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Bibliographic Review

Glutamic acid and protein reduction for broilers and commercial laying hens

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Abstract

The objective was to review the use of reduced protein, the importance of supplementation of nonessential amino acids in diets with reduced protein, the glutamate use as a source of nonessential amino acid in the diet and the interactions between glutamate and the immune system of the birds. Currently there is a growing concern regarding the use of reduced protein and non essential amino acids in the diet of birds. With the reduction in protein, also occurs the reduction of the nitrogen compunds fro formation of nonessential amino acids, requiring a source of nonessential amino acid. The L-glutamate is a synthetic nonessential source of amino acid which has major roles in the immune system and in nitrogen metabolism, plays a key role in transamination (transfer of the amino group for the α-ketoglutarate) and deamidation (liberation of amino group as free ammonia) of amino acids.

Keywords: uric acid; nonessential amino acid; excretion; nitrogen.

Ácido glutâmico e redução protéica para frangos de corte e poedeiras comerciais

Resumo

Objetivou-se revisar o uso da redução protéica, a importância da suplementação dos aminoácidos não essenciais em rações com redução protéica, o uso do glutamato como fonte de aminoácido não essencial na dieta e as interações entre o glutamato e o sistema imune das aves. Atualmente existe uma preocupação crescente em relação ao uso da redução proteica e aminoácidos não essenciais na ração de aves. Com a redução proteica, ocorre também à redução dos compostos nitrogenados para formação de aminoácidos não essenciais, sendo necessária uma fonte de aminoácido não essencial. O L-glutamato é uma fonte sintética de aminoácido não essencial que apresenta grandes funções no sistema imune e no metabolismo do nitrogênio, exerce um papel chave na transaminação (transferência do grupo amino para o α-cetoglutarato) e desaminação

Palavras-chave: ácido úrico; aminoácido não essencial; excreção; nitrogênio.

Ácido glutámico y reducción proteica para pollos de engorde y gallinas ponedoras

Resumen

Objetivo del estudio fue examinar el uso de la reducción proteica, la importancia de la administración de suplementos de aminoácidos esenciales en la ración con reducción proteica, el uso de glutamato como una fuente de aminoácido no esencial en la dieta y las interacciones entre el glutamato y el sistema inmunológico de las aves. Actualmente existe una creciente preocupación con respecto al uso de la reducción proteica y aminoácidos no esenciales en la ración de las aves. Con la reducción proteica también se produce la reducción de compuestos nitrogenados para la formación de aminoácidos no esenciales, se requiriendo una fuente de aminoácido no esencial. L-glutamato es una fuente sintética de aminoácido no esencial que presenta importantes funciones en el sistema inmune y en el metabolismo del nitrógeno, desempeña un papel clave en la transaminación (transferencia del grupo amino para α - cetoglutarato) y desamidación liberación de grupo amino como amonio libre).

Palabras clave : ácido úrico; aminoácido no esencial; excreción; nitrógeno

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Introduction

The proteins earn emphasis for being nutrients essential for the birds, they are related to vital processes of the organism, such as formation of tissues, enzymes and hormones, between others (LEESON and SUMMERS, 2001). In the background are used as sources of energy, where the carbonic skeleton of the amino acids will be forwarded to the cycle of the citric acid and amino group, eliminated in the form of urea or uric acid (NELSON and COX, 2005).

In the past, bird diets were formulated with basis in brute protein, which could result in great losses, both energetic as economical, mainly when occurred unbalancing between amino acids. Actually, it is recommended to formulate diets with amino acids in the ideal proportion, in a way that do not exist deficiencies or excesses (CAMPESTRINI et al., 2008). Since the birds do not have nutritional requirements for brute protein, but for each one of the essential amino acids constituents of the proteins and a quantity of nitrogen sufficient for the biosynthesis of the non essential amino acids (COSTA and GOULART, 2010).

In this sense, the protein reduction is being increasingly used nowadays by the researchers, besides of being seen as one via of possible improvement of the production costs. The level of brute protein of the ration is now defined as the optimal level to respond to the needs of birds in amino acids, considering the cost of the ingredients used in the formulation and the value of the produced meat (SABINO et al., 2004).

