Original Article

Effects of a herbal compound, KIOM-C, on growth performance and immune response in commercial pigs

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The use of non-therapeutic antibiotics as animal feed additives has raised public health concerns due to the increasing resistance of pathogens to antibiotics. It is therefore required to develop safe and effective alternative feed additives to replace non-therapeutic antibiotics. The aim of this study was to assess the effects of the multi-herbal compound, KIOM-C, on growth performance and immune response of growing-to-finishing pigs under farm conditions. The experimental trials were performed in a Korean commercial swine growing-to-finishing complex, and a total of 70-day-old 160 pigs were selected. Eighty pigs were treated with KIOM-C at the level of 2 kg/tonne until slaughter age (KT group), while another 80 pigs were not treated with KIOM-C (NT group). All animals were vaccinated against foot-and-mouth disease (FMD) at 60 and 110 days of age. During the trial period, average daily weight gain (ADWG), average daily feed intake (ADFI), feed conversion ratio (FCR), survival rates, and average slaughter ages were measured. The serum concentrations of tumor necrosis factor-a (TNF-a), interferon-γ (IFN-γ), and IgA were also evaluated. In order to evaluate specific humoral immune responses, the foot-and-mouth disease virus (FMDV) serotype O-specific antibody was measured. The ADWG, ADFI, and FCR of the KT group were significantly greater than those of the NT group (p<0.05). Serum concentrations of IgA in the KT group were statistically higher than the NT group. The antibody levels of the KT group against FMDV serotype O was higher than the NT group, and 86.67% of the KT group tested positive for anti-FMDV antibodies. Overall, these findings suggest that KIOM-C improves growth performance and immune response of pigs under growing-to-finishing farm conditions, and implies that the herbal compound may be used as a suitable alternative feed additive.

Key words: alternative feed additives, herbal compounds, pigs, growth performance, immune responses

Introduction

Antimicrobial feed additives have been widely used as a tool for enhancing growth performance in the swine industry [1, 2]. However, the emergence of antibiotic-resistant pathogens has raised public health concerns, to the extent that non-therapeutic antibiotics in feed additives were prohibited in Europe and South Korea [3–5]. Thus, there is an urgent need to develop effective and safe alternative feed additives, without the residual effects, to improve growth performance and immunity in farm animals [2, 6].

After the use of non-therapeutic antibiotics was prohibited in swine farms, researches have been widely conducted for developing the novel agents as feed additives to increase growth performance and immune responses in the swine industry [7–9]. The immunity of pigs directly affected susceptibility for various bacterial and viral infections in farm conditions. The increased resistance of antibiotics has been reported in swine farms raising public health concerns. Also, the use of antiviral materials was limited in swine farms due to their toxicity, high costs, and restricted effective spectrum for viruses [7–11].

Recently, the herbal mixture compound KIOM-C was found to improve growth performances and immune responses in porcine circovirus associated disease (PCVAD) infected weaning piglets under experimental conditions [12]. Moreover, KIOM-C evoked antiviral cytokines secretion against several viruses and inhibited virus replications in hosts [12–15]. However, the previous reports related to KIOM-C have been performed on only weaning pig...
lets, evaluating non-specific immune responses after short- 
term use of KIOM-C under experimental conditions.

The purpose of this study was to evaluate the effects of 
long-term use of commercialized KIOM-C on growth per-
formance, nonspecific immune response, and specific hu-
noral immune response against the foot-and-mouth disease 
virus (FMDV) in growing-to-finishing commercial pigs 
under farm conditions.

Materials and Methods
Experimental substances
We used commercially available KIOM-C product (Vita-
bio Inc., Daejeon, Korea) in this study [12, 13, 15]. This 
product contains the mixtures of various herbal compounds 
including Zingiber officinale (Z. officinale), Scutellariae radix (S. radix), Platycodon grandiflorum (P. grandi-
florum), Glycyrrhiza radix (G. radix), Paeoniae radix alba (P. radix alba), and Angelicae gigantis radix (A. gigantis radix).

