Effects of Rare Earth Chitosan Chelate Salt on Growth Performance, Serum Biochemical Indices, Nutrient Digestibility, and Fecal Microbiota of Weaned Piglets (Postprint)

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Abstract

This study aimed to investigate the effects of dietary supplementation with rare earth-chitosan chelate (RECC) on growth performance, serum biochemical indices, nutrient digestibility, and fecal microbiota in weaned piglets. A total of 240 healthy 28-day-old purebred Large White piglets were selected and randomly divided into 4 groups with 4 replicates per group and 15 piglets per replicate. The control group was fed a basal diet, while the experimental groups were fed the basal diet supplemented with 0.02%, 0.03%, and 0.04% RECC, respectively. The experimental period lasted 28 days. The results showed: 1) Compared with the control group, dietary supplementation with 0.02% and 0.03% RECC significantly increased average daily gain and average daily feed intake ($P<0.05$), significantly decreased feed-to-gain ratio ($P<0.05$), and all RECC groups significantly reduced diarrhea rate in weaned piglets ($P<0.05$). 2) Dietary supplementation with 0.02% and 0.03% RECC significantly increased serum growth hormone and immunoglobulin G contents in weaned piglets ($P<0.05$). 3) Dietary supplementation with 0.02% and 0.03% RECC significantly improved the digestibility of dry matter, crude protein, and ether extract in weaned piglets ($P<0.05$), and dietary supplementation with 0.02% RECC significantly improved the digestibility of Ca and P in piglets ($P<0.05$). 4) Dietary RECC supplementation had no significant effects on the counts of Escherichia coli, Bifidobacterium, and Lactobacillus in piglet feces ($P>0.05$), but showed a trend toward reducing Escherichia coli count. In conclusion, dietary RECC supplementation can improve growth, immune function, and other functions in weaned piglets by increasing hormone levels and regulating microbial balance, and the appropriate supplementation level of RECC in weaned piglets is 0.02%.

Full Text

Effects of Rare Earth-Chitosan Chelate on Growth Performance, Serum Biochemical Indices, Nutrient Digestibility and Fecal Microbial Flora of Weaned Piglets

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Abstract: This experiment was conducted to investigate the effects of dietary rare earth-chitosan chelate (RECC) on growth performance, serum biochemical indices, nutrient digestibility, and fecal microbial flora of weaned piglets. A total of 240 healthy purebred Large White piglets at 28 days of age were randomly allocated into 4 groups with 4 replicates per group and 15 piglets per replicate. The control group was fed a basal diet, while the experimental groups were fed the basal diet supplemented with 0.02%, 0.03%, and 0.04% RECC, respectively. The experimental period lasted 28 days. The results showed: 1) Compared with the control group, dietary supplementation with 0.02% and 0.03% RECC significantly increased average daily gain and average daily feed intake ($P<0.05$), significantly decreased feed/gain ratio ($P<0.05$), and all RECC groups significantly reduced diarrhea rate ($P<0.05$). 2) Dietary supplementation with 0.02% and 0.03% RECC significantly increased serum growth hormone and immunoglobulin G contents ($P<0.05$). 3) Dietary supplementation with 0.02% and 0.03% RECC significantly improved digestibility of dry matter, crude protein, and ether extract ($P<0.05$), and 0.02% RECC significantly improved digestibility of Ca and P ($P<0.05$). 4) Dietary RECC had no significant effects on the counts of Escherichia coli, Bifidobacterium, and Lactobacillus in feces ($P>0.05$), but showed a trend toward reducing E. coli counts. In conclusion, dietary RECC supplementation can improve hormone levels and microbial balance, thereby enhancing growth performance and immune function in weaned piglets. The appropriate supplemental level of RECC for weaned piglets is 0.02%.

Keywords: rare earth-chitosan chelate; weaned piglets; growth performance; serum biochemical indices; nutrient digestibility; fecal microbial flora

Rare earth elements act as physiological activators that can stimulate animal metabolism, activate growth factors, and promote increased enzyme activity [1]. Chitosan can improve animal production performance, regulate fat utilization, exert broad-spectrum antibacterial effects, and enhance immunity [2]. However, rare earth elements have low absorption when ingested orally, while chitosan is difficult for animals to digest and absorb due to its compact molecular structure [3]. Rare earth-chitosan chelate (RECC) is a novel green feed additive formed by chelating rare earth ions with chitosan molecules through a special process. It exhibits biological effects similar to antibiotics [4] with low toxicity and high safety. In the chelate, chitosan serves as an excellent network carrier [5] that gradually releases rare earth ions into the animal body, preventing enzyme inhibition by metal ions and thereby increasing rare earth ion absorption efficiency. Meanwhile, rare earth elements possess multiple 4f electron orbitals that enable them to coordinate with chitosan molecules to form various spatial geometric configurations, accelerating certain catalytic reactions during chitosan degradation [6]. Therefore, RECC can effectively overcome the low absorption efficiency when either component is used alone.

