

**“No reason to be afraid of
mycotoxins in the feed”**



Feed Additives

Agenda



Süd-Chemie – Products and Product safety

Mycotoxins and Mycotoxin adsorbents

In-vitro results

In-vivo results

Markets

-  AGRICULTURE
-  DOMESTIC PETS
-  BEVERAGES
-  CERAMICS
-  DETERGENTS AND CLEANSING AGENTS
-  FOUNDRY
-  PAPER INDUSTRY
-  EDIBLE OILS
-  CONSTRUCTION AND DRILLING
-  PETROCHEMICALS
-  PLASTICS
-  CHEMICALS
-  OIL REFINERIES
-  PACKAGING SYSTEMS AND COMPONENTS
-  ENVIRONMENTAL TECHNOLOGY

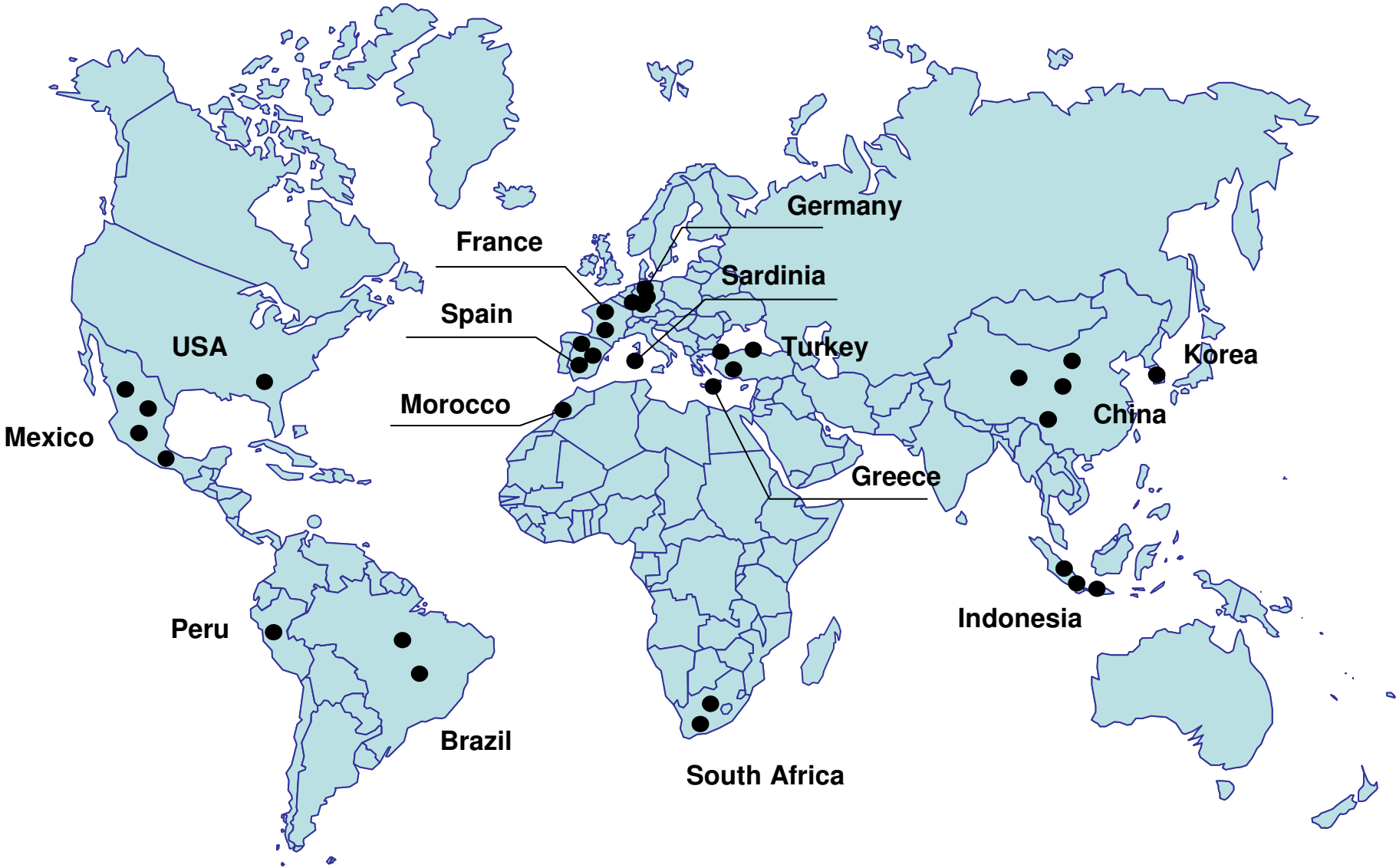


Raw materials

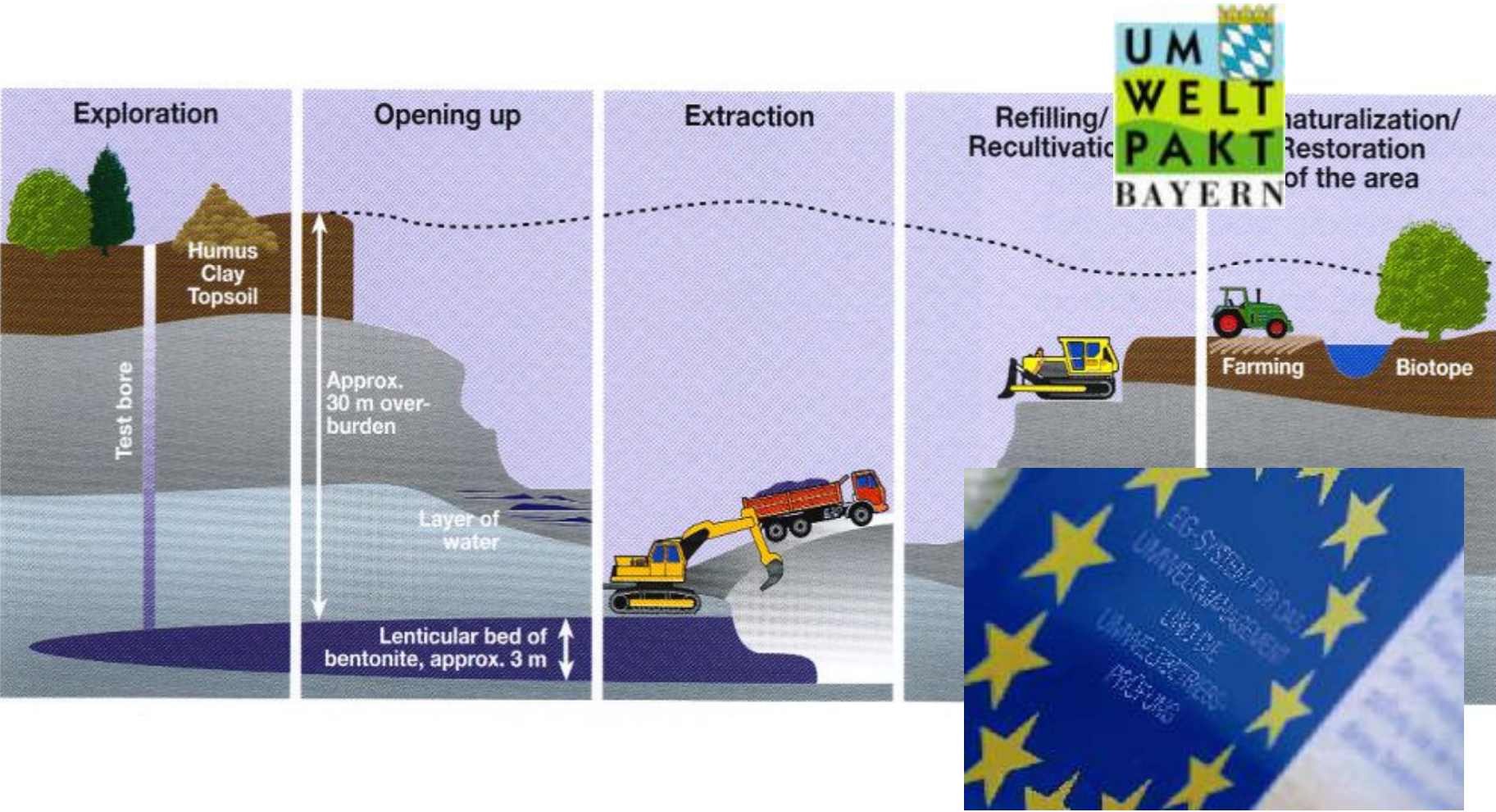


What makes us special?

Full control of raw materials



Responsible mining





Regulated processes and quality management

- Registered as a feed additive producer
(Herstellerbetrieb für Zusatzstoffe gem. § 31
Abs. 1 FMV)
- Certified according to DIN ISO 9001 / 14001,
- HACCP Concept – Implementation by end of 2007.

Safe products for safe feed and food

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Creating Performance Technology



Control of Contaminants

- Dioxins
- Dioxin – like PCB's
- Heavy metals

Lead

Cadmium

Mercury

Arsenic



Agenda