Thus, several researches point to protein reduction, with supplementation of essential amino acids in the diet, as a tool to improve the performance and reduce the nitrogen execration to the environment, since that this reduction do not compromises the provision of nitrogen for the synthesis of non essential amino acids. Some studies show that the supplementation of non essential amino acids in the diet is also used as resource to improve the birds performance, preventing essential amino acids to be used for its synthesis, therefore increasing the protein synthesis (COSTA and GOULART, 2010) and causing reduction of growth, which may compromise the deposition of lean tissue and consequently direct calories for the adipose tissue (DAHIYA et al., 2005).

Among the non essential amino acids, which present great potential to be synthetically used in diets for broilers, there is the glutamic acid. This non essential amino acid is important for the maintenance of the intestinal mucosa, for being source of energy for the mucosa turnover, via the ATP produced from the cycle of Krebs; is source of nitrogen for the synthesis of other amino acids and nitrogen compounds; and glutathione precursor (BERRES et al., 2010). The glutathione is a tripeptide composed by glutamic acid, glutamine and glycine, which acts in the mitochondrial matrix and cytosol as an antioxidant for the cells protection against the oxidative stress caused by peeroxides (CAWTHON et al., 1999; WANG et al., 1997).

The L-glutamic acid is also considered an efficient source of non specific nitrogen, capable of promoting the development and growth, improve the performance, of decreasing the incidence of problems in the legs and mortality in broilers (SILVA et al., 2001a).

Assuming that the nonessential amino acids may be a limiting factor in diets with low content of brute protein, the objective of this study was to approach the aspects of protein reduction and the importance of the L-glutamate use as source of non specific nitrogen and its participation in the immune system of animals.

Protein Reduction

The protein of the ration is one of the most important nutrients of broilers production, which has as objective the efficient conversion in muscle protein (COSTA et al., 2001), and the digestible amino acids being in ideal quantities in the ration promote increase in the protein use efficiency and maximization of use of digestible amino acids for the protein synthesis, minimizing its use as energy source (PINTO et al., 2003) and decreasing the environmental contamination by the quantity of phosphorus and excreted nitrogen (PREZZI et al., 2006).

An adult animal ingesting an adequate and balanced diet is generally in balanced nitrogen, i. e. the quantity of daily ingested nitrogen is equal to the excreted quantity. In fasting state is observed negative nitrogen balance, where more nitrogen is excreted than ingested. In state of animal growth is verified the positive nitrogen balance, where more nitrogen is ingested than excreted. Therefore, the ingestion of diets with protein reduction, depending of the protein quality and the level of consumed energy, promotes a reduction of the urinary nitrogen. After five days of negative nitrogen balance, the organism cannot adapt and the protein deficiency is accompanied by edema, loss of muscle mass, fatty liver, dermatosis, decrease of the immune response and general debility (ANGELES and TIRAPEGUI, 2007).

For this authors, in extreme cases of protein debility, protein malnutrition or in catabolic states, the organism uses adaptive mechanisms, which are regulated by the presence of nutrients or hormones, both anabolic as catabolic, with the intention of preserving the protein mass. When this process is very intense, takes place biochemical, physiological and morphological alterations

AFTAB et al. (2006) point out some probable causes for the performance reduction with diets of low protein: changes in the potassium concentrations and electrolyte balance of the diet; non specific nitrogen insufficiency for the synthesis of non essential amino acids; tendency of broilers in reduce the voluntary consumption in diets with low protein; altered relation essential amino essential and non essential amino acid; insufficient synthesis of non essential amino acid; low efficiency of use of amino acids from a free source vs. from the intact dietary protein, for the deposition of corporal protein; deficiency of some essential amino acids; relation between metabolizable energy and the liquid energy of the diet of low protein vs. diet of high protein.

The adequacy of diets to the animal demands is very hard to be performed, without occurring excessive use of some nutrients. Being common the excessive supplementation of some amino acids when these are not supplemented individually, i. e. in diets with elevated protein in the ration. Thus exceeding the levels considered sufficient to maximize responses of growth performance, immunity and yields after culling. In this context, the protein reduction of diets gains emphasis and more precise relations between the amino acids starts to be more required (BERRES et al., 2010). Among the many advantages of reducing the protein content, are highlighted the reduction of amino acids excesses, approximating the diets of ideal profile, besides of reducing the nitrogen excretion to the environment and the caloric increment of diets, which is well seen in situations of heat stress (SUIDA, 2001).

Formerly it was stated that smaller levels of dietetic protein could be used without compromising the performance of the birds, provided they were only met the requirements of the three first limiting amino acids in broilers (Methionine, Lysine and Threonine). In this sense, BERRES et al. (2010) assessed studies with rations of low protein content, aiming the need of also being met the requirements of limiting amino acids and non essential, such as the valine, isoleucine, glycine and glutamic acid, in order to avoid losses in the animals' performance.

