



PHARMAPEX[®]
CREATING A HEALTHY WORLD[™]

Animal Health Department

YARROWIA LIPOLYTICA strain A-101
Products for Cattle



Pharmapex[®] Group

Headquartered in the U.S., Pharmapex is a multinational group of companies offering a broad range of health-related products to domestic and international markets. Some of the major sectors within the healthcare industry that Pharmapex supports include, but not limited to:

- Animal Health
- Human Pharmaceuticals
- Human Nutrition
- Biotechnology
- Consumer Healthcare
- Medical Device and Consumables



What is *Yarrowia lipolytica*?

- *Y. lipolytica* is a non-pathogenic, entirely safe oleaginous yeast
- It is commonly present in dairy, meat products and in wine
- It is often used as expression system for manufacturing human therapeutic proteins



Our proprietary A-101 strain of *Yarrowia lipolytica* is an excellent prebiotic. It has also many other beneficial properties. Our *Y. lipolytica* A-101 is the key ingredient in some of Pharmapex's product lines involving:

- Pet food
- Feed for farm animals
- Feed supplements for pets and farm animals
- Products for remediation of soil contaminated with hydrocarbons
- Rooting enhancers and fertilizers



WHY Pharmapex's *Y. lipolytica* ? Part I

Pharmapex's *Yarrowia lipolytica* has exceptional biochemical properties:

- High beta-glucans and mannans content of cellular walls
- High levels of unsaturated fatty acids (up to 90%, with ~ 60% monounsaturated fatty acids and ~ 30% polyunsaturated fatty acids)
- High levels of easily digestible protein (up to 50%), with most essential amino acids
- Presence of many unique bioactive substances (e.g. KYNA, citrulline malate)
- Presence of many highly bioavailable microelements



WHY Pharmapex's *Y. lipolytica*? Part II

Pharmapex's *Y. lipolytica* can rapidly improve gut microbiomes:

- Lactic acid-producing and other beneficial bacteria increase in numbers
- Their metabolites lower gut's pH, inhibiting growth of pathogens
- *Y. lipolytica* cell walls, due to their physicochemical properties, bind pathogenic microbes and absorb/neutralize their toxins, which are subsequently excreted
- Those synergistic effects positively influence gut's anatomy (larger villi and deeper crypts), and its function

*NOTE: Supplementing animals with *Y. lipolytica* A-101 offers practical, safe, sustainable and inexpensive method of establishing and maintaining normal, "healthy" gut microbiome, thus improving digestion of food and absorption of nutrients. This, in turn, improves general health and production parameters of animals*



WHY Pharmapex's *Y. lipolytica*? Part III

Pharmapex's *Yarrowia lipolytica*-improved digestion of food and absorption of nutrients, minerals and vitamins result in:

- Improvements in weight gain, feed intake and feed utilization, as shown in calves and dairy cows. In piglets, even rants which would normally be eliminated from production, quickly gained weight and were able to catch up with their littermates
- Better function of calves' digestive system, including significantly limiting diarrhea, decreasing the amount of parasites in feces, and triggering beneficial changes in gastrointestinal microflora



WHY Pharmapex's *Y. lipolytica*? Part III *(cont.)*

- Behavior-improving, calming effects of *Y. lipolytica* across species, most likely via gut-brain axis. Best example of this effect is observed in race horses. Supplementing horses with *Y. lipolytica* has a clear therapeutic effect, benefiting majority of animals suffering from Equine Gastric Ulcer Syndrome (EGUS). Behavior-improving, aggression- and cannibalism-eliminating, calming effect was also observed in calves, beef cattle, piglets and chicken reared in large industrial farms settings





Products for Cattle



Products for horses ■ Products for dogs ■ **Products for farm animals**

Cattle ■ Pigs

YaroBeef™ ■ YaroDairy™ ■ MilkiYar™ ■ Yaro-X™



YaroBeef™

- **Product developed for beef cattle.** Ready to be used in mixer feeders for Total Mixed Rations (TMR). Dose: 1% of Y. lipolytica in total feed mass.

