Research Article
Open Access

Journal of Life Science and Applied Research (JLSAR)
E-ISSN: 2959-8036

THE EFFECT OF USING DIFFERENT LEVELS OF VITAMIN E ON THE ANTIOXIDANTS STATUS OF BROILER CHICKENS

H. Zain[1], A. Tatar[2*], O. M. Alabi[3] and M. Samiei Zafarghandi[4*],

[1] Biology Department, Universiti Pendidikan Sultan Idris, Perak Malaysia.
[2] Department of Animal Science, Animal Science and Food Technology Faculty, Agricultural Sciences and Natural Resources University of Khuzestan, Mollasani, Iran.
[3] Animal Science and Fisheries Management Unit, Agriculture Programme, Bowen University, Iwo, Nigeria.
[4] Pishgam Sepand Alborz Co, Karaj, Iran.
*** Corresponding author:** Ahmad Tatar, Department of Animal Science, Animal Science and Food Technology Faculty, Agricultural Sciences and Natural Resources University of Khuzestan, Mollasani, Iran. Email: ahmadtatar@gmail.com

Article Info:

Received: Nov. 16, 2022
Revised: Feb. 12, 2023
Accepted: April 04, 2023
Published: June 30, 2023

DOI:
10.59807/jlsar.v4i1.58

How to Cite:
H. . Zain, "THE EFFECT OF USING DIFFERENT LEVELS OF VITAMIN E ON THE ANTIOXIDANTS STATUS OF BROILER CHICKENS", JLSAR, vol. 4, no. 1, pp. 37–44, Jun. 2023.

Available From:
https://www.jlsar.com/index.php/journal/article/view/58

Abstract: This study was conducted at the Poultry Research Station of the Livestock Research Department in the Agricultural Research Department. 126 One-day-old chicks were used in the study, with an average starting weight of 38 g from Ross 308 strain. The chicks were distributed randomly into 3 treatments, and each treatment contained three replicates. 14 chicks for each replicate, where the first treatment was control, and the chickens in the second and third treatments were given vitamin E at a level of 350 and 600 mg / kg feed, respectively, as the continuous lighting system was followed (24 hours / day) in the hall until the end of the experiment, which reached 42 days and the temperature was 35 m throughout the study. The results of the study showed a significant ($P<0.01$) in fat oxidation in liver tissue in vitamin E treatments (350 and 600 mg/kg feed) decreased significantly ($P<0.05$) in the level of malondialdehyde, the level of free fatty acids and the peroxide value compared with the control treatment, which indicates the role of the additives used in protecting against infection and effect of exposure to high temperature and its ability to improve the studied traits.

Keywords: Vitamin E, Liver Tissue, MDA, Free Fatty Acids, Lipid Profile.

1. Introduction

High temperatures are dangerous for broiler chickens and make them uncomfortable and lead to an increase in the breathing rate immediately when exposed to broiler chickens [1]. In addition to that, water consumption increases and feed consumption decreases, and accordingly, a rise in the body temperature of chickens occurs to reach more than 43 ° C, and the birds become uncomfortable and unable to breathe normally and then leads to the destruction of broiler chicken [2]. The high temperature leads to a decrease in the antioxidant defense system in the body [3], which leads to an increase in the level of free radicals, which causes an increase in oxidative stress, oxidative stress, and a decrease in immunity [4].

High temperatures weaken antioxidant status through a decrease in feed consumption and feed conversion factor, and then a decrease in live body weight [5], and high temperatures cause the release of corticosterone hormone, which causes disturbances in endocrine function and a decrease in the rate of metabolism with oxidation [6]. Unsaturated fats in the body then weaken the immune response, which makes the body more susceptible to disease [7]. Therefore, it was necessary to use many means and methods in order to reduce the severity of the high temperatures on the birds [8], such as adding aspirin or vitamin E, C, and E is one of the most powerful natural antioxidants because it works to protect unsaturated fatty acids inside and outside the cells of the body from free radicals and also prevents the reactions of the formation of free radicals resulting from respiratory processes [9]. These reactive chemicals are essential in the host-pathogen interaction because they cause pathogen detection, host defense system activation, and gene expression [10]. Organisms have specific antioxidant defense mechanisms that include enzymatic and non-enzymatic substances like catalase (CAT), superoxide dismutase (SOD), glutathione S-transferase (GSH), glutathione (GSH), thioredoxin, melatonin, carotenoids, Vitamin E, and Vitamin C to lessen ROS- and RNS-induced alterations [11]. By boosting the synthesis of reactive chemicals, the RNA virus known as the ND virus is known to cause oxidative stress [12].