In diets with high or normal content of protein, the non essential amino acids (AANE) can be synthesized from essential amino acids (AAE) in excess (AFTAB et al., 2006). However, with the reduction of the protein content above three to four percentage points, the AANE or nitrogen, so that these can be synthesized by the birds is limited, and even meeting the requirements of all essential amino acids, still results in the worse growth (DEAN et al., 2006; PAYNE, 2007) and composition of carcass in broiler chickens in the growth phase (BREGENDAHL et al., 2002). Therefore, the supplementation of AANE, meeting the correct balance between AAE and AANE in the birds, provides greater efficiency of the animal in the use of protein present in the diet.

Importance of supplementation of non essential amino acids

The synthesis of the non essential amino acids occurs from the ammonia and the ternary substances, or then building an amino acid at the expense of another. In the latter instance, it is common the mobilization of an essential amino acid for the synthesis of the non essential. This occurs mainly when there is an unbalance of these amino acids in the ration, because the term non essential amino acid does not mean that the same is dispensable to the growth of the animal (ANDRIGUETTO, 2002). However, in order to take place the protein synthesis, all amino acids which are components of these must be at cellular level, in the synthesis local and in correct relative proportion (MOREIRA et al., 2004).

The essential amino acids must be provided in the diet because of the animal inability in synthesize these in proper quantities, due to the absence of synthesis of appropriate α-keto acids for transamination (REECE, 2006). The non essential amino acids are synthesized from α-keto acids precursors, by the transference of a pre-existing amino group of other amino acids by the aminotransferases, also called of transaminases (DEVLIN, 2011).

The non essential amino acids are called this way for having no need to be provided in the diet.

Yet, they are as necessary to the proper functioning of the animal body as the essential amino acids, and in case of non essential deficiency, essential amino acids are used for its synthesis (COSTA and GOULART, 2010), mainly when the protein levels are very low. Therefore, it is necessary the supplementation of a source of non essential amino acids in the ration, which would save the essential amino acids in the diet (BERTECHINI, 2004).

BERRES et al. (2010), state that the similarity in performance and quality of broilers carcass fed with diets with reduced protein and control diet can be attributed to nitrogen insufficiency for the non essential amino acids synthesis, especially glycine, serine, proline and glutamic acid. It is possible that this occur due a decrease of the potassium level, unbalance between amino acids or alteration in the ionic balance. Besides it, the elevated reduction of protein promotes the unbalance of the relation essential and non essential amino acid, originating the appearing of limiting amino acids in the ration.

In order to the animal be able to synthesize body proteins, all amino acids must be present in adequate quantities in the diets, since it has source of available nitrogen, such as the L-glutamic acid. SILVA et al. (2001b) studied the effects of levels of L-glutamic acid (5, 10 and 15 %) and vitamin D_3 (0, 5,000, 10,000 and 15,000 UI) in the diet of broilers of one day. The authors verified that the proteins (12.6% with 5% L-Glu; 17.1% with 10% L-Glu; 21.7% with 15% L-Glu) balanced in relation to the glutamate are used with greater efficiency with 10% of L-Glutamete and 15,000 UI of vitamin D_3, obtaining improvement in performance and reduction in incidence of legs problems. Confirming that this amino acid is a good source of non specific nitrogen to maximize the performance and reduce the incidence of legs problems.

SILVA et al. (2001b) verified that the unbalancing of glutamic acid in the broilers fed with 5% of L-Glutamate promoted increased incidence of legs problems. Moreover, with 15% of L-Glutamate there was significant decrease in the birds performance, probably due the elevated excretion of nitrogen provided by the diet, once all amino acid causes toxicity when are above the animal need.

HAN et al. (1992) reported the non specific amino nitrogen as a limiting factor in diets of low protein, indicating the need of supplementation of non essential amino acids (glycine and glutamic acid) as alternative for the performance improvement. These same authors verified that broilers between 1 to 21 days of age fed with diet based on maize and soybean meal, with 19% of PB, supplemented with methionine, lysine, threonine, arginine, valine and glutamic acid, had a performance equivalent to those fed with diet of 23% of PB. From 22 to 42 days of age, the broilers that received 16% of PB, supplemented with the same amino acids, had performance similar to those which received the control diet with 20% of PB, not having, including, difference in the body fat content.