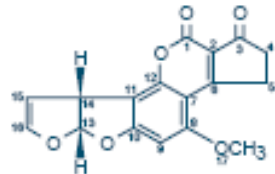
Süd-Chemie – Products and Product safety

Mycotoxins and Mycotoxin adsorbents

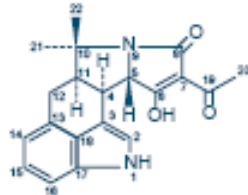
In-vitro results

In-vivo results

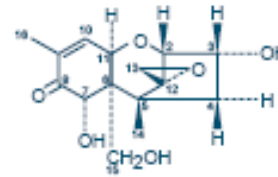
What are mycotoxins?



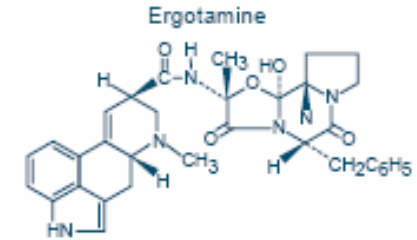
Aflatoxin B₁



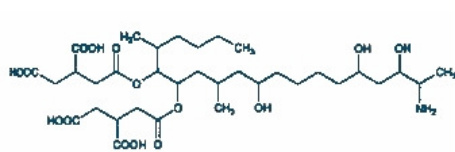
Cyclopiazonic Acid



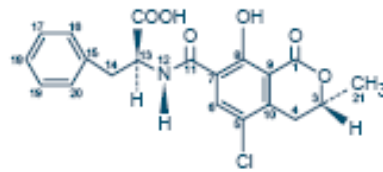
Deoxynivalenol



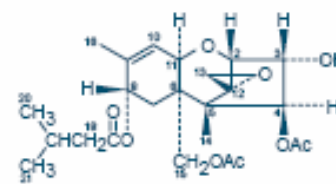
“Mycotoxins are metabolites (by-products) of the growth of the molds. They have very real toxic side effects to other plants, animals, and humans. They are also generally less selective of the hosts they attack and can cross plant species.”



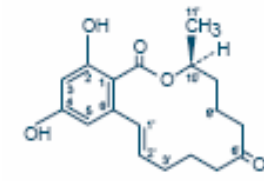
Fumonisin



Ochratoxin A



T-2



Zearaleone

What are mycotoxins ?

Factors affecting mold growth

- Moisture level in grain and feeds
- Relative humidity
- Temperature
- Transit & storage time
- Kernel damage
- pH
- Oxygen



How to prevent mycotoxins?



The ideal situation - always have feed and feedstuffs clean, without presence of any of the mycotoxins.

Once mycotoxins are present, it is difficult to deal with them.

