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REVIEW

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# Antioxidant a Feed Additive: Unravelling the Impact of Antioxidants Supplementation on Productivity and Wellness in Animals

S. Gurusaran*[1] | P. Lokesh[2] | M. Naresh[2] | M. Hariharan[3] | A. Varun[3]

[1]Department of Animal Nutrition, Madras Veterinary College, Tamil Nadu Veterinary and Animal Science University, Chennai, Tamil Nadu, India.
[2]Rajiv Gandhi Institute of Veterinary Education and Research, Kurumbapet, Puducherry, India.
[3]Department of Livestock Production and Management, Rajiv Gandhi Institute of Veterinary Education and Research, Kurumbapet, Puducherry, India.

**Correspondence**

S. Gurusaran, Madras Veterinary College, Tamil Nadu Veterinary and Animal Science University, Chennai, Tamil Nadu, India.

Email: gurusaransivalingam00@gmail.com

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The authors declare that the manuscript was formulated in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

**Authors Contribution**

All authors listed have made a substantial, direct, and intellectual contribution to the work, and approved it for publication.

## Abstract

The global effects of climate change are among the most significant and pressing concerns for the coming decades. The demand for animal products has been expanding as a result of the rapid increase in the global population, rising income levels, and shifting lifestyles. Due to these conditions, there is a rise in the diversity of animal production. While the livestock sector is managing these difficulties, it has also significantly increased the dangers associated with climate change. Multiple etiological factors are involved in oxidative stress, including high humidity, sun radiation, wind speed, and ambient temperature. Oxidative stress compromises animal health and productivity, exhibits numerous chronic inflammatory and cardiovascular disorders, and also possesses carcinogenic properties. Components of animal feed include proteins, lipids, and other organic substances that, on exposure to free radicals, become rancid, lose their nutritional value, and produce toxic substances that damage animal health. Antioxidants are capable of neutralizing the oxidants from metabolism and alleviating the oxidative damage that can be obtained from nutrition, while others are created as byproducts of bodily metabolism. They are broadly classified as natural and synthetic antioxidants. The popular antioxidants used in animal feed are ascorbic acid, alpha-tocopherol, trace minerals (copper, zinc, selenium, etc.), and various plant-derived compounds such as flavonoids and carotenoids. This article focuses on understanding the effects of antioxidants and oxidative stress, including their types and impacts on the various systems of the body.

## KEYWORDS

Antioxidants, free radicals, natural antioxidants, synthetic antioxidants, animal wellness and production

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## INTRODUCTION

The oxidative phosphorylation in the inner mitochondrial membrane generates adenosine triphosphate (ATP), a primary energy source for animals. As a part of this process, a substance is generated, termed a free radical. Reactive oxygen species (ROS) and reactive nitrite species (RNS) are generated as byproducts (Ponnambalam et. al., 2022). The outer shell of the oxidants is unpaired, thereby rendering them more erratic, highly reactive, and transient in nature. In the immune system, ROS play a crucial role in destroying pathogens by targeting vital components of the organism; at a higher level, they deprive the cellular metabolism by creating an unbalanced relationship between oxidants and the antioxidant defense system, which results in oxidative stress (Celi P et. al., 2015). During oxidative stress, the major cellular components like carbohydrates, lipids, nucleic acids, and proteins undergo oxidation, thus altering their physiological function. The cellular membrane is the primary site of target, thus altering the cellular properties (Celi P et. al., 2015). The oxidative stress in animals is linked with multiple factors, including production load, disease status, and environmental factors (diet and ambient temperature) (Ponnambalam et. al., 2022). The extent of the oxidative stress is significantly dependent on the animal's nutritional condition. The body combats free radicals with various endogenous and exogenous elements.

