

Review

Molecular mechanisms and new strategies to fight stresses in egg-producing birds

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Abstract. Commercial egg production is associated with various stresses decreasing productive and reproductive performance of layers. A growing body of evidence indicates that most of stresses in poultry production at the cellular level are associated with oxidative stress due to excess of free radical production or inadequate antioxidant protection. Recently, a concept of the cellular antioxidant defence has been revised with a special attention paid to cell signalling. Indeed, in animals, redox signalling pathways use reactive oxygen species (ROS) to transfer signals from different sources to the nucleus to regulate a number of various functions including growth, differentiation, proliferation and apoptosis. The vitagene concept of fighting stresses emerged as a new direction in a nutritional research. Indeed, by improving the adaptive ability of animals to stress it is possible to substantially decrease negative consequences of various stresses in poultry and farm animal production. The analysis of recently published data clearly showed that the anti-stress composition developed on the vitagene concept and supplied with drinking water is an effective means in fighting stresses in poultry production.

Keywords: stress, poultry, vitagenes, chickens

Introduction

Commercial egg production is associated with various stresses decreasing productive and reproductive performance of layers. It is proven that most of stresses in poultry production (technological: chick placement, vaccinations and transfer to breeder houses; environmental: heat stress, high ammonia, etc.; nutritional: mycotoxins, misbalances of vitamins, minerals, amino acids, etc.; or internal: bacterial and viral challenges) at the cellular level are associated with oxidative stress due to excess of free radical production or inadequate antioxidant protection (Surai, 2002; 2006; Surai and Fisinin, 2012a; 2012b; 2013). Therefore, the antioxidant system of the body is responsible for preventing damages caused by free radicals to various biological molecules including proteins, lipids and DNA. Many of the natural antioxidants are provided with the chicken diet (vitamin E, carotenoids, selenium, etc.), while a range of other antioxidant compounds are synthesised in the body (glutathione, thioredoxins, antioxidant enzymes, etc.) and a delicate balance between antioxidants and pro-oxidants in cells, digestive tract and in the whole body is responsible for maintenance of the redox status of the cell (Surai, 2002), activating various transcription factors and ultimately affects chicken health, their productive and reproductive performances. Therefore, reactive oxygen species (ROS) are no longer viewed as just a toxic by-product of mitochondrial respiration, but are now appreciated for their role in regulating a myriad of cellular signalling pathways (Reczek and Chandel, 2015). In fact, a vita-gene network is shown to be responsible for a regulation of the adaptive ability of animals/human to various stresses (Calabrese et al., 2008; 2010; 2012). Recently a new concept of fighting stresses via antioxidant supplementation via

drinking water (Surai and Fisinin, 2012a; 2012b; 2013) was suggested and a product PerforMax (Magic Antistress Mix) developed based on the vitagene concept was successfully tested in broiler production (Velichko et al., 2013; 2014) as well as for improvement of the reproductive performance of egg breeders (Shatskikh and Latypova, 2014).

The aim of this paper is to review the roles of antioxidant-containing anti-stress compositions supplied with drinking water in maintaining productive and reproductive performance of layer breeders.

Stresses in poultry production

From a physiological point of view stress is related to deviation from optimal internal and external conditions. In general, there are three major types of stress in poultry industry: environmental, nutritional and internal stresses (Surai, 2006). Environmental stresses started from the moment when egg is laid, since temperature variation could cause embryo to start developing (high environmental temperature) or die (low temperature or fast temperature changes). It is well known that temperature and other conditions of egg storage between egg laying and its placement into the hatchery negatively affect embryonic development. In fact, hatchability of fertile eggs declines with length of storage and there is an increase in percentages of early and late embryonic mortality with length of storage period (Elibol et al., 2002; Fassenko, 2007) and most likely could affect chickens in later life. Furthermore, additional time in hatchery during hatching is also considered to be a stress causing detrimental changes in antioxidant defences of the chick (Karadas et al., 2011). The negative effect of high temperature on hatching eggs could be very substantial during summer heat stress.

