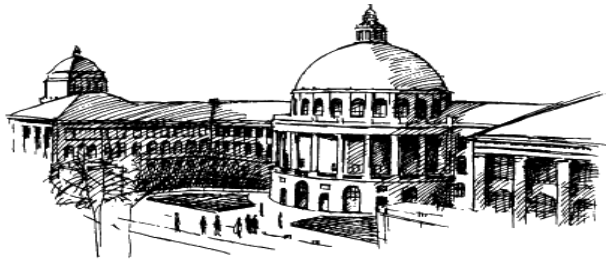
Uppsala, June 7, 2005

Session 5
Coping with New Regulation: Alternatives to Antimicrobial Growth Promoters

Alternatives to Antimicrobial Growth Promoters (AGP)



Caspar Wenk
Federal Institute of Technology
Zürich - Switzerland

KEY FOR HEALTH ANIMALS: EUBIOSIS

Eubiosis: Stable and healthy microflora in the digestive tract

Contribution of the EUBIOSIS:

- Digestion of nutrients
- Vitamin synthesis
- Stimulation of the immune system (e.G. IgA)
- Protection of the mucosa against undesired MO
- Antagonistic effects against undesired MO
- others

WHY Antibiotics in Diets for Pigs

- Reduction of undesired MO in the digestive tract
- Reduction of infections in the digestive tract
  ➡ Less animal losses
- Reduced thickness of the intestinal wall
  ➡ Better nutrient utilization
- Reduced ileal nutrient fermentation
  ➡ Less nutrient and energy losses

The GOOD NEWS

➡ Better health / less animal losses

➡ Higher growth rate

➡ Better feed conversion

Losses of Performance after Withdrawal of Antimicrobial Feed Additives

(under good hygienic conditions) Pfirter et al (1996)

	reduced body mass gain	worse feed conversion ratio
veal calve	7 - 8%	4 - 5%
beef	4%	2%
piglet	8%	5%
growing pig	5%	3%
fattening pig	2%	1%
pig production	5%	2%
broiler	3%	2%
laying hens (egg performance)	1%	1%

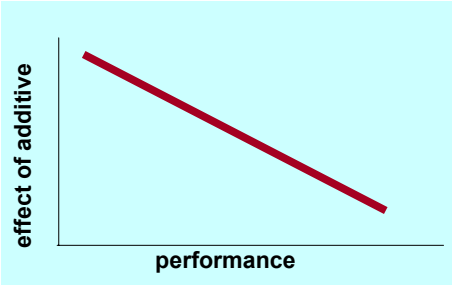
Furthermore eventually less animal losses and costs for veterinarian

When Does a Feed Additive Work ?

Effect of a feed additive is usually higher if:

- Low health conditions of animals
- Low performance
- Low nutrient content of the diet
- ANF (anti nutritional factors)
- Unfavorable environmental conditions
  (space, floor, straw bedding, dust, climate, etc.)
- Stress (e.g. metabolism cages)
- Bad management (e.g. farmer)

Pettigrew (2002):
Use commercial farms instead of laboratory experiments



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The BAD NEWS

➡ Antibiotic resistance: animal - man

➡ Environment (Zn, Cu)

➡ **Consumer says NO**

How Can we Justify the Production and Consumption of Animal Food ?

K. Steigleder, Stuttgart Hohenheim, Germany (2002)

Moralistic Goals in Animal Production

- Economic imperative cannot supercede criteria like wellbeing of man and animals, environmental concerns, good product quality, etc.
- Animal nutrition cannot remediate or repair a basic shortage
- Need of laws to protect animals (local, national, international)

http://www.lah.de/fachinfos/lohmann_info/deutsch/l_i_2_02_artikel5.pdf

What is a Feed Additive?