- **Results:**

- improvement of intestinal and rumen microfloras
- better digestion process and better feed conversion ratio
- significant reduction in aggressiveness, lower hyperactivity
- **higher body mass gains**



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YaroDairy™

- **Product formulated for dairy cows.** Ready to be used in mixer feeders for TMR. Dose: 25-50g/animal/day.

- **Results:**

- **increased productivity: higher milk volume**
- better digestion process and better feed conversion ratio
- improvement & stabilization of rumen & intestinal microflora, better digestion
- better feed conversion and higher dry mass intake
- longer rumination time, improved homeostasis in rumen and utilization of structural carbohydrates, which lowers risk of subclinical rumen acidosis
- milk quality unchanged (protein & fat content not decreased)



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MilkiYar™

- **Specialty product for calves in rearing period.** Ready to be dissolved in mil replacer. Dose: 15-30g/animal/day.
- Results:
 - accelerated development of rumen microflora and transition from monogastric stomach to ruminant (shorter feeding with liquids), increased counts of beneficial microbes, improved absorption of nutrients, higher levels of propionic acid and reduced risk of rumen acidosis
 - **faster growth and development and higher body mass gains (particularly between 40th and 60th day)**
 - **fewer cases of diarrhea, improved immunity**



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Yaro-X™



- **Specialty anti-diarrhea product for calves in rearing period.** Ready to be dissolved in milk replacer, or used as admixture to starter.

Dose: 20 g/animal, 2 times a day for 3 days.

- Results:

- **effective suppression of diarrhea, particularly in stress situations, feeding regime changes, and during first days of life, after transition from colostrum to milk replacer**



- restoration of proper electrolytes levels and prevention of dehydration
- restoration of healthy gut microflora during intestinal infections, including inhibition of pathogenic microbes



YARROWIA LIPOLYTICA A-101

The studies of effects of our proprietary *Yarrowia lipolytica* A-101 strain in cattle, combined with numerous field experiments, showed significant improvement of key production parameters and general health and well-being. Based on those results, we have developed a line of bovine products. Those products are currently used by major European feed producers as raw material supplementing their feed mixes. Examples include:

CARGILL

PIAST FEEDS

MICHEL FEEDS

SOYMAX

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PILOT STUDY

Effects of Pharmapex's *Yarrowia lipolytica* A-101 on milk production in dairy cows

Study conducted by The National Research Institute of Animal Production, Pawlowice Experimental Station, under scientific supervision of Marian Kamyczek PhD, Eng.

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STUDY DESIGN

Purpose: measuring effects of *Yarrowia lipolytica* A-101 on milk production, milk composition and health of udders in dairy cows

30 control animals – without *Yarrowia lipolytica*

30 animals supplemented with *Yarrowia lipolytica*

Length of study: 90 days

Dose of *Y. lipolytica*: 120g/animal/day

Following parameters were measured:

body mass ■ feed intake ■ daily milk yield ■

milk composition (fat, protein, lactose, dry mass, urea, & somatic cell counts)

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RESULTS

Supplementation of milk cows' feed with 120g/day/animal of *Yarrowia lipolytica* resulted in:

increased milk yield by 1.6 – 2kg (4.5 - 5.6%), as compared with control animals

50% reduction in number of cows treated for udder inflammation

lower somatic cell count in milk

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SUMMARY AND FOLLOW-UP

This pilot study showed **positive effects of *Yarrowia lipolytica* supplementation on milk production. It also improved health of udders of supplemented animals.** Therefore, our group decided to conduct more studies in dairy cows, in calves and in beef cattle.

