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Chlorogenic acid protects against lipopolysaccharide- induced ileal injury in piglets

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The intestine is recognized as the 'motor' of sepsis, so protecting it is a critical goal in the prevention and treatment of sepsis. The aim of this study was to investigate the protective effects of chlorogenic acid (CGA) against intestinal injury in a piglet sepsis model induced by lipopolysaccharide (LPS). The weaned piglets were fed with 1 g CGA/kg diet for 21 days before 100 µg LPS/kg body weight administration. After 4 h postinjection, ileal samples were collected. LPS induced ileal morphology atrophy, inhibited the mRNA expression of tight junction proteins, impaired mitochondrial energy metabolism, and disrupted key genes expression involved in mitochondrial quality control mechanisms (i.e., mitochondrial biogenesis, mitochondrial dynamics and mitophagy). CGA supplementation improved ileal morphology, enhanced claudin 3 mRNA abundance, increased ATP production, mediated complex I and III levels, upregulated peroxisome proliferators-activated receptor gamma coactivator 1 alpha, estrogen-related receptor alpha, BCL2 interacting protein 3 like and PTEN induced kinase 1 transcriptional expression in piglets exposed to LPS challenge. These observations reveal the significant protective potential of CGA against LPS-induced intestinal injury through the improvement of intestinal integrity and mitochondrial function, which provides a theoretical basis for application research of the natural product CGA in intestinal sepsis of piglets.

KEYWORDS

chlorogenic acid, intestine, lipopolysaccharide, mitochondria, piglets

1 Introduction

Sepsis, a systemic inflammation syndrome, develops when the host's immune system reacts destructively to an infection and causes multiple organ failure, making the host with considerable morbidity and mortality (Cohen, 2002; Izadparast et al., 2022). The intestine is one of organs most significantly affected by sepsis (Appiah et al., 2020). Besides involving in the nutrients digestion and absorption, intestine epithelial serves as the first barrier against the entry of luminal bacteria and antigens into the bloodstream (Groschwitz and Hogan, 2009; Wang et al., 2023). Sepsis can lead to the breakdown of the intestinal epithelial, promoting the entrance of bacteria and antigens into the systemic circulation, and further exacerbating intestinal and systemic inflammation (Izadparast et al., 2022; Williams et al., 2013). Lipopolysaccharide (LPS), the major component of Gram-negative bacteria cell wall,

is the most effective microbial mediators in the pathophysiology of sepsis (Izadparast et al., 2022). In animal models of sepsis induced by LPS, mitochondrial dysfunction as well as the perturbation of mitochondrial quality control mechanisms are implicated in intestinal damage (Wang et al., 2023; Lu et al., 2024; Cao et al., 2018). Accordingly, a critical goal in the treatment and/or prevention of sepsis is to protect the intestinal tract by modulating mitochondrial function.

Chlorogenic acid (CGA) is a natural polyphenolic compound widely distributed in a variety of plants, including *Eucommia ulmoides leaves*, coffee beans, and *Lonicerae flos*. CGA has attracted increasing attention owing to its potent biological activities, including antidiabetic, anticancer, antioxidant, and anti-inflammatory effects, and it is considered to have no side effects (Xu et al., 2025). CGA has been shown to exert a significant beneficial impact on intestine failure such as inflammatory bowel disease (Gao et al., 2019; Xu et al., 2024; Zhou et al., 2016b), irritable bowel syndrome (Zheng et al., 2023), and colorectal cancer (Bartolomeu et al., 2022) through various mechanism, including the elimination of free radicals, the enhancement of antioxidant defense, the improvement of mitochondrial function, the balance of immune systems, the restored intestinal epithelial barrier, and the maintenance of intestinal microecology. Additionally, previous studies in swine and poultry have demonstrated that CGA exerts beneficial effects on intestinal digestion, absorption, and barrier function (Chen et al., 2018b, 2018; Liu et al., 2023), while also acts as a promising candidate for defending stresses such as heat stress (Chen et al., 2021), oxidative stress (Chen et al., 2022; Zha et al., 2023), infection (Wei et al., 2025), and immunological stress (Tan et al., 2023). However, little is known about the protective effects of CGA against intestinal sepsis. The pig is recognized as an ideal animal model for studying intestinal diseases due to the morphological, physiological, and metabolic similarities between pigs and humans. Consequently, considering the above, we postulated that CGA has the potential to prevent intestinal injury in a sepsis model in piglets induced by intraperitoneal injection of LPS. Therefore, in this study, the protective effects of CGA on intestinal morphology, tight junction protein expression, inflammation mediator, and mitochondrial function were investigated. The results of this study will provide important reference and basis for the application of CGA in sepsis-induced intestinal diseases.