However, only vitamin E supplementation at 120 mg/kg was shown to increase GSH-Px activity in plasma, while at 160 mg/kg vitamin E supplementation was associated with decreased malondialdehyde (MDA) and reactive oxygen species (ROS) in plasma measured fluorometrically by using 2′,7′-Dichlorofluorescin Diacetate as a reactive agent [13]. Furthermore, increased dietary vitamin E levels (from 30 to 60 mg/kg) for 10 wk was shown to be responsible for significant increase in antioxidant defense indexes evidenced by increased serum α-tocopherol concentrations, SOD activity, and the antioxidant capacity of serum measured by FRAP assay based on reduction of Fe3+ to Fe2+ by antioxidants present in the serum with the following formation of a colored complex with 2,4,6 tripyridyltriazine present in the solution [14]. In practically relevant stress conditions of industrial poultry production, antioxidant defense mechanisms are in charge of preventing the negative effects of free radical overproduction and oxidative stress [15]. The principal chain-breaking antioxidant in the cell, found in biological membranes, is thought to be vitamin E, which has been shown to be a key factor in antioxidant defense. In reality, studies have shown that vitamin E is necessary for both male and female reproduction, immune function, efficient growth and development, high-quality eggs and meat, and strong resilience to a variety of stresses [16].

Therefore, this study aimed to find out the effect of adding different levels of vitamin E to the diet on the MDA, free fatty acids, lipid profile and antioxidant status of broiler chickens under heat stress.

2. Materials and Methods

This study was conducted at the Poultry Research Station in the Livestock Research Department of the Agricultural Research Department, as (126) one-day-old chicks were used in the study, with an average starting weight of 38 g of Ross 308 strain. The chicks were distributed randomly to 3 treatments, and each treatment contained three Replicates of 14 chicks for each replicate, where the first treatment (T1) was control, and the chickens in the second (T2) and third treatments (T3) were given vitamin E at the level of 350 and 600 mg/kg feed, respectively, as the continuous lighting system was followed (24 hours/day) in the hall until the end of the experiment, which reached 42 days and was a degree The temperature was 35 C throughout the study, and the birds feeding as ad libitum from the diet used in the study, whose components, percentages, and chemical composition are shown in Table (1), and water was also provided to the birds freely.

Table 1. Composition and calculated nutrient content of the experimental diets (%).

Ingredients	Diets Types		
	Starter (1-10 day)	Grower (11-22 day)	Finisher (23-42 day)
Yellow corn	47.5	50.85	**54.84**
Wheat	10	10	**10**
soybean meal*	32	28	**24**
Proteins concentration **	5	5	**5**

Hydrogenated plant fat	3	4.15	**4.3**
Calcium diphosphate	0.7	0.5	**0.4**
Salt NaCl	0.1	0.1	**0.1**
Limestone	1.2	1.14	**1.1**
Methionine	0.25	0.13	**0.13**
Lysine	0.25	0.13	**0.13**
Total	**100**	**100**	**100**
Calculated nutrient content N [17]			
Metabolism Energy (kcal / kg)	3059	3177	**3277**
Crude protein (%)	22.5	20.9	**19.3**
Crude Fibers (%)	3.5	3.4	**3.2**
Lysine%	1.38	1.19	**1.09**
Methionine + cysteine %	1.08	0.92	**0.88**
Calcium %	1.02	0.95	**0.9**
Available phosphorus%	0.45	0.41	**0.38**

* Soybean meal used from Argentine Origin Crude protein content 48% and 2440 kcal / kg represented energy. ** Proteins used in the production of Dutch Holland (imported) Wafi containing 40% crude protein, 2107 kcal / kg represented energy, 5% raw fat, 2.20% raw fiber, 4.20% calcium, 2.65% phosphorus, 3.85 Lysine, 3.70% methionine, 4.12% methionine + cysteine. It contains a mixture of rare vitamins and minerals that satisfy the bird's needs from these elements.

Vitamin E manufactured by the United Company for Veterinary Pharmaceutical Industry Ltd. (Jordanian Yovidco) was used, which could be obtained from the local markets, as it was added on the basis of the active substance (α-Tochopherol acetate), which was at a level of 50%, so the addition was doubled in the diets to reach The active substance was reduced to 100%, and the idea of doubling the additives was for the purpose of increasing the effectiveness of the vitamin under the condition of heat stress. The diets were prepared in the feed laboratory of the Agricultural Research Department by grinding and mixing the components of the diet according to the required proportions in table (1).

