

Journal of the Hellenic Veterinary Medical Society

Vol 68, No 3 (2017)



Effects of concomitant selenium and vitamin E administration on thyroid hormone metabolism in broilers

A. C. PAPPAS, B. M. KOTSAMPASI, K. KALAMARAS,
K. FEGEROS, G. ZERVAS, D. KALOGIANNIS, S. E.
CHADIO

doi: [10.12681/jhvms.15490](https://doi.org/10.12681/jhvms.15490)

Copyright © 2018, AC PAPPAS, BM KOTSAMPASI, K KALAMARAS,
K FEGEROS, G ZERVAS, D KALOGIANNIS, SE CHADIO



This work is licensed under a [Creative Commons Attribution-NonCommercial 4.0](https://creativecommons.org/licenses/by-nc/4.0/).

To cite this article:

PAPPAS, A. C., KOTSAMPASI, B. M., KALAMARAS, K., FEGEROS, K., ZERVAS, G., KALOGIANNIS, D., & CHADIO, S. E. (2018). Effects of concomitant selenium and vitamin E administration on thyroid hormone metabolism in broilers. *Journal of the Hellenic Veterinary Medical Society*, 68(3), 355–362. <https://doi.org/10.12681/jhvms.15490>

■ Effects of concomitant selenium and vitamin E administration on thyroid hormone metabolism in broilers

Se, vitamin E and thyroid function in broilers

Pappas, A.C.¹ Kotsampasi, B.M.² Kalamaras, K.³, Fegeros, K.¹, Zervas, G.¹,
Kalogiannis, D.³ and Chadio, S.E.^{3*}

¹ Department of Nutritional Physiology and Feeding, Faculty of Animal Science and Aquaculture, School of Agriculture Engineering and Environmental Sciences, Agricultural University of Athens, Athens, Greece

² Animal Research Institute, Hellenic Agricultural Organization (HAO) – DEMETER, Giannitsa, Greece

³ Department of Anatomy and Physiology of Domestic Animals, Faculty of Animal Science and Aquaculture, School of Agriculture Engineering and Environmental Sciences, Agricultural University of Athens, Athens, Greece

ABSTRACT. A total of 400, as hatched, broilers were used to investigate the effect of selenium (Se) and vitamin E supplementation on thyroid hormones metabolism. There were 5 replicates of 4 dietary treatments namely: control (C), a soybean meal maize basal diet with adequate Se and vitamin E (0.3 mg Se per kg diet and 80 mg vitamin E per kg diet), control diet with Se added (Se⁺, with an additional 1 mg of Se per kg of diet), control diet with vitamin E added (E⁺, with an additional 350 mg of vitamin E per kg of diet) and Se⁺E⁺ (with additional 1 mg of Se and 350 mg of vitamin E per kg of diet). Diets were isonitrogenous and isocaloric. Zinc L-selenomethionine complex was used to increase Se content and dl- α -tocopheryl acetate to increase vitamin E content. The experiment lasted 42 days. Plasma Se concentration increased in Se⁺ groups, while whole blood glutathione peroxidase (GPx) activity increased in Se⁺, E⁺ and Se⁺E⁺ groups compared to control. Hepatic type I iodothyronine deiodinase (ID-I) and thyroid hormone concentrations were unaffected by any dietary treatment. It is concluded that supplementation with Se or vitamin E alone or in combination above animal's requirements does not affect thyroid hormone metabolism and liver ID-I activity under the conditions examined.

Key words: Broiler, glutathione peroxidase, selenium, type I iodothyronine deiodinase, vitamin E

Corresponding Author:

Dr Stella E. Chadio,
Department of Anatomy and Physiology of Domestic Animals,
Faculty of Animal Science and Aquaculture,
Agricultural University of Athens,
5 Iera Odos Str, 11855, Athens, Greece.
E-mail address: shad@aua.gr (S.E. Chadio)

Date of initial submission: 27.5.2016
Date of revised submission: 7.7.2016
Date of acceptance: 7.7.2016

