soybeans, pumpkin seeds, perilla seed oil, walnuts, and their derivative oils. ALA requires the enzyme delta-6 and delta-5 desaturases to change over it into EPA and DHA in the body (Bauer, 2011; Fritsch *et al.,* 2010; Roush *et al.,* 2010; Adas *et al.,* 1999; Bibus *et al.,* 1993; Wang *et al.,* 2006). Canines have a constrained capacity to achieve this change (Bauer, 2011; Adas *et al.,* 1999; Bibus *et al.,* 1993; Duda *et al.,* 2009), hence giving preformed EPA and DHA is the most effective approach to raise tissue concentrations of these unsaturated fats.

Omega-6 fatty acids (also referred to as ω-6 fatty acids or *n*-6 fatty acids) are a family of polyunsaturated fatty acids which mainly include Linoleic acid (LA), Gamma linolenic acid (GLA), Arachidonic acid (AA) and Di homo-gamma-linolenic acids (DGLA). LA is chiefly present in corn, canola, safflower, sunflower oils, whole grain and body fat of poultry, while GLA is abundant in black current seed oil, borage oil and evening primrose oil. Moreover, AA is found in body fat of poultry, lean meat, egg yolks and some fish oils and DGLA is predominantly present in organ meats. Among all, linoleic acid is considered to be the most significant essential fatty acid for dogs.

Although most fats and oils are higher in omega-6 than omega-3 unsaturated fats, yet it is significant to contain a diet balanced in both. The ratio of omega-3 to omega-6 fatty acids and the total quantity of each in the diet is crucial in maintaining wellbeing. The National Research Council (NRC) prescribes a proportion of 2.6:1 to 26:1 omega-6 to omega-3 (NRC, 2006). The Association of American Feed Control Officials canine and feline nutrient profiles incorporate a maximum omega-6 to omega-3 ratio of 30:1 (AAFCO, 2016). For comparison, the prescribed intake for humans is 5:1 to 10:1 omega-6 to omega-3 (Institute of Medicine 2005).

All sources of EFAs are very unstable as they are prone to oxidation and destruction by heat, light, and oxygen. Fish oils (an excellent source of Omega 3 fatty acids) are the quickest to go rancid. Therefore, it becomes necessary to assure that dog is getting sufficient quantity of EFAs, which can be attained by incorporating an EFA supplement to the diet, using a guaranteed-fresh source packaged in an oxygen-free container.

Role of essential fatty acids

Fatty acids are considered as essential nutrients in the diet of dogs to ensure optimal health (NRC, 2006; AAFCO, 2016). Essential FAs are required by every mammal for various functions (Torrejon *et al.,* 2007; Calder, 2008; Adhoc Committee on Dog and Cat Nutrition, 2006; Kang and Weylandt, 2008; Zicker *et al.,* 2012) such as:

- Maintenance of structure and function of smooth muscle organs (i.e. heart, reproductive system).
- Protection and formation of liver cells.
- Maintenance of healthy skin structure, functions, coat and strong joint tissues.
- Precursors for eicosanoids such as prostaglandins and leukotrienes.
- Development of brain and immune system as well as eye (retinal) function in puppies and adult dogs by DHA.
- Maintenance of the cutaneous water barrier by Linoleic acid.
- Regulation of epidermal proliferation via prostaglandin E-2 by Arachidonic acid.

Insufficient quantities of EFAs in the body severely disrupt critical body functions. Deficiency of EFAs typically leads to development of chronic skin and coat disorders, digestive problems, cardiovascular

disease, degenerative eye disease, and allergies in dogs and cats. Therefore, EFAs should not be considered as supplemental measures of nutrition, but as crucial components of good health.

