New research into plant-based feed additives

Yanhong Liu & Kwangwook Kim

Department of Animal Science
University of California, Davis, CA
Outline

• Weaning stress on intestinal development and health of pigs
• How to define a healthy gut
• Plant-based feed additives
  • Phytochemicals
  • Algae-derived products
• Take home message
Focus on the GUT

- Digestion and absorption of nutrients
- Physical barrier against pathogenic agents
- Large immune organ
- Nutrient chemo-sensing
Focus on the GUT of weaning pigs

**Critical Window of postnatal GI Development**

- **GI Barrier Development**
  - Epithelial barrier and transport functions
  - Immune system maturation
  - Enteric nervous system

**Maternal Immunity**

**Plasticity**

Birth  2.5 to 4 weeks  12 to 14 weeks  Adult

Moese et al., 2017
Weaning stress

• Maternal separation
• Environmental change
• Increased exposure to pathogens
• Social hierarchy stress
• Move to solid feed
• Transportation stress
Weaning stress on intestinal morphology

- **Pre-weaning:** d 1 to 21, villi surface was increased
- **Post-weaning:** reduced villi number and folding

Wang et al., 2016
Weaning stress on intestinal barrier function

Claudin 1

Occludin

Neunlist et al., 2013; Wang et al., 2016
Weaning stress on intestinal barrier function, cont.

Wang et al., 2016
Weaning stress on intestinal microbial dysbiosis

Intestinal cells

Renewal and apoptosis

Nutrient pool

Proteins and peptides
Lipids
Nucleic acids
Carbohydrates

Ethanolamine
Fucose

Proliferation and breakdown

Microbial communities

Intestinal inflammation

Diseases

Immune cells

Intracellular proliferation

Pathogenic bacteria

ETEC, EHEC, Salmonella

Gut microflora dysbiosis

Loss of bacterial diversity

Stahl et al., 2011; Thiennimitr et al., 2011; Xiong et al., 2019
Weaning stress on intestinal mucosal immunity

- Weaning induces a transient gut inflammation in pigs
  - Enhanced pro-inflammatory cytokines
  - Increased intestinal CD4+ and CD8+ T lymphocytes
  - Up-regulated matrix metalloproteinase
  - Down-regulated MHC I expression
  - Reduced secretory IgA

McCracken et al., 1999; Pié et al., 2004
Weaning stress on intestinal oxidative status

Yin et al., 2014
Focus on the GUT of weaning pigs

Compromised intestinal barrier development and function
- Increased intestinal permeability
- Increased immune cell activity and numbers
- Hyperactive enteric nervous system
- Increased oxidation

Moeser et al., 2017
How to define a healthy gut

• Effective nutrient digestion and absorption

• Effective waste excretion

Overall, should be concomitant with optimal performance

• A functional and protective gut barrier

• A stable and appropriate microbial community (absence of diseases)

• A functional and protective gut immunity

• A minimal activation of stress/neural pathways

Pluske et al., 2018
Nutritional strategies

• Optimization of feed formulation
• Utilization of low protein diet in post-weaning period
• Enhancement of feed processing and manufacturing
• Supplementation of feed additives
Feed additives

- Improvement of nutrient digestion and absorption (i.e. exogenous enzymes)
- Regulation of gut microbiota to more favorable bacterial species (i.e. prebiotics & probiotics)
- Immune modulation to enhance disease resistance of weaned pigs (i.e. β-glucan, phytochemicals)
Plant-based feed additives

• Phytochemicals

• β-glucan
Phytochemicals - plant extracts

• Extracted from parts of plants or synthesized
• Concentrated, hydrophobic, volatile aroma
• Mixtures of secondary plant metabolites
• Liquid or powder
• Phenolic compounds
Anti-inflammatory effects - *In vitro*

LPS-stimulated porcine alveolar macrophages

Liu et al., 2012

*P < 0.05
Frequency of diarrhea

Pig days with diarrhea score ≥ 3
1, normal; 5, watery diarrhea

Sham
Control vs. plant extracts
\( P < 0.05 \)

E. coli
Control vs. plant extracts
\( P < 0.05 \)

Liu et al., 2013
Possible mechanisms for reduced diarrhea

- Possibly improved gut barrier function!