ΠΕΡΙΛΗΨΗ. Τετρακόσιοι νεοσσοί κρεοπαραγωγής, ηλικίας μιας ημέρας, χρησιμοποιήθηκαν για να μελετηθεί η επίδραση του σεληνίου και της βιταμίνης E σε επλεγμένα σεληνιοένζυμα που σχετίζονται με τη λειτουργία του θυροειδούς αδένου. Υπήρχαν τέσσερις διατροφικές επεμβάσεις με πέντε επαναλήψεις η κάθε μία. Οι πειραματικές ομάδες περιελάμβαναν την ομάδα του μάρτυρα στην οποία χορηγήθηκε ένα βασικό σιτηρέσιο επαρκές σε σελήνιο και βιταμίνη E (0,3 και 80 mg/kg αντίστοιχα), την ομάδα Se⁺ στην οποία χορηγήθηκε επιπρόσθετα 1 mg/kg σεληνίου, την ομάδα E⁺ στην οποία χορηγήθηκε επιπρόσθετα 350 mg/kg βιταμίνη E και τέλος την ομάδα Se⁺E⁺ στην οποία χορηγήθηκε συνδυασμός σεληνίου και βιταμίνης E σε συγκεντρώσεις 1 και 350 mg/kg αντίστοιχα. Τα σιτηρέσια ήταν ισοαζωτούχα και ισοενεργειακά. Για την επιπλέον προσθήκη σεληνίου χρησιμοποιήθηκε σύμπλοκο της L-σεληνομεθειονίνης με ψευδάργυρο, ενώ για την προσθήκη βιταμίνης η DL-α-τοκοφερόλη. Το πείραμα διήρκεσε 42 ημέρες. Η συγκέντρωση σεληνίου στο πλάσμα αυξήθηκε στις επεμβάσεις με σελήνιο, ενώ η ενεργότητα της υπεροξειδάσης της γλουταθειόνης στο αίμα αυξήθηκε σε όλες τις επεμβάσεις σε σχέση με τον μάρτυρα. Η αποϊωδίαση της ιωδιοθυρονίνης (τύπου I) στο ήπαρ και οι συγκεντρώσεις των θυροειδικών ορμονών στο αίμα δεν επηρεάστηκαν από οποιαδήποτε επέμβαση. Συμπερασματικά, η συμπλήρωση με σελήνιο ή βιταμίνη E μεμονωμένα ή σε συνδυασμό πέραν των αναγκών του ζώου δεν επηρέασαν τα επίπεδα των θυροειδικών ορμονών, ούτε την ενεργότητα της ηπατικής αποϊωδίασης υπό τις συνθήκες που εξετάστηκαν.

Λέξεις Κλειδιά: Ορνίθια, υπεροξειδάσης της γλουταθειόνης, σελήνιο, αποϊωδίαση της ιωδιοθυρονίνης (τύπου I), βιταμίνη E

INTRODUCTION

Thyroid hormones control metabolic and respiratory rates in virtually all cell types. They are related to oxidative stress not only by their stimulation of metabolism, but also by controlling several antioxidant enzymes (Venditti et al., 2011; 2013; Villanueva et al., 2013). The principal pathway of thyroid hormone metabolism is deiodination, which is mediated by specific selenoproteins, the deiodinases (Kohrle et al., 1999; Darras et al., 2000). Selenium is required for the expression of the selenoenzymes type I (ID-I) and type II (ID-II) iodothyronine deiodinase, which are crucial for the generation of the active hormone 3,3',5-tri-iodothyronine (T₃). Type I iodothyronine deiodinase (ID-I) catalyzes the deiodination of thyroxin (T₄) to 3, 3'5-tri-iodothyronine (T₃). It is mainly expressed in the liver, kidney, thyroid, pituitary, and heart. The tissue-specific expression of ID-I is distinct from that of type II iodothyronine deiodinase (ID-II) and only a few tissues express both enzymes (Kohrle 1999; Bianco et al., 2002; Schmutzler et al., 2007; Drutel et al., 2013). Apart from being an essential component of deiodinases, Se is also an integral part of other selenoproteins involved in the antioxidant defense system. Among them glutathione peroxidases have a prominent role in preventing lipid-free radical chain re-

actions that cause peroxidative damage (Kohrle, 2013).

Vitamin E is well known for preventing peroxidative damage of biological membranes and lipoproteins (Burton and Traber 1990; Packer, 1991). A complementary role in the protection of cells against the detrimental effects of lipid peroxides and free radicals produced during normal metabolism has been postulated for both vitamin E and Se (Rooke et al., 2004). Type I iodothyronine deiodinase, as a membrane bound enzyme (Toyoda et al 1995), is susceptible to lipid peroxidation process (Maiti et al., 1995; Chaurasia et al., 1996; 1997) and previous data showed that administration of vitamin E prevents toxic induced thyroid dysfunction, probably through protecting the stability of microsomal membrane in which ID-I exists (Chaurasia and Kar, 1997).