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RESEARCH PROJECT I

**Effect of supplementing dairy cows with
Yarrowia lipolytica A-101 on milk production**

Trial was conducted under supervision of Prof. Włodzimierz Nowak, D.Sc. of the Poznań University of Life Sciences, Department of Animal Nutrition and Feed Management

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STUDY DESIGN

Trial was carried out on 150 dairy cows for 90 days
in Długie Stare Agricultural Enterprise (Niechłód Farm)

KON – control group, 50
cows, (no *Y. lipolytica*)

YL 50 – 50 cows, 50g *Y.*
lipolytica/day/cow

YL 100 – 50 cows, 100g *Y.*
lipolytica/day/cow

Following parameters were measured:

- milk yield
- rumination time
- content of fat, protein, lactose, and fat/protein ratio in milk
- body mass

Statistical analysis was done using:

- SAS 9.2
- UNIVARIATE, MEANS, GLM procedures
- Duncan test
- $P \leq 0.01$
- $P \leq 0.05$

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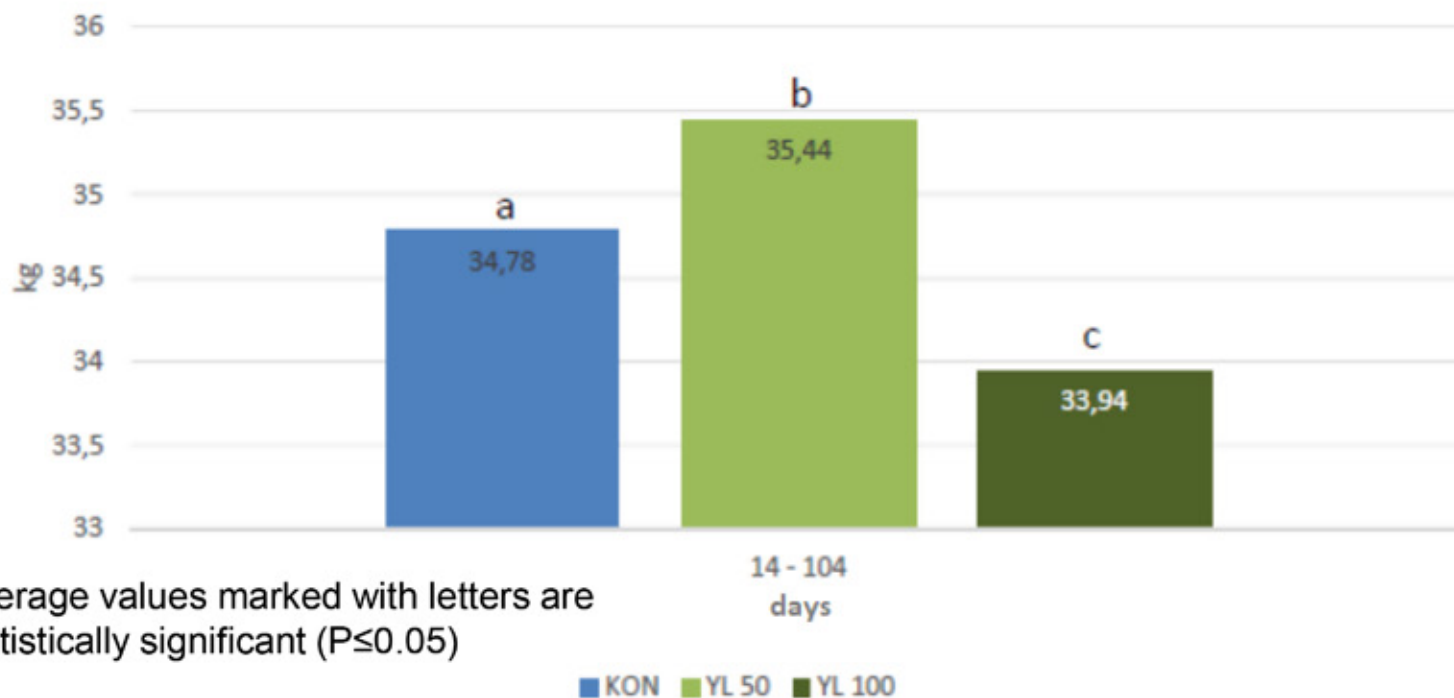
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50g of *Yarrowia lipolytica*/day/cow increases milk production



* Average values marked with letters are statistically significant ($P \leq 0.05$)