EC off. J. 17.10.2001

List of the Permitted Feed Additives in Animal Nutrition:

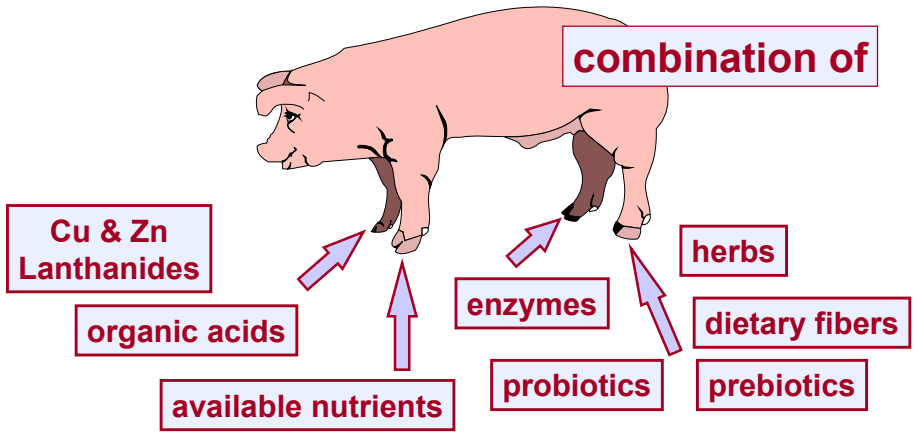
Antibiotics (today only: Salinomycin-Na, Flavophospholipol, Avilamycin)
Coccidiostats and other medicinal substances
Growth Promoters (today only K - di formate)
Coloring matters including pigments
Binders, anti-caking agents etc.
Trace elements (today only Cu)
Enzymes
Microorganisms

Missing on that list:

- antioxidants
- vitamins
- prebiotics
- Aromatic and appetizing substances
- herbs or botanicals
- metabolic modifiers (β-agonists)

PRONUTRIENTS Instead of ANTIBIOTICS for Farm Animals

PRONUTRIENTS as ALTERNATIVES



Minerals as AGPs

ZnO – $CuSO_4$ – Rear Earth Elements

It is well-known that especially ZnO – $CuSO_4$ develop a pronounced antimicrobial activity in the digestive tract. Accordingly 250 - 300 ppm $CuSO_4$ (piglets and fattening pigs) or up to 8000 ppm ZnO (piglets) have been used.

There are obvious toxicological as well as environmental arguments against the use of such high doses.

Recently Rear Earth Elements (Lanthanides) are evaluated as possible alternatives.

Minerals as AGPs

In EU & Switzerland the following maximal dosages are prescribed in mixed feed:

Zn	**all species farm animals**	**150 ppm**
	pet animals	**250 ppm**
	(milk replacer	200 ppm)
Cu	**pigs until 12 weeks**	**170 ppm**
	after 12 weeks	**25 ppm**
	veal calves	**35 ppm**
	sheep	**15 ppm**
	other species	**25 ppm**

(Denmark has again permitted the use of Zn as AGP for piglets)

Rare Earth Elements (REE) in Growing Pigs: European Experiments

Birgit Prause (2005)

PIGS	Dose of REE	BWG (rel. to control)	FCI (rel. to control)	Author
72 piglets, 7 kg BW over 35 days	75 / 150 mg/kg -Chloride	+ 2 % / +0-5 %	-5 % / -3 ; -7 %	Rambeck et al. (1999)
48 piglets, 17 kg BW (8 + 6 weeks)	150 mg/kg -Chloride	**+19 %* / +12 %***	**-11 %*** / -3 %	Borger (2003)
Field trial 18 kg – 100 kg BW	300 mg/kg -Chloride	+4 %	-9 %	Eisele (2003)
24 piglets, 9 kg BW over 41 days	100 / 200 mg/kg -Citrate	+ 9 % / +23 %	-6 % / -6 %	Knebel (2004)
48 pigs 25kg – 104 kg BW	250 mg/kg -Citrate	**+ 9 %***	**-4 %***	Kessler (2004)
147 piglets 8kg over 35 days	150 / 300 mg/kg -Citrate	-1 % / -4 %	-1 % / -4 %	Fritz / Gebert (2004)
40 piglets 8kg – 60 kg	150 / 300 mg/kg -Citrate	0% / (-1%)	**-7 %*** / -2 %	Prause (2005)
40 piglets 35 – 60 kg BW	100 mg/kg chloride/ -nitrate/ -citrate/ -ascorbate	-1 - -4 % * P ≤ 5 %	ND ND = Not Done	Böhme et al (2002)

