Cranberry extract inhibits *in vitro* and *in vivo* adhesion of F4 and F18* E. coli* to pig intestinal epithelium and reduces excretion in experimentally infected pigs

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**Introduction**

Enterotoxigenic or verotoxigenic *Escherichia coli* (E. coli) expressing F4 or F18 fimbriae are an important cause of these diseases, leading to considerable economic losses due to mortality, decreased growth rate and cost of medication. Antibiotics are routinely used to combat these infections, but due to the alarming emergence of microbes resistant to these antibiotics, there is an urgent need to develop alternatives.

Cranberry (*Vaccinium macrocarpon* Ait.) has been shown to be effective in prevention of urinary tract infections (UTIs) in humans caused by type 1- or P-fimbriated *Escherichia coli*. In the present study, we aimed to assess whether cranberry can also act against other types of fimbriated *E. coli*, namely F4+ *E. coli* and F18+ *E. coli*.

**Materials and Methods**

The inhibitory capacity of cranberry on F4+ and F18+ *E. coli* adhesion was assessed via *in vitro* villous adhesion tests, *in vivo* intestinal loop experiments and an F18+ *E. coli* challenge experiment in pigs.

For the challenge experiment with F18+ *E. coli*, 6 F18-sonerative and F18R positive conventionally bred pigs were selected from 1 litter. They were divided into two groups: (i) a control group receiving standard feed (n = 3), (ii) the cranberry group which received 1% cranberry powder (= 10 g/kg) in the feed and 0.1% cranberry powder (= 1 g/L) in the drinking water (n = 3). The pigs were deprived of food and drinking water prior to the challenge infection.

Next, an F18+ *E. coli* infection experiment was performed and it was found that F18* E. coli* excretion tended to be reduced in pigs that received cranberry extract both in feed and drinking water (Figure 3A). Also, diarrhea score was observed to be reduced in the cranberry treated group (Figure 3B).

Higher antibody levels were observed in the control group compared to the cranberry group (Figure 4), which is consistent with a lower exposure to the pathogen of the pigs from the cranberry group.

**Results**

Cranberry extract was found to inhibit *in vitro* F4+ and F18+ *E. coli* adherence to pig intestinal villi (Figure 1A). This effect was not due to antimicrobial activity (Figure 1B).

Furthermore, cranberry extract was found to inhibit *in vivo* adherence of F4 and F18 fimbriae to pig gut epithelium (Figure 2).

In conclusion, we showed that cranberry extract, which has been proven to be a safe and natural product against a variety of pathogens, leads to inhibition of *in vitro* F4+ and F18+ *E. coli* adherence to pig intestinal epithelium. Moreover, a pilot challenge experiment with F18+ *E. coli* revealed that cranberry extract added to both feed and drinking water tended to reduce excretion of the pathogen and the duration of shedding. For this reason, cranberry could be considered as alternative for antibiotics to combat *E. coli* infections in piglets.

Further studies need to be conducted to determine the optimal dose and route of administration. Also, the effects of cranberry on pig health and production parameters and the economic feasibility need to be assessed in future experiments.

**Conclusion**

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