Previous studies in a number of different species have examined the synergistic role of vitamin E and Se under oxidative stress conditions on thyroid hormone metabolism (Sarandöl et al., 2005; Mancini et al., 2013; Kocer-Gumusel et al., 2015; Soliman, 2015). Studies in broilers have mainly focused on their synergistic effects on the antioxidant defense status (Traş et al., 2000; Ozkan et al., 2007; Basmacioğlu Malayoğlu

et al., 2009), while data on their synergism on ID-I activity and thyroid hormone metabolism are sparse.

The present study was designed as part of a project on the effects of antioxidants on thyroid hormone metabolism in broilers. Previously, data showed that excess Se supplementation did not alter thyroid hormone levels, while it increased liver antioxidant enzymes activity (Chadio et al., 2015). Given the role of vitamin E in protecting the stability of microsomal membrane in which ID-I exists (Chaurasia and Kar, 1997; Yue et al., 1998) the aim of the present study was to investigate if concomitant supplementation of additional vitamin E and Se could influence thyroid hormone metabolism and antioxidant enzyme activity in broilers.

MATERIALS AND METHODS

Four hundred (400), as hatched, day-old, Cobb broilers were used in total. The broilers were obtained from a commercial hatchery. Housing and care of animals conformed to Ethical Committee guidelines of Faculty of Animal Science and Aquaculture. There were five replicate pens of four dietary treatments namely, control (C), Se⁺, E⁺ and Se⁺E⁺ randomly allocated in the house. Pen was the experimental unit. Each replicate was assigned to a clean concrete floor pen (2 m²) and birds were raised on a wheat straw shavings litter. There were 20 broilers per pen, 100 per treatment. Broilers of treatment C were fed a commercial diet with adequate Se and vitamin E (0.3 mg Se per kg diet and 80 mg vitamin E per kg diet). In

Table 1. Composition (%) of the experimental broiler diets

Ingredients (%)	Starter (0-14 d)	Grower (15-28 d)	Finisher (29-42 d)
Maize	60.0	63.2	66.8
Soybean meal	26.8	24.8	23.8
Fishmeal	7.1	5.0	2.2
Soybean oil	3.0	4.0	4.0
Limestone	1.6	1.3	1.2
Dicalcium phosphate	0.7	0.9	1.2
Methionine	0.1	0.1	0.1
NaCl	0.3	0.3	0.3
Premix ¹	0.4	0.4	0.4

¹Premix supplied per kg of diet: 12,000 IU vitamin A, 4000 IU vitamin D₃, 80 mg vitamin E, 9 mg vitamin K₃, 3 mg thiamin, 7 mg riboflavin, 6 mg vitamin B₆, 0.025 mg vitamin B₁₂, 50 mg nicotinic acid, 15 mg pantothenic acid, 1.5 mg folic acid, 0.15 mg biotin, 400 mg choline, 0.25 mg cobalt, 1.5 mg iodine, 0.3 mg selenium, 50 mg iron, 130 mg manganese, 20 mg copper, 100 mg zinc. In supplemented diets, an additional 1 mg of Se and 350 mg of vitamin E per kg of diet was provided.

Se⁺ treatment, broilers were fed the C diet with 1 mg of added Se per kg of diet, in E⁺ treatment, they were fed the C diet with 350 mg of added vitamin E per kg of diet and finally in Se⁺E⁺, treatment broilers were fed the C diet with 1 mg of Se and 350 mg of vitamin E added per kg of diet (Table 1). Diets were isonitrogenous and isocaloric. Zinc L-selenomethionine complex (ZnSeMet) was used to increase Se content (Availa-Se 1000, Zinpro Corporation, Eden Prairie, Minnesota, USA) and dl- α -tocopheryl acetate (Rovimix E50 Ads, DSM Nutritional Products Hellas) was

used to increase the vitamin E content.

The duration of the experiment was 42 days. The broilers were raised in a house where light and ventilation were controlled. The lighting program was 23 hours of light and 1 hour of darkness. Heat was provided with a heating lamp per pen. The broilers were fed a starter diet to the 14th day of their life, a grower diet to the 21st day and a finisher diet until the 42nd day (Table 1). Feed and water were provided *ad libitum*. At the end of the 42nd day of the study, one broiler per replicate pen was sacrificed with electrical stunning

so that liver and blood samples were collected. Blood samples were collected in EDTA treated tubes (Aptaca, Canelli, Italy), centrifuged at 1700 g at 4 °C for 10 min and the obtained plasma samples were kept at -20 °C until analysis.