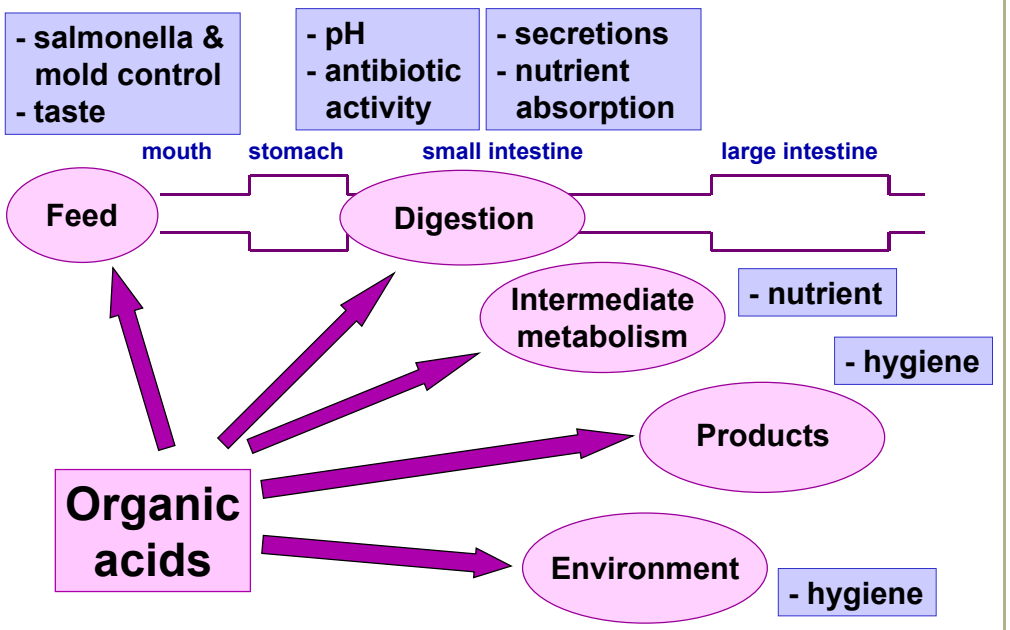
Formula, Physical and Chemical Properties of Organic Acids

Acid	Formula	MW	Dichte (g/ml)	Form	pKa	Sol. in water
Formic	HCOOH	46.03	1.220	liquid	3.75	∞
Acetic	CH3COOH	60.05	1.049	liquid	4.76	∞
Propionic	CH3CH2COOH	74.08	0.993	liquid	4.88	∞
Butyric	CH3CH2CH2COOH	88.12	0.958	liquid	4.82	∞
Lactic	CH3CH(OH)COOH	90.08	1.206	liquid	3.83	*v*
Sorbic	CH3CH:CHCH:CHCOOH	112.14	1.204	solid	4.76	*s*
Fumaric	COOHCH:CHCOOH	116.07	1.635	solid	3.02 4.38	*s*
Citric	COOHCH2C(OH)(COOH)CH2COOH	192.14	1.665	solid	3.13 4.76 6.40	*v*