Omega 3 fatty acids and dog skin

Supplementation of dietary fatty acids in dogs and cats is most commonly recommended for pruritic skin diseases related with hypersensitivity reactions, such as flea allergic dermatitis, atopic dermatitis, food associated hypersensitivity and idiopathic pruritus, along with eosinophilic granuloma complex in cats. Dietary EFAs play an important role in the maintenance of water permeability barrier of the skin and normal cell functioning by providing fatty acid precursors of eicosanoids and other significant physiologic mediators (Watson, 1998). The role of linoleic acid (LA) in maintaining the epidermal permeability barrier and being the precursor of prostaglandins in dogs and cats has been shown in various studies (Whelan and Fritsche, 2013). The epidermal water barrier of skin is composed of ceramide in the cell membrane which is derived from the omega-6 fatty acid (LA). Skin cell cohesion is increased by these lipid components which provide an efficient water barrier to the epidermis. This is the reason that many cases of dry, dull hair coats and scaling, non pruritic skin disorders in dogs show positive effects after supplementation with dietary vegetable oil rich in this fatty acid. Omega-3 fatty acids (ALA) may also work as does LA due to known metabolic competition between these two fatty acid types (Bauer, 2008). Therefore, α-linolenic acid can be advantageous in dog skin wellbeing, because of its sparing effect on LA in skin ceramide lipid fractions with less water loss (Bauer, 2011). Supplementation of omega 3 fatty acids in the diet has been found to increase ceramide and fatty acid content of epidermal layer (Popa *et al.,* 2011). Inflammatory response can also be controlled by omega 3 and 6 FAs via the synthesis of less pro-inflammatory mediators from precursors. During traumatic skin conditions, ω-6 FAs (AA) are transformed into PGE-2 and leuckotrienes-4, while ω-3 FAs are changed into PGE-3 and leukotrienes-5, the less pro-inflammatory than their corresponding ω-6 fatty acid isomers. Neutrophil activation is hindered by these newly synthesized ω-3 based mediators resulting in reduction of any allergic or inflammatory condition (Bauer, 2008, 2011). Several clinical studies have reported the efficacy of fatty acids as adjunctive therapy for pruritic dermatoses (Padmanabhan *et al.,* 2017). Dogs on 180 mg EPA and 120 mg DHA supplemented diet from marine oil displayed considerable improvements in pruritus, alopecia, and coat character over time, showing evidence that high-dose marine oil is an efficient anti-inflammatory treatment of canine allergic skin disease and may provide a safe alternative to glucocorticoids for short-term symptom relief. (Logas and Kunkle, 1994). Along with dietary fatty acids, zinc plays an important part in maintaining healthy skin and hair coat (Watson, 1998). Zinc activates the Δ-6 desaturase enzyme required for conversion of LA to AA and takes part in both inflammatory and immune mechanisms. Addition of marine fish oil at a dosage of 66 mg/kg body weight daily for six weeks may be efficient during skin conditions (Watson, 1998). Linoleic acid is found in higher amount in vegetable oils, like sunflower oil, whereas arachidonic acid is present in greater quantities only in animal fats. Dogs with atopic dermatitis may get benefit from supplementation of one teaspoon (5 mL) of a mixture of vegetable oil and animal fat or fish oil per cup (225 g) of food (Scott *et al.,* 1995). Moreover, the illness may impair the conversion of linoleic acid to the longer-chain (ω-6) fatty acids and their

derivatives, so fatty acid supplemented diet may be advantageous in that condition (Harvey, 1993).

