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Effects of yeast hydrolysate versus plasma powder on growth, immunity, and intestinal morphology of weanling piglets

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Abstract

Yeast hydrolysate (YH) is rich in amino acids, small peptides, B vitamins, glutathione, and nucleotides, which makes it a possible substitute for spray-dried plasma powder (SDPP). This research was conducted to estimate the application of YH instead of SDPP in creep feed of weaned piglets. The experiment had four treatment groups: (1) basal diet (CON group), (2) CON + 4% YH (YH group), (3) CON + 2% YH + 2% SDPP (SY group), and (4) CON + 4% SDPP (SDPP group). Growth performance, biochemical parameters, immunoglobulin levels, and intestinal tissue morphology were measured. No substantial difference in growth performance between the YH, SY, and SDDP groups was found; however, compared with the CON group, the performance of these three groups was substantially improved. The contents of serum globulin and ALP in the CON group were markedly decreased compared to the other groups, but the AST level was substantially increased. The IL-10 concentration in the other groups was substantially higher than the CON group, and the highest content was in group YH; the TNF-α content showed an opposite trend. The levels of serum IgG and IgA in the CON group were the lowest among all groups. There were substantial differences among the groups in villi height and crypt depth in the duodenum, jejunum, and ileum. The results showed that YH effectively increased IL-10 concentration and decreased TNF-α level to promote intestinal development, while not differing from SDPP in terms of growth performance.

Keywords: growth performance, immune function, piglets, yeast hydrolysate, spray-dried plasma protein

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Introduction

Weaning stress in piglets often leads to various weaning syndromes that can severely affect piglet feed intake and later growth rate, and thus various measures can be taken to improve feed intake and health status of post-weaning piglets (Campbell *et al*., 2013; Wojnicki *et al*., 2019). High quality protein sources are effective in relieving weaning stress and improving piglet growth (Che *et al*., 2012a). Spray-dried plasma protein (SDPP) is an excellent source of protein used by many companies in creep feed for piglets (Tucker *et al*., 2011). Numerous studies have shown that SDPP, which is made from animal blood, contains many immunoglobulins and growth factors and can be added to weaning diets for piglets (Ermer *et al*., 1994; Bergstrom *et al*., 1997; Ferreira *et al*., 2010). The SDPP can substantially improve the performance and health of piglets, however, it is expensive and its quality varies widely (Zhang *et al*., 2015). Moreover, as an animal-derived protein raw material, SDPP has potential biosafety issues (Van Dijk *et al*., 2001; Che *et al*., 2012a; Prez-Bosque *et al*., 2016), leading to a non-negligible risk in the future. Therefore, finding safe, reliable, non-animal sources of high-quality protein ingredients is a challenge for pig production and feed companies.

Yeast-derived feed products contain a large amount of protein, amino acids, β-glucan, mannose oligosaccharides, chitin, and nucleotides, which can substantially enhance the immunity of the animal,

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improve the quality of animal products, and promote human food safety, nutrition, and health (Zhou *et al.*, 2019). There are many reports on the effects of yeast feed products on weaned piglets (White *et al.*, 2002; Southern *et al.*, 2010; Yang *et al.*, 2018). Yeast hydrolysate (YH) is obtained from yeast cells through acid, alkali, enzyme, or other hydrolysis methods (Amorim *et al.*, 2016). YH is more easily digested and absorbed by animals and promotes animal immunity because it contains more free immune polysaccharides and small peptides (Shah *et al.*, 2018). The high quality of YH makes it a possible substitute for SDPP. However, few studies (Hu *et al.*, 2014) have demonstrated whether YH can lower stress on piglets as SDPP does. Therefore, the purpose of this study was to investigate the effects of full or semi-replaced SDPP with YH in creep feed on related indices of weaned piglets, including feed intake, serum biochemical indexes, immune function, and intestinal structure.

Materials and Methods

This experiment was conducted at Wuhan, China (114° E, 30° N) according to the experimental procedures approved by the Animal Ethics Committee of Wuhan Polytechnic University (Approval Number WPU202011004), Wuhan, China.

