Arginine: an underrated amino acid in weaned piglets

Abstract

Arginine is a versatile amino acid which exerts multiple key functions in metabolic pathways playing a role in growth and immunity.
Research related to arginine supplementation in swine has mainly focused on sows during gestation, where it is proven to be effective in enhancing reproductive performance. Other physiological stages have received far less attention by researchers and industry. Nowadays, availability of L-arginine, obtained through fermentation has increased and price has dropped, opening the door for a more in-depth look on how arginine can enhance health and performance in all phases of swine production. This article will summarize key elements why arginine should be considered in feed formulations with a focus on young piglets.

Bart Matton
CJ Europe

Background

In contrast to poultry where arginine (Arg) is an essential amino acid as poultry lack a functional urea cycle (uricotelic animals), swine are ureotelic animals and in theory capable of synthetizing Arg *de novo via* the urea cycle. However, this important pathway, responsible for ammonia detoxification, does not provide a net synthesis of Arg due to an exceedingly high activity of cytosolic arginase that rapidly hydrolyzes Arg (Wu & Morris, 1998). The main endogenous production site for Arg in pigs is the so called 'intestinal renal axis'. An interplay between the enterocytes, which produces citrulline (from its precursors glutamine/glutamate and proline) and which is then transformed into Arg in the kidneys and then circulated throughout the body (Figure 1).
In 2012, the NRC classified Arg as conditionally essential for all stages of swine, meaning that under certain conditions such as stress or disease, Arg is not synthesized sufficiently. They recommend a level of SID Arg in the diet of 0.68% and 0.61% for weanling piglets of 5-7kg and 7-11kg respectively (NRC, 2012). The paucity of literature and data on the requirement of Arg in swine combined with current feed formulations usually exceeding NRC recommendations coupled with the fact that mammals are considered to be capable of producing Arg *de novo*, has led for this amino acid to be off the radar of most swine nutritionist for quite some time.

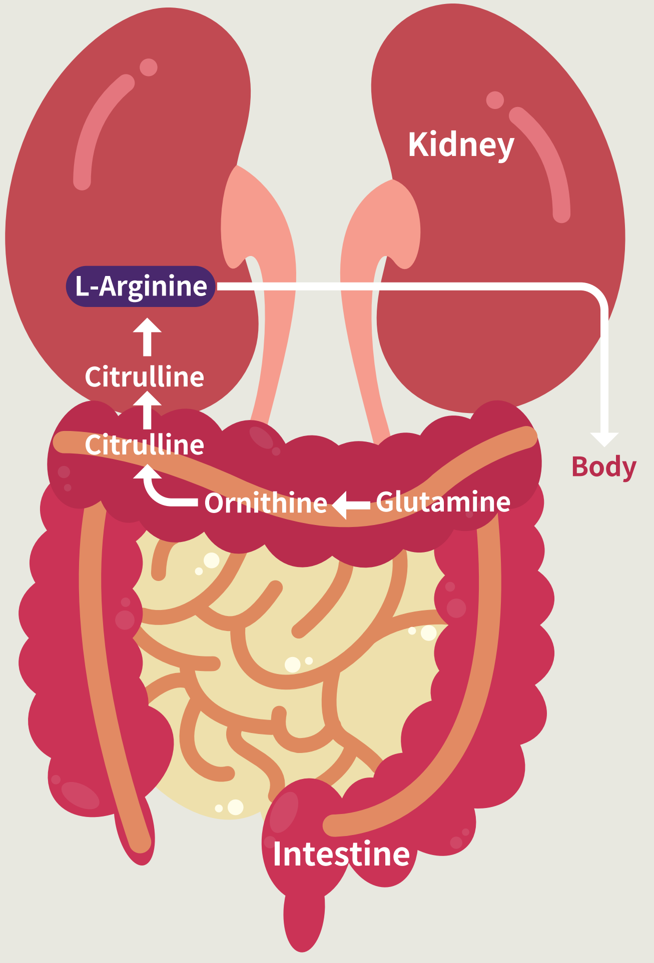

Figure 1. *De novo* synthesis of arginine - intestinal renal axis

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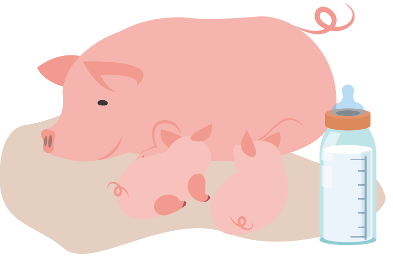
Importance of arginine in the body

