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BUTYRATE:

THE INTESTINAL FUEL

FOR BETTER

PERFORMANCE

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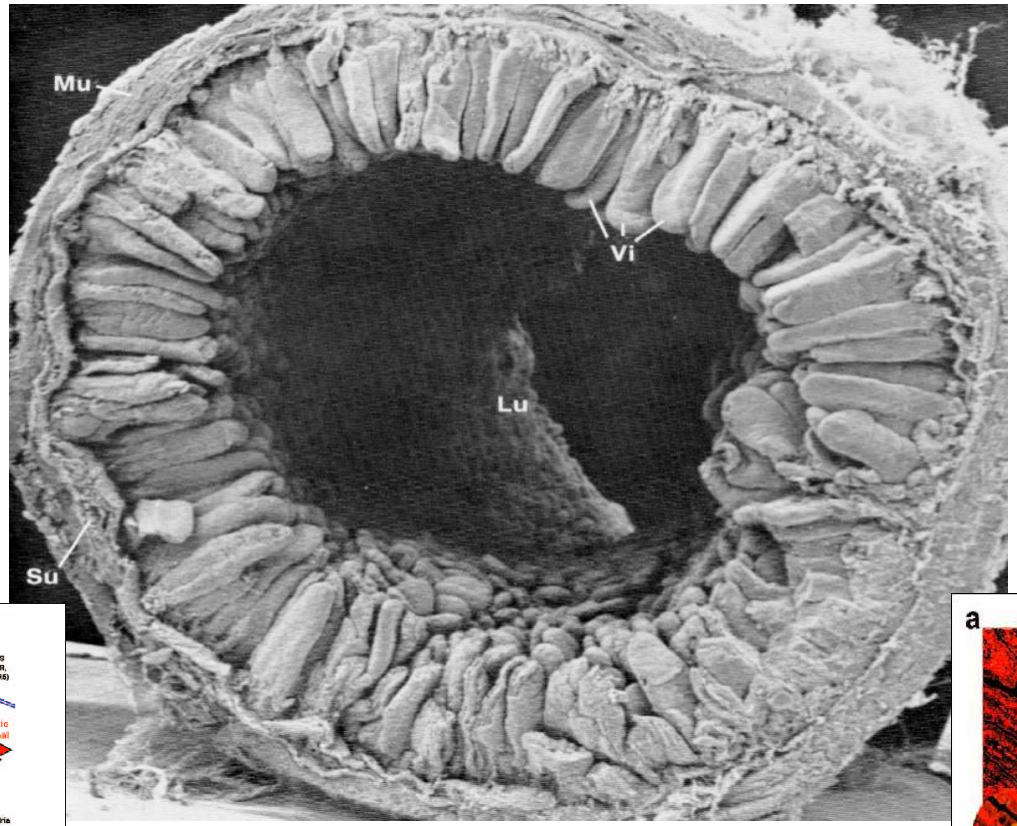
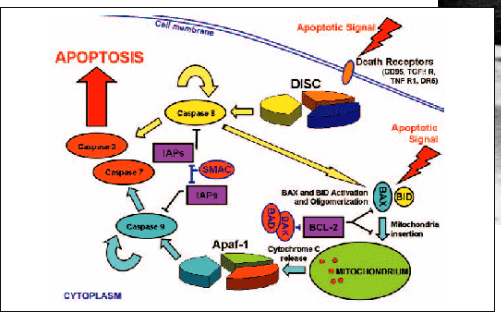
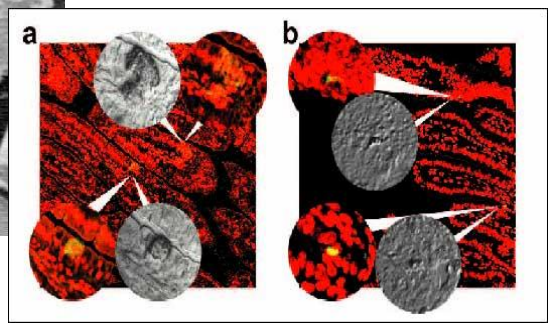
The gut ecology in the small and large intestine is essential to ensure the healthy and normal function of the gut mucosa and its resistance to injury, inflammation and pathological change.







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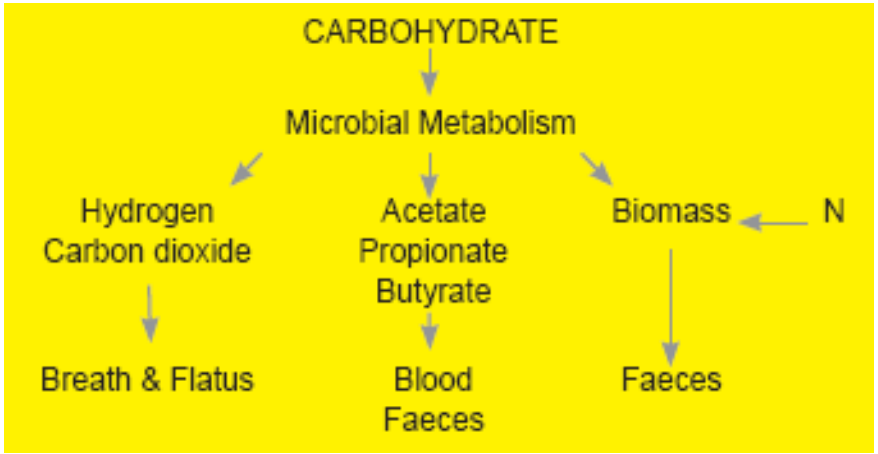
What are Short Chain Fatty Acids?

The major short chain fatty acids (SCFAs), butyrate, acetate and propionate are produced in the large intestine by the microbial fermentation of dietary carbohydrate. The major substrates for their production are resistant starch (RS) and nonstarch polysaccharides (NSP).