Glutathione peroxidase enzyme activity was determined in whole blood and liver samples according to Paglia and Valentine (1967). Units of enzyme activity were expressed as per mg haemoglobin (Hb) or per mg of liver protein (prot). Briefly, livers were minced in 0.9 % NaCl, washed twice with 0.125 M phosphate buffer, pH 7.4, containing 1.0 mM EDTA (PBS-EDTA) and homogenized with a Polytron homogenizer (Brinkmann Instruments, Westbury, NY,

USA) for 1 min in PBS-EDTA (3 ml/g of liver tissue) at 4 °C. Haemoglobin concentration was determined spectrophotometrically using Drabkin's reagent (Sigma-Aldrich, MI, USA). Liver protein concentration was determined according to Bradford (1976) using commercially available kit. (BioRad, CA, USA). ID-I activity was determined in tissue homogenates with substrate of 3 μM ^{125}I rT₃ as previously described (Sawada et al., 1986).

Plasma T₃ and T₄ concentrations were determined by radioimmunoassay, using commercially available kits (Biocode, Liege, Belgium). The sensitivity for the T₃ assay was 0.1 ng/ml, whereas that for T₄ 1.8 ng/ml. Intra- and inter assay coefficients of variation were 2.9

Table 2. Dietary treatment effects on Se concentration in blood plasma and the activity of antioxidant enzymes

Parameter	Treatment				S.E.M.
	C	Se ⁺	E ⁺	Se ⁺ E ⁺	
Plasma Se concentration (ng Se/ g)	211.05 ^a	364.80 ^b	191.49 ^a	314.70 ^b	21.751
Whole blood GPx activity (U/ mg Hb)	497.0 ^a	1680.5 ^b	1173.0 ^b	1860.3 ^b	2.55
GPx activity in Liver (U/ mg prot.)	0.91	1.05	0.97	0.81	0.06

a, b: different superscripts indicate significant ($P < 0.05$) difference between treatments

and 8.4 for T₃ and 3.27 and 4.94 for T₄, respectively.

Finally, Se concentration was determined in plasma using inductively coupled plasma mass spectrometry, ICP-MS (Perkin Elmer, Elan 9000, Perkin Elmer Life and Analytical Sciences Inc, Waltham, MA, USA) as described previously (Pappas et al., 2011).

Statistical analysis

The statistical analysis was performed using SAS software (SAS Institute Inc., Cary NC, USA). All

variables were analyzed by ANOVA. Descriptive statistics, including mean and standard error of the mean (SEM), are presented. The statements of significance presented in this study were based on $P \leq 0.05$ unless otherwise stated.

RESULTS

Selenium supplementation to broiler diets (treatments Se⁺ and Se⁺E⁺) resulted in significantly higher plasma Se concentration ($P < 0.05$) compared to that

of broilers fed diets with no additional Se (treatments C, and E⁺). Most notably, an approximately 1.7 times higher Se levels were found in Se⁺ and Se⁺E⁺ groups (Table 2).

The activity of GPx differed between the four dietary treatments. In particular, a significant ($P < 0.05$) 3-fold increase in blood GPx activity was detected in the two Se supplemented groups compared to control. Interestingly, a significant ($P < 0.05$) 2-fold increase of GPx activity was also detected in group supplemented only with vitamin E. Liver GPx activity was not affected by any of the dietary treatments (Table 2).

Dietary treatments did not significantly affect liver ID-I activity, although a numerical higher activity was detected in all treated groups. Supplementation with Se, vitamin E or their combination did not affect thyroid hormones concentrations or the rate of deiodination of T₄ to T₃ (Table 3).

DISCUSSION

The results of the present study showed that excess Se supplementation resulted in a significant increase in plasma Se levels and blood GPx activity, in good agreement with our previous findings in broilers supplemented with 0.5 ppm Se as zinc L-selenomethionine complex (Chadio et al., 2015). More interestingly elevated GPx activity was also detected in broilers

supplemented with vitamin E alone or in combination with Se. An augmented blood GPx activity has also been reported for humans following vitamin E administration (Giray et al., 2003) while in growing lambs a synergistic action between Se and vitamin E in terms of GPx activity has also been detected (Ramos et al., 1998; Soliman, 2015). These findings support the well-defined antioxidant activity of vitamin E and further emphasize the synergistic action between the two antioxidants. On the other hand hepatic GPx activity was not affected by either Se, vitamin E or their combination, indicating that excess supplementation elicits no further increase in enzyme activity, in accordance with previous results (Whanger and Butler, 1988; Ip and Hayes, 1989).