2 Methods and materials

2.1 Ethics statement

The animal use protocols were reviewed and approved by the Animal Care and Use Committee of Henan University of Technology (Zhengzhou, China) (No. HAUT20230302).

2.2 Experimental animals and design

A total of eighteen healthy weaned piglets (Duroc × Landrace × Yorkshire, 26 days of age, 7.65 ± 0.16 kg) were randomly allotted to three groups (six replicates per treatment and one piglet per replicate): (1) the CON group (piglets were received a basal diet and saline injection); (2) the LPS group (piglets were received a basal diet and LPS injection); (3) the LPS-CGA group (piglets were

received a basal diet supplemented with 1 g/kg CGA [Hunan E.K. Herb Co., Ltd, Changsha, China; purity, 98%] and LPS injection). The supplemental level of CGA used in this study was selected based on the previous study, which reported that providing piglets with a diet supplemented with 1 g/kg CGA improved growth retardation and intestinal injury induced by diquat (Chen et al., 2022). The composition and nutrient levels of the basal diet were formulated based on a previous study (Cheng et al., 2026). Piglets had free access to water and feed throughout the experiment. Piglets were fed the experimental diets for 3 weeks and then intraperitoneally injected with LPS (*Escherichia coli* O55:B5; Sigma-Aldrich, St. Louis, MO, USA) at 100 μ g/kg body weight or the equivalent volume of saline. The dosage of LPS and challenge time referred to the previous study (Wang et al., 2023).

2.3 Sample collection

All piglets were anesthetized (50 mg sodium pentobarbital/kg body weight, intramuscular injection) and sacrificed after 4 h postinjection, and their abdominal cavities were immediately opened to harvest ileum samples. A part of ileum samples were carefully cut, cleaned, and gently washed with saline before being transferred to a 4% paraformaldehyde solution for hematoxylin and eosin, while mucosal samples from the additional parts were snap frozen in liquid nitrogen and stored at -80°C until further analysis.

2.4 Ileal morphology analysis

Ileal segments were dehydrated and embedded in paraffin after fixation. Specimens were sliced into 5 μ m thick sections, deparaffinized, rehydrated, and stained with hematoxylin and eosin for morphological evaluation. The stained section was digitally photographed under a light microscope (RVL-100-G, ECHO Laboratories, USA). Villus height (VH), villus width (VW), and crypt depth (CD) in the ileum were determined using the Image-Pro Plus 6.0 software (Media Cybernetics, San Diego, CA, USA). Ileal VH: CD ratio and villus surface area (VSA) were calculated as reported previously (Dong et al., 2014).

2.5 Ileal tumor necrosis factor alpha (TNF α) concentration analysis

Ileal TNF α concentration was analyzed by commercial enzyme-linked immunosorbent assay (ELISA) kits purchased from HongSong Co. Ltd. (Nanjing, China).

2.6 Ileal ATP and electron transport chain complexes levels determination

Ileal ATP, complex I, complex III, and complex V contents were determined using ELISA kits according to the manufacturer's protocol (Jiangsu Meimian Industrial Co., Ltd., Yancheng, China).

2.7 Ileal genes expression assay

Messenger RNA abundance was measured according to method described by the previous study (Cheng et al., 2024). Total RNA from ileal samples was harvested using the Total RNA Isolation

Reagent (Vazyme, Nanjing, China) and quantified using a nanodrop spectrophotometer. RNA was converted to cDNA using HiScript II Q RT Select SuperMix for qPCR(+gDNA wiper) (Vazyme, Nanjing, China). qPCR was performed with ChamQ SYBR qPCR Master Mix (Vazyme, Nanjing, China) on a qTOWER 3.0 system. Genes were normalized to glyceraldehyde-3-phosphate dehydrogenase using the $2^{-\Delta\Delta Ct}$ method, with primer sequences in Table 1.

2.8 Statistical analysis

Data were analyzed by one-way analysis of variance (ANOVA), using a SPSS statistical software (version 27.0; SPSS Inc., Chicago, IL). The differences among each group were analyzed using Tukey's multiple comparisons. A P -value <0.05 was considered statistically significant. Data are presented as means and standard errors.

3 Results

3.1 Ileal morphology

Relative to CON group, the LPS group exhibited ($P < 0.05$) obvious decreases in VH (Figure 1A) and VH: CD ratio (Figure 1C)

as well as an increase in CD (Figure 1B). Conversely, CGA attenuated the LPS-induced increased CD and decreased VH: CD ratio ($P < 0.05$). However, both LPS and CGA treatments did not alter VW (Figure 1D) and VSA (Figure 1E) in the ileum ($P > 0.05$).