∞, soluble in all proportions, *v*, very soluble, *s*, sparingly soluble

Partanen und Mroz, 1999

Organic Acids: Modes of Action



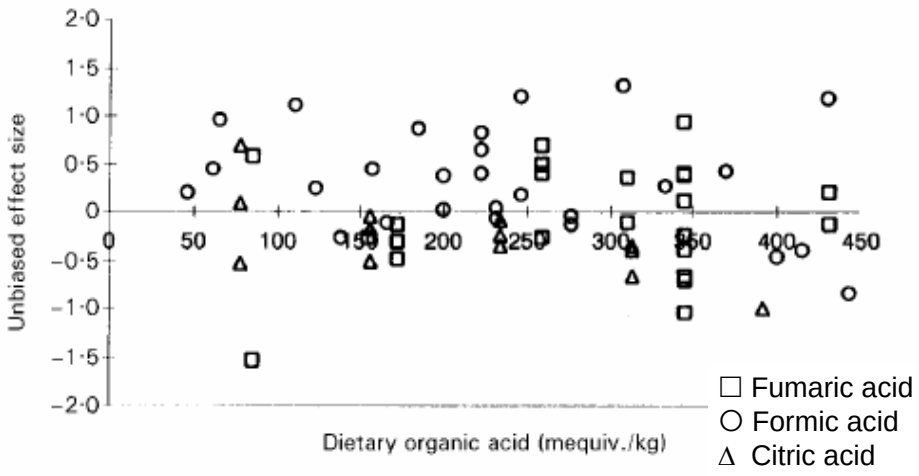
Effect of Organic Acids on pH in the Digestive Tract

Acidifier	Reference	Level (g/kg)	Gastrointestinal pH: Gastric	Ileal	Caecal	Colonic	Gastric dry matter content
Citric acid	Scipioni *et al.* 1978	10	ns	ns			
	Risley *et al.* 1991	15	ns	ns	ns	ns	
	Risley *et al.* 1992	15	ns	ns	ns	ns	
	Risley *et al.* 1993	15	ns	ns	ns	ns	
	Fasshauer & Kienzle, 1995	10		–			
	Radcliffe *et al.* 1998	15	–				
		30	–				
Formic acid	Bolduan *et al.* 1988*a*	3·5	–	ns			ns
		12	–	ns			ns
	Eidelsburger *et al.* 1992*a*	12·5	–	ns	ns	ns	ns
	Roth *et al.* 1992*a*	6	ns	ns	ns	ns	ns
		12	ns	ns	ns	ns	ns
		18	ns	+	+	+	ns
		24	ns	+	ns	+	ns
	Gabert & Sauer, 1995	10		ns			
Fumaric acid	Bolduan *et al.* 1988*b*	5	ns				ns
		15	–				ns
	Risley *et al.* 1991	15	ns	ns	ns	ns	
	Risley *et al.* 1992	15	ns	ns	ns	ns	
	Risley *et al.* 1992	18	–	ns	ns	ns	ns
	Risley *et al.* 1993	15	ns	ns	ns	ns	
	Gabert & Sauer, 1995	15		ns			
		30		ns			
Propionic acid	Bolduan *et al.* 1988*a*	3	ns	ns			ns
		10	ns	ns			ns
Calcium formate	Eidelsburger *et al.* 1992*a*	10	ns	ns	ns	ns	ns
		18	ns	ns	ns	ns	ns
Sodium formate	Roth *et al.* 1992*b*	18	ns	ns	ns	ns	–
Sodium fumarate	Gabert & Sauer, 1995	15		ns			ns

+, significant increase in pH or dry matter content ($P<0·05$); –, significant decrease in pH or dry matter content ($P<0·05$); ns, no significant influence on pH or dry matter content.

Partanen und Mroz, 1999

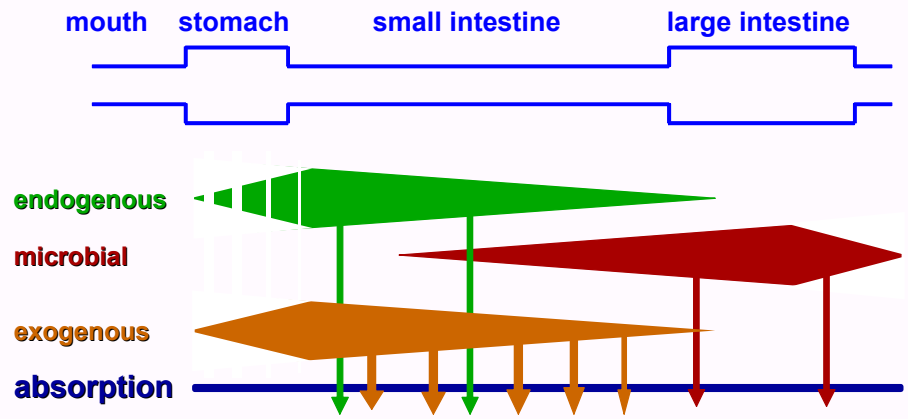
Effect of Organic Acids on Feed Intake in Piglets