Although a considerable number of studies have examined the effects of Se and vitamin E deficiency on plasma thyroid hormone concentrations both in mammals (Beckett et al., 1987; Mitchell et al., 1996; Yue et al., 1998) and birds (Jianhua et al., 2000; Chang et al., 2005), very little is known about the effects of Se and more particularly vitamin E administration on thyroid hormone metabolism and IDs activity. In the present study supplementation with Se, vitamin E or their combination did not influence thyroid hormones levels or the rate of deiodination of T₄ to T₃. The absence of any influence on thyroid hormone metabolism is consistent with the lack of an effect of these

Table 3. Dietary treatment effects on the concentration of iodothyronine deiodinase and thyroid hormones

Parameter	Treatment				S.E.M
	C	Se ⁺	E ⁺	Se ⁺ E ⁺	
ID-I activity in Liver (pmol /min/ mg prot.)	49.42	57.53	53.98	64.91	5.756
T ₄ (ng/ml)	32.67	31.83	29.17	27.83	1.444
T ₃ (ng/ml)	2.78	2.95	2.72	2.82	0.137
T ₄ /T ₃ (ng/ml)	12.53	12.00	11.06	10.31	0.835

antioxidants on hepatic ID-I activity. However, it is of interest to note that a numerically higher, although no significant increase in ID-I activity was detected in groups of broilers received both vitamin E and Se. Therefore, it seems that supplementation with Se or vitamin E above animal's requirements has no effect on thyroid hormone metabolism, providing strong evidence that the upper limit of the tissue concentrations of selenoenzymes are homeostatically controlled and that additional Se does not further increase the selenoenzyme activities, as has already been reported (Behne et al 1992; Chadio et al., 2006).

Previous studies in different animal species revealed a protective role of vitamin E under various stress conditions (Brzezińska-Slebodzińska 2001; Sahin et al., 2001; Sarandöl et al., 2005). Most notably, in lead induced thyroid dysfunction in mice administration of vitamin E has been shown to maintain ID-I activity (Chaurasia and Kar ,1997) and in Se and

vitamin E deficient rats vitamin E administration increased hepatic ID-I activity (Yue et al 1998). Given previous reported data that oxygen radicals may inactivate ID-I through at least reduction of thiol cofactors (Brzezińska-Slebodzińska and Pietras, 2001), it seems that vitamin E protects the stability of microsomal membrane in which ID-I exists, avoiding from free radical damage, as has already been suggested (Chaurasia and Kar, 1997; Yue et al., 1998).

The results of the present study clearly show that supplementation with Se or vitamin E alone or combined above animal's requirements has no effect on thyroid hormone metabolism under physiological conditions. However, given the positive reported effects of vitamin E supplementation under stress conditions it is of particular interest to further elucidate the role of vitamin E and its synergism with Se on ID-I activity and thyroid hormone metabolism. ■