Current studies on RECC in poultry, fish, and ruminants have shown that it can improve feed conversion rate, accelerate animal growth, enhance immune function, and unlock animal potential [7-9], although some reports indicate that RECC does not exhibit good growth-promoting effects [10]. Weaned piglets often experience "early weaning syndrome" characterized by poor appetite, slow growth, diarrhea, and digestive disorders, which seriously troubles swine producers [11]. Research on RECC in weaned piglets is scarce, with only He et al. [12] reporting that RECC can improve daily gain, feed intake, and feed conversion rate in weaned piglets, though its exact effects and mechanisms require further systematic verification. Moreover, the dosage of RECC is considered a key factor in improving animal performance, as excessive supplementation can produce negative effects. Therefore, this experiment was designed to investigate the effects of different dietary RECC levels on growth performance, serum biochemical indices, nutrient digestibility, and fecal microbial flora in weaned piglets, and to determine the appropriate supplemental level to provide a basis for RECC application in piglet production.

1.1 Experimental Materials

The RECC preparation used in this experiment was a rare earth element chelate product produced by Shanghai Debang Animal Husbandry Co., Ltd., appearing as light yellow granules with 13% RECC content. The active rare earth components were cerium and lanthanum.

1.2 Experimental Animals and Design

This experiment was conducted at the breeding farm of Liaoning Debao Aidemeng Pig Farm, with experimental piglets provided by Aidemeng Pig Farm. A completely randomized design was adopted. A total of 240 Large White weaned piglets at 28 days of age with an average body weight of (7.53$±$0.25) kg were randomly divided into 4 groups with 4 replicates per group and 15 piglets per replicate. The groups consisted of a control group (basal diet), 0.02% RECC group (basal diet + 0.02% RECC), 0.03% RECC group (basal diet + 0.03% RECC), and 0.04% RECC group (basal diet + 0.04% RECC). The experiment included a 7-day pre-trial period and a 28-day formal trial period.

1.3 Basal Diet and Management

The basal diet was formulated according to NRC (1998) standards, with composition and nutrient levels shown in Table 1 . Experimental piglets were housed in the same semi-open pig house with fully cemented floors, equipped with fully slatted plastic floors, stainless steel feeders, and nipple drinkers. House temperature was maintained at (25$±$3)°C with good ventilation. Piglets were fed twice daily with ad libitum access to feed and water, and daily feed intake was recorded for each group. Routine immunization and disinfection procedures were followed during the experimental period.

Table 1 Composition and nutrient levels of the basal diet (air-dry basis) %

Note: The premix provided the following per kg of diet: VA 8,000 IU, VD_3 1,228 IU, VE 15 IU, VK_3 3.0 mg, VB_1 1.3 mg, VB_2 3.1 mg, VB_6 1.2 mg, calcium pantothenate 13.4 mg, choline chloride 500 mg, biotin 0.11 mg, niacin 25 mg, folic acid 0.68 mg, VB_{12} 0.03 mg, Fe 120 mg, Cu 10 mg, Zn 130 mg, Mn 100 mg, I 0.3 mg, Se 0.3 mg. ME was a calculated value, while the others were measured values.

1.4 Measurements

1.4.1 Growth Performance Piglet body weight was measured on an empty stomach on days 1 and 28 of the experimental period. Daily feed allowance, feed wastage, and remaining feed were recorded for each group to calculate average daily gain (ADG), average daily feed intake (ADFI), and feed/gain ratio (F/G). Fecal consistency and piglet mental status were observed daily from 07:30 to 19:00, with sensory scoring of each defecation according to Castillo et al. [13]. Diarrhea incidents were recorded to calculate diarrhea rate. Mortality was recorded daily throughout the experimental period.

1.4.2 Serum Biochemical Indices On the final day of the experiment (19:00-21:00), blood samples (10 mL each) were collected from 5 randomly selected piglets per replicate via anterior vena cava puncture. After collection, blood was allowed to clot for 1-2 h, then centrifuged at 3,000 r/min for 15 min to separate serum. Serum was aliquoted into 2 mL tubes and stored at -20°C. Serum biochemical indices were measured using a Hitachi 7160 automatic biochemical analyzer and an r-911 automatic radioimmunoassay counter. Reagent kits were purchased from Beijing Bio-control Co., Ltd. and Beijing Huaying Biotechnology Research Institute.