- **They are complex** – chemical structures are widely different from each other.
- **They are difficult to detect** – by costs and sampling.
- **Symptoms** – in field they show nonspecific signs mainly in lower dosages.

How to prevent mycotoxins?

Currently proposed methods:

- **Resistant Genotypes** – ex. Some corn strains are resistant to development of *Aspergillus* / *Fusarium*,
- **Organic Acids** - to prevent fungi development,
- **Segregation** – physically separating contaminated grains,
- **Heat inactivation** – some mycotoxins are heat sensitive,
- **Mycotoxin Adsorbents.**

What are Mycotoxin Adsorbents?



Usually they are:

- Products made by Hydrated Sodium Calcium Aluminosilicates (HSCAS).
 - Simple
 - Organically modified
- Products made by HSCAS combined with MOS (Mananoligosaccharides).
- Products made by HSCAS combined with enzymes.
- Products only made by MOS.



HSCAS have in general a particular ability to establish a bond with the Aflatoxins molecules. There is a stable link between Aflatoxins and HSCAS making them not absorbable any more by the animal GI tract.

The complex is formed by the β -ceto-lactone system of the Aflatoxin with a non coordinated Calcium and Sodium ion site of the HSCAS.

TOXISORB® Classic & Premium

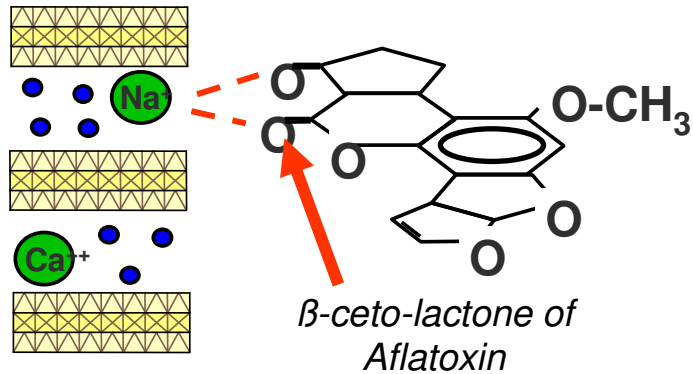
Adsorption mechanism of mycotoxins

1 Attraction

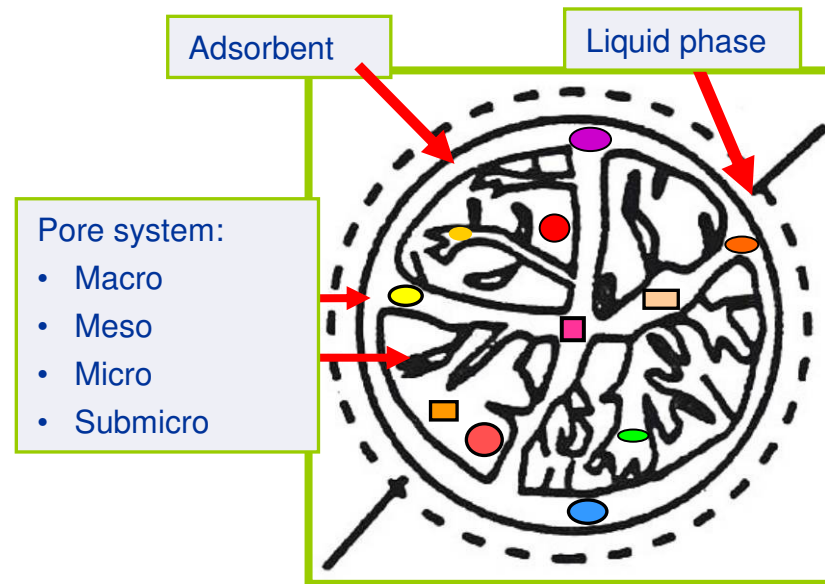
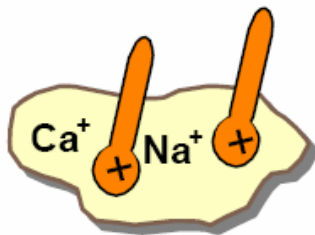


2 TOXISORBion

Polar mycotoxins (Aflatoxin, CPA, Ergot)



Non-polar mycotoxins (DON, FB1, OTA, T-2, ZEA)



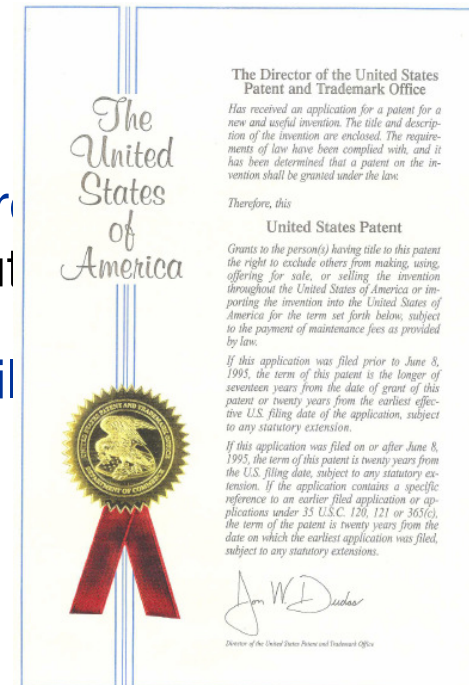
TOXISORB® Basic & Premium Clay activation

TOXISORB® Basic

- Alkaline activation → increase hydrophilic surfaces in aqueous solutions

TOXISORB® Premium

- Alkaline activation → increase hydrophilic surfaces in aqueous solutions
- Organophilic activation → confer lipophilic surfaces



- **PCT/EP99/10088 (Dec. 17, 1999)**
- **PCT/EP 01/11713 (Aug. 13, 2003)**
- **US 6,827, 959 B1 (Dec. 7, 2004)**