3.2 Ileal tight junction protein expression

Compared with the CON (Figure 2), significantly lower claudin (*CLDN*) 1 mRNA expression was observed in the LPS-treated piglets ($P < 0.05$). Compared to the LPS group, CGA supplementation significantly up-regulated mRNA expression of *CLDN3* in the ileum of LPS-challenged piglets ($P < 0.05$). However, *CLDN2* and occludin mRNA expression were not affected among three groups ($P > 0.05$).

3.3 Ileal TNF α content

As illustrated in Figure 3, in the LPS-CGA group in comparison with the LPS group ($P < 0.05$), and the value of which was intermediate in the CON group ($P > 0.05$).

3.4 Ileal energy metabolism

Compared with the CON, LPS challenge reduced ileal ATP (Figure 4A) and complex III (Figure 4C) contents in piglets

TABLE 1 List of primers used in RT-qPCR.

Genes	Forward primer sequence (5' -> 3')	Reverse primer sequence (5' -> 3')
<i>CLDN1</i>	ACAGGAGGGAAGCCATTTC	TTTAAGGACCGCCCTCTCCC
<i>CLDN2</i>	GGATCCTGCGGGACTTCTAC	TGGAGCGATTTCCTGCAGT
<i>CLDN3</i>	GAGACCAGTCCACCCAGATG	AGGTTTCATGGTCCGTGCTG
<i>OCN</i>	CAGGTGCACCCTCCAGATTG	ATGTCGTTGCTGGGTGCATA
<i>PGC1α</i>	CACAATCGCAGTCGCAACAT	ACCCTTGGGGTCATTTGGTG
<i>NRF1</i>	GCTGATGAGTAACAGCCCA	CGTGGCTCGAAGTTTCTAAG
<i>ERRα</i>	TGGTTGAGCCTGAGAAGCTG	TCGAAGAGGTCACAGAGGGT
<i>TFAM</i>	GCTCTCCGTTTCAGTTTTCGG	GGAAGTTCCCTCCACAGCTC
<i>POLG</i>	CAGTGCCCTGTCCCTACAC	GCCAGTCTTCCACCGTC
<i>Fis1</i>	CATCCGTAAGGCCTTGCTC	GCCTTTTCATATTCCTTGAGCC
<i>MFN1</i>	GATGCCAGAAGGTGGTGGG	TGCTGCTGCCACGTTTATTG
<i>MFN2</i>	GCCGGGAAGGTGAAGAATTG	TCGAGAGAAGAGCAGGGACA
<i>OPA1</i>	AGACTTTTTACCCACAGTTTCC	ATGAGCTACCAAGCAGACC
<i>PINK1</i>	ATGTGGAACATCTCGGCGG	GATGATGTTGGGGTGAGGGG
<i>Beclin1</i>	AGAGGCTAACCCAGGAGAGG	GGGGGATGAATCTGCGAGAG
<i>P62</i>	GCTGAGGAATCAGCTTCTGGT	GAGCTGCACTGTCTCTGT
<i>OPTN</i>	AACCATGGCTGTTCTCAGGG	AAGGATTGCCTGCTGGCTC
<i>Map1lc3α</i>	GTCTACGCCTCCCAGGAAAC	CAGGGGCAGAGACAGCTTAG
<i>BNIP3</i>	GGAGAAAAGAACAGCGCTCAG	TTGAAGAGGAGGAACCTTGGC
<i>BNIP3L</i>	AGCAGGGACCATAGCTCTCA	TGCCTGAAGTGAACCTCTTAG
<i>FUNDC1</i>	TAATGGGTGGAGTGAGTGGC	CTGTGACTGGCGATCTGAAG
<i>GAPDH</i>	CCAAGGAGTAAGAGCCCCTG	AAGTCAGGAGATGCTCGGTG

CLDN1, claudin 1; *CLDN2*, claudin 2; *CLDN3*, claudin 3; *OCN*, occludin; *PGC1 α* , PPARG coactivator 1 alpha; *NRF1*, nuclear respiratory factor 1; *ERR α* , estrogen related receptor alpha; *TFAM*, transcription factor A, mitochondrial; *POLG*, DNA polymerase gamma, catalytic subunit; *OPA1*, optic-atrophy-1; *Fis1*, mitochondrial fission 1; *MFN1*, mitofusin 1; *MFN2*, mitofusin 2; *PINK1*, PTEN induced kinase 1; *Map1lc3 α* , microtubule associated protein 1 light chain 3 alpha; *OPTN*, optineurin; *BNIP3*, BCL2 interacting protein 3; *BNIP3L*, BCL2 interacting protein 3 like; *FUNDC1*, FUN14 domain containing 1; *GAPDH*, glyceraldehyde-3-phosphate dehydrogenase.