REFERENCES

- Basmacıoğlu Malayoğlu H, Özkan S, Koçtürk S, Oktay G, Ergül M (2009) 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*, 39:274-285.
- Beckett GJ, Beddows SE, Morris PC, Nicol F, Arthur JR (1987) Inhibition of hepatic deiodination of thyroxine is caused by selenium deficiency in rats. *Biochem J*, 248:443-447.
- Behne D, Kyriakopoulos A, Gessner H, Walzog B, Meinhold H (1992) Type I iodothyronine deiodinase activity after high selenium intake and relations between selenium and iodine metabolism in rat. *J Nutr*, 122:1542-1546.
- Bianco AC, Salvatore D, Gereben B, Berry MJ, Larsen PR (2002) biochemistry, cellular and molecular biology, and physiological roles of the iodothyronine selenodeiodinases. *Endocr Rev*, 23:38-89.
- Bradford MM (1976) A rapid and sensitive for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. *Anal Biochem*, 72:248-254.
- Brzezińska-Slebodzińska E, Pietras B (1997) The protective role of some antioxidants and scavengers on the free radicals-induced inhibition of the liver iodothyronine 5'-monodeiodinase activity and thiols content. *J Physiol Pharmacol*, 48:451-459.
- Brzezińska-Slebodzińska E (2001) Fever induced oxidative stress. The effect of thyroid status and the 5'-monodeiodinase activity Protective role of selenium and vitamin E. *J Physiol Pharmacol*, 52:275-284.
- Burton GW, Traber MG (1990) Vitamin E: antioxidant activity, biokinetics, and bioavailability. *Ann Rev Nutr*, 10:357-382.
- Chadio SE, Kotsampasi BM, Menegatos JG, Zervas GP, Kalogiannis DG (2006) Effect of selenium supplementation on thyroid hormone levels and selenoenzyme activities in growing lambs. *Biol Trace Elem Res*, 109:145-154.
- Chadio SE, Pappas AC, Papanastasatos A, Pantelia D, Dardamani A, Fegeros K, Zervas G (2015) Effects of high selenium and fat supplementation on growth performance and thyroid hormones concentration of broilers. *J Trace Elem Med Biol*, 29:202-207.
- Chang WP, Combs JFJ, Scanes GG, March JA (2005) The effects of dietary vitamin E and selenium deficiencies on plasma thyroid and thymic hormone concentrations in the chicken. *Dev Comp Immunol*, 29:265-273.
- Chaurasia SS, Gupta P, Kar A, Maiti PK (1996) Free radical mediated membrane perturbation and inhibition of type I iodothyronine 5'-monodeiodinase activity by lead and cadmium in rat liver homogenate. *Biochem Mol Biol Int*, 39:765-770.
- Chaurasia SS, Kar A (1997) Protective effects of vitamin E against lead-induced deterioration of membrane associated type-I iodothyronine 5'-monodeiodinase (5'D-I) activity in male mice. *Toxicology* 124:203-209.
- Chaurasia SS, Panda S, Kar A (1997) Lead inhibits type-I iodothyronine