The 96 piglets (Duroc × Landrace Large × White) were selected for the experiment. The weaning time was 25 ± 3 days, and the average initial weight (BW) was 7 kg (CV <15%). The 96 piglets were randomly divided into four groups, containing six replicates each with four piglets (two males and two females). The preliminary trial was 3 days, and the formal trial lasted 14 days.

According to the specific situations, a blind sample test was conducted. Four diets were supplied to piglets: (1) basal diet (CON group), (2) CON + 4% YH (YH group), (3) CON + 2% YH + 2% SDPP (SY group), and (4) CON + 4% SDPP (SDDP group). The YH (crude protein ≥ 50% and total free nucleotides ≥ 2.5%) was supplied by Angel Yeast Co., Ltd (Yichang, China). The SDPP was commercially available (*Emp* low ash plasma), with crude protein ≥ 78%. Basal diets were formulated in accordance with the recommended standards (NRC, 2012). The composition and nutrient level of each group are shown in Table 1.

Table 1 Ingredients and nutrient composition of diets fed to Duroc × Landrace Large × White piglets

Items	CON group	YH group	SY group	SPDD group
Ingredients (%)				
Extruded corn	15	15	15	15
Flour	15	15	15	15
Corn	12.623	11.623	12.593	14.349
Extruded soybean	10	10	10	10
Whey powder	8	8	8	8
Rice	8	8	8	8
Soy protein concentrate	6	3.836	3.047	4.373
Fermented soybean meal	8	8	8	5
Glucose	3	3	3	3
Sucrose	3	3	3	3
Spray-dried plasma protein	0	0	2	4
Yeast hydrolysate	0	4	2	0
Super steam fish meal	3	3	3	3
Soybean oil	2	2	2	2
Calcium phosphate	1.636	1.648	1.52	1.483
Calcium formate	1.238	1.216	1.275	1.336
L-lysine	0.723	0.673	0.619	0.566
DL-methionine	1.13	0.307	0.281	0.256
Threonine	0.302	0.264	0.239	0.215
Tryptophan	0.048	0.034	0.028	0.023
Premix[1]	1.4	1.4	1.4	1.4
Total	100%	100%	100%	100%
Nutrient levels [2]				
Digestible energy (kcal/kg)	2611.926	2623.625	2632.893	2634.161
Crude protein	20	20	20	20
Lys	1.7	1.7	1.7	1.7
Met	0.575	1.435	0.606	0.638
Thr	1.05	1.05	1.05	1.05
Trp	0.28	0.28	0.28	0.28
Ca	0.85	0.85	0.85	0.85
Total phosphorus	0.7	0.7	0.7	0.7

CON- control; YH- Yeast hydrolysate; SY- 2% Yeast hydrolysate + 2% spray-dried plasma powder; SDPP- spray-dried plasma powder

[1] The premix provided following per kilogram of basal diet: Vitamin A, 6350 IU; Vitamin D_3, 2150 IU; Vitamin E, 25 IU; Vitamin K, 3 mg; Vitamin B_1, 1.8 mg; Vitamin B_{12}, 0.024 mg; Vitamin B_2, 6 mg; folic acid, 0.9 mg; Vitamin H, 4.5 mg; niacin, 24 mg; pantothenic acid, 20 mg; Zn, 80 mg; Fe, 150 mg; Cu, 10 mg; I, 0.6 mg; Se, 0.5 mg; Co, 0.8 mg

[2] The nutrient levels are calculated values

According to regulations for normal epidemic prevention in experimental farms, piglets were weighed on an empty stomach before feeding in the morning at the beginning and end of the experiment. The piglets were fed in six meals daily with the feed kept fresh and dry without deterioration. During the entire trial period, the piglets were allowed *ad libitum* access to water and feed. The daily feed intake for each pen was obtained by recording the amount of feed and residue in each pen. The diarrhoea situation and the number of piglets in each pen with diarrhoea were recorded, as well as the incidence, number of pigs with diarrhoea, starting time, and treatment. Any piglets found dead were removed from the test group, and the date, their weight, and cause of death were recorded.

