Phytonutrients: The Next Generation

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Presentation overview

• What is the role of phytonutrients in the diet?
  • Background and history
  • Humans & animals

• How has the science evolved since the first applications in animal production?
  • Insights and shifts from first to second generation paradigms

• Current challenges limiting progress

• Next generation phytonutrients: a new paradigm for the future
Newsflash: diet influences health!

Harvard Women’s Health Watch; June 2018
Traditional medicine refers to the knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures, used in the maintenance of health and in the prevention, diagnosis, improvement or treatment of physical and mental illness. ...often termed alternative or complementary medicine in many countries... ... used a form as primary health care for 70% to 80% of the world.

Pan et al., 2014.
Traditional Medicine: the new chic!
“Traditional medicine can be used as an input to "modern" pharmaceutical research, but also as source of effective treatments in its own right... ...consider ways in which the potential of traditional medicine for providing affordable treatments could be better realised.”
Phytonutrients in human medicine

• The concept that phytonutrients have a direct impact on the health of the animal that ingests the plants is now validated and accepted by the Scientific and Medical communities
  • Mechanisms increasingly clear
  • Preventative & dietary therapies actively explored
  • Global organizations recognize the potential: WHO

• What about health and disease in production animals?
Replace Antibiotic Growth Promoters
Enhance rumen fermentation
Natural therapeutics

Most of the industry today still works under this paradigm.

First generation phytonutrients in animal production
The dangers of oversimplification & lack of science

- Phytonutrients are good because they kill bacteria
- Phytonutrients that do not kill bacteria are not of interest
- Phytonutrients kill bacteria, so they can be used as therapeutics
- Phytonutrients kill bacteria, so they could contribute to antibiotic resistance

Ground-breaking, misunderstood technology

Unhappy customers
Building understanding based on science

What can explain the performance response? It must be due to effects on gut microbes! Same explanation used for antibiotic growth promoters...

Compiled from publications found on https://www.ncbi.nlm.nih.gov/
Building understanding based on science

Antibiotic Treatment Elicits Microbiome-Independent Changes in Host Metabolites

Yang et al., 2017 Cell Host & Microbe.
Eugenol (3 ppm) improves intestinal structure

Eugenol (3 ppm) prevents adhesion of bacteria in the colon...
Second generation phytonutrients in animal production

It’s not the bugs, it’s the Hosts!!!
Host-mediated effects of phytonutrients in production animals: pioneer research

NE = necrotic enteritis challenge; CT = capsicum & turmeric oleoresins (4 ppm); Lee et al., 2013 Brit. J. Nut.
Host-mediated effects of phytonutrients in production animals: pioneer research

CT = capsicum & turmeric oleoresins (4 ppm); Lee et al., 2011 Vet Parasitol.

Altered immune gene expression in the intestine

Increased vaccination response

CT = capsicum & turmeric oleoresins (4 ppm); Lee et al., 2011 Vet Parasitol.
“These results provide new information concerning the molecular mechanisms involved in dietary modulation of host immunity, physiology, and metabolism.

Future studies based on these results will contribute to comprehensive understanding of the molecular mechanism of phytonutrients in the chicken digestive tract and will facilitate the development of novel dietary strategies to immunomodulate host response in normal and disease states.”

Kim et al., 2010. Poultry Sci.
The gut as a sensory organ

John B. Furness, Leni R. Rivera, Hyun-Jung Cho, David M. Bravo and Brid Callaghan

Abstract | The gastrointestinal tract presents the largest and most vulnerable surface to the outside world. Simultaneously, it must be accessible and permeable to nutrients and must defend against pathogens and potentially injurious chemicals. Integrated responses to these challenges require the gut to sense its environment, which it does through a range of detection systems for specific chemical entities, pathogenic organisms and their products (including toxins), as well as physicochemical properties of its contents. Sensory information is then communicated to four major effector systems: the enteric endocrine hormonal signalling system; the innervation of the gut, both intrinsic and extrinsic; the gut immune system; and the local tissue defence system. Extensive endocrine–neuro–immune–organ-defence interactions are demonstrable, but under-investigated. A major challenge is to develop a comprehensive understanding of the integrated responses of the gut to the sensory information it receives. A major therapeutic opportunity exists to develop agents that target the receptors facing the gut lumen.

DECREASED INFLAMMATION + INCREASED ABSORPTION

IMPROVED PERFORMANCE

Loose mucus layer

Inner mucus layer

Artery

Slide courtesy of D. Bravo
Transient receptor potential (TRP)A1 is expressed in enteroendocrine cells of the duodenum.

