Phytonutrients as alternative feeding strategy to improve performance of cattle without using an antibiotics

Sergio Calsamiglia

*Dpt. Ciencia Animal y de los Alimentos*

*Universidad Autónoma de Barcelona*
## Opportunities for improving feed efficiency

<table>
<thead>
<tr>
<th>Description</th>
<th>Energy</th>
<th>Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base feed efficiency</td>
<td>21%</td>
<td>28%</td>
</tr>
<tr>
<td>Increase milk production 10% (2100 lb/year)</td>
<td>+0.7%</td>
<td>+0.4%</td>
</tr>
<tr>
<td>Increase longevity from 3 to 4 lactations</td>
<td>+0.6%</td>
<td>+0.5%</td>
</tr>
<tr>
<td>Decrease maintenance requirement 10%</td>
<td>+1.1%</td>
<td>+1.2%</td>
</tr>
<tr>
<td>Improve efficiency of digestion by 10%</td>
<td>+1.2%</td>
<td>+1.0%</td>
</tr>
<tr>
<td>Reduce age at first calving 2 months</td>
<td>+0.3%</td>
<td>+0.3%</td>
</tr>
<tr>
<td>Reduce calving interval 1 month</td>
<td>+0.4%</td>
<td>+0.4%</td>
</tr>
<tr>
<td>Feed cows &gt;150 DIM a diet with 2% less CP</td>
<td>+0.0%</td>
<td>+1.3%</td>
</tr>
</tbody>
</table>

VandeHaar et al., 2014
Objective: Energy retention

![Chart showing efficiency of Acetate, Propionate, and Butyrate. Efficiency is highest for Propionate and lowest for Acetate.]

Efficiency, %
Energy efficiency in rumen fermentation

Fiber $\rightarrow$ Glucose $\rightarrow$ Starch

Glucose $\rightarrow$ Pyruvate

Pyruvate $\rightarrow$ Methane $\rightarrow$ Acetate $\rightarrow$ Butyrate

Pyruvate $\rightarrow$ Lactate $\rightarrow$ Propionate

$\text{Energy} + 4 \text{ H}^+ \rightarrow \text{Methane} + 8 \text{ H}^+$

$\text{Acetate} + 4 \text{ H}^+ \rightarrow \text{Butyrate} + 4 \text{ H}^+$

$\text{Lactate} + 2 \text{ H}^+ \rightarrow \text{Propionate} + 2 \text{ H}^+$
Effects of monensin

Monensin

↓ Gram +
↑ Gram -

↓ Propionate
↓ Acetate
↓ Butyrate

↑ Catabolism Pep & AA

↓ NH₃
Effects of monensin

Dairy; Duffield et al., 2008

Beef; Duffield et al., 2012

Ban on the use of antibiotics
Objectives

- Search for alternatives:
  - Tradicional approach: a “ionophore-like” product
  - “Unexpected targets”
Plant Extracts

- Products of the secondary metabolism.
- Small size, high diversity
- Classified as GRAS (Generally Recognised as Safe) (D-1999/217/CE; FDA, 2004).
Mechanism of action

Ultee et al., 2002
Modulation of microbial population

Patra and Yu 2012
Phytonutrient selection process

- 500 molecules / extracts
- 100 Tested in vitro - batch
- 10 Tested in vitro
- Continuous Culture
- 5 Tested in vivo
## Nitrogen metabolism

<table>
<thead>
<tr>
<th></th>
<th>CTR</th>
<th>MON</th>
<th>CIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>LPep N</td>
<td>6.8</td>
<td>5.4</td>
<td>6.4</td>
</tr>
<tr>
<td>SPep + AA N</td>
<td>1.9</td>
<td>4.4†</td>
<td>2.5</td>
</tr>
<tr>
<td>Ammonia N</td>
<td>19.2</td>
<td>13.0*</td>
<td>16.0†</td>
</tr>
</tbody>
</table>

* $P < 0.05$  † $P < 0.10$

Busquet et al., 2005 (J. Dairy Sci.)
Mechanism of Action: *(Prevotella)*

**CTR**
- CTR 1 (P2) *HaeIII* digestion

**CIN**
- CIN 1 (P2) *HaeIII* digestion
- GAR 1 (P2) undigested PCR product

![Fluorescence graph](image)