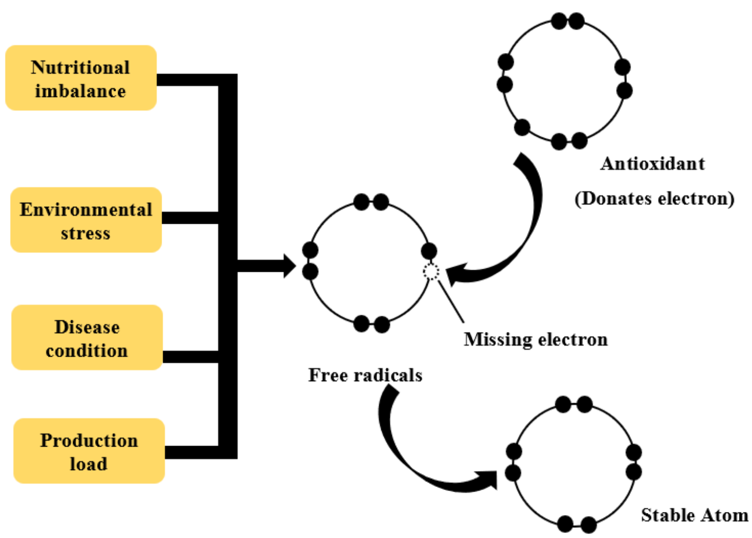


**Figure 1: Diagrammatic representation of Etiological factors for free radical production and antioxidant neutralization (Celi P et. al., 2015)**

## TYPES OF ANTIOXIDANTS

### Natural Antioxidants

Natural sources of antioxidants are fruits, vegetables, herbs, and spices. The natural antioxidant system is clustered into two main groups: endogenous and exogenous. Non-enzymatic antioxidants, known as direct-acting antioxidants, including ascorbic, lipoic, carotenoids, and polyphenols, are said to be obtained through the diet and are crucial to the body's defense against free radicals. The cell itself produces only a small portion of these chemicals. Chelation substances are said to be indirectly acting antioxidants, which bind to redox metals to prevent the generation of oxidants (Celi P et al., 2015).

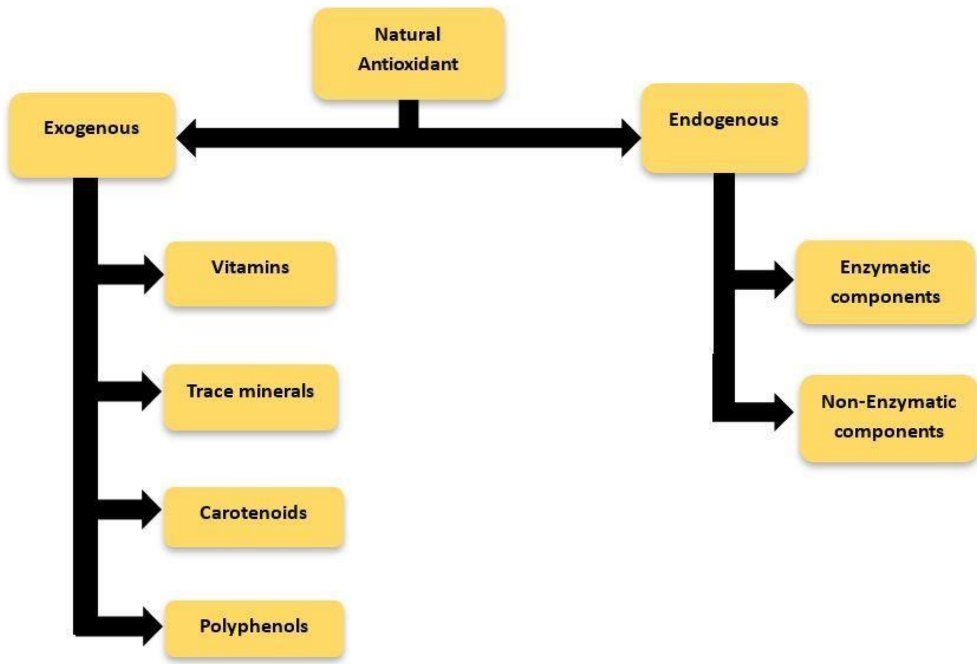


**Figure 2. Classification of natural antioxidant (Rasheed A & Fathima Abdul Azeez R et.al., 2019)**

## Tocopherol

Tocopherol and tocotrienol derivatives, collectively known as vitamin E, are rich in plant food sources such as sunflower seeds, olive oil, almonds, etc. (Ponnambalam et al., 2022). Alpha-tocopherol is crucial in prevention of lipid oxidation, further prevents the free radical formation.

Vitamin C (ascorbic acid and ascorbate)

Naturally, most fruits and vegetables contain vitamin C. Citrus fruits are abundant in vitamin C. Among the common fruits and vegetables, including cruciferous vegetables, peas, pepper corns, berries, tubers, and mustards are considerably rich in ascorbic acid content (L. Hallberg et al., 1982).