Farm history
All pigs were reared in a Korean commercial pig produc-
tion system. The complex produces approximately 
35,000 slaughter pigs from 1,500 crossbred sows (Landrace × Yorkshire) annually. At 10 weeks of age, pigs were 
moved into the growing-to-finishing complex, with slatted 
floor, where they remain until reaching approximately 
110 kg in body weight. Windows and electrical ventilators 
were used for air ventilation and to maintain the tem-
terature at approximately 19 ± 1°C. All animals are vacci-
nated against FMDV at 60 and 110 days old, using the 
commercially available FMDV vaccine (ARRIAH-VAC®, 
FGBI ARRIAH, Vladimir, Russia). The farrowing-to-
weaning complex has a history of Haemophilus parasuis, Streptococcus suis, and Mycoplasma hyopneumoniae in-
fecions. The growing-to-finishing unit was infected by 
pathogenic bacteria from a previous barn. In addition, por-
cine respiratory and reproductive syndrome virus (PRRSV) 
and Actinobacillus pleuropneumoniae (A. pleuropneu-
moniae) were also present.

Feeds
Basal diets fed to pigs at each stage (weaners, growers, 
and finishers) were commercial concentrated feeds ob-
tained from the market with the following specifications: 
1) Weaner feed: ME 3,460 kcal/kg, crude protein 19.01%, 
crude fat 5.10%, crude fiber 3.39%, crude ash 5.19%, 
lysine 1.20%, calcium 0.79%, and phosphorus 0.55%; 2) 
Grower feed: ME 3,200 kcal/kg, crude protein 15.52%, 
crude fat 2.65%, crude fiber 4.01%, crude ash 4.76%, 
lysine 1.05%, calcium 0.85%, and phosphorus 0.45%; and 
3) Finisher feed: ME 3,150 kcal/kg, crude protein 
13.17%, crude fat 3.20%, crude fiber 3.18%, crude ash 
3.91%, lysine 0.80%, calcium 0.58%, and phosphorus 
0.40%. Feed and water were provided ad libitum.

Experimental design
A total of healthy 160 pigs (70 days of age) were se-
lected from the weaner unit. The pigs were then divided 
into 2 groups (80 pigs per group) as follows: KIOM-C 
treated (KT) group and non-treated (NT) group. Each 
group, comprising of pigs of the same sex and body weight ($p>0.05$), was held in separate locations. Each 
group was separated into eight trial pens (ten pigs per pen) and pigs individuals could be identified by their 
ear-markings. The selected groups of weaner pigs were not fed performance enhancers, probiotics, antimicrobials, 
or acidifiers. After moving weaner pigs to their trial pens, 
the KT group was treated with KIOM-C at the level of 
2 kg/tonne of basal feed from 70 days of age to slaughter 
age. KIOM-C was not added to the basal feed components 
of the NT group.

Growth performance
In order to estimate the average daily weight gain 
(ADWG) of each group, pigs were weighed three times 
at the start the growing stage (70 days of age), the start 
of finishing stage (119 days of age), and the end of the 
experiments (182 days of age). The age of pigs reached 
slaughter weight (110 ± 5 kg) was recorded to estimate 
average slaughter ages. Quantities of feed intake per pen 
of pigs were recorded every week by calculating the dif-
fERENCE in weights (kg) between the quantity of feed and 
residual feed, and then the average daily feed intake 
(ADFI) of each group was calculated. The feed conversion 
ratio (FCR) was calculated as the total feed intake divided 
by the total body weight gain of each group in each trial 
period.