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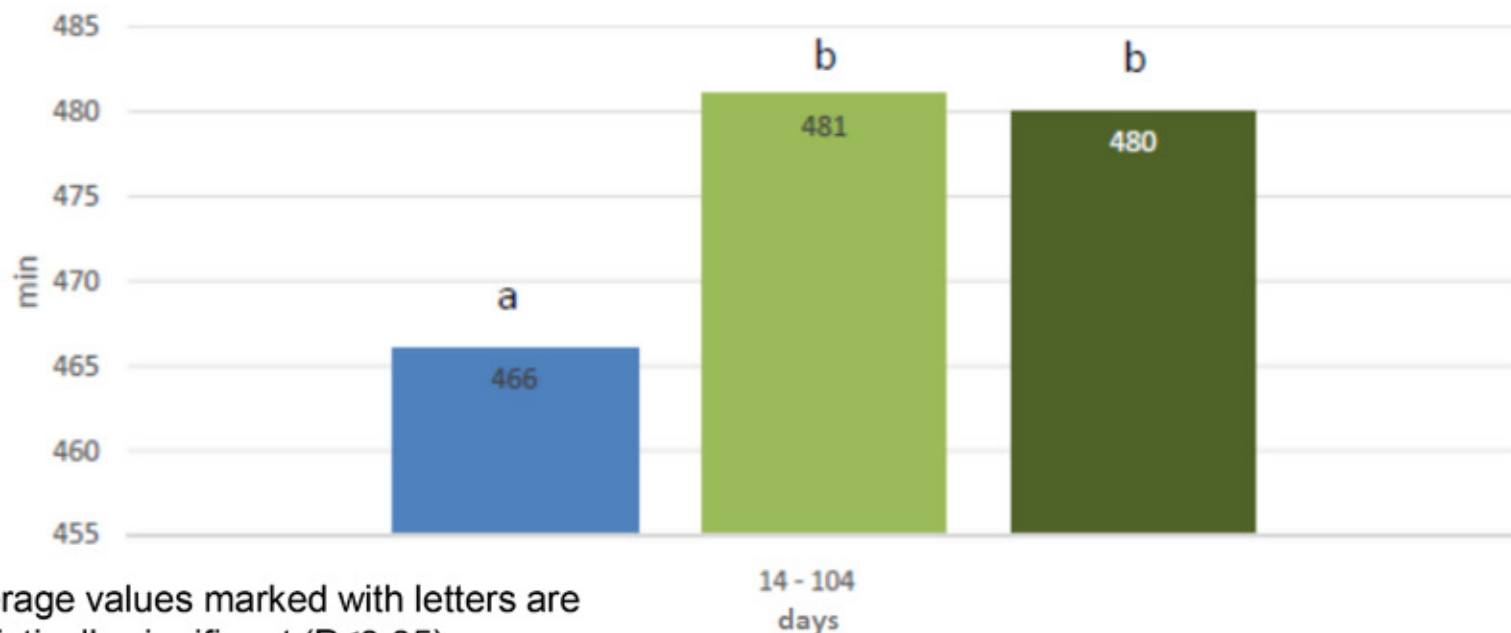
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Yarrowia Lipolytica increases rumination time (daily averages)



* Average values marked with letters are statistically significant ($P \leq 0.05$)