Agenda



Süd-Chemie – Products and Product safety

Mycotoxins and Mycotoxin adsorbents

In-vitro results

In-vivo results

TOXISORB® Basic & Premium

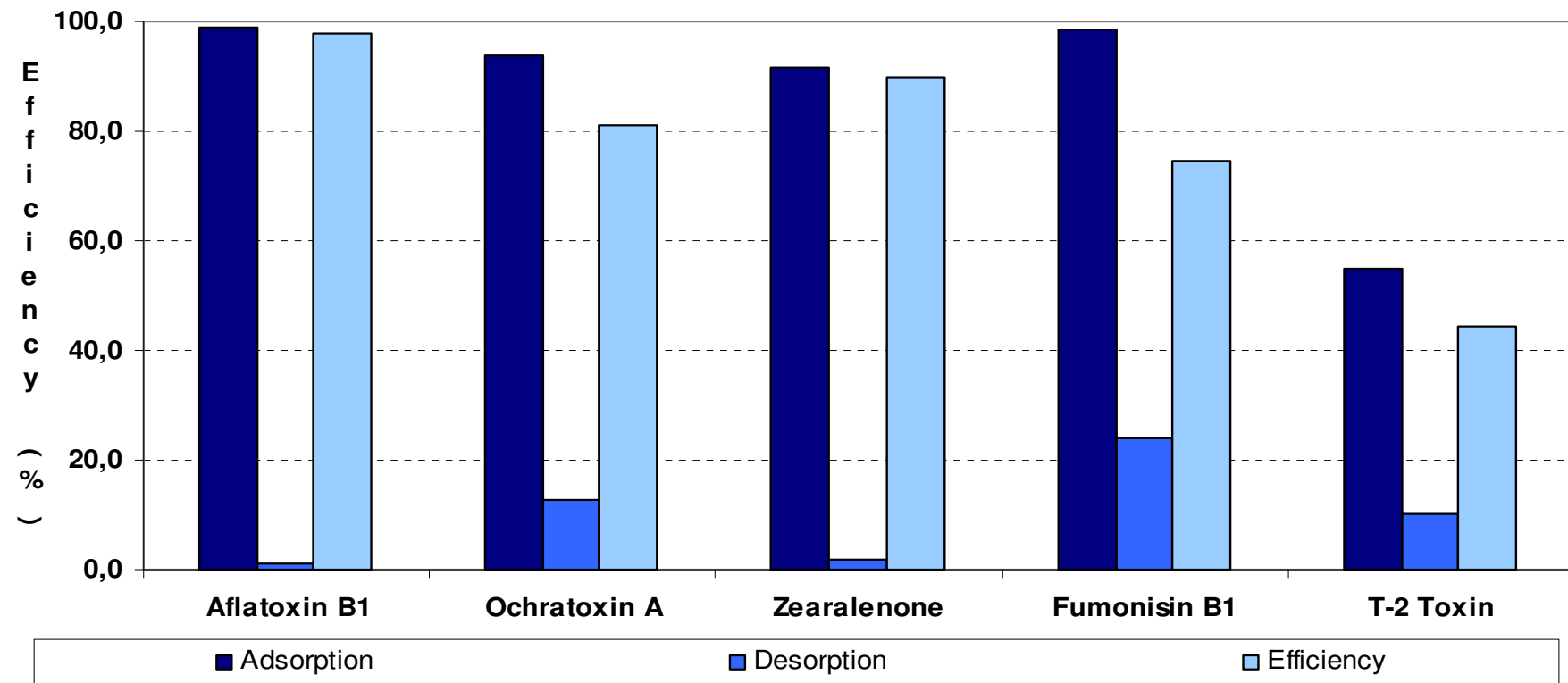
Adsorption efficiency profile of TOXISORB® Premium



TOXISORB In-Vitro Tests at University of Munich

Toxin conc.: AFB1, OTA, ZON, T-2 : 300ppb ; DON, FB1 : 1500ppb

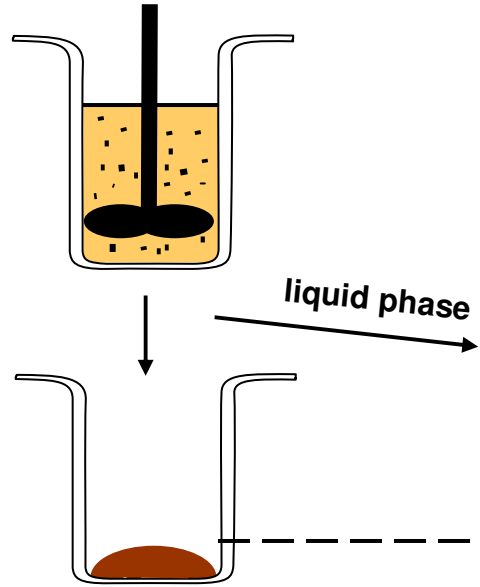
Dosage of adsorbent: 0,4% ; pH_{adsorption} 3,0 (T-2: 4,5) ; pH_{desorption} 6,5



In-vitro trial results

Efficiency vs. adsorption (cont.)

Adsorption under
acidic pH conditions

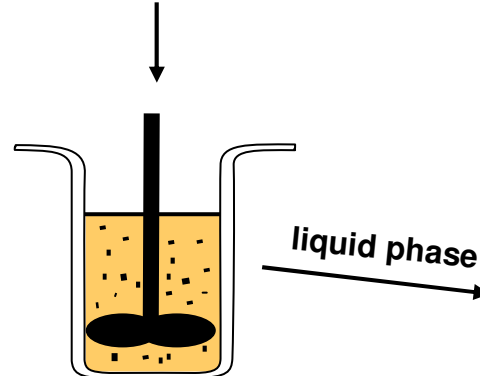


A) aqueous toxin solution (2 ppm toxin), buffered at pH 3 (mimicking stomach pH) + adsorbent (0.2 – 0.4 % [w/w]), agitating 2 h at 37 °C

B) centrifuging (10 min 2800 U / min)