Clinical signs
The clinical signs such as coughing, dyspnea, depression, 
inappetence, vomiting and diarrhea were monitored twice 
a day for all trial pigs by the farm technicians. If disease 
symptoms were detected, the affected pigs were allocated 
to a separate pen designed for sick pigs and treated by 
a swine veterinary expert. Deaths were recorded weekly 
by farm technicians throughout the trial period. We per-
formed an autopsy for all deaths and examine the micro-
organism infection when suspected lesions were found. 
The blood of 30 pigs per group was collected at 70 days 
and 130 days of age, respectively.
Nonspecific and specific immune analysis

Blood samples were collected from jugular veins in pigs. Serum was aseptically obtained from the supernatant of blood samples after centrifugation at 12,000 rpm for 20 min. Serum concentrations of porcine specific tumor necrosis factor-a (TNF-α) and interferon-γ (IFN-γ) were measured using commercial enzyme-linked immunosorbent assay (ELISA) kits (Quantikine; R&D Systems, Minneapolis, Minnesota, USA) according to the manufacturer’s protocols. The serum IgA titers were determined by the Pig IgA ELISA Quantification Kit (Bethyl Laboratories, Montgomery, Texas, USA) following the manufacturer’s instructions. In order to assess the humoral immune responses specific for FMDV, anti-FMDV serotype O antibody levels of experimental animals were measured using the commercial ELISA Kit (PrioCHECK FMDV type O ELISA kit, Prionics AG, Schlieren-Zurich, Switzerland) as per manufacturer’s protocols. The percentage inhibition (PI) values were calculated by measuring the optical density (OD) at 450 nm, where PI values below 50% reflected an absence of anti-FMDV type O antibodies in a test serum.

Statistical analysis

Pens and individual pigs were regarded as an experimental unit for growth performance data and immune analysis, respectively. GraphPad Prism 5 software (GraphPad Software, Inc., San Diego, USA) was used to analyze the data using a one-way ANOVA followed by a Tukey’s HSD post hoc analysis. The difference in the survival rates between the two groups was evaluated by two statistical methods including Kaplan-Meier method and log-rank test. Statistical significance was accepted at the level of $p$ value<0.05.

Results

Growth performances

The growth performance parameters in groups of pigs were described in Table 1. During the entire trial period (70–182 days of ages), the ADWG and ADFI of the KT group was significantly higher than the NT group ($p<0.05$), and the FCR of the KT group was significantly greater than the NT group ($p<0.05$). Compared with the NT group, the KT group had a significantly higher ADWG ($p<0.05$) at the growing stage. The ADFI of the KT group at the growing stage was significantly greater than the NT group ($p<0.05$); however, the FCR was similar in all groups during the growing stage ($p>0.05$). During the finishing stage, the KT group had a significantly higher ADWG and ADFI compared to the NT group ($p<0.05$). According to the FCR calculated for the finishing period, the KT group had a significantly better-feed utilization than that of the NT group ($p<0.05$). When average slaughter age was calculated for pigs reaching slaughter weight (110 ± 5 kg), there was a significant decrease in the time

Table 1. Growth performance parameters of growing-to-finishing pigs in two experimental groups: KIOM-C treated (KT) group and non-treated (NT) group