■ KON ■ YL 50 ■ YL 100

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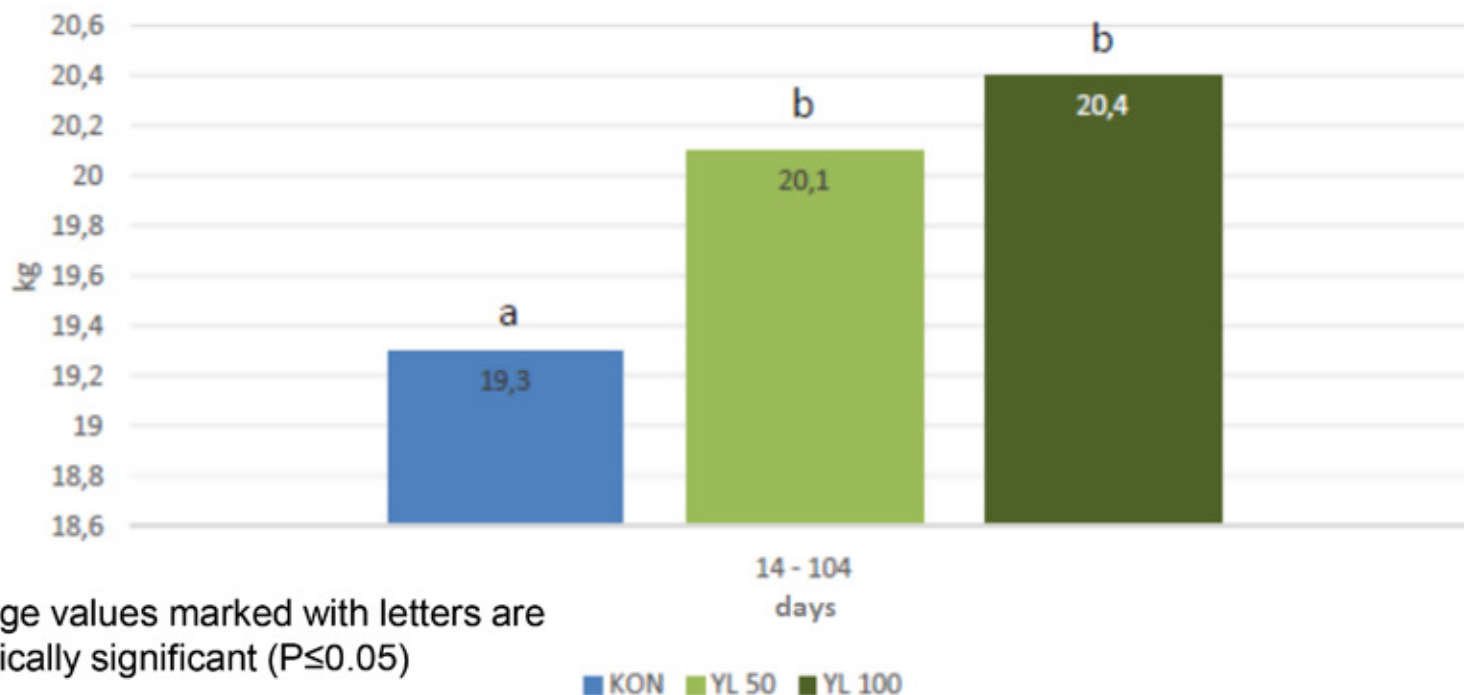
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Yarrowia lipolytica increases dry matter intake (daily averages)



* Average values marked with letters are statistically significant ($P \leq 0.05$)

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RESULTS, in summary

Supplementation with 50g/day/cow of *Yarrowia lipolytica* had positive effect on:

milk production: higher by 0.66 kg/day

rumination time: longer by 15 minutes, and **dry matter intake: larger** by 5%

Quality of milk remained the same (fat and protein content)

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RESEARCH PROJECT II

Effects of supplementing calves with Pharmapex's *Yarrowia lipolytica* A-101

Trial was conducted under the supervision of Professor Wlodzimierz Nowak, DSc. of the Poznan University of Life Sciences, Department of Animal Nutrition and Feed Management

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STUDY DESIGN

The trial was carried out in Manieczki Agricultural Industry, Szoldry Farm

**8 experimental calves (YL) received *Yarrowia lipolytica* for 56 days, twice a day during mornings and evenings, in milk replacer.
Dose: 30g/day/animal. 8 control animals (KON) were not supplemented**

Following parameters were measured/calculated:

- body mass on 4th, 14th, 28th, 42nd and 56th days of life
- body mass gain
- feed intake and feed conversion ratio
- health condition
- feces: parasitology and consistency
- blood tests (hydroxybutyric acid and IGF)
- pH of rumen liquid

- Results were subjected to statistical analysis using the SAS 9.1 program (SAS® / STAT, 2004), PROC TTEST medium-severity test, PROC MEANS and PROC UNIVARIATE.
- Statistical significance of differences between groups was at $P \leq 0.05$ and $P \leq 0.01$ levels.
- Standard error of the mean (SEM) was used as measure of error.