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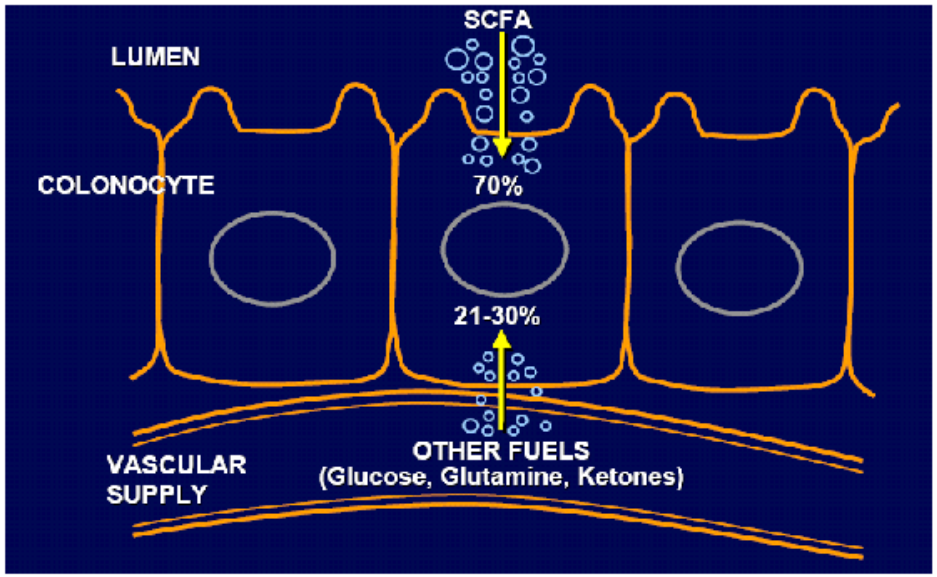
Short Chain Fatty Acids

The SCFAs are required for normal large bowel function where they serve as modulators of the growth, function and differentiation of the epithelium, prevent pathology through their metabolism by colonocytes and produce antimicrobial compounds and stimulate the immune system.

Short chain fatty acids (SCFA) are main source of energy for colonic epithelial cells



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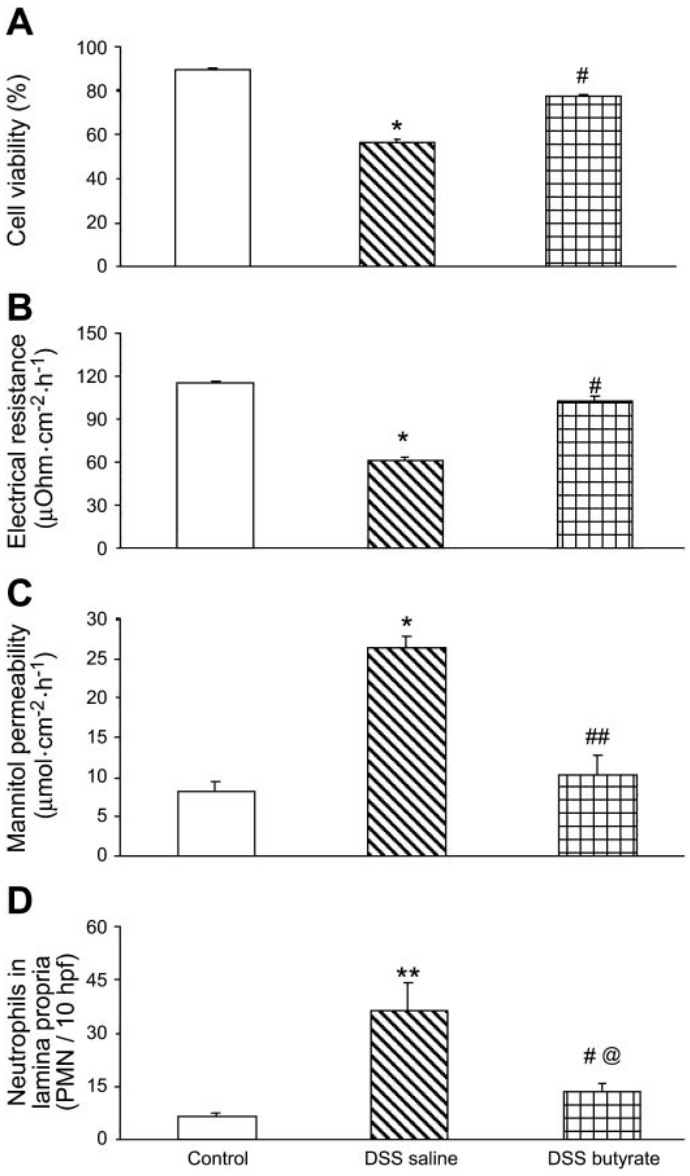
SCFAs are absorbed by the distal ileum and colon, a fraction of the SCFAs is absorbed by diffusion, transported via the portal vein and utilised by other tissues for energy.

Butyrate, in particular, provides an essential energy source for the maintenance of normal colonocytes and is well recognised as an anticancer agent.

Butyrate, produced by intestinal anaerobic bacteria, ameliorates experimental colitis in rats

Fig. 1. Colonocyte viability (*A*), electrical resistance (*B*), mannitol permeability (*C*), and lamina propria polymorphonuclear cell infiltration (*D*) in the colon of normal control rats (control), rats with dextran sulfate sodium (DSS) colitis that had received saline enemas (DSS saline), and rats with DSS colitis that had received butyrate enemas (DSS butyrate). Data are expressed as means SE (*n* 7). **P* 0.01 vs. control; ***P* 0.005 vs. control; #*P* 0.01 vs. DSS saline; ##*P* 0.005 vs. DSS saline; and @*P* 0.05 vs. control.

Venkatraman et al, Amer J Physiol 2003



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What does Butyrate do?

Butyrate is an important source of nutrition for epithelial cells and supplies up to 70 % of their total energy requirements. Butyrate has been shown to be the preferred energy substrate for colonocytes and a potent differentiating agent in cell culture.

Butyrate not only modulates enterocyte differentiation, proliferation and restitution, but also has immunoregulatory effects on intestinal epithelial cells and other mucosal cell population.

Butyrate	• Relaxation of resistance vessels •Metabolism by colonocytes • Maintenance of normal colonocyte phenotype • Stimulation of colonic electrolyte transport	• Greater colonic & hepatic portal venous blood flow • Maintenance of mucosal integrity, repair of diversion & ulcerative colitis, colonocyte proliferation • Reduced risk of malignancy • Greater ion and fluid absorption, prevention of diarrhoea