1.4.3 Nutrient Digestibility On day 28 of the experimental period, 3 piglets with good growth and similar body condition were selected from each replicate to collect fecal samples, which were sealed and transported to the laboratory at low temperature for proximate nutrient analysis. Dry matter (DM), crude protein (CP), ether extract (EE), Ca, and P contents in feed and feces were determined using conventional feed analysis methods. Nutrient digestibility was calculated using the acid-insoluble ash (AIA) marker method [14].

1.4.4 Fecal Microbial Flora On day 28 of the experimental period, 5 piglets with good growth and similar body condition were selected from each replicate. Fecal samples (~50 g per piglet) were collected between 06:00-08:00 and immediately stored at -4°C until analysis. In a laminar flow hood, 0.5 g of feces was placed in a test tube containing 4.5 mL sterile distilled water, vortexed, and allowed to stand for 10 min. Then 0.5 mL of the liquid was transferred to another tube with 4.5 mL sterile distilled water, vortexed, and allowed to stand for 10 min. Serial dilutions were performed, and three dilution levels (10^{-2}, 10^{-3}, and 10^{-4}) were selected with three replicates per dilution. For enumeration, 0.1 mL of diluted solution was plated onto appropriate media: Eosin Methylene Blue (EMB) agar for Escherichia coli (incubated at 37°C for 24 h), Bismuth Sulfite (BS) agar for Bifidobacterium, and Lactobacillus Selective (LBS) agar for Lactobacillus (incubated anaerobically at 37°C for 72 h) [15]. Results were expressed as $\log_{10}$(CFU/g).

1.5 Statistical Analysis Experimental data were analyzed using one-way ANOVA in SPSS 19.0 software. Duncan' s multiple range test was used for post-hoc comparisons. Results were expressed as "mean ± standard deviation." P<0.05 was considered statistically significant, while P>0.05 indicated no significant difference.

2.1 Effects of Dietary RECC on Growth Performance of Weaned Piglets

As shown in Table 2 , ADG and ADFI in all RECC groups were higher than in the control group, with 0.02% and 0.03% RECC groups showing significantly higher ADG and ADFI than both the control and 0.04% RECC groups (P<0.05). The feed/gain ratio in 0.02% and 0.03% RECC groups was significantly lower than in the control and 0.04% RECC groups (P<0.05). Diarrhea rates in all RECC groups were significantly lower than in the control group (P<0.05). Mortality rates in all RECC groups were 0%, which was better than the control group, though the difference was not significant (P>0.05).

Table 2 Effects of dietary RECC on growth performance of weaned piglets

Note: In the same row, values with different small letter superscripts mean significant difference (P<0.05), while with the same or no letter superscripts mean no significant difference (P>0.05). The same as below.

2.2 Effects of Dietary RECC on Serum Biochemical Indices of Weaned Piglets

As shown in Table 3 , serum growth hormone (GH) content in all RECC groups was higher than in the control group, with 0.02% and 0.03% RECC groups showing significantly higher GH content than the control and 0.04% RECC groups ($P<0.05$). Compared with the control group, serum insulin (INS), triiodothyronine (T_3), and thyroxine (T_4) contents in RECC groups showed increasing trends, but the differences were not significant ($P>0.05$).

Table 3 Effects of dietary RECC on serum hormone levels of weaned piglets

As shown in Table 4 , serum immunoglobulin G (IgG) content in 0.02% and 0.03% RECC groups was significantly higher than in the control group ($P<0.05$), with no significant differences among RECC groups ($P>0.05$). Serum immunoglobulin M (IgM) in RECC groups showed increasing trends compared with the control group, but differences were not significant ($P>0.05$). RECC had no significant effect on serum immunoglobulin A (IgA) content ($P>0.05$).

Table 4 Effects of dietary RECC on serum immune indices of weaned piglets (g/L)

As shown in Table 5 , serum superoxide dismutase (SOD) and catalase (CAT) activities in RECC groups showed no significant differences compared with the control group ($P>0.05$).

Table 5 Effects of dietary RECC on serum antioxidant indices of weaned piglets (U/L)

2.3 Effects of Dietary RECC on Nutrient Digestibility of Weaned Piglets

As shown in Table 6 , 0.02% and 0.03% RECC groups significantly improved digestibility of dry matter (DM), crude protein (CP), and ether extract (EE) ($P<0.05$). DM digestibility increased by 11.25% and 8.79%, CP digestibility by 8.81% and 7.15%, and EE digestibility by 8.65% and 5.50% compared with the control group, respectively. The 0.02% RECC group also significantly improved Ca and P digestibility ($P<0.05$), increasing them by 11.67% and 9.69%, respectively.