Liu et al., 2013, 2014
Plant extracts reduced systemic inflammation caused by *E. coli* infection

**White blood cell counts**

- **Control**
- **Capsicum**
- **Garlicon**
- **Turmeric**

**Serum TNF-α**

- **Control**
- **Capsicum**
- **Garlicon**
- **Turmeric**

*P < 0.05

Liu et al., 2013
Plant extracts reduced gut inflammation caused by *E. coli* infection.

Liu et al., 2013
Plant extracts reduced gut inflammation caused by *E. coli* infection

E. coli challenge group

Relative mRNA expression

<table>
<thead>
<tr>
<th></th>
<th>COX-2</th>
<th>TNFA</th>
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<tbody>
<tr>
<td>Control</td>
<td></td>
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<tr>
<td>Capsicum</td>
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<td>Garlicon</td>
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<td>Turmeric</td>
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The Prostaglandin Pathway

- Arachidonic acid
- Cyclooxygenase-2 (COX-2)
- PGG2
- PGH2
- TXA2
- PGF2α
- PGE2
- PGD2
- PGI2

Inflammation!

Liu et al., 2014
Summary
Anti-inflammatory effects of plant extracts

• Suppressed the production of inflammatory mediators \textit{in vitro}

• Reduced diarrhea and enhanced disease resistance of weaning pigs

• Possible mechanisms
  • Gut barrier function
  • Gut mucosa immunity
  • Systemic immunity
  • Reduced oxidative stress ?
  • Modified gut microbiome ?
**β-glucan**

- Heterogeneous group of polysaccharides
- Naturally present in cereal grains, fungi, yeast, seaweed, and algae

Volman et al., 2008
Algae-derived β-glucan

- Extracted from algae *Euglena gracilis*, a freshwater species of single-celled alga
- Linked by (1,3)-glycosidic bonds and categorized as paramylon
- β-glucan from algae *Euglena gracilis* strongly stimulated porcine leukocytes in vitro

Sonck et al., 2010
Low = 54 mg/kg β-glucan in Control; High = 108 mg/kg β-glucan in Control

Diarrhea score: 1, normal feces, 2, moist feces, 3, mild diarrhea, 4, severe diarrhea, 5, watery diarrhea

Kim et al., 2019
Transcellular permeability

HRP flux (ng/cm²/h)

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<tr>
<th></th>
<th>Control</th>
<th>High dose</th>
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<tr>
<td>d 5 PI</td>
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<td>d 12 PI</td>
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High = 108 mg/kg β-glucan in Control

Kim et al., 2019
Tight junction protein
Gene expression in jejunal mucosa, d 12 PI

Low = 54 mg/kg β-glucan in Control; High = 108 mg/kg β-glucan in Control

Kim et al., 2019
Intestinal immunity

Gene expression in ileal mucosa, d 12 PI

Low = 54 mg/kg β-glucan in Control; High = 108 mg/kg β-glucan in Control
Serum cortisol and haptoglobin

Cortisol

Haptoglobin

Low = 54 mg/kg β-glucan in Control; High = 108 mg/kg β-glucan in Control

Kim et al., 2019
Summary
Protective effects of algae-derived β-glucan

• Dietary supplementation of 108 mg/kg of algae-derived β-glucan alleviated diarrhea of F18 E. coli infected pigs
  • Enhanced gut integrity
  • Boosted host immune response
  • Stimulated T-cell activation
Take home message

A healthy gut is extremely important for weanling pigs

Nutrient digestion & absorption
Waste excretion
Functional and protective gut barrier
Stable & appropriate microbial community
Functional and protective gut immunity
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http://animalnutr-ansci.faculty.ucdavis.edu/