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Indeed, high environmental temperature is one of the most serious factors adversely affecting the laying performance in poultry. Egg production (De Andrade et al., 1977; Mack et al., 2013), egg weight (Mashaly et al., 2004; Sahin et al., 2007; Ebeid et al., 2012; Mack et al., 2013), eggshell thickness (de Andrade et al., 1977; Lin et al., 2004; Franco-Jimenez et al., 2007; Ebeid et al., 2012) eggshell percentage (Ebeid et al., 2012), eggshell density (de Andrade et al., 1977) and eggshell breakage (Lin et al., 2004) were negatively affected by high ambient temperature. Elevated temperatures also increase mortality in both layers (Mashaly et al., 2004) and broilers (Quinteiro-Filho et al., 2010).

Furthermore, the gastrointestinal tract is particularly sensitive to stressors, which can cause a variety of changes, including alteration of the normal, protective microbiota (Burkholder et al., 2008) and decreased integrity of the intestinal epithelium (Quinteiro-Filho et al., 2010). Heat stress alters the jejunal glucose and lipid transport in chickens (Sun et al., 2014). Furthermore, heat stress can inhibit the activity of digestive enzymes and reduce absorption and immune functions of intestinal mucosa (Chen et al., 2014). The calbindin concentration was prominently decreased in ileum, cecum, colon, and eggshell gland under heat stress conditions which could be related to the deterioration of eggshell quality characteristics under heat stress conditions (Ebeid et al., 2012). Broilers subjected to the heat stress were characterised by reduced average daily gain and feed intake; lower viable counts of *Lactobacillus* and *Bifidobacterium* and increased viable counts of coliforms and *Clostridium* in small intestinal contents; shorter jejunal villus height, deeper crypt depth, and lower ratio of villus height to crypt depth (Song et al., 2014).

The next stress period is related to the chick placement and the first 24 hours of the chick's life are the most important (Noy and Uni, 2010). It is believed that a chick should have an access to the feed and water as soon as possible after hatching to stimulate the development of the digestive and immune systems. When chicks are placed in winter while outside temperature is quite low there is always a temptation to decrease ventilation to keep energy usage to the minimum. However, it is very important to provide good quality, warm, fresh air that is rich in oxygen for the recently hatched chicks. Indeed, the chick's trachea is very often irritated from being boxed and shipped in the chick trays, often for many hours. Furthermore, chicks can be exposed to formaldehyde gas and contaminated air during hatch. Excessive amounts of irritants such as carbon dioxide and ammonia can cause depression, dehydration, emaciation as well as various problems with the respiratory system of the chick. It is interesting to note that exposure to stressors early on enhanced the chicks' ability to cope with the same or with different stressors later and that compensatory responses occurred as the result of short-term exposure to stressors (Johnson et al., 1991). The increased lipid peroxidation and reduced activities of antioxidant enzymes in healthy chickens reared under unfavorable microclimatic conditions such as higher air temperature and humidity, higher ammonia concentrations, and lower light intensity were indicative about an induced oxidative stress (Georgieva et al., 2011). It should also be mentioned that poor ventilation is often associated with toxic carbon monoxide accumulation. Toxicity causes irreversible physiological and biochemical changes that cannot be corrected with successive additional ventilation. The next stress is related to vaccinations. Indeed, vaccinations are absolutely necessary to maintain chicken protection against various diseases, but when a vaccine activates the immune system there are always negative consequences for productive parameters, since immunity is quite expensive for the body in terms of usage of nutrients and energy. It is generally assumed by immunologists that providing immunological defences

