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Vitamin E: more than nature's most powerful antioxidant

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Summary

Vitamin E is not synthesized by poultry and pigs and is therefore an essential micronutrient to consider in feed formulation. Being the nature's most effective lipid-soluble, chain-breaking antioxidant, it protects cellular membranes from being attacked by lipid peroxyl radicals. This unique function of vitamin E cannot be fulfilled by any other dietary substance with antioxidant-like properties. In addition to being an efficacious membrane antioxidant, vitamin E has a much broader physiological importance, ranging from maintaining tissue's structural integrity to supporting neural growth and reproduction as well as modulating immunity.

Vitamin E also plays an important role in enhancing meat quality as well as the nutritional value and the organoleptic properties of meat and eggs. This is primarily due to the absorption of vitamin E after ingestion, since its accumulation in foods of animal origin improves product quality and storage stability.

Introduction

Vitamin E is the generic term of eight naturally occurring tocopherols and tocotrienol derivatives, i.e., a-, b-, g- and d-tocopherol and -tocotrienol, respectively. Among these eight isomer forms, a-tocopherol exert the highest vitamin E activity (Fig.1). Because of the presence of the a-tocopherol transfer protein (TTP) that preferentially binds to a-T, a-tocopherol, but not b, g and d-tocopherol, is maintained in plasma and tissues. Most of the ingested b, g and d-tocopherol is secreted into the bile and excreted in the feces.

Vitamin E is an essential vitamin and, since it cannot be synthesized by humans and animals, it must be obtained via the diet. In nature, vitamin E is present in the lipid fraction of feed ingredients, especially in vegetable oils, where g-tocopherol contributes with a much higher proportion of vitamin E than a-tocopherol. However, due to its bioavailability, the most frequently used commercial form of vitamin E for animal feed supplementation is a-tocopherol in the form of *all-rac*-a-tocopheryl acetate, containing equimolar amounts of all 8 possible isomers (4 possessing the 2R and another 4 possessing the 2S configuration) (Fig.2). Esterification (acetate) is required for protecting the sensitive active a-tocopherol moiety against oxidation in the feed. After the enzymatic hydrolysis of vitamin E in the ileum, the vitamin E alcohol is absorbed in the gut.

Oxidative stress and antioxidant system

a-Tocopherol functions as a free radical quencher in biological cells (*Machlin 1984*); its localization within the unsaturated fatty acid esters in the phospholipid bilayer of cell membranes provides a means of controlling lipid oxidation at a likely initiation site (*Hafeman and Hoekstra 1977*).

a-Tocopherol from animal diets is probably preferentially incorporated into the plasma membranes of mitochondria and microsomes (*Arnold et al. 1993*). As part of the normal metabolism and energy production, reactive oxygen species (ROS) are formed and it has been estimated that as much as 1–2% of all oxygen consumed may result in the formation of ROS, with the clear majority of ROS being generated in the mitochondria (*Gille and Sigler 1995; Ischiropoulos and Beckman 2003*). The localization of a-tocopherol within the phospholipid bilayer of cell membranes provides a means of controlling lipid oxidation at the initiation site (*Fukuzawa et al., 1994*).An imbalance between prooxidants and antioxidants in favor of the former leads to oxidative stress or damage to biomolecules like proteins, lipids and DNA (*Sies, 1991; Halliwell & Gutteridge 2007*). However, current and short-term oxidative stress may be expected during infectious diseases, in which immune cells generate ROS to eliminate and kill pathogenic bacteria. Hence, the generation of free radicals are part of normal physiology and immune reactions, whereas uncontrolled and chronic production causes local damage (*Beckman and Ames, 1998*). Therefore, during evolution, living organisms have developed specific antioxidant protective mechanisms to deal with ROS and RNS and enabling them to survive in an oxygen-rich environment (Surai, 2002).

The antioxidant system or network in living organisms can be divided in two main groups of compounds: enzymatic and non-enzymatic antioxidants. Enzymatic antioxidants like Superoxide dismutase (SOD), Glutathione peroxidase (GPx) and Catalase (CAT) act primarily as front-line defense to block the formation of free radicals, and especially in the water-soluble cell compartment. Non-enzymatic antioxidants like vitamin E, Vitamin C and glutathione act on formed free-radicals, and the water-soluble vitamin C is capable to regenerate the vitamin E by donating a hydrogen atom to the vitamin E radical once vitamin has been used. Thus, the interplay between these antioxidants and the specific synergy between the vitamins, is very important for the protection of cellular membranes.

It has been very well documented (*Forman et al., 2013*) that because of chemical kinetic constraints, mostly linked to concentration at the site of action and the speed of reactions, antioxidants are a system made of distinct substances with different mode of actions. Every antioxidant has its unique (bio)-chemical profile which is reflected in different sites of action and different biological activities.