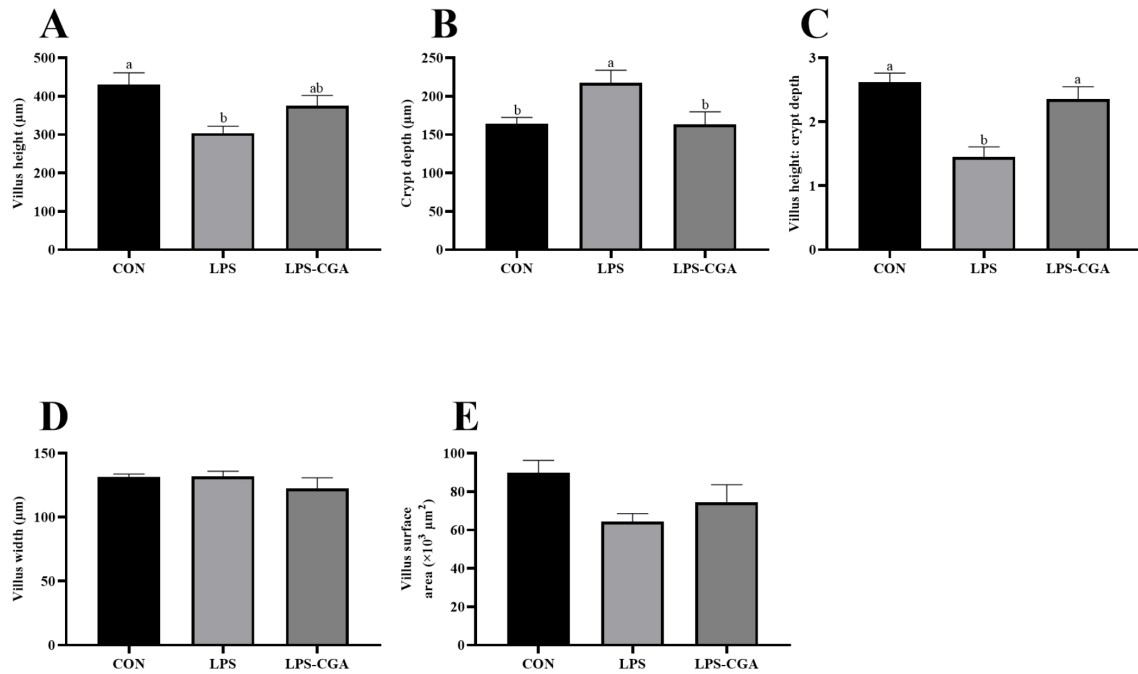


FIGURE 1

Effect of chlorogenic acid on ileal morphology in piglets challenged with lipopolysaccharide. (A) villus height; (B) crypt depth; (C) villus height: crypt depth; (D) villus width; (E) villus surface area. CON, piglets were fed with a basal diet and injected with sterile saline; LPS, piglets were fed with a basal diet and injected with lipopolysaccharide; LPS-CGA, piglets were fed with a chlorogenic acid-supplemented diet and injected with lipopolysaccharide. Results are expressed as means and standard errors. ^{ab}Means without a common letter differ significantly ($P < 0.05$).

($P < 0.05$). Compared with the LPS group, CGA supplementation significantly enhanced ATP, complex I (Figure 4B), and complex III levels in the ileum of piglets exposed to LPS challenge ($P < 0.05$). Treatments did not affect the level of complex V (Figure 4D) in the ileum of piglets ($P > 0.05$).

