Effects of Glutamic Acid and Aspartic Acid on Growth Performance and Intestinal Function in Weaned Piglets: Postprint

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Abstract

This article provides a comprehensive review of the effects of glutamate and aspartate on growth performance and intestinal function in weaned piglets.

Full Text

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Abstract

Glutamate and aspartate serve as crucial energy sources for intestinal epithelial cells and can be converted into other nutrients through decarboxylation or transamination. They play vital roles in maintaining porcine growth performance and normal intestinal function, regulating signaling pathways, alleviating oxidative stress, modulating gene expression, and mediating neural regulation. This review primarily summarizes the effects of glutamate and aspartate on growth performance and intestinal function in weaned piglets.

Keywords: glutamate; aspartate; weaned piglets; growth performance; intestinal function

Classification Code: S828

Glutamate (Glu) and aspartate (Asp) are acidic amino acids containing two carboxyl groups with isoelectric points below 7. Traditionally considered nonessential amino acids in nutrition [1-2], Glu and Asp can be interconverted or metabolized into other amino acids through transamination and decarboxylation in animal tissues such as the small intestine, liver, and kidneys to meet physiological demands. Consequently, exogenous supplementation of Glu and Asp has received limited attention in human diets and animal feed. However, recent research has demonstrated that Glu and Asp play important roles in porcine growth performance, gene expression regulation, cell signaling pathways, hormone secretion, antioxidant capacity, and neural modulation [1,3-5], and show great potential in swine growth, development, reproduction, and lactation [6-7]. Notably, during intestinal absorption and metabolism, glutamine, Glu, and Asp serve as the primary sources for energy production and carbon dioxide generation rather than glucose [8], suggesting that Glu and Asp may function as functional amino acids critically important for intestinal health in pigs. Therefore, this review focuses on the effects of Glu and Asp on growth performance and intestinal function in weaned piglets, aiming to provide a reference for future research on their impact on intestinal health.

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1 Basic Functions of Glu and Asp

Glu and Asp contain two carboxyl groups within their molecular structure and possess a sour, umami taste. Asp, also known as aspartic acid or asparagic

acid, is chemically named aminobutanedioic acid and appears as white crystals or powder. First discovered in asparagus plants in 1962, Asp has an isoelectric point of 2.77. Glu, chemically named aminoglutaric acid or aminocarboxyvaleric acid, forms colorless crystals and was first discovered by Ritthauser in 1866, with its structure confirmed by Wolff in 1890 [4]; its isoelectric point is 3.24. In animal and cellular studies, Glu and Asp can be converted into other substrates (such as glutathione, arginine, citrulline, and glutamine) through transamination and decarboxylation in tissue cells, thereby exerting important physiological functions [7]. Additionally, Glu and Asp serve as crucial excitatory neurotransmitters in the body [9-10] and represent the primary energy source for the small intestine [8]. They can also form chelates with cations for therapeutic applications in cardiac disease and liver injury [11-12].

2 Effects of Glu and Asp on Growth Performance of Weaned Piglets

Current research on the direct effects of Glu and Asp on weaned piglet growth performance remains limited, though these amino acids demonstrate positive effects on pig growth under stress conditions [13-17].

2.1 Direct Effects of Glu and Asp on Weaned Piglet Growth Performance

When dietary protein level is 17%, with Asp at 1.3%–1.5% and Glu at 2.6%–2.9%, growth in weaned piglets is promoted and amino acid utilization is improved. However, at 17% dietary protein, 3.2% Glu inhibits piglet growth, and 3.5% Glu significantly affects blood glucose levels and energy metabolism [18]. Dietary supplementation with 1% Glu promotes healthy growth, reduces feed-to-gain ratio, and alleviates weaning stress in 28-day-old piglets, thereby improving feed conversion efficiency and immune capacity [19]. When lactose is added to the diet, supplementation with 0.8% L-glutamine and L-Glu enhances growth performance in piglets weaned at 21–35 days of age [20].

2.2 Intervention Effects of Glu and Asp in Weaned Piglet Stress Models

Research indicates that Asp shows no significant effect on piglet growth performance before lipopolysaccharide (LPS) injection (days 1–16), but after LPS challenge (days 17–24), 0.5% or 1.0% Asp significantly mitigates the decrease in average daily gain caused by LPS stimulation [14]. Additionally, the dramatic weight loss induced by scalding can be alleviated through Asp injection [15]. In a diquat-mediated oxidative stress model in weaned piglets, dietary supplementation with 2% Glu significantly reduces oxidative stress-induced weight loss [16]. Dietary 2% Glu also alleviates the decrease in average daily feed intake caused by deoxynivalenol (DON) in piglets, significantly increases average daily gain, and reduces feed-to-gain ratio [21]. Supplementing creep feed with monosodium

glutamate or Glu significantly improves feed conversion efficiency in piglets [22].