to minimise such risks to the host is costly in terms of necessitating trade-offs with other nutrient-demanding processes such as growth, reproduction, and thermoregulation (Lochmiller and Deerenberg, 2000). It has been shown that lipopolysaccharide injection decreased feed intake and body weight gain (Lai et al., 2011) and reduced ileal protein digestibility (Yang et al., 2011). It is well appreciated that efficacy of vaccination is very much dependent on the immunocompetence of the birds, which could be compromised in stress conditions (Surai, 2002). Furthermore, there is a range of immunosuppressive diseases in poultry, including bursal disease, infectious chicken anemia and Marek's disease (Fussell, 1998; Hoerr, 2010). High stocking densities have been reported to be another stressful condition (Puron et al., 1995) causing decreased performance, increased mortality and prevalence of leg weakness (Sørensen et al., 2000), and affecting the carcass quality (Feddes et al., 2002) of broiler chickens. Transferring chickens to breeder houses is always associated with increased stress and sometimes causing feather picking and cannibalism (Gunnarsson et al., 1999). The biggest stress for layers comes at the peak of egg production. Indeed, major compounds of the egg yolk are synthesised in the liver and it is working to its maximum ability and any stress can cause a drop in egg production which very often is not coming up after the stress is removed. Finally, egg shell quality during the second part of egg laying is considered to be a problem, especially when layer age is past 80 weeks (Safaa et al., 2008). Indeed, most losses are related to the poor shell quality of eggs produced at the end of the production cycle. For example, Grobas et al. (1999) found that the percentage of broken eggs from Brown egg-laying hens on the farm increased from 0.43% at 22 wk to 1.81% at 74 wk of age. Microbial and virus challenges are considered to be the main internal stresses causing detrimental consequences for productive and reproductive parameters of birds. Mycotoxins are considered to be among major feed-related stressors in poultry production (Awad et al., 2013; Dhama et al., 2013; Rawal et al., 2010; Battacone et al., 2010) and they cause oxidative stress and immunosuppression (Surai and Dvorska, 2005; Fisinin and Surai, 2012; 2012a; 2012b).

In general, all aforementioned stresses suppress reproductive performance of parent birds including reduced fertility and hatchability. Furthermore, stresses are associated with impaired feed conversion, reduced average daily weight gain and increased mortality in growing birds. The immune system is considered to be the most sensitive to various stresses (Hoerr et al., 2010; Surai, 2006; Surai and Dvorska, 2005; Dohms and Metz, 2001). In fact, stress-related dysfunction of the immune system weakens natural resistance to diseases (Antonissen et al., 2014) and reduces efficacy of vaccinations (Ingrao et al., 2013) leading to significant losses in profits.

Molecular mechanisms of stress and antioxidant defenses

It is generally accepted that increased free radical production is the major molecular mechanism of the negative consequences of various stresses in human life and animal/poultry production (Surai, 2002; 2006). Free radicals are atoms or molecules containing one or more unpaired electrons and they are highly unstable and reactive capable of damaging biologically relevant molecules such as DNA, proteins, lipids or carbohydrates. The animal body is under constant attack from free radicals, formed as a natural consequence of the body's normal metabolic activity and as part of the immune system's strategy for destroying invading microorganisms. Recently collective terms ROS and reactive nitrogen species (RNS) have been introduced including not only the oxygen or nitrogen radicals,

but also some non-radical reactive derivatives of oxygen and nitrogen (Surai, 2006).

Reactive oxygen species are constantly produced *in vivo* in the course of the physiological metabolism in tissues. The most important effect of free radicals on the cellular metabolism is due to their participation in lipid peroxidation reactions. In fact, lipid peroxidation is a chain reaction and potentially large number of cycles of peroxidation could cause substantial damage to cells. In membranes the peroxidizable material is represented by polyunsaturated fatty acids (PUFA). It is generally accepted that PUFA susceptibility to peroxidation is proportional to amount double bonds in the molecules. In fact, docosahexaenoic acid (DHA, 22:6n-3) and arachidonic acid (AA, 20:4n-6) are among major substrates of the peroxidation in the membrane. It is necessary to underline that the same PUFAs are responsible for maintenance of physiologically important membrane properties including fluidity and permeability. Therefore, as a result of lipid peroxidation within the biological membranes their structure and functions are compromised. Proteins and DNA are also important targets for ROS.