3.5 Ileal mitochondrial quality control

Mitochondrial quality is regulated by mitochondrial dynamics, mitochondrial biogenesis, and mitophagy. We examined the related

gene expression in the ileum. The mRNA abundance of the following genes were found to be lower ($P < 0.05$) in the LPS-treated piglets than in the CON group: mitochondrial transcription factor A (*TFAM*, Figure 5A), mitochondrial fission 1 (*Fis1*, Figure 5B), mitofusin 1 (*MFN1*, Figure 5B), *Beclin1* (Figure 5C), BCL2 interacting protein 3 like (*BNIP3L*, Figure 5C), optineurin (*OPTN*, Figure 5C), and *p62* (Figure 5C). The ileum of LPS-treated piglets fed the CGA-supplemented diet showed an increase in the mRNA level of peroxisome proliferators-activated receptor gamma coactivator 1 alpha (*PGC1 α* , Figure 5A), estrogen-related receptor alpha (*ERR α* , Figure 5A), PTEN induced kinase 1 (*PINK1*, Figure 5C), and *BNIP3L* (Figure 5C) when compared with the LPS group ($P < 0.05$). The mRNA abundance of ileal nuclear respiratory factor 1 (Figure 5A), DNA polymerase gamma, catalytic subunit (Figure 5A), optic-atropy-1 (Figure 5B), mitofusin 2 (Figure 5B), FUN14 domain containing 1 (Figure 5C), and microtubule associated protein 1 light chain 3 alpha (Figure 5C) were not altered among the three groups ($P > 0.05$).

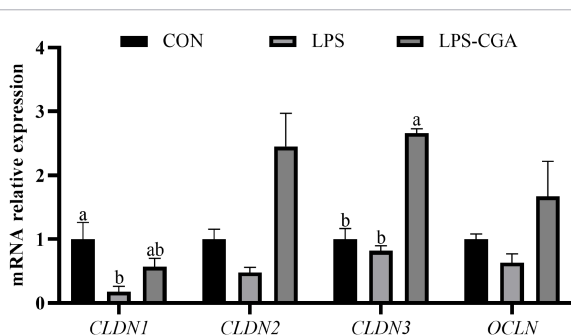


FIGURE 2

Effect of chlorogenic acid on ileal tight junction proteins mRNA expression in piglets challenged with lipopolysaccharide. *CLDN1*, claudin 1; *CLDN2*, claudin 2; *CLDN3*, claudin 3; *OCLN*, occludin; CON, piglets were fed with a basal diet and injected with sterile saline; LPS, piglets were fed with a basal diet and injected with lipopolysaccharide; LPS-CGA, piglets were fed with a chlorogenic acid-supplemented diet and injected with lipopolysaccharide. Results are expressed as means and standard errors. ^{ab}Means without a common letter differ significantly ($P < 0.05$).

4 Discussion

This study presents evidence that CGA is an effective agent for protecting against intestinal injury induced by LPS. The beneficial effects of CGA are associated with, in part, the modulation of tight junction protein transcriptional expression, $TNF\alpha$ production, mitochondrial energy metabolism, mitochondrial biogenesis and mitophagy. Overall, our results indicate that CGA can serve as a promising candidate for intestinal sepsis.

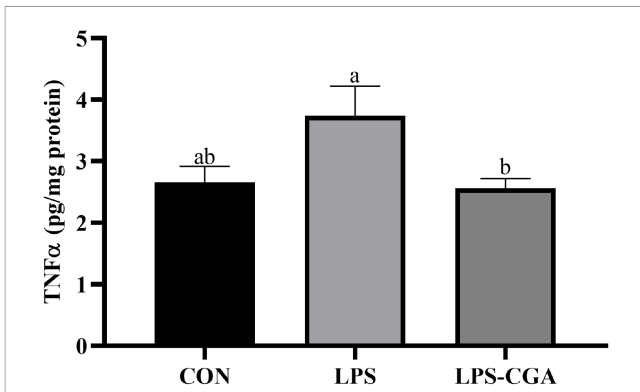


FIGURE 3

Effect of chlorogenic acid on ileal tumor necrosis factor α (TNF α) in piglets challenged with lipopolysaccharide. CON, piglets were fed with a basal diet and injected with sterile saline; LPS, piglets were fed with a basal diet and injected with lipopolysaccharide; LPS-CGA, piglets were fed with a chlorogenic acid-supplemented diet and injected with lipopolysaccharide. Results are expressed as means and standard errors. ^{ab}Means without a common letter differ significantly ($P < 0.05$).