The concentration of malondialdehyde (MDA) equivalents, and the peroxide value and free fatty acid and lipid profile in the liver were determined using the commercial assay kits purchased from Nanjing Jiancheng Institute of Bioengineering (Jiangsu, China) following the standard procedures described by the manufacturer. The water used in the chemical analysis was ultra-purified [18].

The Statistical Analysis System-SAS [19] was used to analyze the data of the study to find out the effect of different coefficients on the studied traits according to a completely randomized design (CRD). Significant differences between the means were compared with the Duncan [20] multinomial test.

3. Results and Discussion

Table (2) shows a significant ($P<0.01$) superiority of the two vitamin E treatments mg/kg feed over the control treatment in fat oxidation in liver tissue in vitamin E treatments (350 and 600 mg/kg feed) decreased significantly ($P<0.05$) in the level of malondialdehyde, the level of free fatty acids and the peroxide value compared with the control treatment the two experimental treatments compared with the control treatment. The reason for the superiority of the additional treatments in antioxidants status over the control treatment is due to the effect of the additions that contributed to reducing the intensity of heat stress on the chickens [21]. Vitamin E is one of the most powerful antioxidants in the body, as it prevents the formation of free radical peroxide in fat cells by hindering the formation of free radicals, and thus provides an important cover in the protection of unsaturated fatty acids [22].

The main function of vitamin E is as an antioxidant, as it inhibits the reactions of the formation of free radicals resulting from a high respiratory rate when exposed to a high temperature or from imbalance and irregular [23], and thus it performs an important function which is to protect unsaturated fatty acids in the body from oxidation and then maintains all body tissues [24]. The reason for the superiority in antioxidants status may be attributed to the effect of additives that worked to reduce high temperatures on chicken, as vitamin E is one of the most powerful natural antioxidants, as it protects unsaturated fatty acids in the body [25]. Vitamin E works to prevent the reactions that form free radicals resulting from the increase in respiratory processes as a result of the entry of large amounts of oxygen in order to cool the body of the bird during exposure to high temperatures. It was found that the oxidation process affects broilers, which leads to a rise in body temperature [26], as it has been proven that vitamin E works to strengthen the antioxidant systems in the body, which reduces the oxidation processes occurring in the body, and this leads to maintaining the temperature of the chickens [27]. Vitamin E breaks the chain of lipid oxidation reactions by donating a hydrogen atom to the peroxyl radical, and this leads to a reduction in the formation of hydroperoxide [28]. As for vitamin C, it controls all active oxygen species, which are hydrogen peroxide radical, negative peroxide, single oxygen, hydroxyl radical, and others. It also has a protective effect against the inhibition of antioxidant enzymes in the body, which causes their concentrations to rise, and this leads to a rise in immunity in chickens [22].

Table 2. Effect of addition of different levels of vitamin E on the antioxidants tratis to diet broiler in antioxidants status (1-42) day, under heat stress conditions.

Traits	Treatments			
	T1	T2	T3	Significant
Malondialdehyde mg/kg	0.857 ± 0.135 a	0.312 ± 0.122 b	0.400 ± 0.111 b	**0.05**
Peroxide mmeq/kg fat	8.32 ± 0.943 a	2.32 ± 0.667 b	2.25 ± 0.245 b	**0.05**
Free Fatty Acids %	4.43 ± 0.326 a	1.50 ± 0.012 b	1.32 ± 0.647 b	**0.05**

*** ±: Average standard error. a, b, c: The different letters within one row indicate significant differences between the coefficients at a significant level (P≤0.05). (T1): basal diet (control) (T2): Vitamin E at the level of 350 mg/kg feed. (T3): Vitamin E at the level of 600 mg/kg feed.**