**Time (seconds)**
- 35 37 39 41 43 45 47 49 51 53 55

**Fluorescence**
- 0 1 2 3 4 5 6 7 8 9 10 11

**Mechanism of Action:** *(Prevotella)*

*(Ferme et al, 2004)*
## Nitrogen metabolism

<table>
<thead>
<tr>
<th></th>
<th>CTR</th>
<th>FEN</th>
<th>CAD</th>
<th>TEA</th>
<th>DIL</th>
<th>GIN</th>
<th>CLO</th>
</tr>
</thead>
<tbody>
<tr>
<td>LPep N</td>
<td>3.8</td>
<td>4.5</td>
<td>6.1</td>
<td>4.3</td>
<td>5.0</td>
<td>4.8</td>
<td>6.9 *</td>
</tr>
<tr>
<td>SPep + AA N</td>
<td>5.2</td>
<td>5.0</td>
<td>5.0</td>
<td>4.5</td>
<td>4.7</td>
<td>4.0</td>
<td>2.8 †</td>
</tr>
<tr>
<td>Ammonia N</td>
<td>7.5</td>
<td>8.7</td>
<td>7.4</td>
<td>8.0</td>
<td>8.5</td>
<td>7.1</td>
<td>6.4</td>
</tr>
</tbody>
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* $P < 0.05$  † $P < 0.10$

Busquet et al., 2005 (Anim. Feed Sci. Technol.)
Essential Oils: Protein metabolism

Dietary Protein → Protein → Peptides → Microbial Protein

Urea → CIN → NH₃ → AA → Peptides → EUG → EO

AA: Amino Acids
Efficiency of energy utilization
(Acetate to propionate ratio)

![Bar chart showing efficiency of energy utilization](chart.png)

**ab** (P<0.05)

Busquet et al., 2005 (J. Dairy Sci.)
Efficiency of energy utilization (Butyrate)

Busquet et al., 2005a (J. Dairy Sci.)

ab (P<0.05)
Hypothesis: Inhibition of methanogenesis
Effects of plant extracts

M (2.3%)  
M (2.5%)

Milk yield, L/d; Bravo et al., 2009  
ADG, kg/d; Bravo et al., 2009

Dairy  
Beef
Summary

- Plant extracts modulate microbial population in the rumen
- Changes in the fermentation profile are similar to ionophores in direction and size, although a different mechanism of action probably takes place
- Production performance in dairy (milk yield) and beef (ADG) is improved with a similar magnitude to that observed with Monensin
The unexpected targets

- The ban on the use of antibiotics has open the door to new opportunities
- Accidental findings are often the start of new discoveries
- Feed efficiency is not only what happens in the rumen, but it is also affected by:
  - Lower digestive tract
  - Metabolism
Immunity and defense in the small intestine

- Goblet cells secreting mucine (Muc2)
- Mucine is a major constituent of inner mucus layer
- Outer mucus layer & microbiota

Jamroz et al., 2006
Defense and immunity (swine)

Piglets infected (challenged) with E. Coli without or with Capsicum oleoresin

MUC2 expression rel. control in ileal mucosa (fold change)
- Uninfected CT
- Infected CT
- Infected + capsicum

TLR4 expression rel. control in ileal mucosa (fold change)
- Uninfected CT
- Infected CT
- Infected + capsicum

↑ physical barrier
↓ Host sensitivity

Improved immunity in cows

Oh et al., 2015
Capsicum and milk production

Oh et al., 2015
Capsicum and immunity: Total treatments (Calves)

Incidence, %

<table>
<thead>
<tr>
<th></th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>56</td>
</tr>
<tr>
<td>XTRACT</td>
<td>48</td>
</tr>
</tbody>
</table>
Capsicum and immunity: Treatments/sick calf

![Bar chart showing treatments for sick calves. The control group had 2.21 treatments, and the XTRACT group had 1.67 treatments.](chart.png)
Capsicum and immunity: Respiratory diseases (feedlot)

Incidence, %

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<tr>
<th></th>
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<tbody>
<tr>
<td>Monensin</td>
<td>15.7</td>
</tr>
<tr>
<td>XTRACT</td>
<td>9.9</td>
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</table>
Incidence of rumen lessions (feedlot)

Hagg et al., 2013
Summary of Capsicum (1)

- Changes in the immune profile is consistent with improved immunity
- Reduction in the incidence of diseases observed in calves and feedlot cattle
- Difficult to justify a 6% increase in milk production (2.9 L/d) due to improved immunity in dairy

![Bar chart showing milk production in kg/d for Control, C250, C500, and C1000 groups]
Capsicum and milk production