Omega 3 fatty acids and Canine Skeletal Health

Osteoarthritis has been estimated to influence up to 20% of dogs > 1 year of age (Johnston, 1997). Dogs of all breeds and ages are affected by the disease. Regular ways to deal with the disease include attempts at prevention, slowing progression, and managing the clinical signs related with OA which can be achieved with balanced diet, body-weight control, exercise, physical therapy, and anti-inflammatory and analgesic medications (Roush *et al.,* 2010; Henrotin *et al.,* 2005). Although non steroidal anti-inflammatory drugs (NSAIDs) are considered as efficient modes of treatment, but have potential negative systemic side effects like gastrointestinal ulceration, liver and kidney damage, and accelerated cartilage degeneration (Henrotin *et al.,* 2005; Hauser *et al.,* 2010). Hence, it becomes urgently important to look for safe options to manage OA. Previous studies in dogs have found the effectiveness of the marine n-3 fatty acids in OA (Roush *et al.,* 2010b; Henrotin *et al.,* 2005; Bauer, 2011; Fritsch *et al.,* 2010b). Studies (Roush *et al.,* 2010a,b; Henrotin *et al.,* 2005; Hauser *et al.,* 2010; Bauer, 2011; Fritsch *et al.,* 2010a,b) have showed that omega-3 fatty acids have helpful impacts in the treatment of rheumatoid arthritis. In addition, the concentration of omega-3 fatty acids in tissues and cell membranes rise by dietary supplementation with omega-3 fatty acids, bringing about a relative decline in omega-6 fatty acid concentration, especially that of arachidonic acid. Additionally, studies (Roush *et al.,* 2010a) have revealed that dietary supplementation with fish oil omega-3 fatty acids increases blood concentrations of these unsaturated fats. Furthermore, owners have reported significant improvements in the clinical signs of osteoarthritis, like walking ability after 12 and 24 weeks on supplementation of diet with approximately 0.11% omega-3 fatty acids and 2.78% omega-6 fatty acids (very high ω-6:ω-3, control diet) or 3.47% omega-3 fatty acids and 2.46% omega-6 fatty acids (low ω-6:ω-3, test food) (Roush *et al.,* 2010a). Furthermore, ingestion of fish oil omega-3 fatty acids improves clinical signs in dogs with osteoarthritis (Roush *et al.,* 2010b). Supplementation of fish oil in the diet containing 1.75 g EPA/kg and 2.2 g DHA/kg diet (ω-6:ω-3 ratio of 3.4:1) does not promote lymphocyte proliferation in dogs (LeBlanc *et al.,* 2007). Moreover, high omega-3 fatty acid revealed better locomotor ability and performance of daily living activities in dogs when the effects of diets containing either 1.47% omega-3 and 1.86% omega-6 fatty acids (ω-6:ω-3 ratio of 1.3) or 0.18% omega-3 and 2.43% omega-6 fatty acids (ω-6:ω-3 ratio of 13.6) were compared. These impacts might be inferable from the partial replacement of arachidonic acid in cell membranes by EPA and DHA which leads to reduced availability of ARA for conversion in to leukotrienes and prostaglandins (Hall *et al.,* 2006; Hansen *et al.,* 2008; LeBlanc *et al.,* 2008). EPA and DHA produce lesser inflammatory molecules (e.g., prostaglandinE3, leukotrieneB5) with a resultant competitive hindrance of ARA metabolism (Wang *et al.,* 2006). This results in a decrease in anti-inflammatory environment systemically and within the joint.

Omega -3 FA in relation to canine cardiovascular system disorders

Cardiac diseases affect approximately 11% of dog and 20% of feline populations (Hundal, 2020). Nowadays, heart failure is the main cause of death in domestic carnivores (Sagols *et al.,* 2011). Nutrition can be optimally used

as a medicine for the treatment of cardiac diseases in dogs and cats. Omega -3 FA has many beneficial effects in cardiac diseases as shown in many experiments. Production of TNF and IL-1 are directly reduced by omega-3 FA and its supplementation has been shown to reduce the muscle loss in dogs with CHF (Freeman, 2010). Supplementation of omega-3 FA decrease the production of inflammatory mediators leading to decrease in platelet aggregation and inflammation and increase in vasodilation (Biagi *et al.,* 2004) , reduce arrhythmogenesis, reduce plasma triacylglycerols and VLDL leading to inhibition of atherosclerosis. In an experiment conducted by Freeman *et al.,* (1998), supplementation of omega -3 FA showed significant decrease in cachexia score, circulatory TNF, IL-1 and PGE. Supplementation leads to decrease in ventricular premature complexes in dogs with arrhythmogenic ventricular cardiomyopathy (Smith *et al.,* 2007). Concentration of EPA and DHA largely decreases in dogs with heart failure when compared to healthy dogs (Freeman *et al.,* 2006). Omega-3 FA also have positive effects on endothelial function, heart rate, myocardial energy metabolism, immune function and heart rate.

Omega-3 FA (EPA+DHA) can be provided as a dietary supplement and the dose of omega-3 FAs currently recommended for dogs and cats with heart failure is 40 mg/kg EPA + 25 mg/kg DHA per day (Freeman., 2010). Supplements are needed to achieve this dose as there are small numbers of commercial pet foods that contain this dose. Most appropriate supplement is fish oil as it is high in omega-3 FA and can be supplemented in either liquid or capsule form. Linseed or flaxseed oil are avoided as dogs and cats are unable to use it due to inefficient conversion. Diet should contain about 80 to 150 mg/100 Kcal of omega-3 FA and ratio of EPA:DHA of approximately 1.5:1 (Freeman, 2010).