<table>
<thead>
<tr>
<th>Stages</th>
<th>Experimental groups</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>KT group</td>
<td>NT group</td>
<td>$p$-value</td>
<td></td>
</tr>
<tr>
<td>Average daily weight gain (kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Growing stage</td>
<td>0.592 ± 0.031</td>
<td>0.541 ± 0.032</td>
<td>$p=0.0056$</td>
<td></td>
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<tr>
<td>Finishing stage</td>
<td>0.864±0.029</td>
<td>0.815 ± 0.025</td>
<td>$p=0.0029$</td>
<td></td>
</tr>
<tr>
<td>Total trial period</td>
<td>0.622*** ± 0.011</td>
<td>0.580 ± 0.008</td>
<td>$p&lt;0.0001$</td>
<td></td>
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<tr>
<td>Average daily feed intake (kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Growing stage</td>
<td>2.149*** ± 0.057</td>
<td>1.935 ± 0.046</td>
<td>$p&lt;0.0001$</td>
<td></td>
</tr>
<tr>
<td>Finishing stage</td>
<td>3.166±0.033</td>
<td>3.132 ± 0.035</td>
<td>$p=0.0673$</td>
<td></td>
</tr>
<tr>
<td>Total trial period</td>
<td>2.056*** ± 0.021</td>
<td>1.978 ± 0.012</td>
<td>$p&lt;0.0001$</td>
<td></td>
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<tr>
<td>Feed conversion ratio</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Growing stage</td>
<td>3.634 ± 0.183</td>
<td>3.588 ± 0.269</td>
<td>$p=0.6903$</td>
<td></td>
</tr>
<tr>
<td>Finishing stage</td>
<td>3.669±0.149</td>
<td>3.847 ± 0.093</td>
<td>$p=0.0124$</td>
<td></td>
</tr>
<tr>
<td>Total period</td>
<td>3.309*** ± 0.086</td>
<td>3.410 ± 0.052</td>
<td>$p=0.0132$</td>
<td></td>
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<tr>
<td>Average slaughter age (days)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total trial period</td>
<td>200.500*** ± 0.756</td>
<td>210.375 ± 1.061</td>
<td>$p&lt;0.0001$</td>
<td></td>
</tr>
</tbody>
</table>

*p<0.05; **p<0.01; ***p<0.001.
taken for pigs to reach slaughter weight in the KT group compared to the NT group ($p<0.05$).

**Pathogenicity evaluation**

The survival rates in pigs of the NT and KT groups were evaluated throughout the trial periods. The survival rates of the KT group seemed to be higher than that of the NT group; however, this difference was not statistically significant ($p>0.05$) (Fig. 1). The concomitant infection of PRRSV and *A. pleuropneumoniae* was identified in pigs in the growing and finishing stages. Disease symptoms during experimental trials were evaluated for all pigs. NT pigs tended to represent various clinical symptoms more frequently compared to the KT group including coughing, dyspnea, depression, Inappetence and diarrhea (Table 2).

**Nonspecific and specific immunity**

Concentrations of IFN-$\gamma$, TNF-$\alpha$, and IgA in the experimental groups were successfully obtained in serum samples collected from pigs. Serum IFN-$\gamma$ and TNF-$\alpha$ levels in the KT group increased slightly after treatment with KIOM-C; however, no significant difference was found between the KT and NT groups ($p>0.05$). Interestingly, the IgA level of the KT group at 130 days of age increased significantly, by more than 7 times, compared to the NT group ($p<0.05$) (Fig. 2). Additionally, the level of FMDV type O specific antibodies increased significantly in the KIOM-C supplemented group compared to the NT group ($p<0.05$) (Fig. 3). The percentages of antibody positive animals against the structural protein of serotype O after the second vaccination were 86.67% and 66.67% in the KT group and NT group, respectively.

**Discussion**

Feed additives are necessary for improving productivity in the swine industry. However, with the demands of consumers tending towards safe animal products, antimicrobial feed additives have been banned in Korea and

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Fig. 1. Survival rates (%) of growing-to-finishing pigs in two experimental groups: KIOM-C treated (KT) group and non-treated (NT) group. The deaths were evaluated weekly in pigs aged from 70 days of age to slaughter.

Table 2. Disease signs of growing-to-finishing pigs in two experimental groups, KIOM-C treated (KT) group and non-treated (NT) group.