- clear supernatant to HPLC for analysis of remaining toxin amount
- remaining solid phase is used in a desorption step

Desorption under
neutral pH conditions



C) re-suspension of solid phase (adsorbent + bound toxin) in aqueous solution at neutral pH (mimicking intestine), agitating 2 h at 37 °C

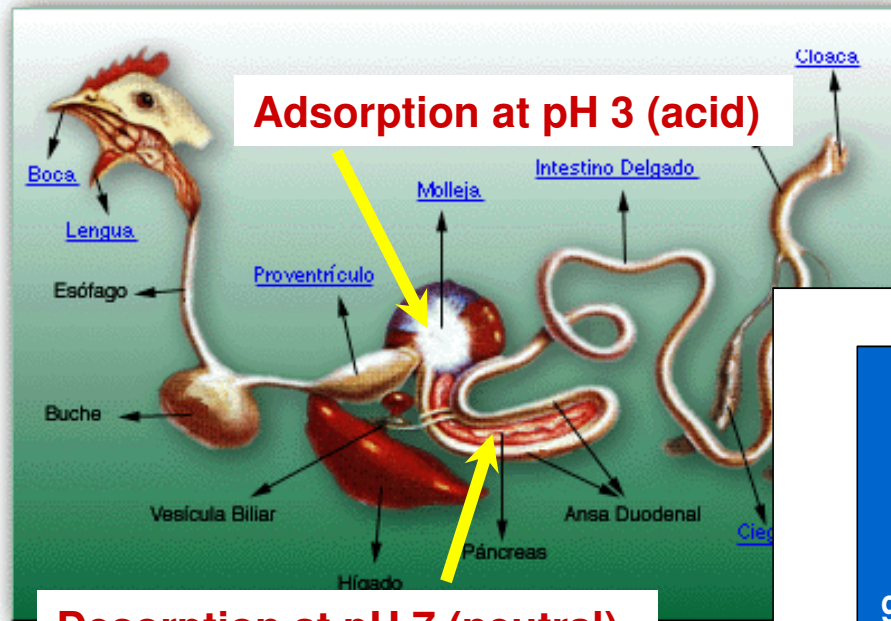
D) centrifuging (10 min 2800 U / min)