Body weight and feed intake were recorded on days 1, 7, and 14, respectively, and average daily gain (ADG), average daily feed intake (ADFI), and feed/gain (F/G) were calculated.

At the end of the experiment, two healthy piglets with similar body weight (a total of 48 piglets) were randomly selected from each pen, and 10 ml of blood was collected from the anterior vena cava on an fasting basis, and centrifuged at 3000 × *g* for 10 min after 30 min of rest. Serum was separated and stored at -20 °C for testing.

Total protein (TP), albumin (ALB), globulin (GLB), glucose (GLU), alkaline phosphatase (ALP), and aspartate aminotransferase (AST) were determined using an automatic biochemical analyser (Hitachi 7180, Hitachi Limited, Tokyo, Japan).

The levels of cytokines (IL-1β, IL-2, IL-10, TNF-α, and INF-γ) in serum and the levels of antibodies (IgG, IgM, and IgA) were determined. The ELISA kits were purchased from Nanjing Jiancheng Biological Co., Ltd (Nanjing, China). The instructions and procedures for the relevant tests were strictly followed.

At the end of the trial, two piglets (one male and one female) from each pen were slaughtered, the abdominal cavity dissected, the digestive tract removed, and the duodenum, jejunum (distal duodenum), and ileum were separated. The tissues of the duodenum (3 cm from the gastric pylorus), the mid-jejunum, and the mid-ileum, ~2 cm respectively, were collected, washed with saline, and kept in 4% neutral formalin.

The fixed tissues were dehydrated in ethyl alcohol, diaphanized in xylol, and embedded with paraffin. Each slide had two 5-μm-thick sections and then the tissue sections were made with hematoxylin-eosin staining. Under the microscope, 10 typical fields of view (villi intact) were randomly selected from each section, and the height of the longest villi (V) in each field of view and the corresponding crypt depth (C) were measured. The V/C ratio was then calculated.

The experimental data were organized using Excel 2016 and analysed using SPSS 19.0 for both control and experimental groups. Variability of all experimental data was expressed as the standard error of the mean. Duncan multiple comparisons were used to test the data for each group, with significance determined at *P* <0.05.

Table 2 Effects of substituting spray-dried plasma powder with yeast hydrolysate (YH) in creep feed on growth performance of piglets[1]

Items		d 1–7	d 8–14	d 1–14
ADFI (g/day)	CON group	393.36 ^{b}	530.93 ^{b}	462.14 ^{b}
	YH group	404.21 ^{ab}	544.71 ^{ab}	474.46 ^{ab}
	SY group	405.57 ^{ab}	546.64 ^{ab}	477.61 ^{ab}
	SDPP group	428.50 ^{a}	551.08 ^{a}	489.75 ^{a}
SEM		17.70	35.21	30.51
Significance		*	*	*
ADG (g/day)	CON group	269.29 ^{b}	251.07 ^{b}	260.18 ^{b}
	YH group	312.00 ^{a}	353.93 ^{a}	334.46 ^{a}
	SY group	314.07 ^{a}	354.87 ^{a}	336.47 ^{a}
	SDPP group	317.50 ^{a}	361.79 ^{a}	339.64 ^{a}
SEM		25.62	32.89	31.54
Significance		*	*	*
F/G	CON group	1.46 ^{a}	2.11 ^{a}	1.78 ^{a}
	YH group	1.28 ^{b}	1.53 ^{b}	1.41 ^{b}
	SY group	1.35 ^{b}	1.53 ^{b}	1.44 ^{b}
	SDPP group	1.35 ^{b}	1.52 ^{b}	1.44 ^{b}
SEM		0.02	0.03	0.03
Significance		*	*	*