The production of Arg in neonatal piglets starts with endogenous production of Arg via citrulline in the enterocytes. In the suckling piglet, sow milk supplies Arg metabolites such as proline and glutamine rather than Arg itself (Wu et al., 2018). Around weaning, intestinal arginase activity increases and dietary Arg is catabolized to a larger extent as compared to suckling piglets in which arginase activity is absent (Wu et al., 1996). We also need to take into account that piglets have reduced feed intake around weaning and an immature gastrointestinal tract that threatens the supply of Arg or precursors such as glutamine/proline. Only about 60% of the dietary Arg reaches the portal vein (Wu et al., 2018); where it is further used for the formation of others physiological compounds such as nitric oxide, creatine and polyamines.
Nitric oxide is an important signaling molecule and impacts the cardiovascular system, e. g. regulating blood flow and pressure (Lundberg and Weitzberg, 2022). Polyamines on the other hand are important for cell differentiation (Pegg, 2016) and finally creatine is essential for cellular energy metabolism (Balestrino, 2021). The Arg metabolites first found in the milk and later produced by the piglet itself are essential for neonatal performance, gut development, and immune function in the weanling pig (Liao 2021 & Yang and Liao 2019). Even though the Arg de novo synthesis is present in pig (lets), it is not clear if the amount of Arg produced is sufficient to cover the Arg requirement since a multitude of processes require Arg along with immune function.



Game changers in piglet nutrition

In the past years, weaned piglet feed formulations have changed dramatically, especially in the European Union. Prohibition to use medicinal dosages of zinc oxide after weaning has led to reduction of feed crude protein (CP) content. Lowering CP in the diet and meeting essential amino acid requirements has been proven as an effective strategy to keep up performance while supporting intestinal health, because excess protein is fermented in the hindgut and enhances proliferation of pathogenic bacteria leading to post-weaning diarrhea (Rodrigues et al., 2022). Ecofriendly swine production on the other hand has been a second driver to reduce feed CP content further as excessive CP will lead to higher N-excretion. On average, 1% CP reduction leads to a 10% reduction of the total nitrogen excretion (Dalibard et al., 2014). Due to mainly ecological motives, the amount of soybean meal (SBM) is reduced or fully banned and replaced by other, often local protein sources. However, these protein sources may not have the same amino acid profile or digestibility as SBM.

All above reasons have led to:

- **A more challenging environment for weaned piglets, which can no longer benefit from a basic intestinal protection offered through preventive usage of antimicrobials**
- **A change in formulation habits which leads to a change in amino acid supply.**

Applying the ideal protein concept and consequently the use of free amino acids such as lysine (Lys), methionine (Met), threonine (Thr), tryptophan (Trp) and valine (Val) and the recent development of new fermentation based free amino acids such as L-isoleucine (Ile) and L-histidine (His) have helped to maintain performance in a low CP diet. However, the amount of Arg in the diet has been declining largely unnoticed over the past years, whilst conditions changed. Increased stress and reduced intestinal health led to a change in metabolic state and might therefore require even higher amounts of Arg than before.

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Concentration of Arg needed in post-weaning piglet

Due to the large variety of raw materials used, varying CP content and Lys concentration in piglet formulations around the globe, it is hard to pinpoint an average value of the actual digestible (d) Arg or dArg to dLys ratio (dArg/dLys). However, in most of the cases, the values are above the recommendations set by the NRC namely 0.61% dArg in the diet of 7 to 11 kg piglets. The optimal concentration of true digestible amino acids in diets for swine from Texas A&M university (Wu, 2014) are 1.19% and 1.01% dArg in the diet as optimal values for piglets ranging from 5-10kg and 10-20 kg respectively, corresponding to a ratio of about 100% dArg/dLys. Recently, two proof of concept trials on the topic were executed in the US supported by CJ BIO. A first trial showed 1.66% dArg in the diet as an optimal concentration (Perez-Palencia et al., 2022). A second trial, executed at Iowa State University, also looking at intestinal effect of adding Arg in weaned piglets' feed indicated an optimal value of 1.55% dArg (Greiner et al., 2023). The values described above correspond to overall dArg/dLys ratios ranging from 100-110% for weaned piglets, which is closer to the recommendations of Wu (2014) than NRC (2012).