- clear supernatant to HPLC for analysis of desorbed toxin amount

Efficiency = Adsorption - Desorption

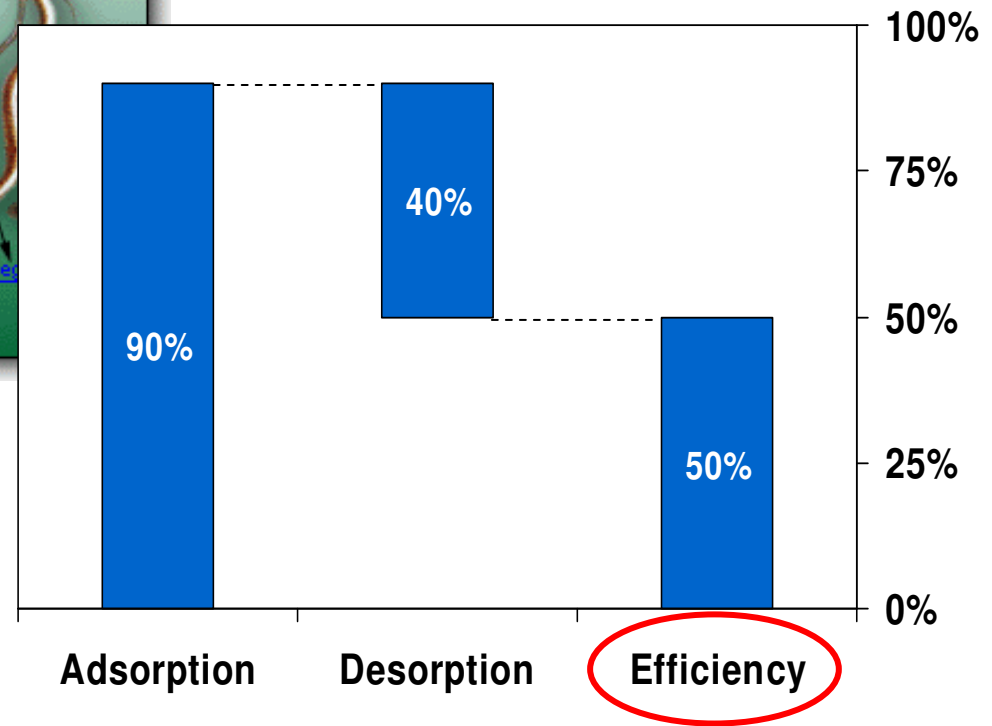
TOXISORB® Basic & Premium

Efficiency vs. adsorption



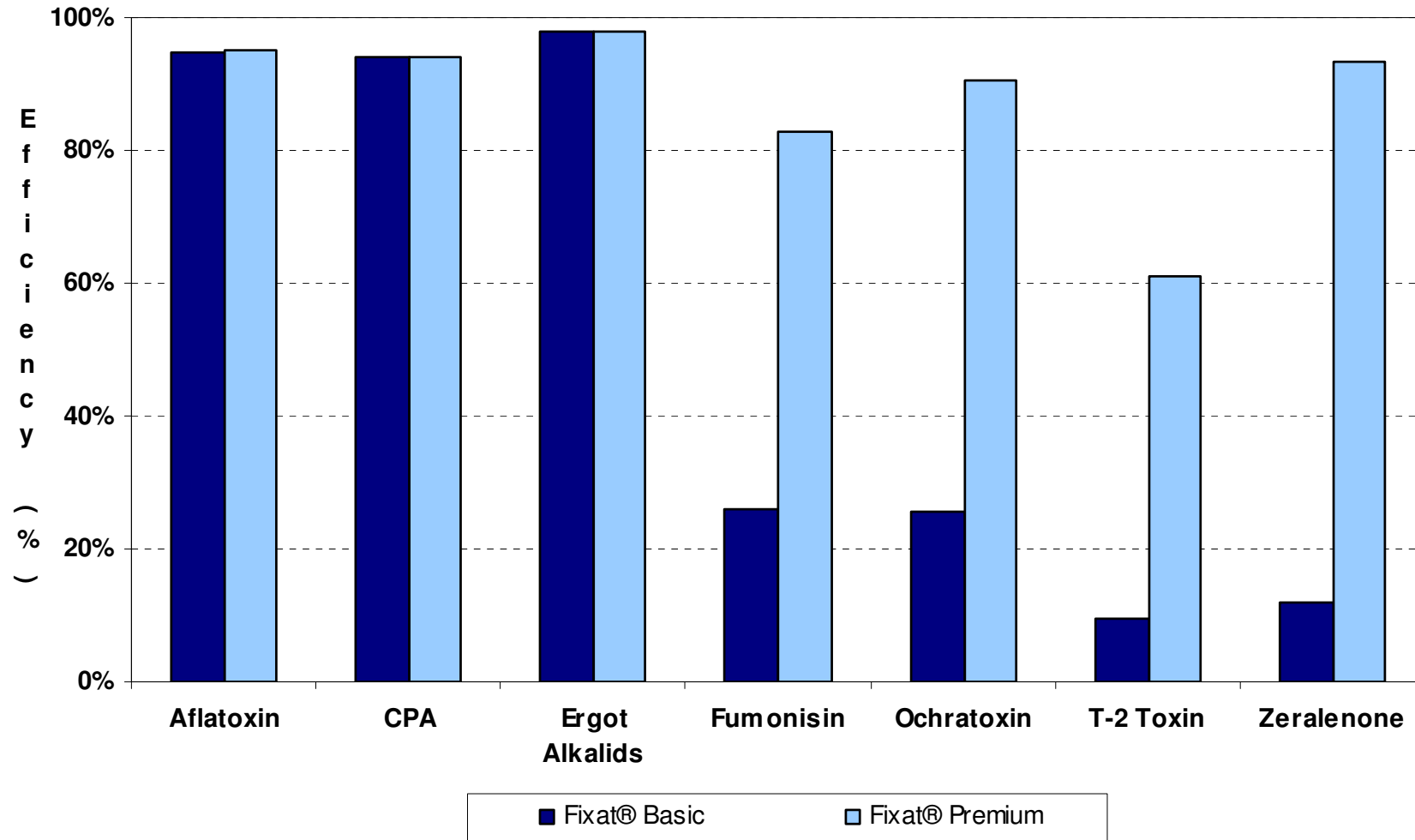
Desorption at pH 7 (neutral)

Efficiency =
Adsorption - Desorption



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Mycotoxin adsorption efficiency profile at 4kg/t