Figure 1 shows Effect of addition of different levels of vitamin E on the HDL, LDL and VLDL mg/dl to diet broiler in antioxidants status (1-42) day, under heat stress conditions, if a significant decrease is observed in the second and third treatments compared with the control treatment in the value of the HDL, while there was a significant decrease of the second and third treatment over the first treatment (the control treatment) in the value of the LDL. However, there was a significant decrease of the second and third treatment over the first treatment (the control treatment) in the value of the VLDL. The reason for the improvement in the treatments of the experiment in the HDL, LDL and VLDL mg/dl may be due to the role of vitamin E on the meat quality and immunological response of broiler chickens are widely acknowledged. Vitamin E acts directly on the cell or indirectly modifies metabolic and endocrine characteristics as a main antioxidant of cell membranes [29]. Recent research, however, has produced conflicting findings on the effects of vitamin E on broiler chicken development performance, particularly in relation to the size of the vitamin E response in accordance with the quantity of supplementation used [30]. As an antioxidant, vitamin E lessens the pathology caused by free radicals in both inflammatory and regular metabolic conditions [31]. Vitamin E modifies the expression of genes that are regulated by free radical signaling by regulating free radical synthesis, which in turn impacts free radical-mediated signal transduction processes [30].

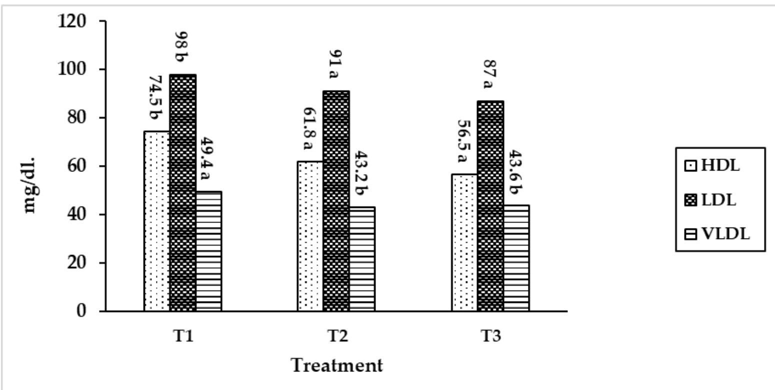

Figure 1. Effect of addition of different levels of vitamin E on theVLDL, LDL HDL mg/dl to diet broiler in antioxidants status (1-42) day, under heat stress conditions.

* ±: Average standard error. a, b, c: The different letters within one row indicate significant differences between the coefficients at a significant level (P≤0.05). (T1): basal diet (control) (T2): Vitamin E at the level of 350 mg/kg feed. (T3): Vitamin E at the level of 600 mg/kg feed.

4. Conclusions

In conclusion that adding different levels of vitamin E in the diets as appetite stimulants in the antioxidants status of broiler chickens under heat stress conditions. led to a significant improvement in the Malondialdehyde, Peroxide, and Free Fatty Acids in (1-42) days, and improvement in the VLDL, LDL HDL especially in the treatments T2 and T3 compared with the control treatment in (1-42) days of broiler chickens.

Supplementary Materials:

No Supplementary Materials.

Author Contributions:

H. Zain and A. Tatar, writing—original draft preparation, O. M. Alabi and M. Samiei Zafarghandi; writing—review and editing, A. Tatar; paraphrasing. All authors have read and agreed to the published version of the manuscript.

Funding:

This research received no external funding.

Institutional Review Board Statement:

The study was conducted in accordance with the protocol authorized by the Animal Science and Food Technology Faculty, Agricultural Sciences and Natural Resources University of Khuzestan, Mollasani, Ethics Committee, Iran in cooperation with Universiti Pendidikan Sultan Idris, Perak Malaysia, from a commercial farm, fertile eggs from Ross (308) strain broiler breeder hens were obtained.

Informed Consent Statement:

No Informed Consent Statement.

Data Availability Statement:

No Data Availability Statement.

Conflicts of Interest:

The authors declare no conflict of interest.

Acknowledgments:

The authors are thankful for the help of the Animal Resources Field Manager, The College Dean, and the Head of the Department of Animal Science, Faculty of Animal Science and Food Technology, Agricultural Sciences and Natural Resources University of Khuzestan, Mollasani, Iran. We would also like to thank the undergraduate students for their valuable help and technical assistance in conducting this research.

Disclaimer/Journal’s Note:

The statements, opinions, and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of JLSAR and/or the editor(s). JLSAR and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions, or products referred to in the content.

5. References

[1] Z. J. M. Saed, S. M. Abdulateef, T. T. Mohammed, and F. M. H. AL-Khalani, “Effect of dried tomato pomace as alternative to vitamin C supplemented diets in hematological indices and oxidative stability of egg yolk of laying hens in high-ambient temperature,” *Biochem. Cell. Arch.*, vol. 18, no. 2, 2018.