Vitamin E Metabolism

Being a fat-soluble vitamin, vitamin E follows the digestion and absorption of other lipids. In general, vitamin E metabolism is well documented. Active absorption in the gut depends on several factors but on average achieves 42% expressed as a-tocopherol equivalents (*Villaverde et al., 2004; Barroeta, 2007*). Vitamin E is packaged into lipid-bile micelles and is transported via the lymphatic pathway to the liver, where it is transiently stored. A specific transport-protein (a-tocopherol transfer protein) moves a-tocopherol from the liver into the blood circulation and attaches it to lipoproteins for the transport to the various organs and cells (*Hosomi et al., 1998*).

Vitamin E is the most powerful antioxidant of lipid membranes

Vitamin E is deposited, in a dose-dependent way, in cellular and subcellular membranes (mitochondria, microsomes), which are rich in fatty acids, and thus becomes an integral part of these structural elements, (Fig.3) beneficially influencing the fluidity, the structural integrity and the functionality of biological membranes in all cells of the organism (*Lauridsen and Jensen, 2012*).

As mentioned above, a-tocopherol is well recognized and accepted as the nature's most effective lipid-soluble, chain-breaking antioxidant, protecting cellular membranes from being attacked by lipid peroxyl radicals. Vitamin E prevents the propagation of lipid peroxyl radicals in cellular membranes. Lipid peroxyl radicals react 1,000 times faster with vitamin E than with polyunsaturated fatty acids (*Buettner, 1993*).

The physiological importance of vitamin E goes beyond being a powerful antioxidant. It is required for normal growth and reproduction; it helps maintain the structural integrity of all tissues, it supports the development of the nervous system and substantially contributes to optimum health and disease resistance of farm animals due to its modulating effects on the immune system. Deficiency of vitamin E in pigs and poultry results in severe diseases such as the Mulberry heart disease and muscular dystrophy ("white muscle disease") in pigs, and encephalomalacia (known as "crazy chicken syndrome") and exudative diathesis (chicken) (Fig.4). Sub-clinical vitamin E deficiency is hardly detectable but can result in retarded growth, impaired feed conversion, diminished fertility, higher susceptibility to infectious diseases, reduced stress resistance and impaired welfare of farm animals. In addition to the above, animal physiological requirement, vitamin E plays an important role for the nutritional value, and the product quality, e.g. organoleptic properties of meat and eggs.

The minimum vitamin E requirements, those required primarily for avoiding deficiency symptoms, are set by NRC (*National Research Council, 2012*) in the range of 10 mg/kg feed and 45 mg/kg feed respectively for swine for fattening and breeders and around 10 mg/kg feed for broilers (*National Research Council, 1994*).

However, more recent nutritional specifications of poultry genetic companies suggest a much higher supplementation for broilers in the range of 80, 50-65 and 50-55 mg/kg feed respectively for starter, grower and finisher (*Aviagen, 2014; Cobb, 2015*[LG1] *; Hubbard, 2014*).

National Swine Nutrition Guide (2010) recommends 60 mg/kg feed for piglets and around 40 for fatteners.

DSM Optimum Vitamin Nutrition (2016) for example, recommends 100-150 mg/kg feed for piglets and 60 to 100 mg/kg feed for fatteners whereas for broilers supplementation level is set at 100 to 250 mg/kg feed in the starter feed and 50 to 100 mg/kg feed for grower and finisher phases.

For both species, highest levels are suggested for taking advantage of the impact of vitamin E at supra-nutritional levels on immune modulation in early phases (*Tengerdy and Nockels, 1975*; *Franchini et al., 1986*; *Leshchinsky and Klasing, 2003*; *Lauridsen and Jensen, 2005*; *Lauridsen, 2002*) and on meat quality attributes in later stages (*Grau et al., 2000*; *Koreleski et al., 2006*; *Hoppe et al., 1993; Morrissey et al., 1996*; *Sales J. and Koukolová V., 2011)*

Moreover, Vitamin E requirements may increase under conditions of heat stress as it has been demonstrated in layers (*Bollengier-Lee et al., 1998 and 199*9) and broilers (*Maini et al., 2007*).

Conclusion: higher levels of vitamin E have multiple benefits

It looks reasonable to conclude that vitamin E functionalities are peculiar and its supplementation in feed is recommended at levels higher than minimum requirements (*NRC, 2012/swine; NRC, 1994/poultry*) for benefiting of its multiple functionalities according to specific needs. Based on the existing knowledge we would like to remind that the network of antioxidants in the body does not call for replacement of one antioxidant with another but supply all the required elements for the antioxidant system to ensure an efficient protection of the body towards oxidative stress.

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