When 1% Asp and 2% Glu are added individually or in combination to the diet, they alleviate the growth performance inhibition caused by hydrogen peroxide ($H_{2O}2$)-mediated intestinal oxidative damage, increase average daily feed intake (Figure 1 [Figure 1: see original paper]), and reduce feed-to-gain ratio [23].

In summary, Asp and Glu can alleviate stress and improve growth performance in weaned piglets to a certain extent.

Red arrows indicate intraperitoneal injection with 10% $H_{2O}2$ on days 8 and 11. Data are presented as means ± SEM, n=8. NC: control group; PC: $H_{2O}2$ group; PG: basal diet + 2% Glu + $H_{2O}2$ group; PA: basal diet + 1% Asp + $H_{2O}2$ group; PGA: basal diet + 2% Glu + 1% Asp + $H_{2O}2$ group.

Figure 1 Effects of Glu and Asp on average daily feed intake of piglets after $H_{2O}2$ injection [23]

3 Effects of Glu and Asp on Intestinal Function of Weaned Piglets

The small intestine is the primary site for nutrient digestion and absorption and serves as a natural barrier against harmful substances [24]. Research shows that amino acids are preferentially utilized nutrients in the intestine [25], and small intestinal structural and functional integrity is supported by substantial ATP consumption, making it highly susceptible to damage during energy deficiency. Glu and Asp are the main sources of ATP for mammalian intestinal cells [3,26] and thus play crucial roles in porcine intestinal morphology, amino acid absorption and transport, energy metabolism, and oxidative stress.

3.1 Effects of Glu and Asp on Intestinal Morphology of Weaned Piglets

Glu and Asp can be converted into glutamine through decarboxylation during animal metabolism, and glutamine improves intestinal morphology and promotes intestinal growth [23,27]. Dietary supplementation with 1% Glu improves small intestinal villus height, crypt depth, villus width, and villus surface area in weaned piglets [28]. When lactose is added to the diet, simultaneous supplementation with Asp and Glu increases villus height in the duodenum, jejunum, and ileum of weaned piglets [20]. Dietary 0.5% or 1.0% Asp alleviates LPS-induced damage to small intestinal and colonic structures and enhances antioxidant enzyme activity in piglet intestinal mucosa, thereby improving intestinal morphology [29]. Asp and Glu can also restore intestinal tissue and morphological damage caused by hydrogen peroxide and reduce intestinal cell apoptosis [23]. Studies have also revealed that Asp supplementation inhibits the expression of Toll-like receptor 4 (TLR4) and nucleotide-binding oligomerization domain protein/nuclear factor- B (NODs/NF- B) signaling pathways in the intestine of weaned piglets under LPS challenge, indicating that Asp can

enhance intestinal immune function and maintain intestinal barrier function during inflammatory responses [30].

3.2 Effects of Glu and Asp on Intestinal Amino Acid Absorption and Transport in Weaned Piglets

The small intestine is the primary site for amino acid absorption in the body. Using in situ intestinal loop perfusion techniques, studies have shown that Asp (171 mg/L) and Glu (307 mg/L) are mainly absorbed in the middle and terminal ileum. Ussing chamber experiments demonstrate that Asp and Glu increase electrical resistance during transport, and high concentrations of Glu or Asp inhibit the absorption of Asp or Glu [31].

Free amino acids hydrolyzed in the intestinal lumen are primarily transported into the bloodstream via amino acid transporters on intestinal epithelial cells for utilization by tissues throughout the body [32]. The main transporters responsible for Glu transport in the intestine include excitatory amino acid transporter-3 (SLC1A1), excitatory amino acid transporter-2 (SLC1A2), and glutamate-cystine transporter (SLC7A11) [33]. Dietary supplementation with 1% Glu significantly increases intestinal SLC1A1 gene expression while decreasing cationic amino acid transporter-1 (SLC7A1) gene expression [34]. Glu and Asp can downregulate the expression of T-type transporter-1 (SLC16A10) and y+L amino acid transporter-1 (SLC7A7) in the intestine and increase the content of lysine, methionine, threonine, alanine, proline, and citrulline in the mesenteric vein, hepatic portal vein, and jugular vein under oxidative stress conditions. Dietary 2% Glu increases the gene expression of neutral amino acid transporters in the jejunal mucosa of weaned piglets, which is beneficial for promoting nutrient digestion and absorption in the jejunum [35].