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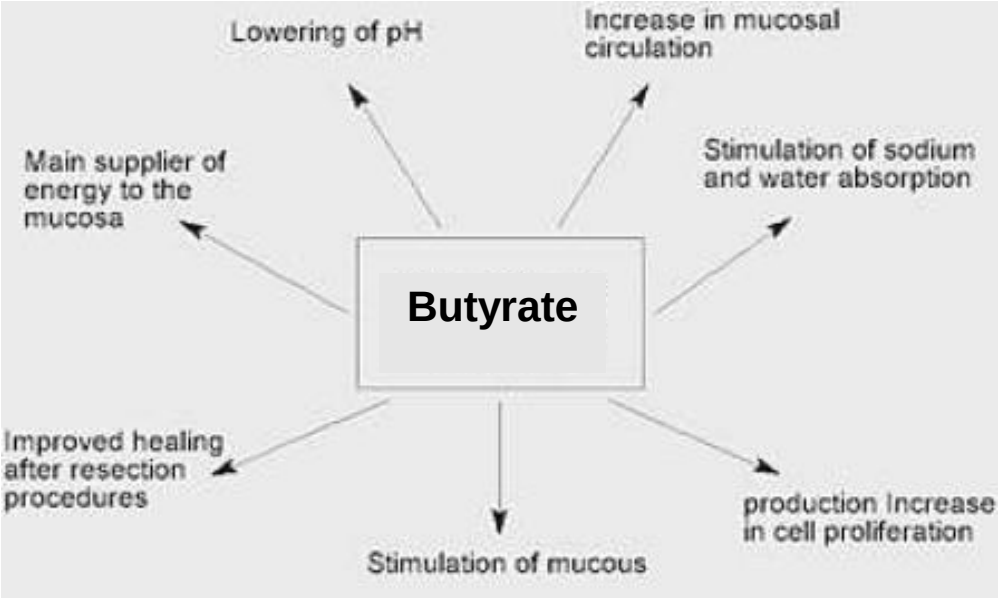
What does Butyrate do?



Butyrate stimulates water and sodium absorption. This mechanism is responsible for the uptake of water from the colon and for an antidiarrhea effect.

Butyrate is also found to enhance mineral absorption. Although the small intestine is the major site for mineral absorption, the colon also facilitates the absorption of calcium and magnesium with the aid of Butyrate.

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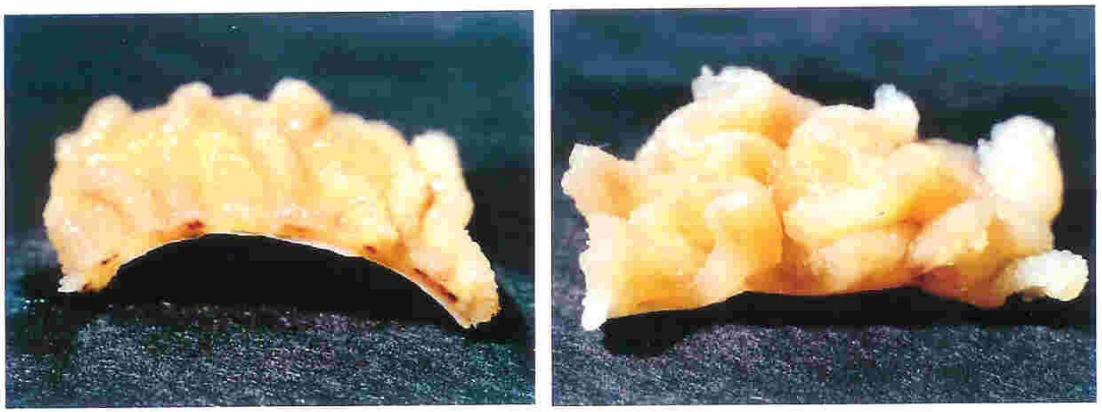
What does Butyrate do?

Butyrate promotes apoptosis in tumor cells and inhibits this process in normal nontransformed cells. The result is that damaged cells are eliminated while the development of healthy cells is promoted. Butyrate also promotes the repair of damaged epithelial cells.

Butyrate contributes to the detoxification of harmful substances by the induction of the detoxification enzyme glutathione-S-transferase and other mechanisms. It increases the production of mucin which traps reactive genotoxic compounds.

Effect of Calcium-butyrate on the intestinal wall (Prof. R. Claus – University Hohenheim - 2004)



Energy deficit

Energy + Butyrate

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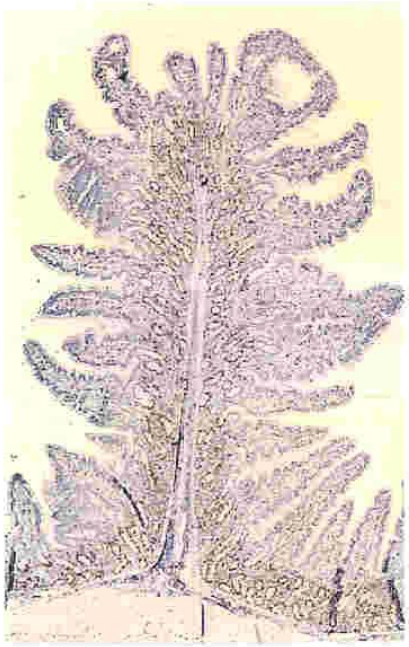
What does Butyrate do?

Slice-cut of jejunum villus:
low energy group versus butyrate group

Plica eines Hungertieres



Plica eines Tieres der Butyratgruppe

Effect of Calcium-butyrate on the intestinal villi
(Prof. R. Claus – University Hohenheim - 2004)