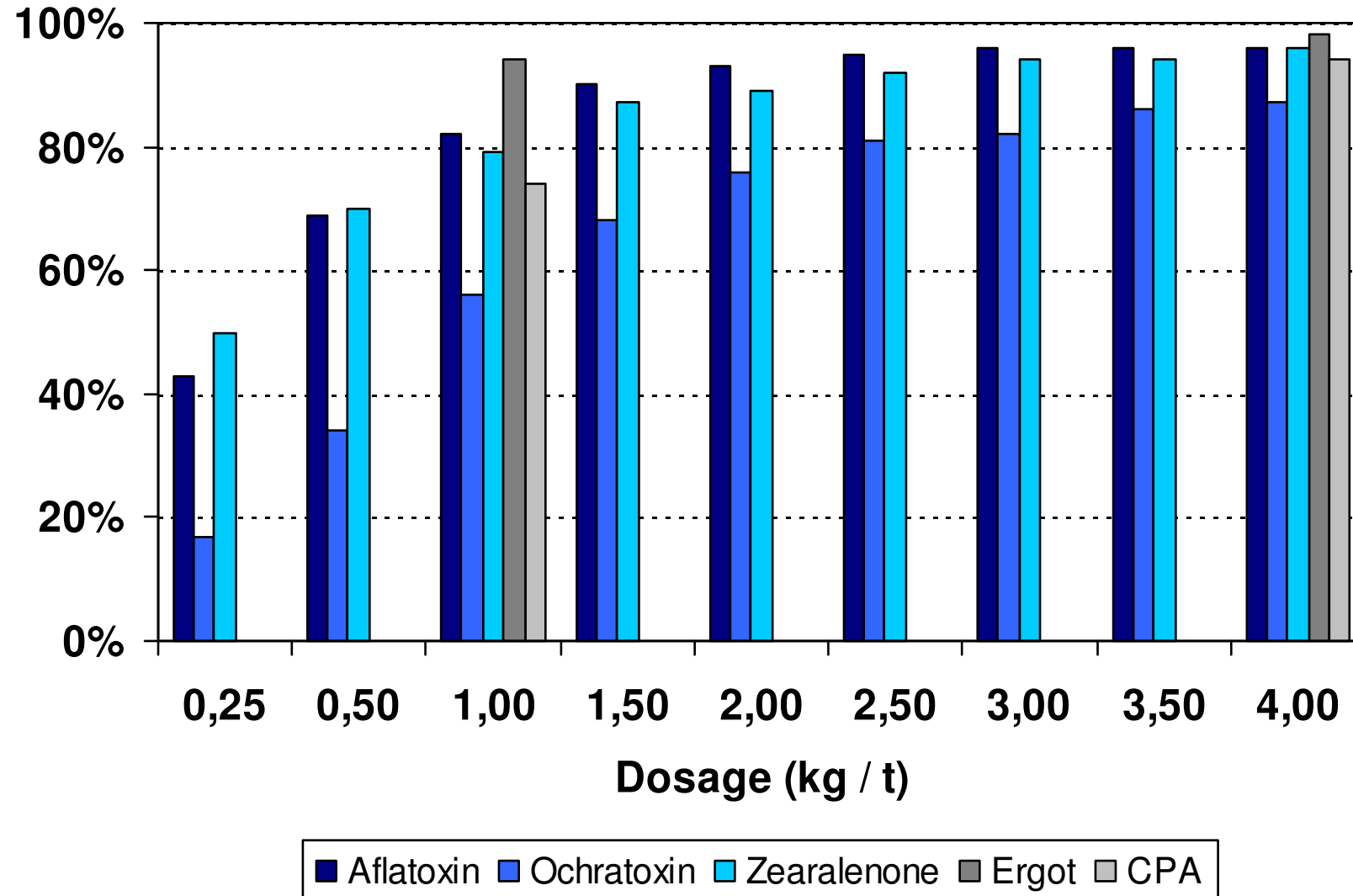
Source: Süd-Chemie

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Dosage dependent efficiency of TOXISORB® Premium



Source: Süd-Chemie

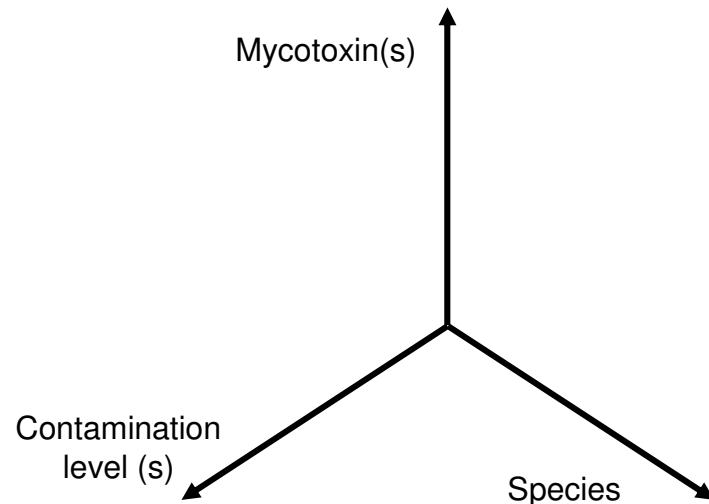
TOXISORB® Basic & Premium

Product and dosage recommendation



- | | | |
|--------------------------------------|---|--------------------------|
| • Aflatoxin only | → | TOXISORB® Basic |
| • Any mycotoxins, incl. cocktail mix | → | TOXISORB® Premium |

Dosage = f(species, mycotoxin(s), contamination level(s))



Mycotoxin	Poultry	Swine	Ruminants
Aflatoxin	●	●	●
Deoxynivalenol	◐	◐	◐
Fumonisin	◐	◑	
Ochratoxin	◐	◑	
T-2 Toxin	●	◑	◑
Zearalenone	◐	●	◐

TOXISORB® Basic & Premium

Product and dosage recommendation



- | | | |
|--------------------------------------|---|--------------------------|
| • Aflatoxin only | → | TOXISORB® Basic |
| • Any mycotoxins, incl. cocktail mix | → | TOXISORB® Premium |
- Low contamination (below NOAEL levels) and/or preventive use
 - **1 – 2 kg/t of feed**
 - Medium contamination levels of only one mycotoxin or low mycotoxin levels of “cocktail mix”
 - **2 – 3 kg/t of feed**
 - High contamination levels and/or medium mycotoxin levels of “cocktail mix”
 - **3 – 4 kg/t of feed**

TOXISORB® Basic & Premium

Compatibility analysis with amino acids, phosphate and trace elements

Test procedure:

- Zearalenone: 2,000 ppb
- DL-Tryptophan: 0.4%
- L-Methionine: 0.4%
- Phosphate: 0.55%
- Iron: 60 ppm
- Zinc: 6 ppm
- Manganese: 20 ppm
- Copper: 4 ppm

- Time:
- Adsorbent: TOXISORB® Basic
TOXISORB® Premium
- Dosage: 4 kg/t

Mycotoxin/ nutrients	Adsorption efficiency TOXISORB® Basic	Adsorption efficiency TOXISORB® Premium
Zearalenone	2%	95%
DL-Tryptophan	0%	0%
L-Methionine	0%	0%
Phosphate	0%	0%
Iron	0 ppm	0 ppm
Zinc	0 ppm	0.06 ppm
Manganese	0.2 ppm	0 ppm
Copper	0.04 ppm	0.06 ppm

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Compatibility analysis with PO₄ and phytase



Phytase

Test procedure:

- **PO₄ source:** Phytic acid (Fluka)
- **Enzyme:** Phytase
- **Time:** 1 hour of stirring
- **Temp.:** 37 °C
- **Adsorbent:** TOXISORB® Premium
- **Dosage:** 4 kg/t



Phytase dosage	Liberated PO ₄ without TOXISORB® Premium	Liberated PO ₄ with TOXISORB® Premium
-	11.55 ppm	15.15 ppm
0.1%	36.8 ppm	41.0 ppm
1.0%	50.4 ppm	54.9 ppm

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Compatibility analysis with different nutrients

Author	Source	Animal	Bentonite dosage	Results
Lindemann, M.D., et. al. - 1993	J. Animal Science, 71	Swine	0.25–0.75%	Content of Ca, Mg, P, Na, K, Cl in blood serum unchanged
Southern, L. L., et. al. (1994)	Poultry Science, 73	Broiler	0.50 %	No significant changes of trace elements content in ash of tibia but increasing feed consumption and daily weight gain
Santurio, J. M., et. al. (1990)	Brit. Poultry Science, 40	Broiler	0.50 %	No significant changes of trace elements and enzyme contents in blood serum
Chung, T. K., et. al. (1990)	J. Animal Science, 68	Broiler	0.5–1 %	P-utilization from the diet unchanged
Chung, T. K., et. al. (1989)	Poultry Science, 69	Broiler	0.5–1 %	Vitamin A in liver and ash content of tibia unchanged; Mn content in ash of tibia unchanged, Zn content slightly reduced, significant only with 1 %
Briggs, G. M. et. al. (1995)	Poultry Science, 35	Broiler	5 %	With 5 % of bentonite in a synthetic diet vitamin A deficiency was found
Laughland, D. H., et. al. (1956)	Poultry Science, 35	Broiler	2–6 %	In a diet with vitamin A deficiency a negative effect caused by bentonite was observed. With a normal diet no effect was obvious.
Röhrmoser, G. (1988)	BLW, 50	Cattle	500 g / animal / d	Even after 6 month of application no effects could be detected regarding trace elements and vitamin A content in liver.