## Trace minerals

Copper, iron, zinc, selenium, manganese, molybdenum, cobalt, and chromium are the trace elements with antioxidant activity. Since selenium is a cofactor for various antioxidant enzymes, including glutathione peroxidase (GPx), thioredoxin reductase (TrxR), and iodothyronine deiodinases (IDD), selenium plays a vital role in countering the pro-oxidants (Gulcin et al., 2020). Copper, zinc, and manganese are cofactors for the superoxide dismutase enzyme. However, iron in increased concentrations catalyzes the generation of free radicals (Celi P. et. al., 2015).

### Carotenoids

Carotenoids are naturally existing lipid soluble colorants; among them, the most vital one is beta-carotene, which is abundant in dark green leafy vegetables and orange-colored fruits (Celi P et. al., 2015). Others like zeaxanthin, lycopene, beta-cryptoxanthin, and lutein are rich in citrus fruits, berries, and tubers.

### Polyphenols

Flavonoids have the ability to scavenge oxidants and chelate them, whereas the phenolic acids exhibit their antioxidant activity by trapping oxidants (Nele Gheldof et al., 2002). Most of the polyphenols are obtained from the pant and falls into the four categories: diterpenes, flavonoids, phenolic acids, and volatile oils.

### Enzymatic Antioxidants

Superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione reductase, and heme peroxidase are the vital enzymes that assist in combating oxidants. These enzymes either reduce the potential of the oxidants or donate the electrons to make them stable. SOD, GPx, and CAT are the first line of defense against free radicals. Cabbage, Brussels sprouts, wheat grass, and barley grass are the natural sources of SOD. Animal cells consist of an enzyme called catalase, which is responsible for the degradation of hydrogen peroxide (Celi P et al., 2015). GPx cause a reduction of lipid hydroperoxide to their respective alcohols. GPx levels are highly related to the glutathione (GSH) level. Selenium, glutathione peroxidase, glutathione, and vitamins C and E interact together as a potent antioxidant combination to support the body's defenses against free radical damage. Glutathione reductase (GR), a key enzyme in maintaining the level of intracellular glutathione, has a vital role in countering oxidative stress (M.J. Speranza et al., 1993).

### Synthetic Antioxidants

Synthetic antioxidants are clustered into phenolic structures and nano-antioxidant and used for their ability to stabilize the lipid in feeds. Since natural antioxidants are inherently unstable, the use of synthetic antioxidant has gained importance to stabilize the lipids from oxidation. The most frequently employed synthetic antioxidants in animal feeds are butylated hydroxytoluene (BHT), tertbutyl hydroxyquinone (TBHQ), and butylated hydroxyanisole (BHA). Others compound employed in the animal feeds are ethylene diaminetetraacetic acid (EDTA), propyl 3,4,5-trihydroxy benzoate, lauryl gallate (LG), and octylgallate (OG). The disadvantage of using synthetic antioxidants is that they may be contaminated with toxic solvents, chemical precursors, or harmful byproducts (Gulcin et al., 2020).

## SIGNIFICANCE OF DIETARY ANTIOXIDANTS ON THE LIVESTOCK AND POULTRY

Oxidative stress degrades animal health and production, which in turn affects profitability; hence, maintaining and improving oxidative status, particularly through natural nutritional strategies, is critical for normal physiological processes in animals. Various studies have suggested that the use of antioxidants as feed additives has ameliorated productivity, internal physiological changes, apparent performances, and the health of animals (Lee M.T. et al., 2016). Animal products keeping quality and nutritive value may compromised due to oxidant stress induced damage to fat, nucleic acid, protein, etc. Negative energy balance and the formation of lipid peroxide result in the oxidation of dietary fats, which has an adverse impact on the health and performance of livestock (Castillo et al., 2013). Dietary anti-oxidants, endogenous anti-oxidants, and metal-binding proteins all contribute to the anti-oxidant defenses that keep free radicals at bay inside biological systems. For better productive efficiency and health, these productive mechanisms are crucial by reducing the generation of oxidants and minimizing oxidative damage. Therefore, for the optimal use of key nutrients and energy in the feed, animals must be fed a diet rich in key vitamins and trace minerals (Ponnambalam et al., 2022).