Wall and Bravo, 2016
Capsicum and milk production

Week of lactation

Milk yield (kg/d)

Capsicum vs Control

30.1 vs 32.1

Stelwagen et al., 2016
XTRACT and milk yield (Heat stress)

Blanck et al., 2016
The “other effect” of Capsicum

<table>
<thead>
<tr>
<th>Variation, % Control</th>
<th>Monensin</th>
<th>C+E</th>
<th>C+E+C</th>
<th>CAP</th>
<th>CAP</th>
<th>CAP</th>
<th>bST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duffield et al., 2008</td>
<td>2.3</td>
<td>3.0</td>
<td>6.7</td>
<td>6.2</td>
<td>6.6</td>
<td>9.1</td>
<td>13.0</td>
</tr>
<tr>
<td>Bravo, 2009</td>
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<td>Bauman et al., 1999</td>
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</table>
Capsicum and insulin

(Penn State U., Unpublished)
Glucose metabolism

Adipose tissue

INSULIN

Glucose

Mammary gland
Glucose and early lactation (and bST)

Adipose tissue → R → INSULIN → Glucose

Glucose → Mammary gland
Glucose and early lactation

Adipose tissue

INSULIN

Glucose

Mammary gland

Glucose
Summary

- Capsicum enhances milk production (~6-9%)

- The changes in insulin effects are parallel to those observed in early lactation or bST and may explain the mechanism of action that justified the increased production.

- Although capsicum increases feed intake, results suggest that this may not be the cause of increased production, rather the consequence.
“Playing with glucose”

- Sucram is a sweetener that stimulates sweet receptors.
- It may be used to increase DM intake.
## Receiving calves (190 kg)

<table>
<thead>
<tr>
<th></th>
<th>CTR</th>
<th>SUCRAM</th>
<th>±%</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{DMI, kg/d}^{1,2}$</td>
<td>4,45</td>
<td>4,77</td>
<td>+7,2%</td>
</tr>
<tr>
<td>$\text{ADG, g/d}^{1,2}$</td>
<td>1242</td>
<td>1333</td>
<td>+11,4%</td>
</tr>
<tr>
<td>$\text{ADG/DMI}^{1,2}$</td>
<td>0,257</td>
<td>0,266</td>
<td>+5,9%</td>
</tr>
<tr>
<td>Pulls, %$^1$</td>
<td>59,7</td>
<td>58</td>
<td>-2,9%</td>
</tr>
<tr>
<td>Re-Pulls, %$^1$</td>
<td>52,6</td>
<td></td>
<td>-22,0%</td>
</tr>
</tbody>
</table>

How can we explain the improved efficiency?

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1. Texas A&M;  
2. Texas Tech U
Glucose absorption

Small Intestine

Blood

(Shirazi-Beechey, U Leeds, UK)
Regulation of glucose transport

Sensor T1R2/T1R3

Gustducin

Increased Ca^{2+}

GLP-2

GLP-2R

Enteric neuron

(VIP/PACAP, AC)

ATP,cAMP

VPAC1

SGLT1

Na^+

(Shirazi-Beechey, U Leeds, UK)
Changes in glucose transporters induced by Sucram in calves

Control

Sucram

Moran et al., 2014
Results in calves: glucose transporters
GLP-1 and insulin release

(Shirazi-Beechey, U of Leeds)
Sucram and insulin release

Ponce et al., 2007

Insulin, ng/mL vs. Time, minutes

- Control
- Sucram
Insulin in dairy and beef

- Insulin release may reduce body fat mobilization and help in the control of ketosis (energy balance) post partum
- Insulin increases growth of muscular and adipose tissue
- The effect on intramuscular fat is higher compared with external fat
- The effects on marbling is higher early in the growing period
Conclusion

- Antibiotic growth promotants have been used successfully in animal nutrition.

- The ban on the use of antibiotic growth promotants (in the EU and likely in other countries) has stimulated the research on alternative approaches.

- The need for such alternatives has also opened new opportunities to identify “unexpected targets”:
  - Immunity
  - Glucose metabolism
Conclusion

- Phytonutrients (namely Cinnamaldehyde and Eugenol) modify rumen microbial population, the fermentation profile and dairy and beef performance, in a direction and size similar to some AGP.

- Capsicum has shown immune enhancing capabilities.

- Capsicum and Sucram may enhance production performance of dairy and beef through the modification of glucose metabolism.