Intestinal morphology is regarded as a reliable reflection for intestinal integrity, development status, nutrient absorption (Xu et al., 2003). Impaired intestinal morphology such as lower VH, deeper CD, suppressed VH: CD ratio is accompanied by decreased absorption, fewer mature and functional enterocytes (Cairo et al., 2018). Additionally, intestinal physical barrier, mainly composed of tight junction proteins (e.g., OLCN and CLDN), is a key determinant for preventing the infiltration of bacterial toxins and other exogenous

substances into intestinal tissues and activation of intestinal inflammation (Dai et al., 2020). Similar to previous studies (Ruan et al., 2014; Tan et al., 2023; Wang et al., 2023), LPS exposure resulted in a lower VH, a higher CD, a lower VH: CD ratio, and a decrease in *CLDN1* mRNA expression, indicating that LPS induced impaired morphology, increased permeability and barrier damage in the ileum. CGA administration could counteract the changes of CD and VH: CD ratio, and increase *CLDN3* mRNA expression in the ileum of piglets exposed to LPS, thereby improving intestinal integrity, structure, and barrier function. Consistent with our findings, Ruan et al. (2014) also found that CGA improves intestinal morphology and tight junction protein expression in weaned rats challenged with LPS. Interestingly, studies in colitic rats have shown that CGA enhances intestinal barrier partly by regulating the expression, dynamic distribution, and reassembly of CLDN1 via the inhibition of myosin light chain kinase (Ruan et al., 2016). Similar beneficial effects of CGA were observed in pigs subjected to diquat (Chen et al., 2022) and broilers challenged with LPS (Tan et al., 2023), and avian pathogenic *Escherichia coli* (Wei et al., 2025). In the present study, the protective effects of CGA against intestinal damage may be associated with the improvement of mitochondrial function.

Mitochondria produce the ATP in enterocytes through the mitochondrial electron transport chain consists of five multisubunit enzyme complexes I-V, which contributes to the restoration of the intestinal barrier (Cheng et al., 2025; Pi et al., 2014). Considerable evidence shown that mitochondrial dysfunction is implicated in sepsis-induced intestinal injury through excess reactive oxygen species generation and components of mitochondria (Fock and Parnova,