Glutamate in the diet

Most of the glutamate ingested in the diet is metabolized by the intestine, both for energy generation and conversion in other amino acids. In providing of elevated protein reduction for the animal, without supplementation of a source of nitrogen, the organism capacity to synthesize amino acids can get compromised and the non essential amino acids can become limiting in the animal organism (REEDS, 2000).

The glutamic acid acts in the intestine, and its effects are observed directly on the enterocytes, cells which compose the villosities of the intestinal mucosa, responsible by the nutrients absorption. The enterocytes present high rates of turnover during the animal growth and depend of this amino acid as precursor for the cellular metabolism (AJINOMOTO, 2007).

The glutamic acid and the glutamine are two non essential amino acids which are closely related, they have a vital role in the nitrogen metabolism due to its amino groups get together with the α-amino and amido group (NEWSHOLME et al., 2003), providing half of the nitrogen demand for the purine and pyrimidine synthesis and also for some amino acids (LOBLEY et al., 2001). Yet, present different functionally roles in the intestine. The metabolism extension of glutamate in the lumen of the small intestine is superior to the metabolism of the arterial metabolism. Nevertheless, the glutamate concentration in the intestine has no significant effect on the use of intestinal glutamine (REEDS et al., 2000).

This authors studied the intestinal metabolism of glutamate, glucoses and glutamine in swine and verified that the greatest contributor to the energy generation by the intestine was the glutamate of the diet. The authors showed that the enteral glutamate, enteral glucose and arterial glutamine contribute with 36.6 and 15%, respectively, of production of CO_2 by the viscera drained through the portal vein, i. e. the enteric glutamate is an oxidant much more important in the Krebs cycle to generate energy than the enteric glucoses or arterial glutamine. This study provides subsides to understand that the glutamate of the diet performs an important role in the intestine. Moreover, these functions are apparently different from those of arterial glutamine.

However, the glutamate, especially the originated from the diet, can easily substitute the glutamine in many of its metabolic roles, including the generation of energy and the synthesis of amino acids (REEDS et al., 2000). Therefore, the glutamate is used in some ways for the substitution of glutamine, being the common way between these two amino acids the metabolization of glutamine to glutamate, plus ammonia through the glutaminase. The glutamate is degraded in α-cetoglutarato via transamination through the glutamate synthase enzyme (REEDS and BURRIN, 2001), and can also be transformed in glutamine by the action of glutamine synthetase (MAIORKA et al., 2002), being then considered as exchangeable substrates in the intestinal mucosa (WU et al., 1995).

The dietary glutamate participates as specific precursor of biosynthesis of glutathione, arginine and proline in the mucosa of the small intestine (REEDS et al., 2000). The glutathione is a tripeptide (glutamic acid, glutamine and glycine) that acts as an antioxidant for the cells protection against the oxidative stress caused by peroxides (CAWTHON et al., 1999; WANG et al., 1997). Therefore, the glutamate performs an important role in the removal of oxidants and in regulation of the antibody response (LI et al., 2007; WU et al., 2004).

The glutamate is also a precursor of arginine and proline. In the mammals, the arginine is synthesized through the glutamate-5-semialdehyde which is transaminated to ornithine in a catalyzed reaction by the ornithine aminotransferase. From there, the ornithine enters in the urea cycle and forms arginine. Therefore, the ornithine precursor of citrulline, arginine and proline is also synthesized from the glutamate (NELSON and COX, 2005). Yet, the enzyme carbamyl phosphate synthetase is absent in the birds. Thus the arginine is not regenerated from the ornithine, as occurs in the mammals. With this the arginine is nutritionally essential for the birds (MOREIRA and SCAPINELLO, 2004).

The proline is formed through the reaction between carboxyl gamma of glutamate and the ATP, resulting in a compound named glutamate -5-phosphate. The enzyme that acts in this reaction is the glutamyl kinase. The glutamate 5 phosphate is reduced by NADPH to glutamate-5-semialdehyde (semialdehyde glutamic), which becomes spontaneously cyclical forming the pyrroline-5-carboxylate, this undergoes a final catalyzed reduction by the pyrroline-5-carboxylate reductase, a enzyme which requires NADPH. This last reduction results in the formation of proline (REECE, 2006).