- 5%-monodeiodinase in the Indian rock pigeon, *Columba livia*: A possible involvement of essential thiol groups. *J Biosci*, 22:247–254.
- Darras VM, Van der Geyten S, Kühn ER (2000) Thyroid hormone metabolism in poultry. *Biotechnol Agron Soc Environ*, 4:13–20.
- Drutel A, Archambeaud F, Caron P (2013) Selenium and the thyroid gland: more good news for clinicians. *Clin Endocrinol*, 78:155–164.
- Giray B, Kan E, Bali M, Hincal F, Basaran N (2003) The effect of vitamin E supplementation on antioxidant enzyme activities and lipid peroxidation levels in hemodialysis patients. *Clin Chim Acta*, 338:91–98.
- Ip C, Hayes C (1989) Tissue selenium levels in selenium-supplemented rats and their relevance in mammary cancer protection. *Carcinogenesis*, 10:921–925.
- Jianhua H, Ohtsuka A, Hayashi K (2000) Selenium influences growth via thyroid hormone status in broiler chickens. *Br J Nutr*, 84:727–732.
- Kocer-Gumusel B, Erkekoglu P, Caglayan A, Hincal F (2015) The ameliorating effects of vitamin E on hepatic antioxidant system and xenobiotic metabolizing enzymes in fenvalerate-exposed iodine-deficient rats. *Drug Chem Toxicol*, 8:1–8.
- Kohrle J (1999) Local activation and inactivation of thyroid hormones: the deiodinases family. *Mol Cell Endocrinol*, 151:103–119.
- Kohrle J (2013) Selenium and the thyroid. *Curr Opin Endocrinol Diabetes Obes*, 20:441–448.
- Maiti PK, Kar A, Gupta P, Chaurasia SS (1995) Loss of membrane integrity and inhibition of type-I iodothyronine 5'-monodeiodinase activity by fenvalerate in female mouse. *Biochem Biophys Res Commun*, 214:905–909.
- Mancini A, Raimondo S, Di Segni C, Persano M, Gadotti G, Silvestrini A, Festa R, Tiano L, Pontecorvi A, Meucci E (2013) Thyroid hormones and antioxidant systems: focus on oxidative stress in cardiovascular and pulmonary diseases. *Int J Mol Sci*, 14:23893–23909.
- Mitchell JH, Nicol F, Beckett GJ (1996) Selenoenzyme expression in thyroid and liver of second generation selenium- and iodine-deficient rats. *J Mol Endocrinol*, 16:259–267.
- Ozkan S, Malayoğlu HB, Yalçın S, Karadas F, Koçtürk S, Cabuk M, Oktay G, Ozdemir S, Ozdemir E, Ergül M (2007) Dietary vitamin E (α -tocopherol acetate) and selenium supplementation from different sources: performance, ascites-related variables and antioxidant status in broilers reared at low and optimum temperatures. *Brit Poultry Sci* 48:580–593.
- Packer L (1991) Protective role of vitamin E in biological systems. *Am J Clin Nutr*, 53:1050S–1055S.
- Paglia DE, Valentine WN (1967) Studies on the quantitative and qualitative characterization of erythrocyte glutathione peroxidase. *J Lab Clin Med*, 70:158–169.
- Pappas AC, Zoidis E, Georgiou CA, Demiris N, Surai PF, Fegeros K (2011) Influence of organic selenium supplementation on the accumulation of toxic and essential trace elements involved in the antioxidant system of chicken. *Food Addit Contam Part A Chem Anal Control Expo Risk Assess*, 28:446–454.
- Ramos JJ, Fernandez AMT, Verde T, Sanz MC, Marca MC (1998) Effect of inoculation with selenium and / or vitamin E on the immune response of lambs. *Med Vet*, 15:291–296.
- Rooke JA, Robinson JJ, Arthur JR (2004) Effects of vitamin E and selenium on the performance and immune status of ewes and lambs. *J Agric Sci*, 142:253–262.
- Sahin N, Sahin K, Kucuk O (2001) Effects of vitamin E and vitamin A supplementation on performance, thyroid status and serum concentrations of some metabolites and minerals in broilers reared under heat stress (32 °C). *Vet Med Czech*, 46:286–292.
- Sarandöl E, Taş S, Dirican M, Serdar Z (2005) Oxidative stress and serum paraoxonase activity in experimental hypothyroidism: effect of vitamin E supplementation. *Cell Biochem Funct* 23:1–8.
- Sawada K, Hummel BC, Walfish PG (1986) Properties of cytosolic components activating rat hepatic 5'-deiodination in the presence of NADPH. *Biochem J*, 234:391–398.
- Schmutzler C, Mentrup B, Schomburg L, Hoang-Vu C, Herzog V, Köhrle J (2007) Selenoproteins of the thyroid gland: expression, localization and possible function of glutathione peroxidase 3. *Biol Chem*, 388:1053–1059.
- Soliman EB (2015) Dose-response of vitamin E and selenium injection on growth performance, physiological and immune responses of Ossimi lambs. *Egypt J Sheep & Goat Sci* 10:27–40.
- Toyoda N, Berry MJ, Harney JW, Larsen PR (1995) Topological analysis of the integral membrane protein, Type I iodothyronine deiodinase (D1). *J Biol Chem*, 270:12310–12318.
- Traş B, Inal F, Baş AL, Altunok V, Elmas M, Yazar E (2000) Effects of continuous supplementations of ascorbic acid, aspirin, vitamin E and selenium on some haematological parameters and serum superoxide dismutase level in broiler chickens. *Brit Poultry Sci*, 41:664–666.
- Villanueva I, Alva-Sánchez C, Pacheco-Rosado J (2013) The Role of Thyroid Hormones as Inductors of Oxidative Stress and Neurodegeneration. *Oxidative medicine and cellular longevity*. Article ID 218145, <http://dxdoi.org/10.1155/2013/218145>.
- Venditti P, Di Stefano L, Di Meo S (2013) Vitamin E management of oxidative damage-linked dysfunctions of hyperthyroid tissues. *Cell Mol Life Sci*, 70:3125–3144.
- Venditti P, Napolitano G, Di Stefano L, Chiellini G, Zucchi R, Scanlan TS, Di Meo S (2011) Effects of the thyroid hormone derivatives 3-iodothyronamine and thyronamine on rat liver oxidative capacity. *Mol Cell Endocrinol*, 341:55–62.
- Whanger PD, Butler JA (1988) Effects of various dietary levels of selenium as selenite or selenomethionine on tissue selenium levels and glutathione peroxidase activity in rats. *J Nutr*, 118:846–852.
- Yue L, Wang F, Li G (1998) Changes of peripheral tissue thyroid hormone metabolism in rats fed with selenium- and vitamin E-deficient artificial semisynthetic diet. *Chin Med J (Engl)*, 111:854–857.