Table 6 Effects of dietary RECC on nutrient digestibilities of weaned piglets (%)

2.4 Effects of Dietary RECC on Fecal Microbial Flora of Weaned Piglets

As shown in Table 7 , RECC groups showed a trend toward reducing E. coli counts, though the difference was not significant ($P>0.05$). Bifidobacterium counts in 0.02% and 0.03% RECC groups were higher than in the control group, while the 0.04% RECC group was slightly lower, but none reached significant levels ($P>0.05$).

Table 7 Effects of dietary RECC on fecal microbial population of weaned piglets

3.1 Effects of Dietary RECC on Growth Performance of Weaned Piglets

RECC possesses the chemical properties and physiological functions of both rare earth elements and chitosan. When applied in animal feed, it can produce antibiotic-like effects on animal growth performance, nutrient metabolism, immune system, and various enzymes [16]. Research on RECC as a novel feed additive is limited, but studies on rare earth elements have shown they can significantly improve animal production performance [17]. Lanthanum and cerium constitute the majority of rare earth elements and can substitute for Ca^{2+}, Mg^{2+}, Fe^{3+}, Fe^{2+}, and Mn^{2+}. Since Ca^{2+} plays a crucial role in cell metabolism, rare earth ions with similar properties and structures may replace Ca^{2+} at binding sites, promoting the activity of certain proteins and enzymes. Zhao et al. [18] reported that cerium ions at certain concentrations affect bacterial growth, promoting E. coli growth at concentrations below 350 g/mL but inhibiting it above 400 g/mL. Rare earth elements can alter bacterial membrane surface structure, causing bacterial flocculation [19] and exerting antibiotic-like effects that inhibit gastrointestinal bacteria and promote piglet growth. Additionally, lanthanum and cerium ions can increase nucleotide levels in the animal intestine, accelerating intestinal cell differentiation, growth, and repair, promoting small intestine maturation, repairing damaged intestinal mucosa, improving intestinal function, and reducing diarrhea rates [19-20]. Wang et al. [21] reported that feeding finishing pigs a diet containing 100 mg/kg lanthanum increased daily gain by 12.95%, reduced feed conversion ratio by 6.78%, and significantly increased serum growth hormone peak, baseline, and overall levels by 80.42%, 70.99%, and 64.91%, respectively. Studies have shown that appropriate chitosan supplementation can improve animal production performance, but excessive amounts produce negative effects [22]. Shi et al. [23] found that 0.05% chitosan significantly improved broiler growth performance, while Tang et al. [24] reported that 0.1% chitosan reduced daily gain by 7.48% and feed conversion ratio by 0.88% in weaned piglets.

This study demonstrated that appropriate RECC supplementation significantly improved ADG and ADFI while reducing F/G in piglets, increased serum GH and INS contents, and decreased diarrhea and mortality rates. The improved performance may be related to increased serum GH levels, consistent with Xiao [25]. RECC can regulate serum hormone levels, promote protein synthesis, enhance immunity, and balance gastrointestinal microflora, thereby improving piglet growth performance [26]. Gu et al. [27] reported that adding 0.2%-1.0% rare earth chitosan to growing pig diets increased body weight by 5.4%-14.4% and economic benefits by 7.3%-36.8%. Dietary supplementation with 250 g/t rare earth amino acid chelate increased feed intake by 2.88% and daily gain by 3.57% in nursery piglets, while 350 g/t reduced feed intake by 11.39% but still increased daily gain by 2.90% and significantly reduced feed/gain ratio, improving nursery piglet performance [28]. Wan [29] reported that 0.2% RECC supplementation in laying hens achieved peak egg production, increasing average egg weight and egg mass by 0.73% and 6.83%, respectively, significantly higher than the control group. These findings are consistent with our results and confirm that chelated rare earth-chitosan is superior to individual supplementation.