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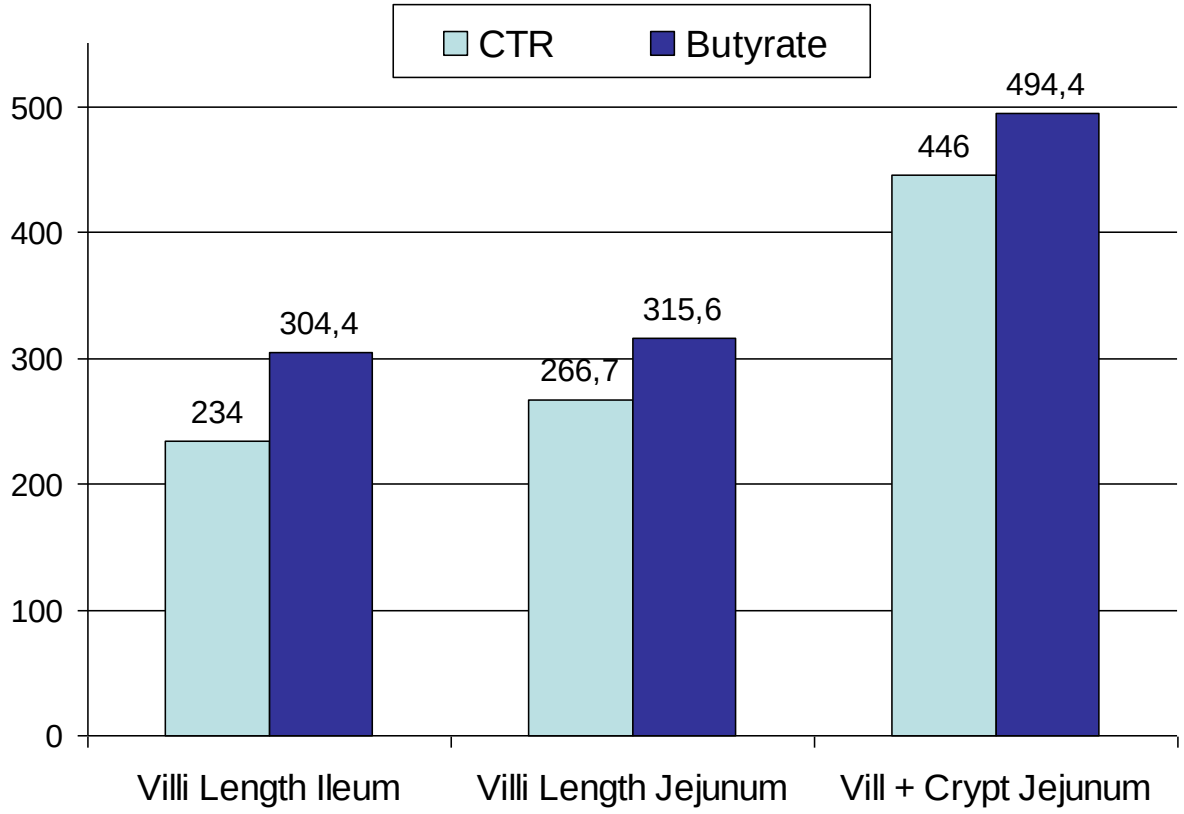
What does Butyrate do?

Effect of butyrate on digestive tract

(Galfi & Neogradi - Department of Physiology and Biochemistry)



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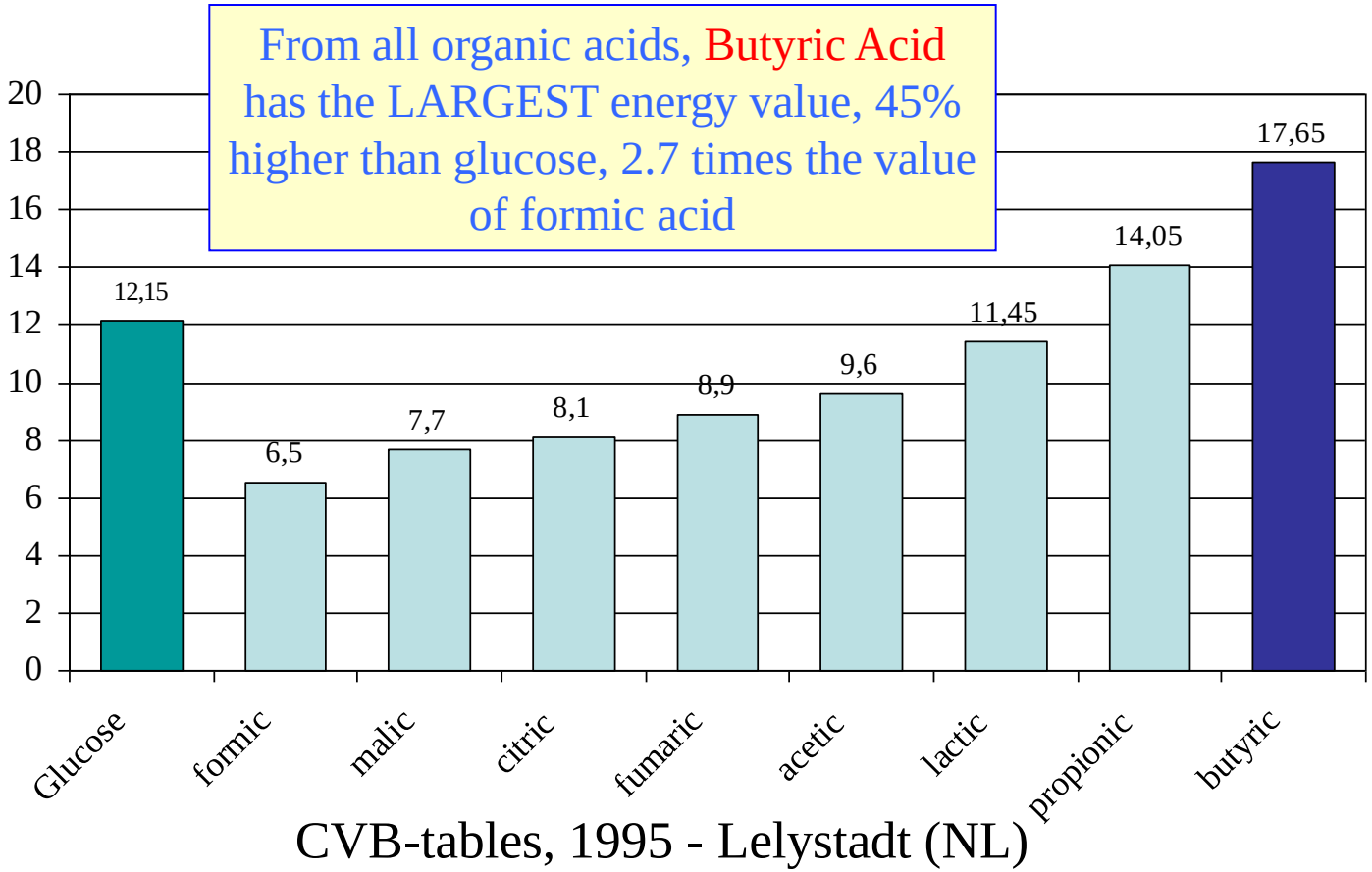
Energy value of organic acids

NE-v (pigs) : MJ/kg



CVB-tables, 1995 - Lelystadt (NL)