Omega-3 FA and brain development

From the last 20 years, there is an increased evidence of the essentiality of n-3 fatty acids in brain development (Heinemann *et al.,* 2005). Diets deficient in omega-3 FA are not optimal for early neural development (Pawlosky *et al.,* 1997). These FA are required for brain development as well as its function. Deficiency can lead to the development of functional abnormalities of neural system. Electroretinogram recorded retinal activity and trainability in puppies improved by feeding bitches food supplemented with n-3 FA during gestation and lactation (Zicker *et al.,* 2012). Omega-3 FA act as neuroprotectors and in animals with epilepsy, they can increase the threshold of seizures (Schlanger *et al.,* 2002). In animals with epilepsy they function by new interneurons formation and increasing transmission through GABAergic receptors (Scorza *et al.,* 2009). Diet enriched with n-3 FA alleviates convulsive symptoms in epileptic dogs (Schlanger *et al.,* 2002). Supplementation of n-3 FA in dogs with drug-resistant epilepsy leads to the reduction of about 85% seizures (Scorza *et al.,* 2009). These also improve memory and cognitive function. Dosage of EPA and DHA recommended by NRC (2006) for neurologic diseases are: 130 mg EPA + DHA per 1,000 kcal of metabolizable energy for pregnant bitch and growing puppy after weaning, whereas 25 mg EPA+ DHA per 1,000 kcal of metabolizable energy for pregnant queen and growing kitten after weaning.

Behavior problems are common in the domestic dog (*Canis familiaris*) population (Voith *et al.,* 1992; Wells *et al.,* 2000; Bradshaw *et al.,* 2002; Kobelt *et al.,* 2003; Hiby *et al.,* 2004). A usual behavioural problem in dogs is aggression, leading to bite injuries reaching great numbers (Mikkelsen and Lund, 2000; Berg *et al.,* 2005). Lipid

metabolism is shown to play an essential role in canine aggression which has been shown by hypocholesterolemia in aggressive dogs (Sentürk and Yalçin, 2003). A significantly lower quantity of docosahexanoic acid (22:6 n-3) concentration and a prominently higher omega-6/omega-3 ratio has been reported in German Shepherds dogs with aggressive behaviour in contrast to non-aggressive ones (Re *et al.,* 2008). Serotonergic function in the central nervous system is greatly affected by omega-3 fatty acid status in the rat (DeMar *et al.,* 2006) and in humans (Hallahan and Garland, 2004). Higher docosahexanoic acid levels increase the concentrations of cerebrospinal fluid 5-hydroxyindole-acetic-acid, which is the main breakdown product of serotonin metabolism (Hibbeln *et al.,* 1997). In addition, decreased serotonin content has been reported with omega-3 fatty acid deficient diet in rat (Olsson *et al.,* 1998). Therefore, serotonergic dysfunction may be regarded as one mechanism relating low omega-3 fatty acids and aggressiveness. A combination of omega-3 fatty acids, magnesium and zinc has been reported to improve some of the behavioral disorders in dogs with common behavior problems (Niyyat *et al.,* 2018).