3.2 Effects of Dietary RECC on Immune and Antioxidant Function of Weaned Piglets

The digestive and active immune systems of piglets are not fully developed at weaning, and they cannot completely synthesize immunoglobulins independently [30], making them susceptible to stress from environmental pathogens. Chitosan has immunomodulatory effects, enhancing macrophage phagocytosis and stimulating macrophages to produce lymphokines that initiate immune responses and improve immunity. Tang et al. [24] showed that 0.025% dietary chitosan increased serum IgA, IgM, and IgG contents in early-weaned piglets. Bianco et al. [31] reported that chitosan, as a degradation product of RECC, can affect arachidonic acid synthesis and release in immune cells by increasing phospholipase A2 activity, thereby initiating specific immune responses. Mills [32] demonstrated that RECC can increase inducible nitric oxide synthase activity, affecting nitric oxide synthesis in immune cells and initiating non-specific immunity through its cytotoxic effects. These studies confirm that RECC can enhance immunity, consistent with our findings. In humoral immunity, IgM and IgG contents positively correlate with immune function. This experiment showed that different RECC levels increased serum IgM and IgG contents to varying degrees, with 0.02% and 0.03% RECC groups showing significantly higher IgG than the control group, indicating that RECC improves piglet immune function by enhancing immunoglobulin synthesis.

Free radicals protect the organism, but excessive amounts cause damage. Under certain conditions, rare earth elements can enhance SOD activity as free radical scavengers. Mice injected with carcinogens and given rare earth solution showed significantly higher SOD activity than untreated mice [33]. Su et al. [33] found that 0.03% dietary RECC significantly improved growth performance and feed utilization in flounder while enhancing immune and antioxidant indices, though excessive supplementation produced negative effects. Although RECC supplementation did not significantly affect serum SOD and CAT activities in this study, both enzyme activities were higher in RECC groups than in the control group, similar to previous results, suggesting that RECC can improve antioxidant capacity to some extent, eliminate excess free radicals, and reduce cellular damage.

3.3 Effects of Dietary RECC on Nutrient Digestibility of Weaned Piglets

Both rare earth elements and chitosan can improve nutrient digestibility. Rare earth elements are beneficial and auxiliary nutrients that participate in material metabolism and activate enzymes to varying degrees. Han et al. [4] reported that rare earth mineral-yeast supplementation in weaned piglets resulted in higher DM, CP, EE, Ca, and P metabolism than zinc oxide or antibiotic groups. Prause et al. [35] found that 0.015% rare earth supplementation significantly improved nitrogen absorption, energy balance, carbohydrate absorption, and nutrient digestibility, but 0.030% supplementation showed no significant effects, suggesting that rare earth may affect small intestine permeability and promote digestive juice secretion to improve nutrient digestibility. Many scholars believe that appropriate chitosan can improve protein digestion and utilization. Wada et al. [36] reported that chitosan significantly improved Ca absorption in rats. Chitosan can increase small intestinal villi, expand absorption area, and enhance nutrient absorption. This study showed that 0.02% and 0.03% RECC significantly improved DM, CP, and EE digestibility, and 0.02% RECC significantly improved Ca and P digestibility, consistent with the above reports. Additionally, the significant improvement in piglet performance indicates enhanced nutrient digestibility.

3.4 Effects of Dietary RECC on Fecal Microbial Flora of Weaned Piglets

Rare earth elements regulate bacterial growth, with appropriate concentrations of light rare earth elements showing slight stimulation during early growth phases, though this effect diminishes over time [37-38]. Chitosan also has broad-spectrum antibacterial activity. Deng et al. [39] reported that chitosan oligosaccharide is an important bifidogenic factor that regulates intestinal microbial metabolism, improves intestinal microflora distribution, inhibits harmful bacteria, and promotes Bifidobacterium growth. Zhang and Wang [40] showed that 0.05% chitosan at pH 5.5 significantly inhibited E. coli, with antibacterial effects increasing as molecular weight decreased, and low-molecular-weight chitosan (~1,500 Da) showing the best effect. The antimicrobial mechanism may involve the positive charge and polymeric structure of chitosan adsorbing to and agglutinating bacterial flagella and capsules, inhibiting pathogen proliferation while promoting beneficial bacteria such as Bifidobacterium and Lactobacillus, thereby improving small intestinal metabolic capacity. This study showed that RECC supplementation inhibited E. coli counts while increasing Bifidobacterium and Lactobacillus counts in piglet feces, favoring intestinal microbial balance, consistent with previous studies and the observed reduction in diarrhea rates.

Conclusions: 1. Dietary RECC supplementation significantly improved ADG and ADFI while significantly reducing feed/gain ratio and diarrhea rate in weaned piglets. 2. Dietary RECC supplementation significantly increased serum GH and IgG contents, with a trend toward increased IgM content. 3. Dietary RECC supplementation significantly improved digestibility of DM, CP, EE, Ca, and P in weaned piglets. 4. The appropriate supplemental level of RECC in weaned piglet diets is 0.02%.

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Note: Figure translations are in progress. See original paper for figures.