Formic acid slightly better than others

Partanen und Mroz, 1999

Competition between Enzymes in the Digestive Tract



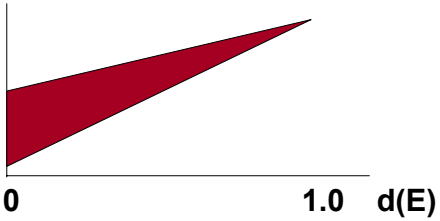
Feed enzymes are active in the digestive tract

ENZYMES: What can we expect from them?

1 **Replenishment of lacking endogenous enzymes**

2 **Better availability of feed nutrients**

Effect of an enzyme on performance



3 **Inactivation of ANF: Phytate, inhibitors, mycotoxins, etc.**

Enzymes, Antibiotics and Microbials as Feed Additives for Broilers (Gordon Rosen, 2003)

Parameter	A	E	M
n	5159	2557	234
FDIC (g)	2478	2106	2636
FDIeff	15 (970)	32.4 (451)	6 (1449)
LWGC (g)	1075	1043	1331
LWGeff (g)	**39.8** (129)	**54.3** (147)	**25.3** (192)
FCRC	2.16	1.99	1.87
FCReff	**-.073** (164)	**-.105** (185)	**-.030** (195)
DUR (days)	41.0	30.3	35.8
YEAR - 1900	71.6	87.0	86.6
Improvement frequency (%)**	**74**	**75**	**70**

**) percentage of tests with feed conversion ratio and live weight gain improvement

Enzymes, Antibiotics and Microbials as Feed Additives for Pigs (Gordon Rosen, 2003)

Parameter	A	E	M
n	2702	509	238
FDIC (kg/day)	1.614	1.481	.993
FDIeff (kg/day)	.067 (185)	.029 (319)	.015 (483)
LWGC (kg/day)	.541	.584	.431
LWGeff (kg/day)	**.049** (104)	**.042** (104)	**.021** (142)
FCRC	2.90	2.39	2.12
FCReff	**-.136** (156)	**-.124** (121)	**-.082** (206)
DUR (days)	65.8	53.1	43.7
YEAR - 1900	69.3	93.3	85.1
Improvement frequency (%**)	**69**	**76**	**56**

**) percentage of tests with feed conversion ratio and liveweight gain improvement

Pronutrients in Animal Nutrition

Probiotics: Microbial food / feed supplements that beneficially affect the host by improving its intestinal microbial balance

Prebiotics: Non digestive food / feed ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacterial species already resident in the digestive tract and thus attempt to improve host health

GIBSON & ROBERTFROID, 1995

Prebiotics

Non digestive food / feed ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacterial species already resident in the digestive tract and thus attempt to improve host health

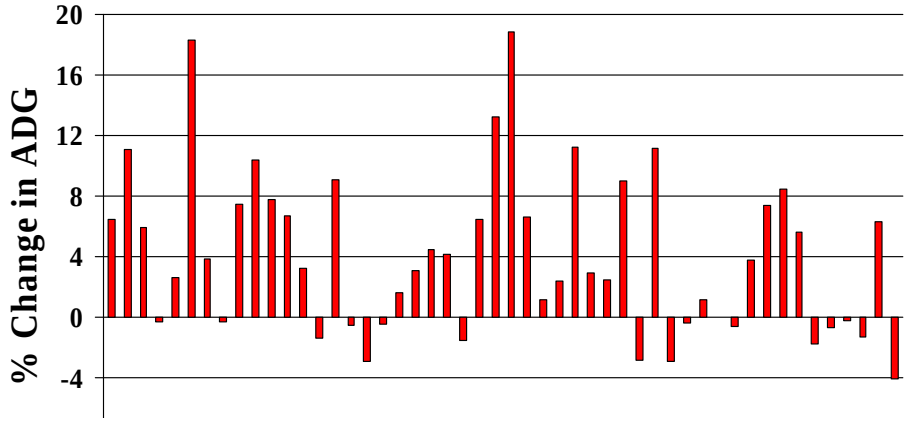
	Mode of action (examples)
FOS / RS Lactose	Specific substrate for MO (e.g. Bifidus or Lactobacilli)
MOS	Competitive exclusion of pathogenic MO