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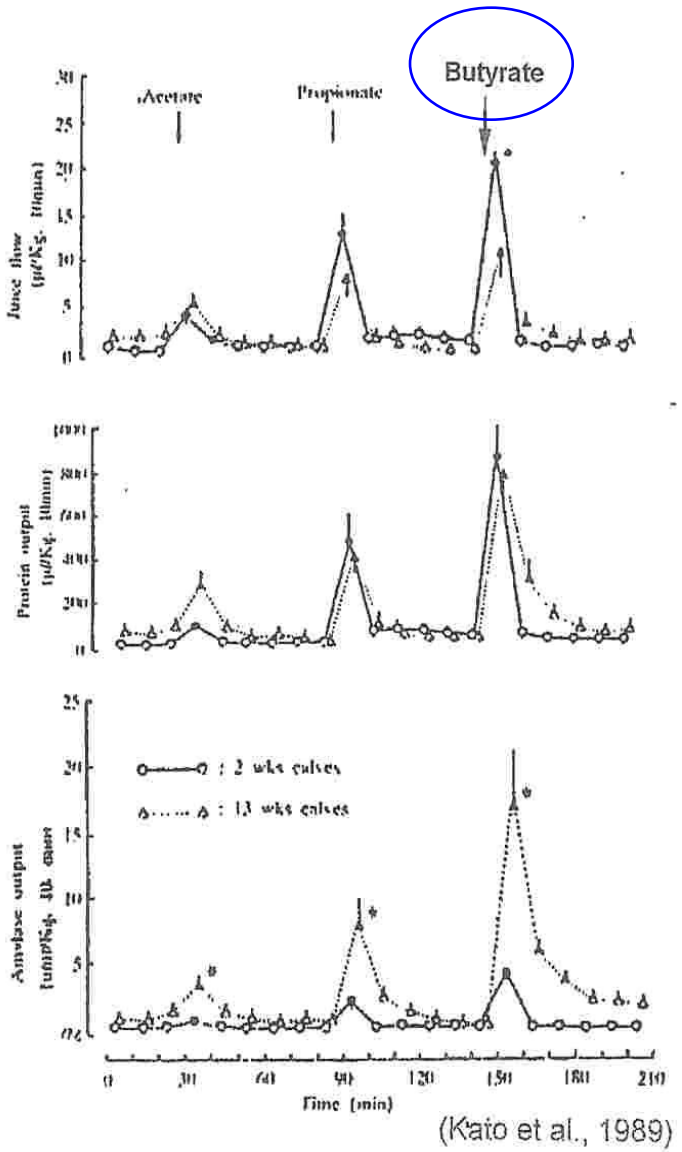
Stimulation of pancreas enzymes by BUTYRATE

GASTRIC JUICE →

PROTEINES →

AMYLASE →



(Kato et al., 1989)

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Effect of coated Calcium-Butyrate on small intestinal mucosa

D. Günthner, H. Letzguß, R. Claus

Background

Previous work clearly showed that energy as well as purine content in feed has a positive influence on the mitotic rate of the small intestine in the pig.
In the large intestine butyrate produced by bacterial fermentation in the colon exerts an apoptosis inhibiting effect and thus is also leading to enhanced mucosal proliferation.

The aim of this study was to clarify whether butyrate in the diet has an effect in the small intestine leading to an even more pronounced proliferation in addition to the effects of energy and purines.

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Effect of coated Calcium-Butyrate on small intestinal mucosa

D. Günthner, H. Letzguß, R. Claus

Experiment

The experimental group (n=5) was fed a diet with high energy (13,5 MJ/kg) and purine (brewing yeast as protein source) content and was supplemented with 3 % fat-coated calcium-butyrate.
One control group(n=5) was fed a ratio with low energy (5,4 MJ/kg) and purine content (casein as protein source).
The other control group (n=5) was fed the same ratio as the experimental group but without calcium-butyrate.
Each diet was fed for 5 days.
Tissue samples were obtained for morphological and histochemical evaluation. Sucrase activity, a brush border enzyme, was determined in chyme.

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Effect of coated Calcium-Butyrate on small intestinal mucosa

D. Günthner, H. Letzguß, R. Claus

Results

Calcium-butyrate clearly increased small intestinal mucosa proliferation (fig.1).

Morphometry exhibited an enormous enlargement of the plicae intestinales (height and cutting area) mainly due to formation of additional villi by crypt fission (fig.2). Crypt fission (principle fig.4) meansthat increased mitotic activity leads to additional villi instead of excessive prolongation of existing villi. Inconsequence brush border enzyme activity increased accordingly (fig.3).

Fig.1: Morphological changes

deficit

butyrate

Fig.2 : Villi per plica in medial Jejunum

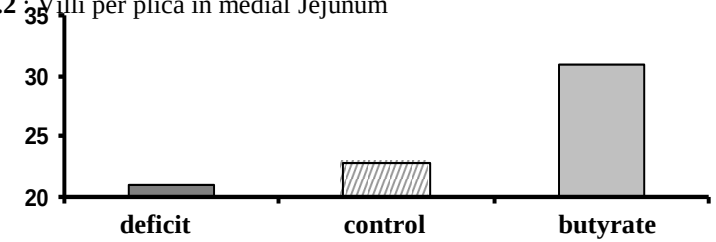


Fig.3: Sucrase activity in chyme

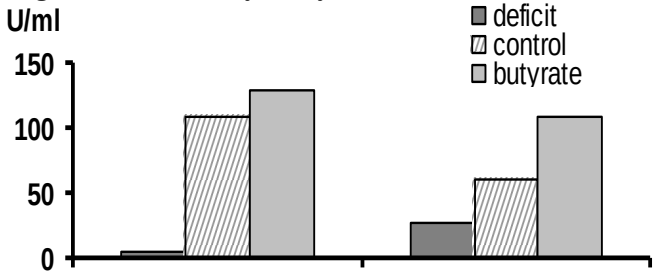
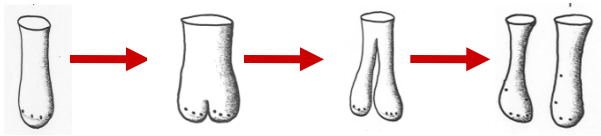


Fig.4: Crypt fission



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Effect of coated Calcium-Butyrate on small intestinal mucosa

D. Günthner, H. Letzguß, R. Claus

Conclusion

The data show that calcium-butyrate, in addition to energy and purines, increases the digestive and absorptive surface of the small intestinal mucosa.

Literature

Raab et al. 1998: Journal of Metabolism
Mentschel et al. 2003: Journal of Metabolism

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Calcium-Butyrate and "bacterial inhibition"

Likewise the main part of organic acids, also butyric acid and butyrate exert a pronounced bacterial inhibition, but not in the same way.

Bacterial inhibition by butyric acid distinguish clearly from most other acids :

- The effect is more SELECTIVE : this means some bacteria are inhibited, some are not. The majority of Lactobacilli are not touched, while several Coliforms and Clostridium strains are inhibited.

- The effect is LESS pH DEPENDENT

Traditional organic acids exert bacterial inhibition only in a low pH range, but have no single effect in the neutral to less acid range (see chart from Prof. Decuypere 1996).