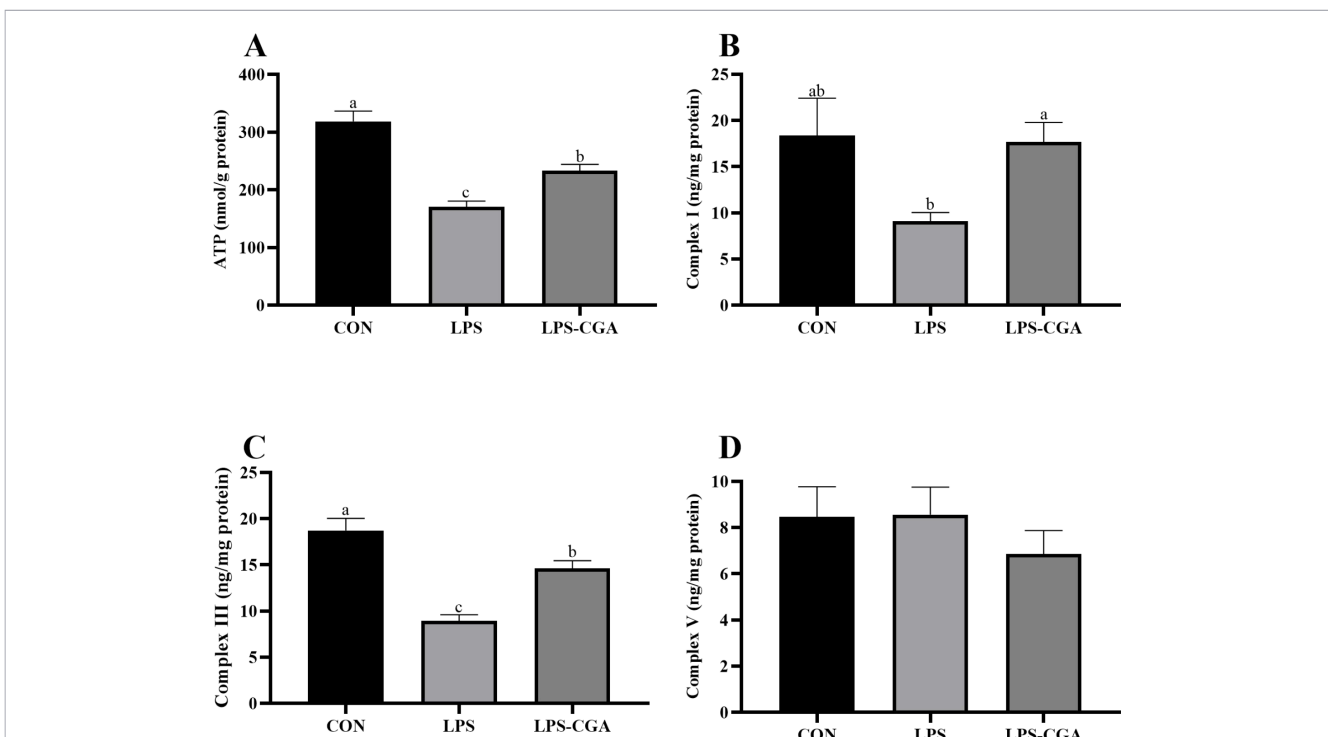


FIGURE 4

Effect of chlorogenic acid on ileal mitochondrial energy metabolism in piglets challenged with lipopolysaccharide. (A) ATP; (B) complex I; (C) complex III; (D) complex V. CON, piglets were fed with a basal diet and injected with sterile saline; LPS, piglets were fed with a basal diet and injected with lipopolysaccharide; LPS-CGA, piglets were fed with a chlorogenic acid-supplemented diet and injected with lipopolysaccharide. Results are expressed as means and standard errors. ^{ab}Means without a common letter differ significantly ($P < 0.05$).

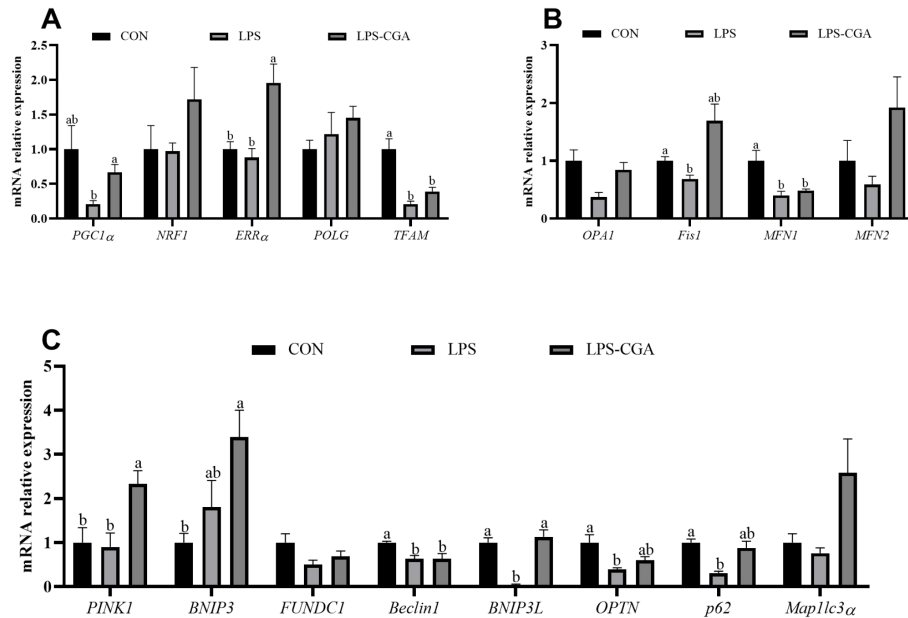


FIGURE 5

Effect of chlorogenic acid on ileal mitochondrial quality control-related genes expression in piglets challenged with lipopolysaccharide. (A) genes expression related to mitochondrial biogenesis; (B) genes expression related to mitochondrial dynamics; (C) genes expression related to mitophagy. *PGC1α*, peroxisome proliferators-activated receptor gamma coactivator 1 alpha; *NRF1*, nuclear respiratory factor 1; *ERRα*, estrogen related receptor alpha; *POLG*, DNA polymerase gamma, catalytic subunit; *TFAM*, mitochondrial transcription factor A; *OPA1*, optic-atropy-1; *Fis1*, mitochondrial fission 1; *MFN1*, mitofusin 1; *MFN2*, mitofusin 2; *PINK1*, PTEN induced kinase 1; *BNIP3*, BCL2 interacting protein 3; *FUNDC1*, FUN14 domain containing 1; *BNIP3L*, BCL2 interacting protein 3 like; *OPTN*, optineurin; *Map1lc3α*, microtubule associated protein 1 light chain 3 alpha; CON, piglets were fed with a basal diet and injected with sterile saline; LPS, piglets were fed with a basal diet and injected with lipopolysaccharide; LPS-CGA, piglets were fed with a chlorogenic acid-supplemented diet and injected with lipopolysaccharide. Results are expressed as means and standard errors. ^{ab}Means without a common letter differ significantly ($P < 0.05$).