Indeed, the intestine has great need of glutamate, has been verified that from every ingested glutamate through food, only 4% is transported from the enterocyte to the blood, to be reused by the body. Thus, the organism needs to virtually synthesize all glutamate that is necessary. This applies specially to the brain, where the glutamate is used as a neurotransmitter. The hematoencephalic barrier that controls the type of molecules that enter the brain does not allow the passing of the glutamate, thus the brain needs to produce its own glutamate from the glucoses and from other amino acids (REEDS et al., 1997).

The glutamate also acts as excitatory neurotransmitter widely distributed by the central nervous system. The glutamate is recycled in the neurons and in glial cells (astrocytes). The glial cells transform the glutamate in glutamine, which then diffuses back to the neuron. The mitochondrial glutaminase in the neuron produces agains the glutamate for reuse. The activation of its N-methyl-D-aspartate receptor increases the sensibility to the stimulus of other neurotransmitters (MOTTA, 2003).

Glutamate as nutrient for the immune system

The body defense comes from a complex system of overlapped and interlocked mechanisms, named immune system. A failure of this mechanism can result in diseases or even in death of the animal. So that the organism can expel invaders which cause illnesses, are necessary many defense systems which can interact against several types of invaders or destroy specific organisms. Some systems act only in the body surface (innate immunity), others act internally combating pathogens that have managed to overcome the external mechanism of defense, and learning to recognize them when finding them again (acquired immunity) (TIZARD, 2002).

The nutrients have a direct role in the immunology for serving as a substrate and enzyme cofactors for cellular multiplication during the immune response (phagocytes, lymphocytes), and for the synthesis of effector molecules (antibodies, nitric oxide, lysozyme) or molecules of communication (cytokines, inflammatory mediators). They can also have an indirect effect in the immune response by modifying the intra and extra cellular routes of communication (cytokines) or limiting undesired effects of effector molecules. Finally, the immune system is regulated by many hormones, many of which respond to nutrients such as glucose, relation protein/energy, amino acids, among others (GENTON and KUDSK, 2003; KLASING et al., 1980).

In this sense, the high yield observed in the animal exploitation depends, amongst other factors, of the adequate obtaining of nutrients by the organism. For so, specific diets for each stage of life, lineage and different weathers have been exhaustively researched and used. However, for these diets being properly digested and absorbed, the intestinal mucosa must present adequate morphophysiological structural characteristics. The absorption processes are dependent of transport mechanisms, which occur in the mucosa epithelial cells membrane, being in this sense, of great importance the integrity of the same, since that it is the via of nutrients entry for the animal development (MAIORKA et al., 2000).

Therefore, it is always good to supplement with some nutrients which can positively influence the absorption capacity of the intestinal mucosa, because they modify its structure and metabolism, resulting in improvement of the digestion capacity and absorption of nutrients by the birds (FREITAS et al., 2001). These substances are considered trophic agents, that according to MAIORKA et al. (2002) are capable of stimulating the mitotic process and, as consequence, increase the number of cells and size of the villi.

Amongst the important amino acids for the reestablishment of the animal, there is the glutamate. This amino acid performs several functions in the metabolism and in the function of leukocytes (NEWSHOLME et al., 2003). The glutamate regulates the inducible nitric oxide synthase (iNOS) in specific tissues, such as the brain. The expression of iNOS is considered as a fundamental mechanism in the protection against parasites, bacteria, fungi, malignant cells, intracellular protozoa and viruses in different animal species, including both mammals and birds (LI et al., 2007).

The nitric oxide (NO) is synthesized from the arginine by the inducible nitric oxide synthase (iNOS), being produced in many areas of the brain where its function is related to the neurotransmitter function of the glutamate. When the glutamate is freed from a neuron, it binds to receptors, where is triggered a flux of Ca^{2+} through the post synaptic membrane, estimulating the synthesis of iNOS. Once synthesized, the nitric oxide diffuses from the source cell to the pre-synaptic cell, promoting a liberation of glutamate. In this sense, the NO acts as a retrograde neurotransmitter, and promotes a cycle in which the glutamate is released from the pre synaptic neuron connecting and promoting potentials of action in the post synaptic neuron (MOTTA, 2003).

Moreover, the decarboxylation of glutamate originates the γ-aminobutyrate (GABA), inhibitor neurotransmitter of the central nervous system, produced by some cells of the peripheral tissue, such as the β cells of pancreatic islets. It is also present in lymphocytes (TIAN et al., 2004) and macrophages (STUCKEY et al., 2005). The glutamate also acts in the metabolism of leukocytes, as energy substrates. It is considered a central and peripheral neurotransmitter of the nervous system, acting on the ionotropic and metabotropic receptors, which perform several functions in the modulation of the immune system (NEWSHOLME et al., 2003).