Co-expression with CCK: possible mechanism for digestive effects of cinnamon and garlic?

Host-mediated effects of phytonutrients in production animals: pioneer research

Cinnamaldehyde increases nutrient flux in the duodenum via TRPA₁

Fothergill et al., 2016. Nutrients.
Host-mediated effects of phytonutrients in production animals: pioneer research

Immune and production responses of dairy cows to postruminal supplementation with phytonutrients


Phytonutrients as additives in ruminants: the unexpected target organ
J. Oh,1 E. H. Wall,2 D. M. Bravo,2 and A. N. Hristov1
1The Pennsylvania State University, University Park, U.S.A.
ADSA-ASAS Joint Annual Meeting, July 2016

Host-mediated effects of phytonutrients in ruminants: A review1
J. Oh,* E. H. Wall,† D. M. Bravo,† and A. N. Hristov*2
*Department of Animal Science, The Pennsylvania State University, University Park 16802
Host-mediated effects of phytonutrients in production animals: pioneer research

Effects of rumen-protected *Capsicum* oleoresin on productivity and responses to a glucose tolerance test in lactating dairy cows

J. Oh,* M. Harper,* F. Giallongo,* D. M. Bravo,† E. H. Wall,† and A. N. Hristov*†
*Department of Animal Science, The Pennsylvania State University, University Park 16802

Effects of rumen-protected *Capsicum* oleoresin on immune responses in dairy cows intravenously challenged with lipopolysaccharide

J. Oh,* M. Harper,* F. Giallongo,* D. M. Bravo,† E. H. Wall,† and A. N. Hristov*†
*Department of Animal Science, The Pennsylvania State University, University Park 16802

Oh et al., 2017a; Oh et al., 2017b J. Dairy Sci.
In this experiment, dietary supplementation of RPC, but not artificial sweetener, appeared to increase milk production and feed efficiency in dairy cows following feed restriction to induce sub-clinical ketosis and
Second generation phytonutrients in animal production

- Important discoveries revealed that phytonutrients elicit host-mediated effects in production animals

Molecular detectors in the gut → Physiological reactions
- Improved gut health
- Improved antioxidant status
- Enhanced immunity
- Resistance to disease

Most of the Scientific community today works under this paradigm.

- Observed across species
- Phytonutrients detected by gut sensing machinery
- Molecular reactions lead to systemic responses
- Clear opportunity for next generation phytonutrients
Second generation phytonutrients in animal production

• And yet...
• Industry continues to work under the first-generation paradigm
• Virtually all phytonutrients are positioned as natural replacements for antibiotic growth promoters or antibiotics
  • Efficacy, ROI, application
• Oversimplified, silver-bullet approaches are expected
• Regulatory status continues as flavoring agents and concerns loom regarding classification as drugs, chemicals, microbials
How can we apply the knowledge & move forward?

ANIMAL NUTRITION

MEDICINE

We need insights!!

We have some!!
The effects of food essential oils on cardiovascular diseases: A review.

Saljoughian S1, Roohinejad S2,3, Bekhit AEA4, Greiner R2, Omidizadeh A1, Nikmaram N5, Mousavi Khaneghah A6.

TRPV1 Antagonists as Novel Anti-Diabetic Agents: Insulin

Essential Oils as Treatment Strategy for Alzheimer's Disease: Current and Future

Anticancer Properties of Essential Oils
Andrade MA1, Braga MA2, Cesar PHS2, Trento MVC2, Esp
Martins J1, S B2.

Phytochemistry and pharmacology of anti-depressant medicinal plants: A review

Dietary nutraceuticals as backbone for bone health.
Pandey MK1, Gupta SC2, Karelia D3, Gilhooley PJ4, Shakibaee M5, Aggarwal BB6.

Essential oils and functional herbs for healthy aging.
Anatopnous-KustRin S1, KustRin F2, Morton DW3.

The Role of Phytochemicals in the Inflammatory Phase of Wound Healing.
Shah A1, Amini-Nik S2,3,4.
Phytonutrients: the next generation

• What do we need to get there?
  • Resist the tempting cause-and-effect trap
  • Acknowledge host-mediated responses
  • Work on regulatory classification and positioning
  • Educate the industry
  • Integrate and align the progress of science with industry understanding/use and regulatory frameworks! (alternative: death of the technology)
  • Actively explore next-generation concepts!
Integrating next-generation phytonutrients with animal feeding, nutrition, and management

+probiotics
+prebiotics
+optimized management
+enzymes
+vaccines
+...
+technologies

Complex challenges

Complex solutions

Let’s move together towards this paradigm!
Thank you.