2021; Wang et al., 2023; Cao et al., 2018). In animal models of sepsis induced by the systemic LPS administration, impairment of the electron transfer chain and oxygen consumption, deficiency in ATP production, and a decline in mitochondrial number were observed (Wang et al., 2023; Cao et al., 2018; Zhou et al., 2016a). Similarly, the reduced ileal mitochondrial ATP generation and complex III level induced by LPS were also found in our study. Additionally, the suppressed mRNA expression of TFAM, Fis1, MFN1, Beclin1, BNIP3L, and p62 in the ileum were induced due to the LPS injection. TFAM is an essential mitochondrial protein regulating the replication and transcription of mitochondrial DNA and respiratory chain biogenesis (Kozhukhar and Alexeyev, 2022). Previous study conducted in dendritic cells shown that TFAM deficiency leads to mitochondrial dysfunction (Lu et al., 2023). Mitochondrial fission and fusion events regulate mitochondrial dynamics, and alteration in these events results in mitochondrial dysfunction and contributes to many diseases, including septic intestinal injury (Ashraf and Kumar, 2022; Wang et al., 2023). MFN1 and Fis1 are involved in mitochondrial fusion and fission, respectively. Mitophagy is an important mitochondrial quality control mechanism that selectively eliminates damaged mitochondria. This process can be partly achieved by p62, BNIP3L, and Beclin1 (Leduc-Gaudet et al., 2021). Thus, the negative effects of LPS on ileal mitochondrial function could be attributed to the inhibition of mitochondrial biogenesis, mitochondrial dynamics, and mitophagy. The effect of LPS injection on mitophagy seems to be tissue-specific. For example, Cao et al. (2018) reported that LPS induced an increase in expression of mitophagy

related proteins (PINK1 and Parkin) in the jejunal mitochondria, suggesting that LPS triggers the jejunal mitophagy. It has been confirmed that LPS reduces the transcriptional and translational expression of key proteins related to mitochondrial fusion in the intestine of piglets (Wang et al., 2023; Lu et al., 2024), but its impact on mitochondrial fission is controversial. Wang et al. (2023) found that LPS had no effect on Fis1 expression in the jejunum of piglets at 62–64 d of age. However, Lu et al. (2024) discovered that LPS increased Fis1 expression in the jejunum of piglets at 51–53 d of age. However, this study found that LPS decreased Fis1 expression in the ileum of 47-day-old piglets. These contrasting responses of mitochondrial fission key proteins in the intestine of piglets subjected to LPS may be due to differences in age and tissue. In this study, CGA supplementation increased ileal ATP content, complex I and III levels in piglets exposed to LPS challenge. This indicates that CGA improves ileal mitochondrial energy metabolism, which explains its beneficial effects on ileum in piglets injected with LPS. Mechanistically, CGA shows significant potential for the transcriptional regulation of proteins associated with mitochondrial biogenesis (i.e., *PGC1α* and *ERRα*) and mitophagy (i.e., *PINK1* and *BNIP3L*). Similarly, pretreatment with CGA against kainic acid-induced neurotoxicity through preservation of *PGC-1α*-mediated mitochondrial biogenesis and *PINK1*/*Parkin*-induced mitophagy to maintain adequate mitochondrial homeostasis and function (Pai et al., 2023). Previous study also demonstrated that CGA supplementation improves intestinal mitochondrial oxidative metabolism and energy production in piglets

with intrauterine growth retardation in part through mediating PINK1 and BNIP3L expression (Cheng et al., 2025). Interestingly, CGA is a well-known activator of AMP-activated protein kinase (AMPK). AMPK balances mitochondrial quantity and quality through mitochondrial biogenesis, mitophagy, and mitochondrial dynamics pathways (Herzig and Shaw, 2018). The role of AMPK in the protective effects of CGA on ileal mitochondrial function in piglets exposed to LPS needs to be further investigated.

5 Conclusions

In conclusion, CGA supplementation alleviated the LPS-induced ileal injury by improving intestinal integrity and mitochondrial function, which may provide a theoretical basis for practical application research of the natural product CGA in the treatment of intestinal sepsis.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The animal study was approved by Animal Care and Use Committee of Henan University of Technology. The study was conducted in accordance with the local legislation and institutional requirements.

Author contributions

KC: Funding acquisition, Supervision, Conceptualization, Project administration, Writing – original draft, Methodology, Formal analysis, Data curation, Validation, Resources, Investigation. JY: Writing – review & editing, Formal analysis. ZS: Funding acquisition, Writing – review & editing. XY: Formal analysis, Writing – review & editing. YW: Formal analysis, Writing – review & editing. ZL: Formal analysis, Writing – review & editing. LK: Formal analysis, Writing – review & editing. JH: Data curation, Funding acquisition, Writing – review & editing. JW: Resources, Writing – review & editing, Supervision. YZ: Writing – review & editing, Resources.

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Conflict of interest

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