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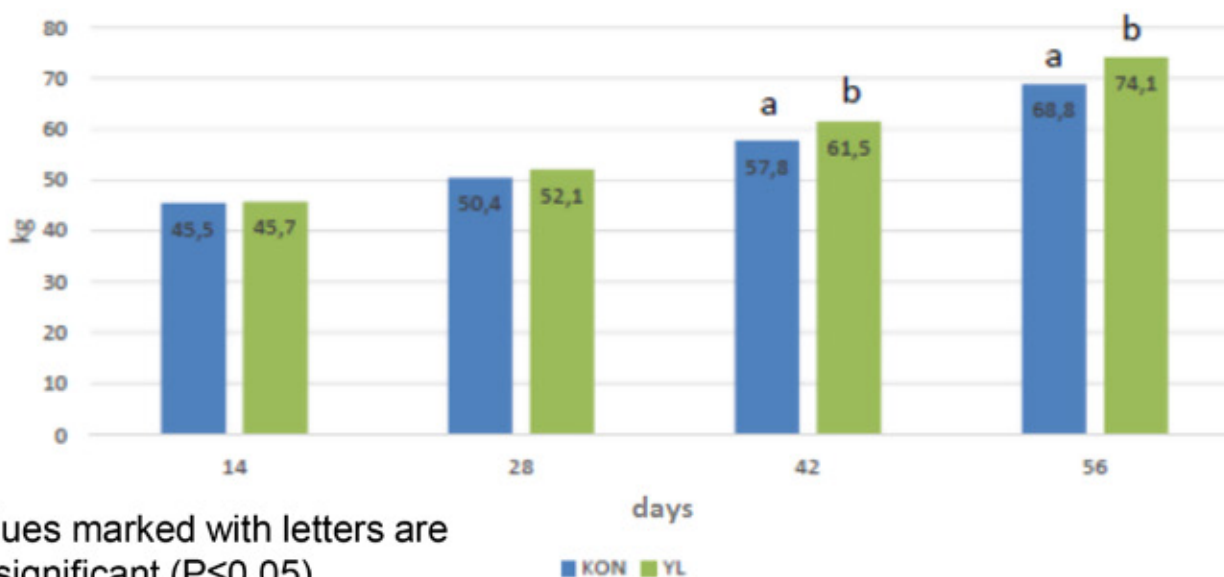
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RESULT I

Yarrowia lipolytica increases calves' body mass



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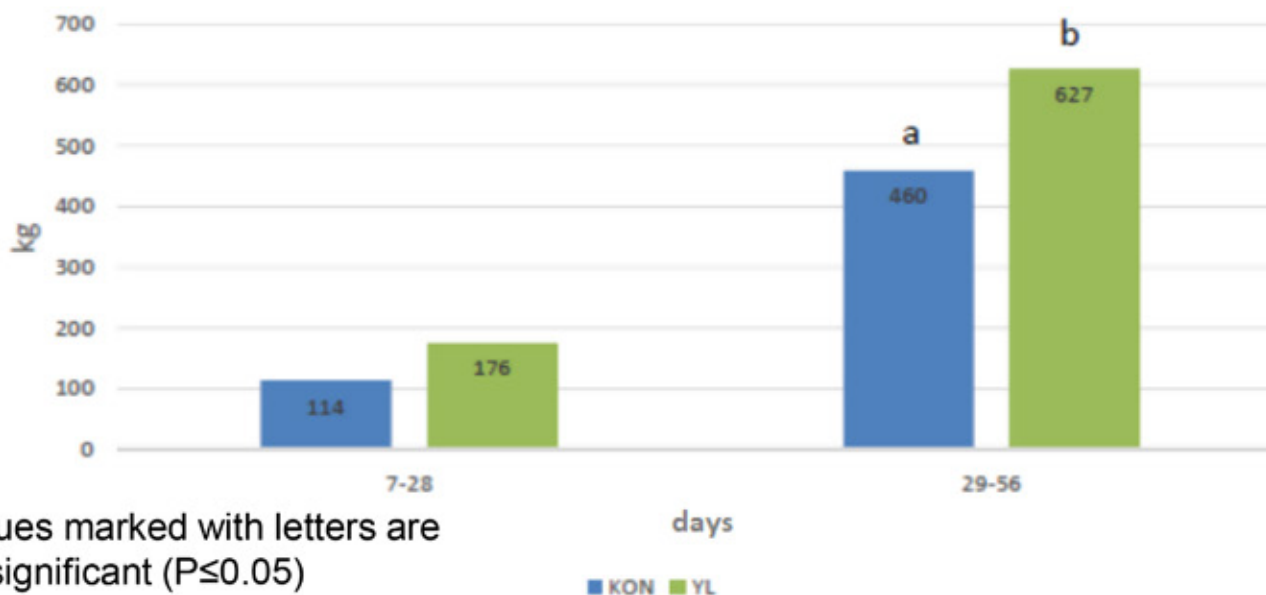
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RESULT II