In this sense, it can be considered that the glutamate is one of the main fuels for enterocytes (WU, 1998), keeping the integrity of the intestinal barrier and preventing the intestinal translocation of microorganisms for the systemic circulation (VAN DER HULST et al., 1993).

In studies with swine, MOLINO et al. (2012) assessed in one of their experiments the effects of use or not of 0.80% glutamine + acid glutamic in rations with different levels of lactose (0, 4 and 8%) for piglets weaned at 21 days of age. The author observed that the supplementation of amino acids influences positively in the weight gain of piglets from 21 to 49 days old and promoted increase of the villus height in all three segments of the small intestine (duodenum, jejunum and ileum). According to the author, the effect of glutamine and of glutamic acid proved to be evident even that was not induced any inflammatory response in animals.

Conclusions

The formulation of ration with protein reduction must provide all necessary nutrients to the animals' demand, without excess or lack, therefore being formulated according to the concept of ideal protein.

The non essential amino acids are as essential to the proper functioning of the animal organism as the essential amino acids, and when we reduce the protein in the ration we are reducing as well the necessary nitrogen for the non essential amino acids synthesis. In this sense, it is expected that the supplementation of glutamic acid in rations for broilers and laying hens meet the necessary requirement of nitrogen to provide improvements in the performance and quality of carcass and eggs of the birds, and consequently provide income to the producer.

References

AFTAB, U.; ASHRAF, M.; JIANG, Z. et al. Low protein diets for broilers. **World's Poultry Science Journal**, v.62, p.688-701, 2006.

AJINOMOTO ANIMAL NUTRITION. **AminoGut-Aminoácidos para a função intestinal,** 2007. Disponível em: <http://www.lisina.com.br/upload/Artigo%20Amino Gut_port (1).pdf.>. Acesso em: 29/10/2012.

ANDRIGUETTO, J.M. Nutrição animal. As bases e os fundamentos da nutrição animal - alimentos. Editora Nobel, v.1, 395p. 2002.

ANGELES, R.C.; TIRAPEGUI, J. **Fisiologia da Nutrição Humana**. Aspectos Básicos, Aplicados e Funcionais. Metabolismo de proteínas. Cap.06, p.69-109, Editora Atheneu, São Paulo, 2007.

BERRES, J. ; VIEIRA, S.L.; DOZIER III, W.A. et al. Broiler responses to reduced-protein diets supplemented with valine, isoleucine, Glycine, and glutamic acid. **Journal of Applied Poultry Research**. v.19, p.68-79, 2010.

BERTECHINI, A.G. **Nutrição de Monogástricos**. Lavras :Editora UFLA/FAEPE, 2004. 450p.

BREGENDAHL, K.; SELL, J.L.; ZIMMERMAN, D.R. Effect of low protein diet on performance and body composition of broiler chicks. **Poultry Science**, v.81, p.1156-1167, 2002.

CAMPESTRINI, E.; BARBOSA, M.J.B.; NUNES, R.V. et al. Níveis de lisina com dois balanços eletrolíticos para frangos de corte na fase de crescimento (22 a 40 dias). **Revista Brasileira de Zootecnia.** v.37, n.8, p.1405-1411, 2008.

CAWTHON, D.; MCNEW, R.; BEERS, K. et al. Evidence of mitochondrial dysfunction in broilers with pulmonary hypertension syndrome (Ascites): effect of t-butyl hydroperoxide on hepatic mitochondrial function, glutathione, and related thiols. **Poultry Science**, v.78, p.114–124. 1999.

COSTA, F.G.P.; GOULART, C.C. Exigências de aminoácidos para frangos de corte e poedeiras. **In. Anais** II Workshop de Nutrição de Aves. Universidade Federal da Paraíba, UFPB, 2010.

COSTA, F.G.P.; ROSTAGNO, H.S.; ALBINO, L.F.T.; et al. Níveis dietéticos de proteína bruta para frangos de corte de 1 a 21 e 22 a 42 dias de idade. **Revista Brasileira de Zootecnia.** v.30, p.1498-1505, 2001.

DAHIYA, J.P.; HOEHLER, D.; WILKIE, D.C. et al. Glycine concentration affects intestinal clostridium perfringens and lactobacilli populations in broiler chickens. **Poultry Science**, v.84, p.1875-1885, 2005.