Calcium-butyrate does inhibit several pathogenic bacteria like Coli, Clostridium and Salmonella at intestinal pH levels (Decuypere, Decostere, Van Immerseel).

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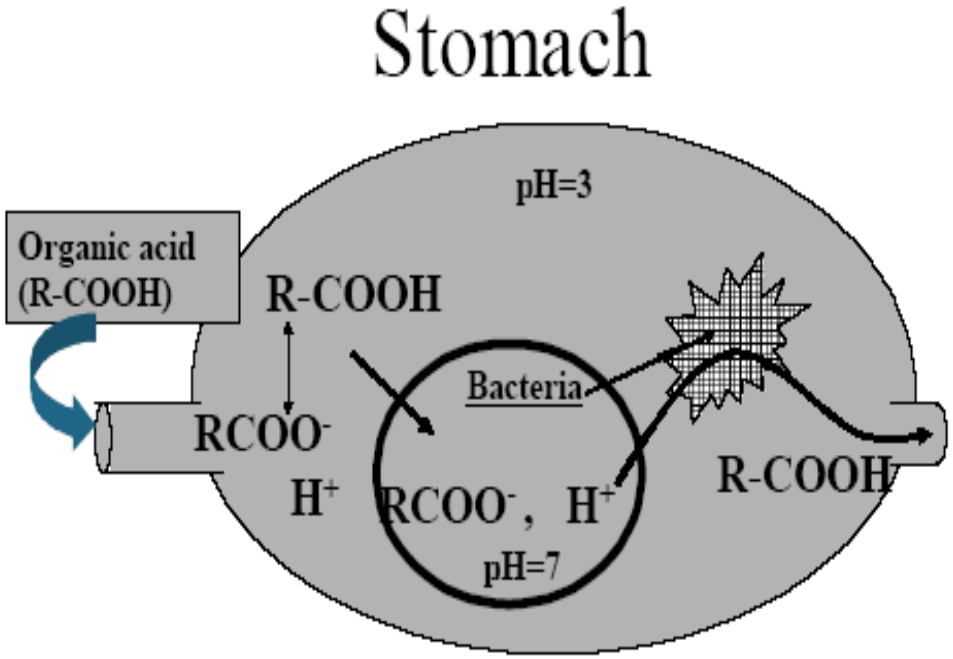
What does Butyrate do?

Butyrate is considered as an alternative to antibiotic growth promoters. In addition to its role in development of the intestinal epithelium butyrate has a bactericidal activity especially against coli, salmonella and clostridium. Bacterial cells take up the undissociated fatty acid, and once this dissociates, the change in intracellular pH is usually bactericidal.



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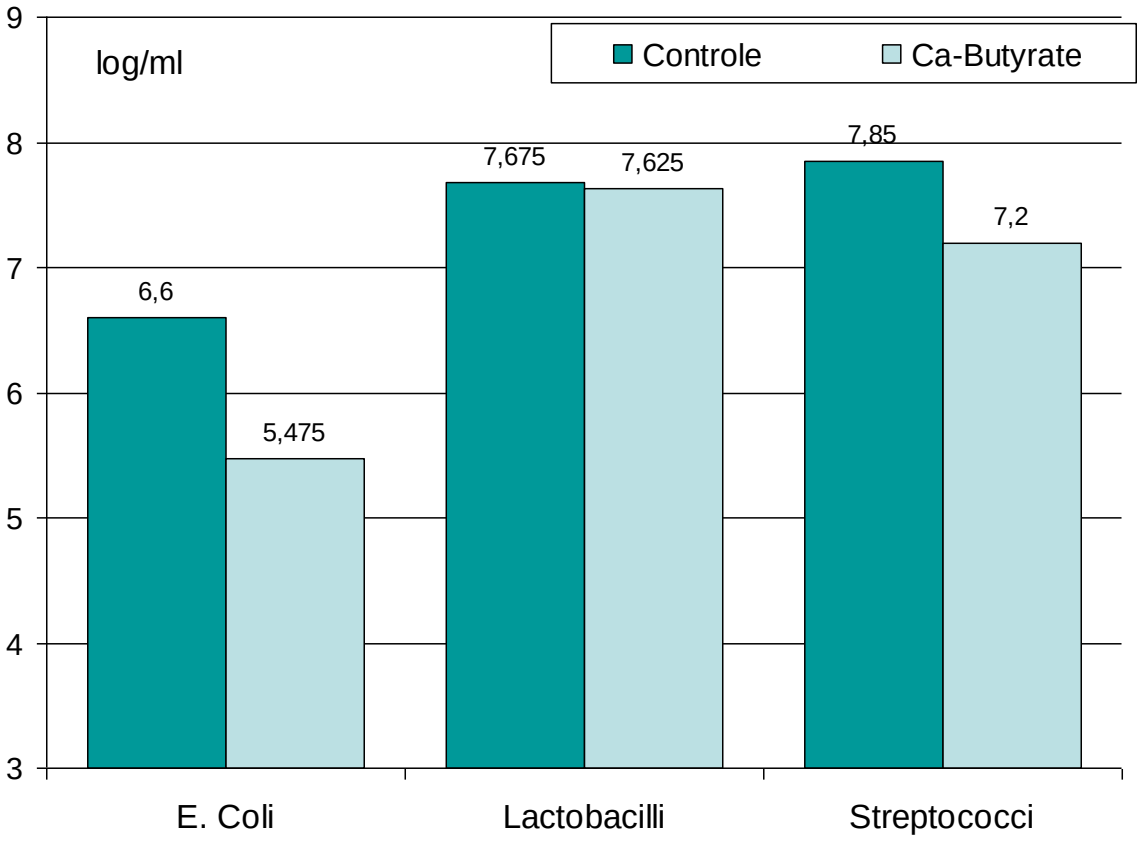
Influence of butyrate on bacterial development (Incubation at pH 5.5 : Feed + ileumcontent)



Prof. Dr. J. Decuypere & I Vackier (2002) : Type II incubations (50 mM salt - log phase - inoculated feed suspension)

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Sintobutyl

The coated calcium butyrate for piglets and laying hens

PIGLETS: 0.5-1.5 kg/t

LAYING HENS: 0.2-0.3 kg/t

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The calcium butyrate source is especially studied for **piglets** and **laying hens**.

Piglets and laying hens need extra energy to support stressed conditions like weaning and eggs laying. Stressed conditions require more fuel directly in the intestine.