[2] N. G. Gregory, “How climatic changes could affect meat quality,” *Food Res. Int.*, vol. 43, no. 7,

2010, doi: 10.1016/j.foodres.2009.05.018.

[3] N. Č. A. Puva *et al.*, "Spices and herbs in broilers nutrition : Effects of garlic (Allium sativum L .) on broiler chicken production," vol. 71, no. September, pp. 533–539, 2015, doi: 10.1017/S0043933915002214.

[4] B. H. Mousa, S. M. Abdulateef, H. A. Alhamdani, N. N. Alhayani, A. A. Alhamdani, and H. H. Nafea, "EFFECT OF DIETARY NATURAL FEED ADDITIVES TO MINIMIZE NEGATIVE ROLE OF PEROXIDE HYDROGEN IN BROILER," *Biochem. Cell. Arch*, vol. 20, no. 2, pp. 5223–5230, 2020, [Online]. Available: https://connectjournals.com/03896.2020.20.5223.

[5] F. I. Al-Bazy, S. M. Abdulateef, and B. F. Sulimn, "IMPACT OF FEEDS CONTAINING OPTIFEED®, VÊO® PREMIUM, AND OLEOBIOTEC® ON THE LIPID PEROXIDATION OF MALE BROILERS UNDER HEAT STRESS," *J. Life Sci. Appl. Res.*, vol. 3, no. 2, pp. 25–31, Dec. 2022.

[6] S. K. Al-Maksousi, W. K. Al-Hayani, and F. M. Hussein, "Effect of the level of corticosteron hormone in the blood of local Iraqi chicken mothers on the sex ratio of the produced offsprings," *Plant Arch.*, vol. 19, 2019.

[7] K. M. Abdul-Lateif and S. M. Abdulateef, "The effect of injecting hatching eggs with different concentrations of biotin on the quality and physiological characteristics of the hatched chicks," *Iraqi J. Vet. Sci.*, vol. 26, 2012, doi: 10.33899/ijvs.2012.168764.

[8] A. K. Al-Delaimy, "The Prospective Effects of Climate Change on Neglected Tropical Diseases in the Eastern Mediterranean Region: a Review," *Curr. Environ. Heal. Reports*, vol. 9, no. 2, pp. 315–323, 2022, doi: 10.1007/s40572-022-00339-7.

[9] K. Sahin, M. Onderci, N. Sahin, M. F. Gursu, F. Khachik, and O. Kucuk, "Effects of lycopene supplementation on antioxidant status, oxidative stress, performance and carcass characteristics in heat-stressed Japanese quail," *J. Therm. Biol.*, vol. 31, no. 4, pp. 307–312, 2006, doi: 10.1016/j.jtherbio.2005.12.006.

[10] K. Aquilano, S. Baldelli, and M. R. Ciriolo, "Glutathione: New roles in redox signalling for an old antioxidant," *Frontiers in Pharmacology*, vol. 5 AUG. 2014, doi: 10.3389/fphar.2014.00196.

[11] A. V. Ivanov *et al.*, "Oxidative Stress during HIV Infection: Mechanisms and Consequences," *Oxidative Medicine and Cellular Longevity*, vol. 2016. 2016, doi: 10.1155/2016/8910396.

[12] E. Peterhans, "Sendai virus stimulates chemiluminescence in mouse spleen cells," *Biochem. Biophys. Res. Commun.*, vol. 91, no. 1, 1979, doi: 10.1016/0006-291X(79)90630-2.

[13] Y. F. Lin, H. L. Tsai, Y. C. Lee, and S. J. Chang, "Maternal vitamin E supplementation affects the antioxidant capability and oxidative status of hatching chicks," *J. Nutr.*, vol. 135, no. 10, 2005, doi: 10.1093/jn/135.10.2457.

[14] Z. Zduńczyk, A. Drazbo, J. Jankowski, J. Juşkiewicz, A. Czech, and Z. Antoszkiewicz, "The effect of different dietary levels of vitamin e and selenium on antioxidant status and immunological markers in serum of laying hens," *Pol. J. Vet. Sci.*, vol. 16, no. 2, 2013, doi: 10.2478/pjvs-2013-0045.

[15] P. F. Surai, I. I. Kochish, and V. I. Fisinin, "Glutathione peroxidases in poultry biology: Part 1. Classification and mechanisms of action," *World's Poultry Science Journal*, vol. 74, no. 2. 2018, doi: 10.1017/S0043933918000284.