[1] Data are means of 24 pens of four piglets at the age of 28–42 days

CON- control; YH- Yeast hydrolysate; SY- 2% Yeast hydrolysate + 2% spray-dried plasma powder; SDPP- spray-dried plasma powder; ADFI- average daily feed intake; ADG- average daily gain; F/G- feed gain ratio; SEM - pooled standard error of the mean

^{a,b} Different letters in the same column differ significantly, *P* <0.05

* *P* <0.05

Results

The effect of diets on ADFI, ADG, and F/G are presented in Table 2. The SDPP group had the highest ADFI (*P* <0.05). Compared with the CON group, ADG of the other groups were higher, while F/G was lower. There was no difference in growth performance among the YH, SY, and SDPP groups (*P* >0.05), indicating that partial or complete replacement of SDPP with YH had no significant effect on growth of early weaned piglets.

There were no differences (*P* >0.05) in levels of TP, ALB, and GLU in serum among the four groups (Table 3). However, the GLB content in the YH group was higher than in the other treatments. There were differences (*P* <0.05) in ALP between the CON group and groups YH, SY, and SDPP. The AST content was higher in the CON than the other three groups (*P* <0.05).

Table 3 The effect of replacing spray-dried plasma powder with yeast hydrolysate (YH) in pig creep feed on serum biochemical variables[1]

Items	CON group	YH group	SY group	SDPP group	SEM	Significance
TP, g/l	47.32	49.85	49.82	50.41	1.25	NS
ALB, g/l	20.78	21.22	22.24	21.25	0.86	NS
GLB, g/l	26.54[b]	28.63 [a]	27.57 [a]	27.15 [a]	1.35	*
GLU, mmol/l	1.82	2.18	2.04	2.04	0.21	NS
ALP, U/L	474.8[b]	689.2[a]	691.8[a]	694.7[a]	56.24	*
AST, U/L	172.0[a]	158.8 [b]	136.6[c]	133.7[c]	20.65	*

[1] Data are means of 24 pens of two piglets at the age of 42 days
CON- control; YH- Yeast hydrolysate; SY- 2% Yeast hydrolysate + 2% spray-dried plasma powder; SDPP- spray-dried plasma powder; TP-total protein; ALB-albumin; GLB- globulin; GLU- glucose; ALP- alkaline phosphatase; AST- aspartate aminotransferase; SEM - pooled standard error of the mean; NS- nonsignificant
[a,b,c] Different letters in the same row differ significantly, *P* <0.05
* P <0.05

The IL-10 concentration in the YH, SY, and SDPP groups was higher (*P* <0.05) than in the CON group, and the highest content was for YH (Table 4). Compared with the CON group, the TNF-α content was lower in the other three groups, and was lowest for YH (*P* <0.05). The contents of serum IgG and IgA in the YH, SY, and SDPP groups were higher than in the CON group (*P* <0.05).

Table 4 The effect of replacing spray-dried plasma powder with yeast hydrolysate (YH) in pig creep feed on serum cytokine and immunoglobulin concentrations[1]

Items	CON group	YH group	SY group	SDPP group	SEM	Significance
IL-1β, pg/mL	31.24	32.34	31.83	31.91	1.24	NS
IL-2, pg/mL	605.48	598.51	596.47	601.41	18.63	NS
IL-10, pg/mL	212.59 [a]	345.95 [c]	324.82 [c]	287.11 [b]	11.24	*
TNF-α, pg/mL	480.24 [a]	422.15 [c]	435.24 [bc]	445.65 [b]	10.65	*
INF-γ, pg/mL	178.65	155.82	164.38	169.27	8.64	NS
IgG, g/l	2.11 [a]	3.22 [b]	3.13 [b]	3.37 [b]	0.45	*
IgM, g/l	0.54 [a]	0.58	0.65	0.59	0.13	NS
IgA, g/l	1.01 [a]	1.32 [b]	1.34 [b]	1.41[b]	0.55	*