ADVANTAGES:

- Easy to handle
- Without bad smell
- Slow release
- High energy source directly in the intestine
- Useful in animal stressed conditions

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Trials with Ca-butyrate in piglets versus ABGP

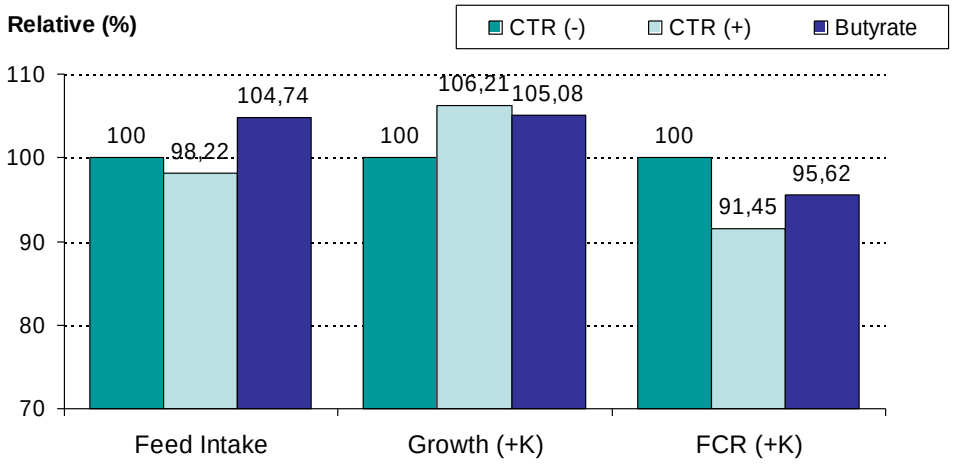
Highschool Thesis - E. Matthys - CTL Ghent 2002

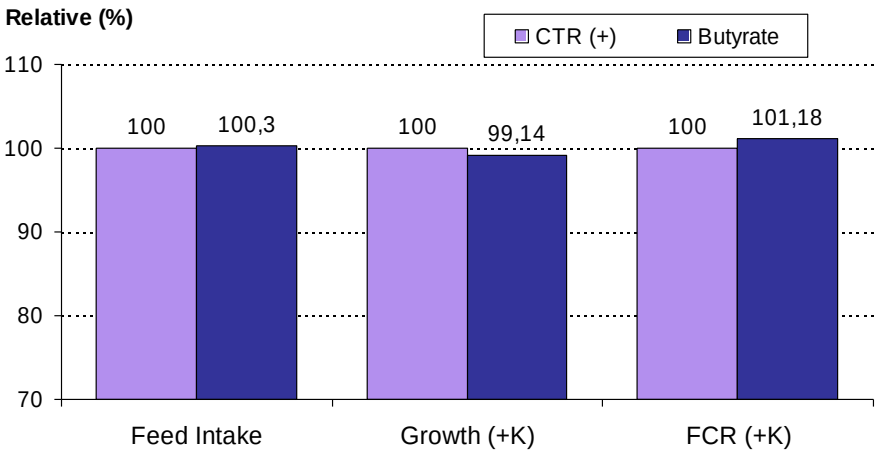
→Trials set up at a practical farm and followed up by the Industrial School - CTL Ghent. Trials in the frame of student scription (thesis).

→CTR-: blanc control without ABGP and without calciumbutyrate
CTR +: feed with ABGP: 60 ppm salinomycin
Butyrate : calciumbutyrate at 2 kg per ton

→ Trial 1 : 96, 96 and 98 piglets in two shifts of 6 replicates. Trial 2 : 68 piglets per group in two shift of 6 replicates.

→ General conclusion :
- Large variations in the trial groups.
- First trial : Calcium butyrate performed in between salinomycin and negative control. Gave 5.1 % better DWG and 4.5% better FCR
- second trial : Calcium butyrate performed similar to salinomycin.





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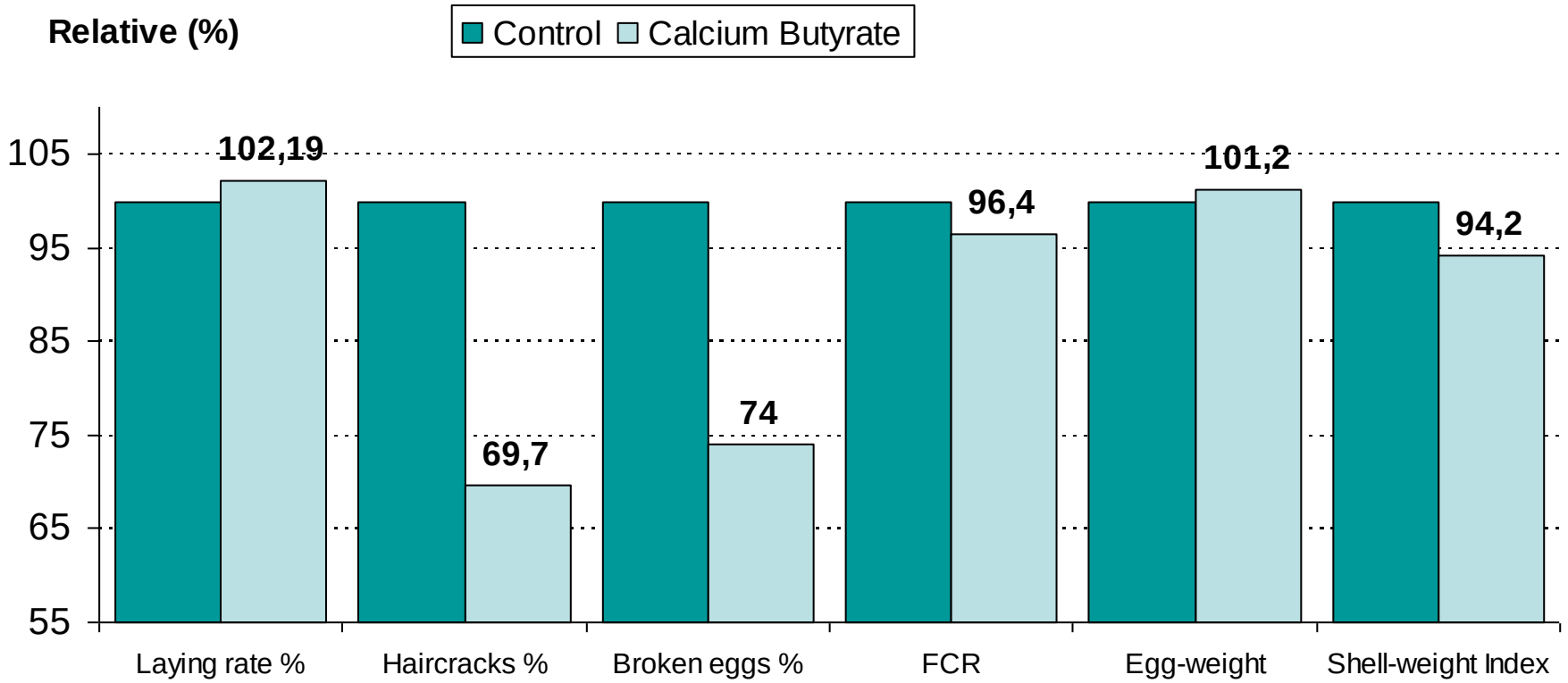
Effect of Ca-butyrate in Laying hens