Omega 3 FA and reproductive health

Nowadays, the reproductive failure in the canine species is one of the principle concern of breeders and practitioners, who look for specific treatments to deal with it. As indicated by the literature, poor sperm concentration and/or function are considered as the major constraining factors of breeding programs. Along these lines, several investigators examined various protocols to improve semen quality, in both human and veterinary medicine, supplementing a certain daily intake of micronutrients (Surai *et al.,* 2000; Rooke *et al.,* 2001; Wathes *et al.,* 2007; Safarinejad *et al.,* 2012). Little data is accessible for dogs (Domosławska *et al.,* 2015; Kirchhoff *et al.,* 2017). Several human and animal clinical research studies recommend that, fish-derived n-3 polyunsaturated unsaturated fats (PUFA) can have a beneficial effect on sperm motility and fertility (Surai *et al.,* 2000; Rooke *et al.,* 2001; Wathes *et al.,* 2007; Safarinejad *et al.,* 2012; Mitre *et al.,* 2004). In addition, few authors recommended that the n-6:n-3 ratio of spermatozoa is altered by supplementation of n-3 PUFA enriched diet, further improving sperm motility (Mitre *et al.,* 2004). Diet enriched with n-3 PUFA may enhance sperm functions, by altering membrane properties, along with reducing spermatozoa lipidic peroxidation (Liu *et al.,* 2016). Other studies demonstrated that spermatozoa fatty acid (FA) profile gets modified by n-3 PUFA diet (Mitre *et al.,* 2004; Castellano *et al.,* 2010), which promote the susceptibility of membrane PUFA to lipid peroxidation (Marin-Guzman *et al.,* 1997; Cerolini *et al.,* 2000), therefore alters membrane integrity and function, which improves sperm motility and fertility (Cerolini *et al.,* 2000; Yeste *et al.,* 2011).

Omega-3 FA and Renal health

Renal diseases especially renal failure is not uncommon in dogs and important medical management is dietary modification. There is reduction in renal function with low plasma PUFA level and higher plasma n-3 FA reduces the risk of developing renal insufficiency (Brown *et al.,* 1998). Omega-3 FA has been found to slow the progression of kidney disease in dogs and reduce glomerular capillary hypertension (Asif, 2015). These reduce kidney inflammation due to its anti-inflammatory effect and improve blood flow to the kidneys. Progressive canine nephropathies reduced with dietary n-3 FA supplementation and maintain the GFR (glomerular filtration rate) and thereby

preserve renal structure (Brown *et al.*, 1998). Rise in creatinine level become slowly on n-3 FA supplementation and thereby improve serum albumin levels, proteinuria and lead to reduction in cholesterol and triglyceride levels in serum. Dietary n-3 FA supplementation in renal insufficiency dogs lead to significant reduction in BUN and triglycerides (Brown *et al.*, 1998). A study conducted by Valle *et al.*, (2015) showed significant increase in GFR and decrease in creatinine level after supplementation of renal feed with omega-3 and antioxidants. These also prevent the progression of chronic renal failure (CRF) due to its action on the abnormalities (lipid and immune) that are secondary to CRF. Dosage of EPA and DHA recommended as adjunctive dietary treatment for kidney diseases is 140 ($mg/kg^{0.75}$) and approximate dose for 10 kg dog is 790mg (Bauer, 2011).

Potential adverse effects of omega-3 fatty acids in Dogs

Excess doses of omega-3 fatty acids may be related with immune function impairment, platelet dysfunction, and altered glucose and lipid metabolism, based on the review of literature (Hall, 1996; Nabavi *et al.*, 2015). Vitamin E can be added or supplemented in diets enriched with omega fatty acids to prevent or reduce lipid peroxidation and to avoid vitamin E deficiency. Furthermore, there are chances of omega fatty acid-drug interactions. Simultaneous administration of the NSAIDs caprofen or the antiplatelet medication clopidogrel and omega-3 fatty acids may have a negative effect on hemostasis (Lenox and Bauer, 2013). Consideration of individual animal is important prior to omega-3 fatty acid treatment because animals with less platelet counts may not be fit for supplementation. All animals fed diet rich in omega-3 fatty acids must be observed for possible harmful effects.

In conclusions, omega-3 fatty acids have many beneficial effects on the overall health of canines. They play an important role in animals with osteoarthritis, atopy, or other inflammatory conditions. They are advantageous for neurologic development and can improve skin and coat. In dogs, diet enriched with fish oil help to maintain renal function by increasing the efficacy of renal feed in CKD dogs, as well as prevent cardiovascular disorders. Supplementation of EPA and DHA @ 30 $mg/kg^{0.75}$ BW is recommended in the diet of healthy dogs. Nevertheless, more research is needed to firmly establish the amount of and the type of omega fatty acids, as well as the ω-6:ω-3 fatty acid ratio required for the treatment of various diseases in dogs. Once these studies become available, refinements in the current recommendations or the establishment of recommended doses for clinical veterinary applications can be implemented.

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