Interaction with specific (soluble) fiber fractions

Practical Response to MOS in Nursery Pigs

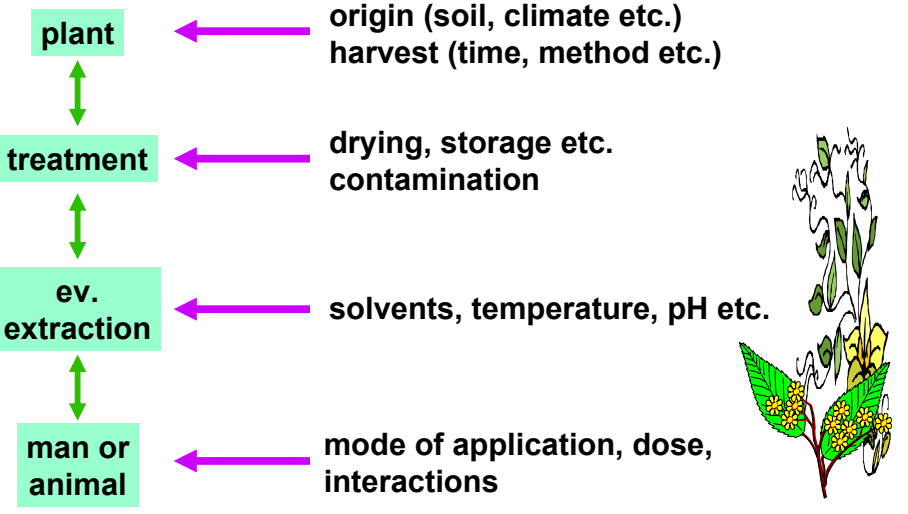
J. C. Miguel, S. L. Rodriguez - Zas & J. E. Pettigrew (2002)
University of Illinois

Overall average daily gain (ADG) Ø = + 4.04 %; P<0.0001



From Herbs to Botanicals

Influence on Activity



Antimicrobial Activity of Herb Extracts (Botanicals)

Stéphanie Good (2003)





Water and ethanol extracts from:
Oregano, Clove, Fenugreek, Black cumin and Curcuma

Antimicrobial Activity of Herb Extracts (Botanicals)

Stéphanie Good (2003)

	Ent. faecalis	E. coli	Candida magnoliae
Water extract			
Oregano	-	(*)	-
Clove	-	(*)	-
Fenugreek	-	-	-
Black cumin	-	-	-
Curcuma	-	-	-
Ethanol extract			
Oregano	**	**	*
Clove	**	**	*
Fenugreek	-	(*)	-
Black cumin	(*)	(*)	-
Curcuma	*	*	-

Literature Results with Herbs and Essential Oils in Piglets

Rodehutscord, M., Kluth, H. (2002) Tierfütterung ohne antibiotisch wirkende Leistungsförderer. Züchtungskunde, 74, (6) S. 455-4527

Supplement	Dose	Feed intake		BM gain		Feed efficiency		Autors
	g/kg	C[1]	Rel.[2]	C	Rel.	C	Rel	
	Feed	g/d	%	g/d	%	kg/kg	%	
Herb								
Oregano	2	553	-1	367	+9	1,51	-10	Schuhmacher et al. (2002)
Oregano	2	601	+4	480	+5	1,25	±0	
Garlic	1	553	-7	367	+2	1,51	-8	
Garlic	1	601	+5	480	+1	1,25	+4	
Rose of sharon	2	553	-7	367	-3	1,51	-6	
Rose of sharon	2	601	+3	480	+2	1,25	+1	
Coriander	2	558	+4	409	+7	1,37	-3	
Sage	2	558	+3	409	+7	1,37	-4	
Thyme	2	558	+4	409	+6	1,37	-3	
Yarrow	2	558	+1	409	+4	1.32	-4	
Echinacea purpurea	18	622	-2	389	+1	1,60	-4	Maass et al. (2002)
Herb mixture								
ENTEROGUARD	1	573	-2	330	-3	74	±0	Richter et al. (2002)