CTR	77.7 %	16.5 %	21.5 %	2.21	64.9	86.8
Calcium Butyrate	79.4 %	11.5 %	15.9 %	2.13	65.7	81.8

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Effect of Calcium Butyrate on Egg Shell Quality

Action	Effects
a) Gut integrity (villi, mucosa) => better absorption of nutrients => minerals (Ca)	Significantly : * Less Broken eggs * Less Dirty eggs * Less Hair cracks * Less Eggs without shell
b) Synthesis of the matrix proteins of the shell, around which calcium (mineral) crystallisation takes place	Non significant increasing effect : * Shell Weight, Thickness * Egg Shell %, SWUSA
c) Highly available Organic Calcium	Improvement vibration parameters : * K-dyn, Resonance Frequency, * Damping ratio
d) Physiologic and metabolic effect on energy and Ca-metabolism	More intense Shell Colour (brown eggs)

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Sintobutyl The deodorised calcium butyrate for the basal energy request of all the species

- Calves: 1.0 - 1.5 kg/t
- Growing pigs : 0.3 - 0.5 kg/t
- Piglets up to 35 Kg: 0.5 – 1.0 Kg/ton
- Lactating sows : 1.0 - 2.0 kg/t
- Broilers : 0.20 – 0.5 kg/t
- Laying hens: 0.2 – 0.3 Kg/ton
- Turkeys : 0.25 – 1.0 Kg/t
- Rabbits: 1.0 – 2.0 kg/t

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Sintobutyl

ADVANTAGES:

It is a deodorised calcium butyrate source formulated to supply the basal energy requested by all the animal species.

Thanks to it special formulation it is well accepted from the operators, easy to handle and without bad smell.

It could be used in milk replacer for calves.

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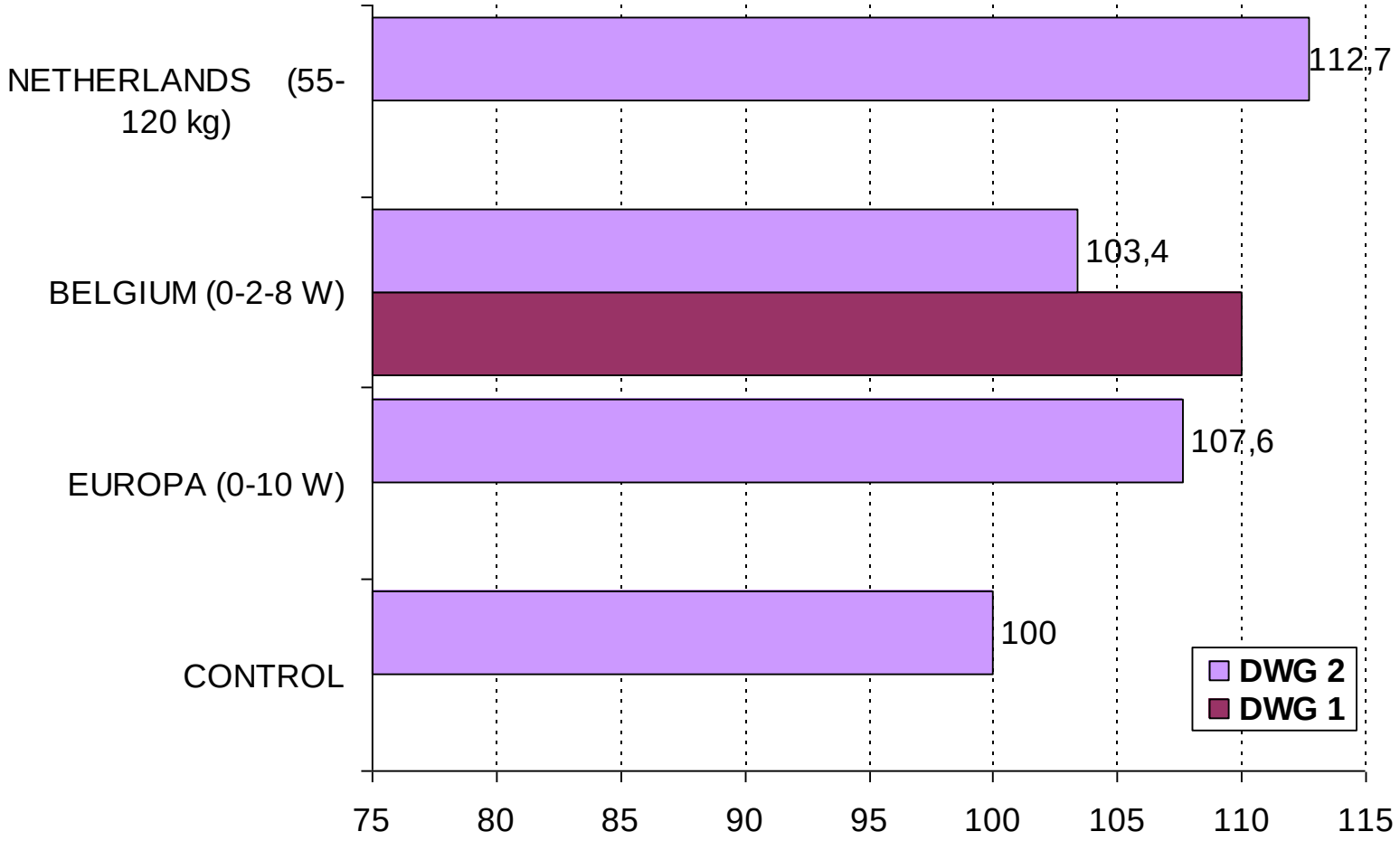
Trial overview with Sintobutyl in CALVES



Daily weight gain expressed as percent of non supplemented control.