The complex structure of proteins and a variety of oxidizable functional groups of the amino acids make them susceptible to oxidative damage. In fact, the accumulation of oxidized proteins has been implicated in the aging process and in other age-related pathologies (Wani et al., 2014; Zhang et al., 2014). A range of oxidized proteins and amino acids has been characterised in biological systems. In general, the accumulation of oxidized proteins depends on the balance between antioxidants, pro-oxidants and removal/repair mechanisms. Oxidation of proteins leads to the formation of reversible disulfide bridges. More severe protein oxidation causes a formation of chemically modified derivatives e.g. Schiff's base (Surai, 2006).

During evolution, living organisms have developed specific antioxidant protective mechanisms to deal with ROS and RNS (Surai, 2002). Therefore, it is only the presence of natural antioxidants in living organisms which enable them to survive in an oxygen-rich environment. The general term "antioxidant system" describes these mechanisms, which are diverse and responsible for the protection of cells from the actions of free radicals. This system includes:

- Natural fat-soluble antioxidants (vitamins A, E, carotenoids, ubiquinones, etc.);
- Water-soluble antioxidants (ascorbic acid, uric acid, taurine, carnitine, etc.);
- Antioxidant enzymes: glutathione peroxidase (GSH-Px), catalase (CAT) and superoxide dismutase (SOD);
- Thiol redox system consisting of the glutathione system (glutathione/glutathione reductase/glutaredoxin/glutathione peroxidase and a thioredoxin system (thioredoxin/thioredoxin peroxidase/thioredoxin reductase).

The protective antioxidant compounds are located in organelles, subcellular compartments or the extracellular space enabling maximum cellular protection to occur. The antioxidant system of the body is responsible for prevention of damaging effects of free radicals in stress conditions. Therefore, dietary supplementation of antioxidant compounds is a way to improve efficiency of broiler production in commercial conditions associated with various stresses.

Oxidative stress and transcription factors

Recently, a concept of the cellular antioxidant defence has been revised with a special attention paid to cell signalling. Indeed, in

animals, redox signalling pathways use ROS to transfer signals from different sources to the nucleus to regulate a number of various functions including growth, differentiation, proliferation and apoptosis. Various transcription factors are involved in a regulation of the antioxidant defence system (Ma and He, 2012; Majzunova et al., 2013; Song and Zou, 2014; Kweider et al., 2014). These pathways operate in coordinated manner and several are critically important for animals to cope with oxidative stress insults. They include Keap1/Nrf2, NF- κ B, Mapk and AP-1 (Luschak, 2011). Particularly great attention has been paid to a basic leucine zipper transcription factor, Nuclear factor-erythroid-2- (NF-E2-) related factor 2 (Nrf2). The recent information can be summarised as follows:

Based on the existing evidence, Nrf2, is considered to be the master regulator of oxidative stress signalling and growing evidence has demonstrated that the Nrf2 antioxidant response pathway plays an important role in the cellular antioxidant defense by activating a great variety of genes involved in early defence reactions of higher organisms (Ma, 2013; van der Wijst et al., 2014). Indeed, Nrf2, has a significant role in adaptive responses to oxidative stress being responsible for the induction of the expression of various antioxidants to combat oxidative and electrophilic stress. In particular, critical components of the cellular antioxidant defence mechanisms include the ROS scavengers, phase II detoxification enzymes, and other detoxification proteins, which contain antioxidant response elements (AREs) in their promoter regions (Howden, 2013; Buelna-Chontal and Zazueta, 2013; Keum and Choi, 2014). There is considerable experimental evidence suggesting that under normal physiological conditions, Nrf2 is kept in the cytoplasm by Kelch-like-ECH-associated cytoskeletal protein 1 (Keap1) and the ubiquitin scaffold protein Cullin 3 targeting Nrf2 for ubiquitylation and subsequent degradation. Indeed, Cullin 3 ubiquitinates its substrate, Nrf2. Furthermore, Keap1 serves as a substrate adaptor, which facilitates the ubiquitination of Nrf2 by Cullin 3 with the following proteasomal degradation resulting in a short (about 20 min) half-life of Nrf2 under normal conditions. Emerging evidence has revealed that Keap-1 acts as a redox sensor and upon exposure to oxidative stress, critical cysteine thiols of Keap1 are modified resulting in Nrf2 to be released from Keap1 and translocate to nucleus. In the nucleus, Nrf2 combines with a small musculoaponeurotic fibrosarcoma protein called Maf to form a heterodimer, and, by binding to the ARE in the upstream promoter region, it initiates the transcription of a number of antioxidative genes, leading to the expression of antioxidant proteins, thiol molecules and their generating enzymes, detoxifying enzymes, and stress response proteins. This includes enzymes of the first line of the antioxidant defence, namely superoxide dismutase (SOD), glutathione peroxidase (GSH-Px) and catalase (CAT), as well as heme oxygenase-1 (HO-1), NAD(P)H dehydrogenase (quinone 1) (NQO1), glutathione-S-transferase (GST), γ -glutamylcysteine synthase (γ -GCS) and others contributing to counteracting oxidative damages (Zhou et al., 2014). It is believed that, Nrf2 is controlled through a complex transcriptional/epigenetic and post-translational network that ensures its activity increases during redox perturbation, inflammation, growth factor stimulation and nutrient/energy fluxes, thereby enabling the factor to orchestrate adaptive responses to diverse forms of stress (Hayes and Dinkova-Kosova, 2014). Beyond activation of synthesis of antioxidant enzymes, Nrf2 also contributes to adaptation by up-regulating the repair and degradation of damaged macromolecules, and by modulating intermediary metabolism conducting direct metabolic reprogramming during stress (Luschak, 2011). Furthermore, Nrf2 may

serve as a major regulator of several cellular defence associated pathways by which various cells combat oxidative stress. Moreover, Nrf2 contributes to cellular proteostasis by regulating the expression of molecular chaperones, as well as of additional players of proteome stability and maintenance, namely the proteasome subunits (Niforou et al., 2014). Through inducing the expression of this battery of genes, Nrf2 can augment a wide range of cell defence mechanisms, thereby enhancing the overall capacity of cells to detoxify potentially harmful substances and adapting to various stress conditions. As such, the Nrf2-Keap1 pathway is generally considered to be a major cellular defence pathway (Zhou et al., 2014). It has been suggested that low intensity oxidative stress is mainly sensed by Keap1/Nrf2 system which downstream up-regulates the genes encoding antioxidant enzymes. Intermediate oxidative stress also increases the activity of antioxidant enzymes, but mainly via NF- κ B and AP-1 pathways. At both, low and intermediate intensity oxidative stresses, MAP-kinases and other kinases seem to be also involved in signal sensing and cellular response, leading to enhanced antioxidant potential (Luschak, 2011).

Vitagenes and a new concept of fighting stresses

Recently a new concept of how vitagenes regulate the adaptive ability of humans and animals to various stresses has been developed (Calabrese et al., 2008; 2010; 2012). This concept postulates that there is a range of genes responsible for the synthesis of various antioxidant compounds (heat shock proteins, antioxidant enzymes, sirtuins, etc.) and that there are nutrients, which can affect expression of such genes. Carnitine, betaine, and some other elements are proven to be effective regulators of vitagenes.