DEAN, D.W.; BIDNER, T.D.; SOUTHERN, L.L. Glycine supplementation of low protein, amino acid-supplemented diets supports equal performance of broiler chicks. **Poultry Science**, v.85, p.288-296, 2006.

DEVLIN, T.M. **Manual de bioquímica com correlações clínicas**. 7ª ed. São Paulo: Editora Edgard Blücher Ltda, 2011. 1252p.

FREITAS, B.C.F.; BAIÃO, N.C.; NUNES, I.J. Fisiologia digestiva do frango de corte nos primeiros dias de vida: digestão da gordura. **Cadernos técnicos de veterinária e zootecnia**, Belo Horizonte: FEP MVZ, n.34, p.7-13, 2001.

GENTON, L.; KUDSK, K.A. interactions between the enteric nervous system and the immune system: role of neuropeptides and nutrition. **The American Journal of Sugery**. v.186, p.253-258, 2003.

KLASING, K.; KNIGHT, C.D.; FORSYTH, D.M. Effects of iron on the anti-coli capacity of sow's milk in vitro and in ligated intestinal segmentes. **The Journal of Nutrition,** v.110, p.1914-1921, 1980.

HAN, Y.; SUZUKI, H.; PARSONS, C.M. et al. Amino acid fortification of a lowprotein corn and soybean meal diet for chicks. Poultry Science, v.71, p.1168-1178, 1992.

LEESON, S.; SUMMERS, J.D. **Nutrition of the chicken**. 4.ed. University Books: Ontario, Canadá, 2001. 591p.

LI, P.; YIN, Y.L.; LI, D. et al. Amino acids and immune function. **British Journal of Nutrition**, v.98, p.237-252. 2007.

LOBLEY, G.E.; HOSKIN, S.O.; MCNEIL, C.J. Glutamine in animal science and production. **The Journal of Nutrition**, v.131, p.255-2531, 2001.

MAIORKA, A.; BOLELI, I.C.; MACARI, M. Desenvolvimento e reparo da mucosa intestinal. In: MACARI, M.; FURLAN, R.L.; GONZÁLES, E. (Eds) F**isiologia aviária aplicada a frangos de corte**, Jaboticabal: FUNEP/UNESP, 2002. 375p.

MAIORKA, A.; SILVA, A.V.F.; SANTIM, et al. Influência da suplementação de glutamina sobre o desempenho e o desenvolvimento de vilos e criptas do intestino delgado de frangos de corte. **Arquivos Brasileiros de Medicina Veterinária e Zootecnia**, v.52, n.5, 2000. n.pag.

MOLINO, J.P.; DONZELE, J.L.; OLIVEIRA, R.F.M. et al. L-glutamate in diets with different lactose levels for piglets weaned at 21 days of age. **Revista de Zootecnia,** v.41, p.98-105, 2012.

MOREIRA, I.; SCAPINELLO, C. Metabolismo Protéico em Aves. **In:** SAKOMURA, Nilva Kazue; MORAES, Vera Maria Barbosa de; MENDES, Ariel Antonio; FUKAYAMA, Ellen Hatsumi. (Org.). **Curso de Fisiologia da Digestão e Metabolismo dos Nutrientes em Aves**. Jaboticabal-SP, 2004.

MOREIRA, I.; SCAPINELLO, C.; SAKAMOTO, M.U. Fisiologia da digestão e absorção de proteínas em aves. **In:** SAKOMURA, Nilva Kazue; MORAES, Vera Maria Barbosa de; MENDES, Ariel Antonio; FUKAYAMA, Ellen Hatsumi. (Org.). Curso de Fisiologia da Digestão e Metabolismo dos Nutrientes em Aves. Jaboticabal-SP, 2004.

MOTTA, V.T. **Bioquímica clinica para laboratório: metabolismo do nitrogênio.** 4ª Ed. Porto Alegre: Editora Médica Missau, Cap.11, p.319-357, 2003.

NELSON D.L.; COX M.M. **Lehninger – Principles of Biochemistry**, 4ª ed. Freeman, NY. 2005.

NEWSHOLME, P. et al. Glutamine and glutamate as vital metabolites. **Brazilian Journal of Medical and Biological Research**, v.36, p.153-163, 2003.

PAYNE, R. L. The potential for using low crude protein diets for broilers and turkeys. **Degussa AminoNews**, v.8, p.2-13, 2007.