[1] Data are means of 24 pens of two piglets at the age of 42 days
CON-control; YH-Yeast hydrolysate; SY-2% Yeast hydrolysate + 2% spray-dried plasma powder; SDPP- spray-dried plasma powder; SEM- pooled standard error of the mean; IL-1β- interleukin-1β; IL-2- interleukin-2; IL-10- interleukin-10; TNF-α- tumour necrosis factor alpha; INF-γ- interferon gamma; IgG- immunoglobulin G; IgM- immunoglobulin M; IgA- immunoglobulin A; NS- nonsignificant
[a,b,c] Different letters in the same row differ significantly, *P* <0.05
* *P* <0.05

There were difference among the groups (*P* <0.05) in duodenal V and C (Table 5 and Fig. 1). The V/C ratio, in order of SDPP > YH > SY > CON groups, suggested that the SDPP group had the best duodenal development, followed by the YH group, and the CON group had poorer intestinal development.

Growth of jejunal villi was better in groups SDPP and SY than in YH and CON. The V/C ratio in the SDPP and CON groups differed (*P* <0.05).

The piglets in the SDPP, SY, and YH groups differed from the CON group in ileum V (*P* <0.05). The V/C ratio of SDPP and YH groups was higher than in the other groups (*P* <0.05).

Table 5. Effect of replacing spray-dried plasma powder with yeast hydrolysate (YH) in creep feed on villi height (V) and crypt depth (C) of the duodenum, jejunum, and ileum of piglets[1]

Items		CON group	YH group	SY group	SDPP group	SEM	Significance
duodenal	villi height (μm)	73.24 [a]	78.58 [b]	76.04 [b]	79.30 [b]	8.62	*
	crypt depth (μm)	71.20 [a]	66.48 [b]	69.77[b]	63.74 [b]	6.98	*
	V / C	1.03 [a]	1.18 [a]	1.09 [a]	1.24 [b]	0.35	*
jejunal	villi height (μm)	59.91 [a]	65.69 [a]	70.70 [b]	74.98 [b]	7.32	*
	crypt depth (μm)	52.10	51.15	52.28	54.56	5.90	NS
	V / C	1.15 [a]	1.28 [a]	1.35 [b]	1.37 [b]	0.35	*
ileum	villi height (μm)	50.27 [a]	57.87 [b]	56.73 [b]	61.80 [b]	6.25	*
	crypt depth (μm)	47.09	47.54	50.66	48.22	5.03	NS
	V / C	1.06 [a]	1.22 [b]	1.12 [a]	1.28 [b]	0.25	*

[1] Data are means of 24 pens of two piglets at the age of 42 days
CON, control; YH, Yeast hydrolysate; SY, 2% Yeast hydrolysate + 2% spray-dried plasma powder; SDPP, spray-dried plasma powder; SEM- pooled standard error of the mean; V/C- villi height / crypt depth; NS- nonsignificant
[a,b] Different letters in the same row differ significantly, P <0.05
* P <0.05