<table>
<thead>
<tr>
<th>Clinical signs</th>
<th>No. of pigs in pens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>KT group</td>
</tr>
<tr>
<td>Total no. of pigs with any clinical signs</td>
<td>9</td>
</tr>
<tr>
<td>Coughing</td>
<td>6</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>2</td>
</tr>
<tr>
<td>Depression</td>
<td>6</td>
</tr>
<tr>
<td>Inappetence</td>
<td>4</td>
</tr>
<tr>
<td>Vomiting</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1</td>
</tr>
</tbody>
</table>

Fig. 2. Mean (± S.D.) serum concentration levels of IFN-$\gamma$ (A), TNF-$\alpha$ (B) and IgA (C) in two experimental groups of pigs: KIOM-C treated (KT) group and non-treated (NT) group. Statistical significance was determined as $p$-values under 0.05. Error bars indicate standard deviations.
has both anti-inflammatory and antibacterial effects [22, 23]. *P. grandiflorum* activates B cell and macrophage responses, and improves intestinal health and immune responses of pigs, and when combined with *G. Radix*, has antiviral activity against rotavirus infection in piglets [24, 25]. Therefore, the combined effects of these herbal compounds could improve growth performance of the KIOM-C treated group in this study.

In a previous study, KIOM-C proved to increase protection against PCVAD infection in weaning piglets [12]. In this study, the levels of IFN-γ and TNF-α in KT group showed significant differences compared to those of NT groups. Interestingly, total serum IgA titers increased significantly in KT group. IgA is a major immunoglobulin of humoral immunity, which mainly contributes to protection against local pathogens in the mucosal surface in the form of secretory IgA (sIgA) [26, 27]. Serum IgA acts as a second line of defense by forming an immune complex with the aggressive pathogens and then interacting with receptors in the Fc region of IgA (FcαR) on the surface of the immune effector cells. This mechanism promotes antibody-dependent cell-mediated cytotoxicity (ADCC) and phagocytosis [27–30]. Thus, the substantial increase in serum IgA levels in this study signifies immune-stimulatory effects of KIOM-C, especially as mucosal and inflammatory immunity.

IgA might have the positive effects on growth performance (Table 1). IgA proved to form passive immunity in the intestinal environment of newborn piglets by secreting from the mother’scolostrum or milk through the gut-mammary axis, and IgA synthesis increases temporarily postpartum in order to deliver maternal immunity to neonatal piglets [31, 32]. Therefore, further studies are necessary to determine the effects of KIOM-C on a sow’s lactogenic immunity and its protective effects against intestinal pathogens for neonatal piglets. High levels of serum IgA, however, could elicit the accumulation of FeR-IgA complexes into the kidney and induce nephropathy in older humans [33, 34]. Although any evidence of disease derived from IgA nephropathy was not found in the present study, additional studies are necessary to determine the possibility of IgA nephropathy following the long-term use of KIOM-C.

FMDV infection, a highly contagious viral disease mainly occurring in cloven-hoofed animals, has resulted in economic losses in the swine industry by increased costs associated with vaccination and disease eradication policies [35]. Vaccination policies have been adopted worldwide to prevent FMD outbreaks, however, the vaccination of pigs generally induces poor humoral immune responses compared to those of cattle [36, 37]. This issue has prompted several approaches to enhance immune responses.
to vaccinations [38–40]. The results of the present study showed that KIOM-C supplementation in the diets of pigs elicited significantly higher anti-FMDV antibody levels and showed more than 80% seroconversion rates, which were an adequately positive rates for herd immunity, as mentioned in previous studies [37, 41, 42]. Therefore, these findings suggest that KIOM-C may be a potential immune-stimulator for enhancing the efficacy of FMDV vaccination, although further research should be performed to investigate the accurate mechanism study for enhancement of KIOM-C on humoral response.

In conclusion, KIOM-C compound had a positive effect on growth performance, an elevated activity on serum IgA levels and antibody response against FMD serotype O in growing-to-finishing pigs. Therefore, KIOM-C may have the potential to be applied as a feed additive to improve humoral immunity and productivity in commercial pigs. However, further research should be performed to clarify the underlying mechanisms associated with the positive effects of KIOM-C in this study and to establish the long-term safety of KIOM-C usage on pigs.

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References

20. Ali BH, Blunder G, Tanira MO, Nemmar A. Some phytochemical, pharmacological and toxicological properties of