Practical application of arginine in piglet diets

In order to test the outcomes from the two US trails under commercial rearing conditions and EU formulations (no ZnO, low CP), a practical 3-phase feeding post weaning (PW) trial was organized with a German compound feed producer (phase 1: 0-10 days PW, phase 2: 11-28 days PW - phase 3: 29-49 days PW). The study contained a market-usual piglet feed (control), formulated with crystallin amino acid (Lys, Met, Thr, Trp, Val) to meet assumed requirement of essential amino acids proposed by CJ Europe. The control was compared to a reduced CP diet also corrected to meet the assumed requirement of the essential amino acids (T1) -extra addition of His and Ile was needed and to a 2nd treatment (T2) in which T1 was further corrected to SID 105% dArg/dLys by an on top addition of L-Arg. The control diet had a CP level of 17.7% in phase 1, 17.6% in phase 2 and 17.4% in phase 3. In the treatment diets the dietary CP level was reduced by about 1%-point to 16.5% in phase 1 and phase 2, but was not reduced in phase 3.

1173 piglets were weighed prior to the trial start and equally allocated to one of 3 treatments, to provide a uniform distribution between the groups regarding start weight and sex. Average starting weight was about 6.3 ± 0.030 kg. The diets were mainly based on barley, wheat, and soy products.

There were no statistically significant differences in performance of the piglets in the low-CP group and the Arg enriched feed (T1 and T2, respectively) in comparison to the control group at the end of the trial. However, animals which received the low-CP feed and the Arg enriched feed showed a numerically higher ADG and lower FCR compared to the control (Figure 2). Consequently, final body weight of the piglets in the treatment groups (27.95 ± 2.36 kg and 28.59 ± 1.60 kg, respectively) were also numerically higher compared to the control (27.46 ± 2.42 kg) (Figure 3). The results of this study showed that a CP reduction around 1%-point is possible while maintaining animal´s performance and that addition of Arg to reach 105% dArg/dLys in the feed further increases performance in a low CP diet when properly corrected for essential amino acids.

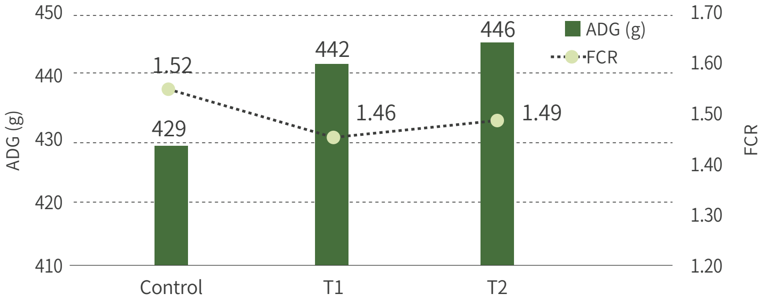

Figure 2. Effect of a low CP or an Arg rich low CP diet on FCR and ADG of weaned piglets during a seven week study period.

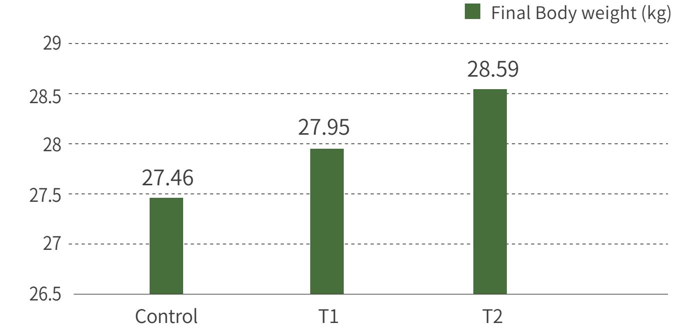

Figure 3. Effect of a low CP or an Arg rich low CP diet on final body weight of weaned piglets during a seven week study period.

Conclusion

The importance of Arg to maintain optimal health and performance in swine and especially piglets cannot be underrated since Arg is involved in many metabolic processes. Huge evolutions in piglet rearing conditions such as lower milk provision by the sow due to hyper prolificacy, increased stress on the immature digestive system and the use of low CP formulations around weaning to prevent post-weaning diarrhea are triggering a reduction of dietary Arg or its precursors (e.g. glutamine, glutamate, and proline) for the young pig. Supported by advancements in research and availability of crystalline amino acids, we need to be aware that some amino acids, not considered in the formulation until now, such as Arg, will enable us to exploit the full potential of piglets in the new reality of pig breeding.

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