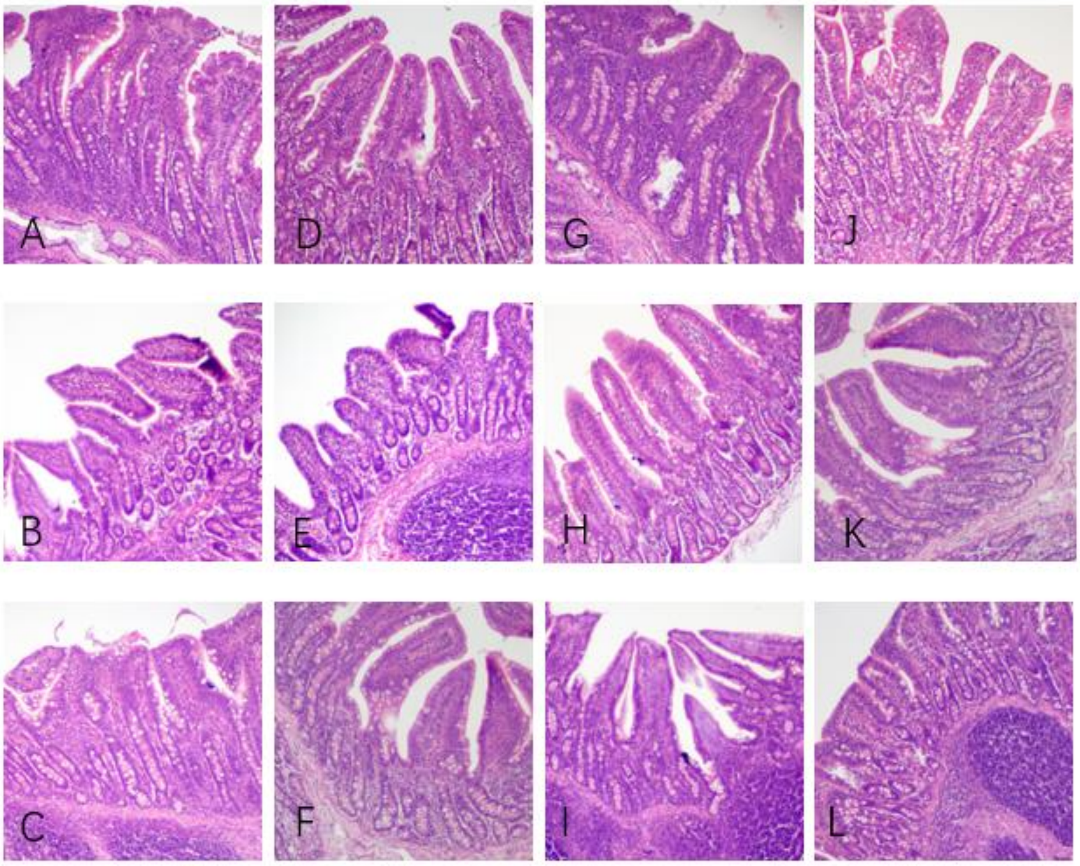

Figure 1 Effects of dietary supplementation on histological evaluation of intestinal morphology (HE, ×400): (A, B, C) control group; (D, E, F) 4% yeast hydrolysate group; (G, H, I) 2% yeast hydrolysate + 2% spray-dried plasma powder group; and (J, K, L) 4% spray dried plasma powder group. (A, D, G, J) Duodenum; (B, E, H, K) jejunum; and (C, F, I, L) ileum

Discussion

Weaning is considered to be one of the most challenging parts of the pig breeding cycle, often leading to anorexia, health problems, damage to the intestinal structure and digestive tracts (because the digestive glands of the piglets are not well developed), and increased pathogenic diseases (Heo *et al*., 2013). The results of this experiment agreed with those of Rigueira *et al*. (2013) and Hu *et al*. (2014), who showed that dietary supplementation of plasma protein powder or yeast extract had similar effects on weight gain, feed intake, and feed conversion efficiency of weaned piglets, and the effects were all better than those of basal diet group.

ALP exists in all tissues of the body, especially in bone, liver and kidney. ALP in normal serum mainly comes from bone, is produced by osteoblasts, travels through the blood to the liver, and is excreted from the biliary tract system (Tang *et al*., 2019). Yang *et al*. (2016b) reported that the ALP activity in the ileal mucosal of piglets on a chito-oligosaccharide diet was greater than that in basal-diet piglets. In our study, the SDPP group had the highest ALP activity, and the CON group had the lowest, indicating that the CON group had weaker osteogenic activity and slower skeletal growth than the other groups. The AST exists in a variety of cells and is a sensitive marker of liver cell damage (Xiong *et al*., 2015). Our results showed that AST concentration was highest in the CON group, with no significant differences among the other groups, indicating that YH or SDPP in piglet feed could protect the liver of piglets. Feng *et al*. (2020) reported that antimicrobial peptide, cathelicidin-BF, treatment in piglets decreased levels of serum blood AST but increased levels of serum ALP compared to the basal-diet group, consistent with our results.