Agenda



Süd-Chemie – Products and Product safety

Mycotoxins and Mycotoxin adsorbents

In-vitro results

In-vivo results

In-vivo trials

Broilers // Aflatoxin B₁ // TOXISORB® Premium



Institute: Universidad Federal de Santa Maria (Brazil)
Species: Broiler chicken
Duration: 42 days
Repetitions: 5 with 15 heads each

Aflatoxin B1 dosage	TOXISORB® Premium dosage	Weight gain	Feed intake	Feed conversion rate	Mean daily weight gain
-	-	2464 g	4436 g	1.81	59 g
-	2.5 kg /t	2423 g	4482 g	1.85	58 g
3,000 ppb	-	1685 g	3168 g	1.88	40 g
3,000 ppb	2.5 kg /t	1810 g	3312 g	1.83	43 g

In-vivo trials

Broilers // Aflatoxin B₁ + T-2 Toxin // TOXISORB® Basic



Institute: Farm (Peru)
Species: Broiler chicken
Duration: 45 days
Repetitions: 1 with 10,000 in each group (50% male, 50% female)

TOXISORB® Basic dosage	Weight gain	Feed intake	Feed conversion rate	Mean daily weight gain	Productive efficiency index (PEI)
-	2,417 g	4,880 g	1.99	53.7 g	260
2.5 kg/t	2,561 g	4,790 g	1.84	56.9 g	295

$$PEI = (ALW \times (TGW \div ns) \times 10000) \div (age \times (TFC \div nf) \times 2.2)$$

ALW = Average _ Live _ Weight

TGW = Total _ Group _ Weight

ns = number _ started

TFC = Total _ Feed _ Consumption

nf = number _ finished

In-vivo trials

Broilers // Ochratoxin A // TOXISORB® Premium



Institute: Instituto Tecnológico y de Estudios Superiores de Monterrey (Mexico)
Species: Broiler chicken
Duration: 42 days
Repetitions: 4 with 12 heads each

Ochratoxin A dosage	TOXISORB® Premium dosage	Ochratoxin A in liver	Femur* weight (full)	Femur* resistance (full)
-	-	0 µg/kg	20.45 g	27557 N/m ²
-	5 kg/t	0 µg/kg	21.07 g	27789 N/m ²
500 ppb	-	84 µg/kg	20.91 g	21167 N/m ²
500 ppb	2.5 kg/t	36 µg/kg	21.06 g	26336 N/m ²
500 ppb	5 kg/t	12 µg/kg	20.06 g	27168 N/m ²

*) proxy to egg-shell resistance

In-vivo trials

Swine // Fumonisin B₁ // TOXISORB[®] Premium

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Institute: Instituto Nacional de Investigaciones Forestales, Agrícolas y Pecuarias (Mexico)
Species: Swine
Duration: 2 weeks adaption, 6 weeks testing
Repetitions: 2 with 4 heads each (2 male, 2 female)

Fumonisin B1 dosage	TOXISORB [®] Premium dosage	Weight gain	Feed conversion rate	Diseases	Histopathology
-	-	36.5 kg	2.8		-
-	4 kg/t	36.7 kg	2.7		-
43 ppm	-	32.7 kg	3.0	<ul style="list-style-type: none"> • Pneumonia • Diarrhea 	<ul style="list-style-type: none"> • Medium liver problems (hyperemia, size increase, color change) • Minor kidney issues (hyperemia, color change) • Severe lung problems (consolidation, multifocal petequies) • Severe heart problems (hydropercardiac, cardiomegalia) • Nephrotoxicity
43 ppm	2 kg/t	36.6 kg	2.9		<ul style="list-style-type: none"> • Minor lungs problems
43 ppm	4 kg/t	39.0 kg	2.7		<ul style="list-style-type: none"> • Minor lungs problems

In-vivo trials

Swine // Zearalenone // TOXISORB[®] Premium



Grupo Porcicola Mexicano

Farm: Grupo Porcícola Mexicano (Mexico)
Species: Swine (piglets)
Duration: 80 days
Repetitions: 1 with 4,400 heads

TOXISORB [®] Premium dosage	Weight gain	Feed conversion rate	Mean daily weight gain	Mortality
-	68.88 kg	2.77	846 g	3.4%
2.5 kg/t	74.95 kg	2.67	907 g	1.0%

In-vivo trials

Swine // Nutrients // TOXISORB® Premium



Institute: Institut für Klinische Prüfung Ludwigsburg GmbH (Germany)
Species: Swine (piglets)
Duration: 14 days

Amounts found in blood serum	Group without TOXISORB® Premium	Group with 4 kg/t TOXISORB® Premium	Group with 6 kg/t TOXISORB® Premium	Expected normal values
Calcium (mmol/l)	2.62	2.56	2.5	2.0 – 3.0
Magnesium (mmol/l)	1.75	1.39	1.67	0.7 – 1.6
Iron (µg/dl)	149	150	127	93 – 107
Copper (µg/dl)	183	194	138	80 – 150
Zinc (µg/dl)	1119	881	1059	700 – 1500
Vitamin A (mg/l)	0.29	0.27	0.35	0.2 – 1.2
Vitamin E (mg/l)	0.7	1.4	1.2	2.8 – 7.4