Based on the aforementioned positive effects of dietary antioxidants on protection against various stresses in poultry production, a range of anti-stress compositions/premixes has been developed. However, in stress conditions feed consumption is substantially decreased so the effects of feed supplements are also decreased. The new concept was based on an idea that supplying birds with various antioxidants via the drinking water could help them deal with stress conditions more effectively. Indeed, it was proven that inclusion of vitagene-regulating compounds (carnitine, betaine, vitamin E, etc.) in water, as well as some minerals, vitamins, electrolytes and organic acids could be effective in fighting various stresses (Fisinin and Surai, 2011; Surai and Fisinin, 2012a; 2012b; 2013; Fotina et al., 2013). This helps at chick placement, when the antioxidant system is crucial for the digestive and immune system development (Fisinin and Surai, 2012a). In particular, it was proven that inclusion of an anti-stress composition (Antistress Magic Mix, PerforMax) into the drinking water at the University trial improved chicken growth and feed conversion ratio (FCR, Fotina et al., 2011; Fotina et al., 2014). Using the same anti-stress composition in commercial conditions improved FCR during a 39-day broiler growth trial. At the end of the trial, the improvement in FCR due to the anti-stress composition during the first three days post-hatch as well as before and after vaccination was highly significant (Velichko et al., 2013; 2014). In addition, it was shown that the anti-stress composition had an immune-modulating effect in broilers (Fotina et al., 2011), growing ducklings (Surai et al., 2012) and could be successfully used to prevent immunosuppression (Fisinin and Surai, 2013a; 2013b). Improvement of the antioxidant system via supplying the antioxidant composition via the drinking water could help deal with various mycotoxins in feed, including DON (Fisinin and Surai,

2011b; 2011c), ochratoxin A (Fisinin and Surai, 2012d; 2012e) and T-2 toxin (Fisinin and Surai, 2021f; 2012g). Furthermore, such a technology could help fight heat stress (Surai and Fotina, 2013).

Effect of the anti-stress composition on layer breeders

The importance and efficacy of using the anti-stress composition (PerforMax, Magic Antistress Mix) for rearing birds and adult egg-type parent stock (Hy-Line) at one of the biggest egg producing farms in Russia (Borovskaya poultry farm, Tumen region) have been described recently and below there is a summary of major findings. The study was conducted with rearing birds as well as with adult laying hens and cockerels of the parent stock (Hy Line Brown, line SD). There were two poultry trials, two physiological trials and a big commercial trial. In total 53400 birds were used (Latypova, 2014).

In the first phase of the experiment, the effect of Magic Antistress Mix (PerforMax) on the rearing birds was studied. There were a control and an experimental group with 2000 females and 400 males in each group. The control group was fed in accordance with Hy Line recommendations with the diet formulated to meet all requirements in major nutrients and energy. The experimental group had an additional antistress supply via drinking water at the level of 100 g per 100 L of drinking water during days 1–5, 9–13, 21–25, 27–31, 45–49, 63–67 and 75–79 which were related to stresses imposed by vaccinations, grading, and transfer to the breeding houses. The experiment lasted for 105 days (Shackih and Latypova, 2014).

In general, growth and development of chickens were similar in both groups with slight increase in body weight (1242 g vs 1200 g) at 15 weeks of age in the experimental female birds. Therefore, the experimental birds were closer to target body weight (1230 g) than control birds. The usage of antistress composition positively affected testes development of 15-week old cockerels (2.47 g vs 1.05 g, $P < 0.05$) (Shackih and Latypova, 2014a). It is interesting to note that in the experimental cockerels testes weight was also improved at 26 and 56 weeks of age (Shatskikh and Latypova, 2013). The liver of experimental birds was characterised by a significant increase in vitamin A content of the liver at various ages ($P < 0.05$). There was an increase in Ca content of the bones of female birds at 15 weeks indicating better Ca reserves for future egg production. Results of balance experiments indicated that females and males of the experimental group were characterised by improved ($P < 0.05$) usage of nitrogen, calcium and phosphorus from the diet. Indeed, usage of the antistress composition with water in period of chicken stress positively affected experimental birds (Shackikh and Latypova, 2014).

The second phase of the experiment was a continuation of the first phase and lasted from day 106 until day 448 and similar to a previous experiment Performax (Magic Antistress Mix) was used with water at 100 g per 100 L of drinking water at days 106–107, 109–111, 148–157 and 238–246 associated with increased stresses of vaccinations, first egg laying, active egg production growth and peak of egg production (Latypova, 2014b). The main results of egg production are shown in Table 1.