Yarrowia lipolytica increases starter mixture intake



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RESULT III

Yarrowia lipolytica improves rumen microbiome

PARAMETER	GROUP	TIME PERIOD	
		28d	42d
Total bacteria count [10 ⁷]	KON	14.9	14.7
	YL	17.5	18.5
Total protozoa count - Holotrich [10 ²]	KON	0.35	3.09
	YL	1.75	5.60
Total protozoa count - Entodiniomorph [10 ³]	KON	8.05	15.4
	YL	13.7	34.7

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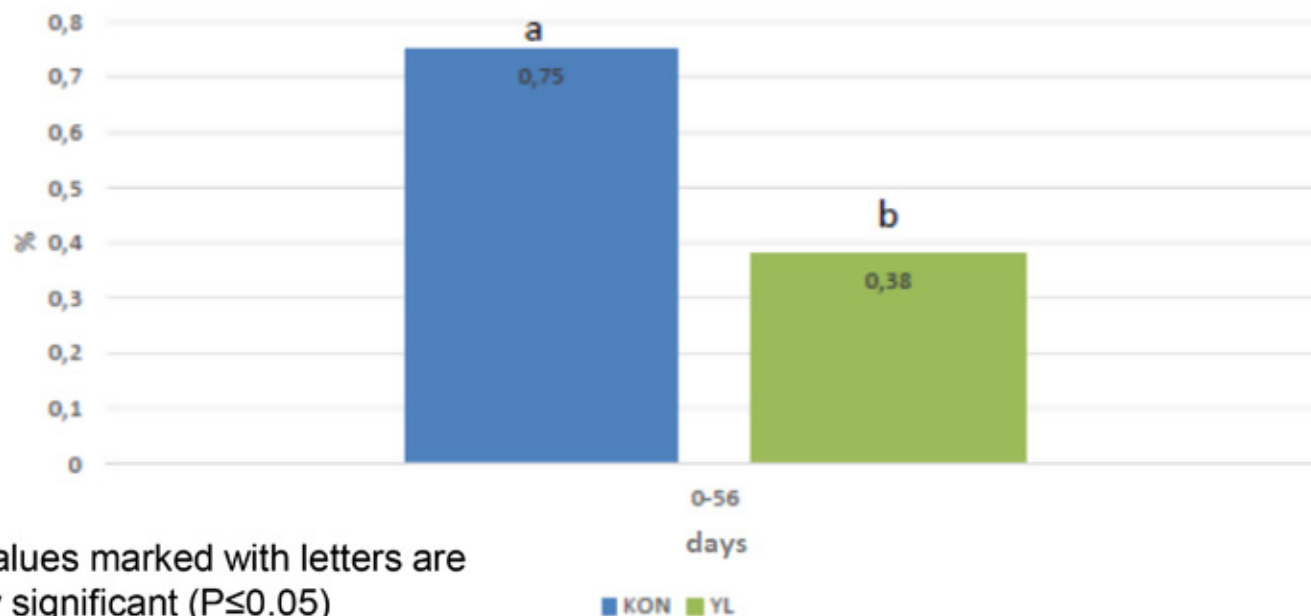
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RESULT IV