3.3 Effects of Glu and Asp on Intestinal Energy Metabolism in Weaned Piglets

Asp can be converted into citrulline via argininosuccinate synthetase to enter the urea cycle, can be transformed into Glu to enter the tricarboxylic acid cycle, and can also enter the malate-aspartate shuttle to affect energy metabolism [26,36]. Supplementation with 0.5% or 1.0% Asp increases intestinal ATP, ADP, and total adenine nucleotide content as well as adenylate energy charge, while reducing AMP/ATP ratio. Asp downregulates the gene expression of AMP-activated protein kinase (AMPK) $\$ 1, AMPK\ 2, silentinformationregulator1(SIRT1), andproliferator - activatedreceptorgammacoactivator - 1\ \$$ (PGC1α) in the intestine and muscle, and reduces AMPKα oxidative phosphorylation in the intestine, thereby affecting intestinal energy supply through the AMPK signaling pathway [26]. Additionally, Asp increases the activity of key enzymes in the tricarboxylic acid cycle (such as citrate synthase, isocitrate dehydrogenase, and α-ketoglutarate dehydrogenase) and the activity of intestinal mucosal disaccharidases [26,37].

Glu is an abundant amino acid in the diet, but it is extensively oxidized for energy during transcellular transport from the intestinal lumen to the mesenteric vein, with only a small portion being absorbed and metabolized by the circulatory system [38-39]. When dietary Glu intake increases 3–4 fold, most of it is catabolized and converted into other amino acids in the intestine, generating substantial ATP for utilization [38]. Glu upregulates the expression of the mammalian target of rapamycin (mTOR) pathway in energy metabolism and increases blood citrate and fumarate content [40]. In the body, Glu can also be converted into glutathione, N-acetylglutamate, Asp, α-ketoglutarate, and CO_2 through decarboxylation and transamination (Figure 2 [Figure 2: see original paper]) [1,15,35-36]. These substances can provide nutrition for the intestine and serve as substrates for various metabolic processes, playing major roles particularly in intestinal integrity, protein synthesis [35], nitrogen sparing, oxidative stress [38-39,41], and energy metabolism [4].

Figure 2 Glutamate metabolism in the intestinal tract [38]

3.4 Effects of Glu and Asp on Oxidative Stress in Weaned Piglets

Since Glu and Asp can be converted into glutathione and other antioxidant substances in the body, they play important roles in alleviating oxidative stress and can enhance intestinal antioxidant capacity to a certain extent [38-39,41]. Studies show that Asp tends to increase antioxidant enzyme activity in piglet intestinal mucosa while reducing oxidative product formation, thereby improving intestinal structure and alleviating systemic oxidative stress [29]. Glu may upregulate the gene expression of acidic amino acid transporters in piglet intestine through specific cell signal transduction processes, increasing its metabolic level in the intestine and effectively alleviating oxidative stress responses while reducing reactive oxygen species-induced tissue damage [16,34]. Additionally, in a porcine oxidative stress model established with $H_{2O}2$, Glu and Asp reduce intestinal cell apoptosis, increase the activity of hexokinase (Hexok) and carnitine palmitoyltransferase-1 (CPT-1), and activate the AMPK-acetyl-coenzyme A carboxylase (ACC) signaling pathway [23].

4 Other Biological Functions of Glu and Asp

Glu and Asp possess important biological functions in food and clinical medicine. In the food industry, Asp is the primary raw material for producing aspartame (an artificial sweetener) and alitame (a dipeptide sweetener) [42-44]. Monosodium glutamate, commonly known as MSG, is widely used as a flavor enhancer in food products and is a common condiment in daily life. Since Glu is an amino acid with umami taste, it can bind to umami receptors in the body to alter feeding behavior and promote gastric acid secretion and gastrointestinal motility [45-46]. Asp and Glu are important neurotransmitters in the central nervous system, primarily participating in detoxification reactions of intracellular oxygen free radicals and regulating functions related to nerve activity, reproduction, memory, and movement [42,47-48]. Therefore, in clinical

medicine, Asp and Glu can be used to treat and prevent liver injury [12,49], fatty liver [50], myocardial infarction [51-52], gastrointestinal diseases [53], and improve intestinal microbiota.

Glu and Asp are the primary energy sources for the intestine and can be converted into other substances to exert important biological functions in the body. Particularly, Glu functions as a functional amino acid that plays significant roles in growth performance, intestinal health, immunity, and oxidative stress in weaned piglets. However, further research is needed to determine the precise supplementation doses of Glu and Asp under normal conditions and low-protein diets, as well as their digestion, absorption, and metabolic mechanisms.

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