As can be seen from the presented data, usage of the antistress composition with drinking water at specific periods of the increased stress can improve breeder's performance. In particular there was an increase by 2% of the egg peak production and peak plateau lasted about 50 days longer than that in the control birds. It is interesting to note that hen housed egg production in the control group (260.8 eggs) was higher than the target for the line (253.4

Table 1. Egg production of Hi Line parent laying hens per 64 weeks (Latypova and Shatskikh, 2014)

Parameter	Group	
	Control	Experimental
Total egg produced	504958	517200
Age of the first egg laid, days	108	106
Age of achieving 50% laying, days	143	142
Peak of egg production, %	94.3	96.9
Age of achieving egg peak production, days	180	172
Plateau of peak production, days	59	110
Egg production intensity, %	86.5	87.0
Eggs per hen housed (T – 253,4 eggs)	260.8	266.9
Eggs per hen day (T – 259,5 eggs)	263.6	268.1
Feed per 10 eggs, kg (T – 1,35 kr)	1.36	1.33

T – target for Hy Line Brown

eggs) and in the experimental group it was increased by 6 eggs. Improved egg production was associated with increased weight of the oviduct in the experimental layers (Shackih and Latypova, 2013). It is also important to mention that FCR (feed per 10 eggs) was also improved by usage of the antistress composition and was better than the target for the line. As a result more than 12000 additional eggs were obtained in the experimental group (Latypova and Shackih, 2014). It is interesting to note that egg shell strength at age 26, 36 and 56 weeks was improved in the experimental group by 2.8, 5.6 and 5.6%, respectively. The most interesting finding was related to a significant increase of the carotenoid level in the egg yolk of the experimental birds. Since carotenoids were not supplied with the antistress composition, this increase could be due to improved absorption of nutrients resulting from antistress composition usage. This can also explain improved FCR in the experimental birds. Vitamin A level in the egg yolk from the experimental layers was also increased probably reflecting its transfer from the antistress composition. Antistress composition usage was associated with improved fertility at 16, 40, 48 and 56 weeks by 2.5; 2.7; 2.8 and 3.7%, respectively. In the same experimental group the hatch of condition chickens improved at 26, 32, 40, 48 and 56 weeks by 3.6; 2.1; 3.4; 4.9 and 4.3%, respectively (Latypova, 2014a). In another study with the same antistress composition increased concentrations of the essential amino-acids in the layer's blood were shown (Fotina, 2011). Furthermore, vitamin A concentration in the liver of newly hatched chicks from the experimental group was significantly ($P < 0.05$) increased. During 28-day growth of the hybrid chickens there was a positive effect of the maternal diet on the progeny. In particular, evenness of the birds at day 28 hatched from the eggs of the experimental group at 26, 32, 40, 48 and 56 weeks was improved in comparison to the control group by 14.0; 8.7; 14.4; 7.5 and 11.7%, respectively (Latypova, 2014a; 2014c). A positive effect of the usage of PerforMax (Magic Antistress Mix) was confirmed in a big commercial trial and it was proven that the antistress composition supplied with water can improve hatching egg production efficacy and it is an economically valuable tool to be used in industry (Latypova et al., 2014).

Since molecular mechanisms of the stresses are similar in monogastric animals, the vitagene concept of fighting stresses was successfully applied for pigs as well (Surai and Melnichuk, 2012). In

particular, using PerforMax (Magic Antistress Mix) for piglets to fight stresses at weaning (Gaponov et al., 2011) and heat stress (Surai and Fotina, 2013) is shown to be effective.

Conclusions

The vitagene concept of fighting stresses emerged as a new direction in a nutritional science. Indeed, by improving the adaptive ability of animals to stress it is possible to substantially decrease negative consequences of various stresses in poultry and farm animal production. The aforementioned data clearly showed that the anti-stress composition developed on the vitagene concept is an effective means in fighting stresses in poultry and pig production.

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