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Supplement	Dose	Feed intake		BW gain		Feed efficiency		Autors
	g/kg	C[1]	Rel.[2]	C	Rel.	C	Rel	
	Feed	g/d	%	g/d	%	kg/kg	%	
„Essential" oil								
Oregano	0,1	596	+3	398	+2	1,50	±0	Gollnisch et al. (2001)
Oregano	0,1	724	±0	444	+5	1,63	-5	Wald et al. (2001)
Cassia	0,1	596	+5	398	+2	1,50	+3	Gollnisch et al. (2001)
Cassia	0,1	724	-5	444	±0	1,63	-5	Wald et al. (2001)
Clove leaf	0,1	596	+1	398	-1	1,50	+3	Gollnisch et al. (2001)
Clove leaf	0,1	724	+3	444	+7	1,63	-4	Wald et al. (2001)
Lemon grass	0,1	887	-2	531	+2	1,67	-4	
Piment	0,1	887	-8	531	-4	1,67	-5	
Teebaum	0,1	887	-2	531	±0	1,67	-2	
Mints	0,1	887	-9	531	-3	1,67	-7	
Mints	0,1	717	-6	457	-5	1,57	-1	Wald (2002)

[1] Control [2] relative to control

Herbs and Botanicals in Livestock Nutrition
Current Trends, Efficacy and Safety

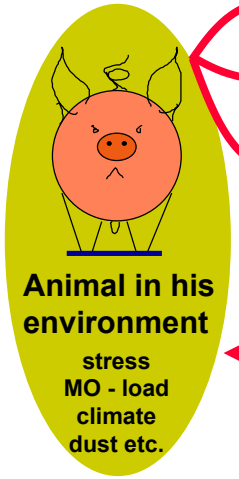
HERBS - BOTANICALS

are effective as feed additives

What they ***cannot*** do:
Suppress (like AGP)
- any illness
- digestive disorders
- stress
  (climate, dust, management . . .)

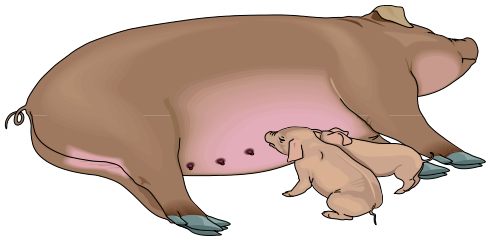
What they ***can*** do:
Stimulate
- feed intake
- digestive secretions
- eubiosis of intestinal MO
- antioxidative protection

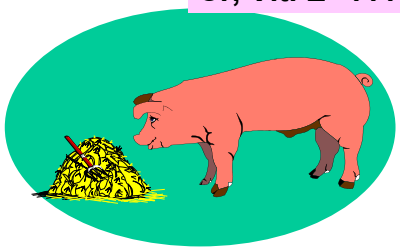
Alternatives after the Ban of Antibiotics in Pigs



AGP = Anti microbial growth promoter

Feeding of Piglets Begins with the Feeding of the Sow





Piglets, sow milk and starter diet:
Fe is the 1st limiting nutrient for Escherichia coli !!!

At weaning: ➡ see that all piglets drink water & eat dry feed
➡ see that piglets do not ingest to big quantities of feed (regular intake of small quantities !!!)

Feeding Factors to Minimize Digestive Disorders in Weaned Piglets

1 Lower acid binding capacity
- less minerals (Ca (6 g/kg), P (5 g/kg))
- less protein (ess. AS according to requirement)
- organic acids (fumaric and lactic acid)

2 Enzymes, prebiotics and dietary fibers
- carbohydrases, phytases
- pectins, other soluble dietary fibers
- prebiotics: FOS, RS, MOS, others

3 Liquid feeding with fermentation

4 Herbs, botanicals, essential oils

5 Probiotics: lactobacilli (others)