**Impact of Antioxidants in Performance and Production**

In animals with greater metabolic rates, there is a disparity between the generation of pro-oxidants and the ability to counter, results in oxidative stress. A high metabolic rate is always linked with production (milk and meat), growth, and reproduction. Hence, it is critical to provide exogenous antioxidants as feed additives in animal diets to maintain a balance between pro-oxidants and antioxidants at the tissue level (Surai et al., 2014). The addition of anti-oxidants such as glutathione, selenium, omega-3 fatty acids, and vitamin A and E has boosted immunity and reduced oxidative stress (Ponnambalam et al., 2022). According to Gulcin et al. 2020, adding lucerne hay to sheep has improved antioxidant status and shown better growth and carcass traits. In sheep, incorporating anti-oxidants and mineral mixtures into diets improves appetite, daily weight gain, and reproduction traits and reduces plasma cortisol levels, a primary heat stress-relieving hormone (Sejian et al., 2014). It was also stated that giving dietary anti-oxidants reduce the negative effects of heat stress, by reduce the production of ROS in sheep (Chauhan et al., 2014). Improves follicular growth by stimulating gonadotropin secretion from adenohypophysis and stimulating steroid hormone synthesis (Rizzo et al., 2009). Supplementing alpha tocopherol along with the selenium potentiates the function of metabolic hormones during the heat stress. The supplemented group had considerably higher mean values of both metabolic hormones T3 and T4 in diverse breeds of sheep than the control group (Shakirullah et al., 2017). The addition of antioxidants to the poultry diet establishes a balance between pro-oxidants and antioxidants, thus lowering the influence of oxidation on egg quality and egg deterioration (Habeeb o. Yusuf and Ruth T.S. Ofongo et al., 2024). Due to a lack of sweat glands, birds are much more susceptible to heat stress, which diminishes vitamin A, E, and C and elevates cortisol levels as it induces lipid peroxidation of the cell membrane (Bohler, M. W. et al., 2021) Hence, supplementing vitamin E in the diet has a critical role in neutralizing the effects of stress hormones. While vitamin C helps in the synthesis of collagen and vitamin D, it also regulates body temperature, immune system activation, corticosterone secretion, and the conversion of tocopherol to its active form. Inclusion of tannins in the diet of sheep has shown improved antioxidant status and carcass quality (Chedea et al., 2019).

**Impact of Anti-oxidants on Milk production**

Current investigations suggest that supplementing with rumen-protected methionine potentiates the levels of endogenous glutathione and carnitine, exhibits a beneficial effect on milk production and the inflammatory response (Osorio et al., 2014). In addition, it significantly improves milk casein production and reduces oxidative damage to udder epithelial cells (Batistel et al., 2017). Dietary antioxidant supplementation can help to decrease the somatic cell count and generation of pro-oxidants in milk, which leads to an increase in production and reduces spoilage. Taking dietary supplements, such as alpha tocopherol, ascorbic acid, carotenoids, and trace minerals (selenium, manganese, and zinc), reduces the incidence of mastitis and improves the shelf life of milk (Stobiecka, M et al., 2022). According to Walker et al. 2010, presence of glutathione peroxidase and selenium substances in milk can inhibit the oxidation of fat and extend its function as anti-oxidants in human tissues upon consumption. The amount of selenium in sow milk increased significantly when fed as a supplement (Surai and Fisinin et al., 2016).

**Impact of antioxidants on the physical and functional characteristics of meat/carcass**

Recent investigations have found that secondary products derived from the olive oil and grape pomace have increased the shelf life of meat, and health of productive animals (Chedea et al., 2019). Alpha- tochpherol (vitamin E) is naturally obtained as an antioxidant when combined with polyphenols and flavonoids, which decrease lipid peroxidation and myoglobin oxidation and preserve the texture and color of the meat (McDowell et al., 1996). According to Kafantaris et al. 2018, feeding grape pomace to lambs and weaned piglets significantly reduced oxidative stress damage and enhanced gut barrier function, resulting in increased body weight, and n-3 PUFA in meat has shown significant anti-oxidant effects. Studies have pointed out that using mill wastewater and polyphenol from olives in animal feed enhances the color, stability, and quality of the meat (Rolia et al., 2018). Even though the use of antioxidants in meat is beneficial, some synthetic anti-oxidants have a carcinogenic effect on consumption (Andree et al., 2010).

## CONCLUSION

Incorporating antioxidants into the feed of livestock and poultry helps to defend against oxidative stress by lowering the synthesis of prooxidants and countering them. It safeguards the vital components of a cell from oxidation and improves the wellness and productivity of an animal by boosting fertility rate and immunity. When used in livestock feed, it preserves their nutritional value by decreasing the risk of rancidity and the production of harmful substances. It improves the quality of the livestock products by enhancing their oxidative status, thus extending their shelf life and benefiting consumers health. Hence, there is a need for further in-vivo research studies using anti-oxidants as feed additives in order to comprehend their biological action and elucidate their appropriate amount that improves animal welfare, production, performance, health, farmer profitability, and consumer satisfaction.

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