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The potential of phytogenic feed additives in disease prevention and reduction of medications

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Introduction

Weaning is a stressful period in the life of pigs with increased susceptibility to environmental and pathogenic challenges (Pluske & Hampson, 1997). These challenges can cause a severe decrease in growth performance and an increase in the need for medications, causing overall considerable economic losses. In the past, antimicrobial growth promoters (AGP) like antibiotics and zinc oxide have been used to counteract these problems (Vondruskova et al., 2010). Increasing occurrence of antimicrobial resistances and a negative environmental impact of these feed supplements, however, raised the need to investigate alternatives to prevent disease development in livestock animals. Phytogenic feed additives (PFA), based on plants and plant derived products like essential oils, have the potential to support health and well-being of animals, in particular during critical periods of their lives (Yang et al., 2015). Consequently, the hereby presented current studies aimed to characterize the modes of action and benefits of PFA with regard to post-weaning diarrhea (PWD) in piglets.

Material and Methods

Three studies have been conducted to evaluate the potential of PFA on piglets' health. In study 1, the effects of fimbriae expression on the surface of pathogenic *Escherichia coli* was studied using an *in vitro* mucus adhesion assay. In brief, microtiter plates coated with ileal mucus of piglets were incubated with a radioactive labelled F4+ fimbriated *E. coli* strain and four different phytogenic substances at non-growth inhibiting concentrations (sub-MIC). Unbound bacteria were removed by washing and the measured remaining radioactivity corresponded to proportion of adhered bacteria.

In study 2 a trial with 132 piglets (6 per pen, 11 pens per treatment) was conducted to determine gut barrier integrity (Aumiller et al., 2018). Piglets received diets with or without supplementation of a phytogenic additive. At day 14 and day 42 one piglet per pen was slaughtered and samples from distal small intestine were used for an *ex vivo* FITC-4kDa permeability assay.

Study 3 was carried out in a commercial farm with history of high incidence of PWD. Piglets were assigned to two groups (200 male and 200 female animals per group): Whereas one group was fed an unsupplemented diet, a PFA was added to feed of the second group. Mortality, appearance of diseases and use of medication was recorded.

Results

Study 1: In untreated microtiter wells nearly 20% of radioactive labelled pathogens adhered to the mucus coating, indicating the occupation of all available receptor sites in the wells. Test substance 1 increased attachment to the mucus whereas substance 2 had no effect, and substances 3 and 4 reduced mucosal attachment compared to the control.

Study 2: Permeability for the FITC-4kDa marker was reduced in the PFA group at day 14 by 69.3% (P=0.049) compared to the control group. At day 42, a non-significant reduction was observed (difference of PFA to control -28.2%; P=0.465).

Study 3: Overall mortality was at a low level with 1.75% in the control and 1.0% in the PFA group. Occurrence of PWD (118/82 in control/PFA group) was reduced by 30.5% (P<0.001). Respiratory disorders (46/44 in control/PFA group, P=0.833) and other diseases (7/8 in control/PFA group, P=0.761) were not affected by treatment. Antibiotic treatments against PWD (82/45 in control/PFA group) were reduced by 45.1% with supplementation of the PFA.

Discussion and Conclusion

The occurrence of PWD in piglets is frequently associated with the presence of F4-positive *E. coli* strains (Fairbrother et al., 2005). These fimbriae are important for intestinal adhesion and colonization of *E. coli* and previous studies demonstrated, that quorum sensing is involved in their expression (Sturbelle et al., 2015). The results of study 1 strongly suggest, that several phytogenic substances are capable to influence adhesion behavior of F4 fimbriated *E. coli in vitro* at sub-MIC concentrations. It can be speculated, that this is a result of interference with bacterial quorum sensing. Reduced adhesion of pathogenic *E. coli* protects the intestinal tract from loss of gut barrier integrity. For this purpose a PFA was formulated, using efficient substances from study 1 and evaluated regarding its effect on gut barrier integrity in piglets in study 2. The reduction of FITC-4kDa in the *ex vivo* permeability assay suggests, that the prototypes were able to support the integrity of the piglets' small intestinal barrier at day 14 after weaning. During further maturation of the animals, this effect was nearly lost, although numerically lower permeability for FITC-4kDa was also seen at day 42. Using the same PFA in study 3 revealed its potential to protect piglets from the outbreak of PWD, indicated by both,

a significantly reduced number of sick piglets and reduction of medications needed to treat these animals. Due to the specific formulation of the PFA for PWD prevention no additional benefits could be detected with regard to respiratory and other disorders between control group and PFA treated animals.
In summary, it can be concluded, that specific PFAs are suitable to support post-weaning piglets against *E. coli* associated PWD. Application of these products can therefore reduce the negative economic impact of post-weaning health issues.

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