Yarrowia lipolytica decreases incidences of diarrhea



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RESULTS, overview I

Supplementing calves' feed with Pharmapex's *Yarrowia lipolytica* A-101 resulted in:

higher final body mass (by 7.7%)

higher daily body mass gains (in the second half of study, 28th - 56th day, by 130g on average - statistically significant increase)

improved zoometric indices that characterize growth rate: body length, hip height and girth

improved appetite and increased starter intake (by 122g-167g)

improvement of fermentation processes in rumen, leading to increased pH, and helping with preventing subclinical acidosis, a common problem in calves fed liquid diet

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RESULTS, overview II

improvement of rumen's microflora
(faster transition from monogastric stomach to adult rumen)

improved general health: significantly fewer incidences of diarrhea,
also 100 % elimination of pneumonia

KEY: Accelerating initial growth of female calves has significant impact on production results when they become dairy cows. Increasing their daily weight gain by 100g/day at the time of feeding with liquid feeds increases yields during first half of lactation by 225g/day/animal.

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FIELD STUDIES: BEEF CATTLE

**Positive effects of supplementing beef cattle with Pharmapex's
Yarrowia lipolytica A-101: general health and behavior**

Field experiment on herd of beef cattle carried out in Czeslawa Kruk's
feed lot in Bedon-Wies

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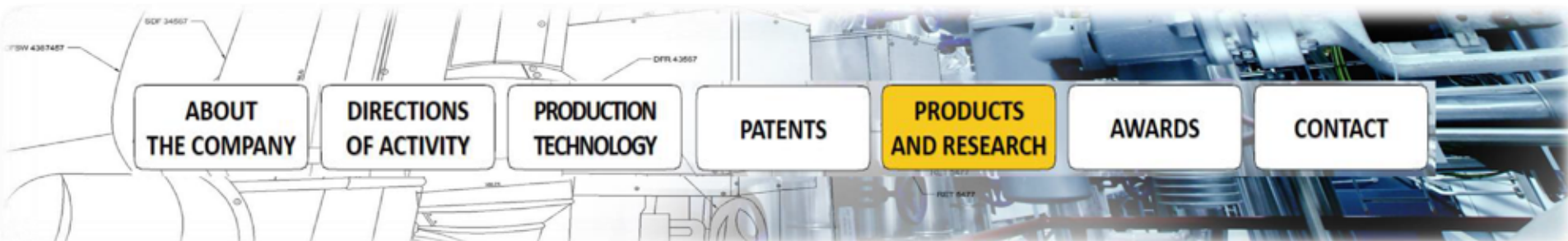
STUDY DESIGN AND CONCLUSIONS

Beef cattle's feed was supplemented with *Yarrowia lipolytica* at 100 g/day/animal for first 30 days, and 30-50g/day/animal for following 30 days.

Following observations were made in this and several other, similar field studies:

- **Lower aggression levels (calming effect)**
- **Improvement in general physical condition and health**
- **Fewer cases of diarrhea, more solid feces**

Higher body mass gains were also observed in supplemented animals.




SUMMARY: *Y. lipolytica* A-101 as supplement in cattle

Supplementing calves, dairy cows and beef cattle with Pharmapex's *Yarrowia lipolytica* is an effective, easy, inexpensive, and sustainable way to increase key production parameters, health and overall wellbeing of animals

Those positive effects are achieved without use of antibiotics or other means that are harmful to human consumers, environment or animals

Additional aspect of our successes with *Y. lipolytica* A-101 is crystalized in the context of our evolving partnership in the cattle sector with other multinational companies, such as Cargill, as well as several major feed companies worldwide



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