[16] P. F. Surai, I. I. Kochish, M. N. Romanov, and D. K. Griffin, "Nutritional modulation of the antioxidant capacities in poultry: the case of vitamin E," *Poult. Sci.*, vol. 98, no. 9, 2019, doi: 10.3382/ps/pez072.

[17] N. Dale, "National research council nutrient requirements of poultry — ninth revised edition (1994)," *J. Appl. Poult. Res.*, vol. 3, no. 1, 1994, doi: 10.1093/japr/3.1.101.

[18] Z. U. Rehman *et al.*, “Supplementation of Vitamin E Protects Chickens from Newcastle Disease Virus-Mediated Exacerbation of Intestinal Oxidative Stress and Tissue Damage,” *Cell. Physiol. Biochem.*, vol. 47, no. 4, 2018, doi: 10.1159/000490984.

[19] S. a S. S. A. System., *SAS user´s guide*. 2004.

[20] D. B. Duncan, “Multiple Range and Multiple F Tests,” *Biometrics*, vol. 11, no. 1, 1955, doi: 10.2307/3001478.

[21] A. Nawab *et al.*, “Heat stress in poultry production: Mitigation strategies to overcome the future challenges facing the global poultry industry,” *Journal of Thermal Biology*, vol. 78. 2018, doi: 10.1016/j.jtherbio.2018.08.010.

[22] A. K. Panda, S. V. Ramarao, M. V. L. N. Raju, and R. N. Chatterjee, “Effect of dietary supplementation with vitamins e and C on production performance, immune responses and antioxidant status of White Leghorn layers under tropical summer conditions,” *Br. Poult. Sci.*, vol. 49, no. 5, 2008, doi: 10.1080/00071660802337233.

[23] Y. Bi, X. Yuan, Y. Chen, G. Chang, and G. Chen, “Expression analysis of genes related to lipid metabolism in peripheral blood lymphocytes of chickens challenged with reticuloendotheliosis virus,” *Poult. Sci.*, vol. 100, no. 5, 2021, doi: 10.1016/j.psj.2021.101081.

[24] N. Skiepko, I. Chwastowska-Siwiecka, J. Kondratowicz, and D. Mikulski, “Fatty acid profile, total cholesterol, vitamin content, and TBARS value of Turkey breast muscle cured with the addition of lycopene,” *Poult. Sci.*, vol. 95, no. 5, pp. 1182–1190, 2016, doi: 10.3382/ps/pew005.

[25] S. A. Stotz, “Academy of Nutrition and Dietetics Complete Food and Nutrition Guide,” *J. Nutr. Educ. Behav.*, vol. 52, no. 1, 2020, doi: 10.1016/j.jneb.2019.11.002.

[26] M. Valko, H. Morris, and M. Cronin, “Metals, Toxicity and Oxidative Stress,” *Curr. Med. Chem.*, vol. 12, no. 10, 2005, doi: 10.2174/0929867053764635.

[27] R. N. Reis, S. L. Vieira, P. C. Nascimento, J. E. Peña, R. Barros, and C. A. Torres, “Selenium contents of eggs from broiler breeders supplemented with sodium selenite or zinc-L-selenium-methionine,” *J. Appl. Poult. Res.*, vol. 18, no. 2, 2009, doi: 10.3382/japr.2008-00069.

[28] J. Boyle, “Lehninger principles of biochemistry (4th ed.): Nelson, D., and Cox, M.,” *Biochem. Mol. Biol. Educ.*, vol. 33, no. 1, 2005, doi: 10.1002/bmb.2005.494033010419.

[29] T. V. Leshchinsky and K. C. Klasing, “Relationship between the level of dietary vitamin E and the immune response of broiler chickens,” *Poult. Sci.*, vol. 80, no. 11, 2001, doi: 10.1093/ps/80.11.1590.

[30] H. B. Malayoğlu, S. Özkan, S. Koçtürk, G. Oktay, and M. Ergül, “Dietary vitamin E (α-tocopheryl acetate) and organic selenium supplementation: Performance and antioxidant status of broilers fed n-3 PUFA-enriched feeds,” *S. Afr. J. Anim. Sci.*, vol. 39, no. 4, 2009, doi: 10.4314/sajas.v39i4.51122.

[31] L. Packer and Y. J. Suzuki, “Vitamin E and alpha-lipoate: Role in antioxidant recycling and activation of the NF-κB transcription factor,” *Mol. Aspects Med.*, vol. 14, no. 3, 1993, doi: 10.1016/0098-2997(93)90009-3.