Serum GLB is a mixture of various proteins (including immunoglobulin and complement) that have a defensive effect and are abundant, and a variety of glycoproteins. The GLB is produced by the immune organs of the body. Most of the GLB is produced outside the liver cells and is related to immunity of the body (Ye *et al*., 2020). It was reported that, compared with the basal diet, the supplementation of *Lactobacillus planplanum* GF103 and *Bacillus subtilis* B27 increased the serum GLB concentration at day 14 (Dong *et al*., 2014). Our results showed that the GLB content was lowest in the CON group, indicating that the immune function of piglets in this group was poor. There was no marked difference among the SDPP, SY, and YH groups, indicating that YH could effectively improve the immune function of the body.

Cytokines are a kind of small molecular protein with wide biological activity, synthesized and secreted by immune cells through stimulation. They regulate cell growth, differentiation, and are effective by binding to corresponding receptors to regulate the immune response. The balance and regulation between pro-inflammatory cytokines (IL-1β, IL-2, TNF-α, and INF-γ) and anti-inflammatory cytokines (IL-10) in animals is of great physiological significance in maintaining the normal immune response of the body (Sabbioni *et al*., 2012; Ramani *et al*., 2015). It was found that dietary inclusion of YH enhanced the serum IL-10 level (Fu *et al*., 2019). Deng *et al*. (2017) reported that yeast polysaccharide could increase serum IL-10 and TGF-β levels, and decrease serum IL-1β and IL-6 levels. Che *et al*. (2012b) found that dietary manna oligosaccharide supplementation had no effect on serum TNF-α concentration of weaned piglets but tended to increase serum IL-10 level. Our experiments showed that SDPP and YH could reduce an excessive immune response and increase the utilization of nutrients by increasing IL-10 secretion and decreasing TNF-α secretion, thus improving the performance of weaned piglets.

Natural antibodies are all kinds of antibodies that exist naturally in the body of animals without obvious infection or artificial injection of antigens, and play an early defence role by preventing and delaying the spread of pathogenic bacteria to vital organs (Holodick *et al*., 2017). In our study, the serum IgG and IgM were lower in the CON group than the other groups, indicating that the CON group had poorer immunity and was more prone to diarrhoea. This concurs with the study of Xiong *et al.* (2015), in which supplementation of yeast product in the diet of weaned piglets increased serum IgG and IgM contents compared to the control group.

Having a healthy small intestine is important because this is the major site of nutrient, water, and electrolyte absorption by the enterocytes located in the villi. Enterocytes are produced in the crypts and migrate to the tip of the villi. Reduction of V and increase in C are associated with a reduced capacity for absorption (Nabuurs *et al*., 1993; Pluske *et al*., 1996). The functionality of the small intestine depends greatly on V and C. It is common to observe villus atrophy during the first weeks after weaning, which is caused by an increase in cell loss and a slow recovery process (Yang *et al*., 2016a; Fu *et al*., 2021). In this experiment, the V and V/C of the SDPP group were greater than those of other groups, indicating that the SDPP group had the best effect in promoting villi growth and epithelial cell maturation rate. The SY group was slightly better than the YH group in jejunal development; however, the YH group had better duodenum and ileal development than the SY group. The CON group had poorer intestinal development than the other groups. These results are consistent with the results of growth and immunization.

Conclusions

The experimental results showed no significant difference in growth performance between piglets fed YH and those fed SDPP (P >0.05), but these two groups had better growth performance than the CON group. Adding YH improved IL-10 and TNF-α levels compared to other groups (P <0.05). In summary, YH effectively increased the concentration of IL-10 and decreased the content of TNF-α to promote intestinal development, while not differing from SDPP in terms of growth performance. These results suggested that YH could replace SDPP as a high-quality protein source in piglet creep feeds.

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Author Contributions

XQH, JPH, JJD, and XDW designed and supervised the work, and edited the paper. ZG and WBW performed laboratory work and drafted the manuscript. AQG assisted in laboratory work. All authors have read and agreed to the published version of the manuscript.

Conflicts of interest

The authors declare no conflicts of interest.

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