PINTO, R.; DONZELE, J.L.; FERREIRA, A.S. et al. Exigência de metionina mais cistina para codornas japonesas em postura. **Revista Brasileira de Zootecnia**, v.32, n.5, p.1166-1173, 2003.

PREZZI, J.A.; ARAÚJO, L.F.; JUNQUEIRA, O.M. et al. Redução do nível protéico da dieta com a suplementação de aminoácidos. **Revista Brasileira de Ciência Avícola** (Suplemento 8), p.87, 2006.

REECE, W.O. **Dukes, Fisiologia dos animais domésticos**, 12ª Ed. Rio de Janeiro: Guaanabara Koogan, 2006. 926 p.

REEDS, P.J.; BURRIN, D.G. Glutamine and the bowel. **The Journal of Nutrition**, v.131, p-2505-2508, 2001.

REEDS, P.J. Criteria and Significance of Dietary Protein Sources in Humans. Dispensable and Indispensable Amino Acids for Humans. **Journal Nutrition**. v.130, p.1835-1840, 2000.

REEDS, P.J.; BURRIN, D.G.; STOLL B.; et al. Intestinal glutamate metabolism. **Journal Nutrition**. v.130, p.978-982, 2000.

REEDS, P.J.; BURRIN, D.G.; STOLL, B. et al. Enteral glutamate is the preferential source for mucosal glutathione synthesis in fed piglets. **American Journal Physiology,** v.273, p.408-415, 1997.

ROSTAGNO, H.S; TOLEDO, R.S; ALBINO, L.F.T. **Programa de alimentação com "5" fases para frangos de corte.** 2002. Disponível em: <http://www.polinutri.com.br/upload/artigo/156.pdf.>. Acesso em: 27/10/2012.

SABINO, H.F.N.; SAKOMURA, N.K.; NEME, R. et al. Níveis protéicos na ração de frangos de corte na fase de crescimento. **Pesquisa Agropecuária Brasileira**, v.39, n.5, p.407-412, 2004.

SILVA, J.H.V.; ALBINO, F.T.; NASCIMENTO, A.H. et al. Níveis de energia e relações energia: proteína para frangos de corte de 22 a 42 dias de idade. **Revista Brasileira de Zootecnia**, v.30, n.6, p.1791-1800, 2001a.

SILVA, F.A.; MORAES, G.H.K.; RODRIGUES, A.C.P. et al. Efeitos do Ácido L-Glutâmico e da Vitamina D3 no Desempenho e nas Anomalias Ósseas de Pintos de Corte. **Revista Brasileira de Zootecnia**, v.30, n.6, p.2059-2066, 2001b.

SUIDA, D. Formulação por Proteína Ideal e Conseqüências Técnicas, Econômicas e Ambientais. In: **I Simpósio Internacional de Nutrição Animal:** Proteína ideal, energia líquida e modelagem – Santa Maria, RS – Brasil, p.1-17, 2001.

STUCKEY, D.J.; ANTHONY, D.C.; LOWE, J.P. et al. Detection of the inhibitory neurotransmitter GABA in macrophages by magnetic resonance spectroscopy. **Journal Leukocyte Biology,** v.78, p.393-400, 2005.

TIAN, J.D.; LU, Y.X.; ZHANG, H.W. et al. G-Aminobutyric acid inhibits T cell autoimmunity and the development of inflammatory responses in a mouse type I diabetes model. **Journal Immunology**, v.173, p.5298-5304, 2004.

TIZARD, I.R. **Imunologia veterinária: Uma introdução**. 6ª edição. São Paulo: Rocca; 2002.

VAN DER HULST, R.R.; VAN KREEL, B.K.; VON MEYENFELDT, M.F. et al. Glutamine and the preservation of gut integrity. **Lancet,** v.341, p.1363-1365, 1993.

WANG, S.; BOTTJE, W.; MAYNARD, P. et al. Effect of santoquin and oxidized faton liverand intestinal glutathione in broilers. **Poultry Science**, v.76, p.961-967, 1997.

WU, G.; FANG, Y.Z.; YANG, S. et al. Glutathione metabolism and its implications for health. **Journal of Nutrition**, v.24, p.134-489. 2004.

WU, G. Intestinal mucosal amino acid catabolism. **The Journal of Nutrition,** v.128, p.1249-1252, 1998.

WU, G.; KNABE, D.A.; YAN, W. et al. Glutamine and glucose metabolism in enterocytes of the neonatal pig. **American Journal Physiology**, v.37, p.334- 342, 1995.