

# CitriStim

## a novel ingredient based on *Pichia guilliermondii* yeast

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### Introduction

The European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control report a high resistance for commonly used antimicrobials in its summary report (2019). Despite the EU-wide ban of antibiotic growth promoters in animal feed, significant levels of these products are still used in the livestock industry and the search for alternatives remains high on the agenda.

Yeast preparations are a primary ingredient in this context since, amongst others, they contain mannan-oligosaccharides (also known as MOS) and  $\beta$ -glucans. These components of the yeast cell wall exert specific functions in supporting the immune system and fend off pathogen invasion in the intestines of the host.

Almost all products are based on *Saccharomyces cerevisiae* yeast. CitriStim, consisting solely of inactivated non-GMO *Pichia guilliermondii* yeast, has already been used in the United States for some years.

### *Pichia guilliermondii*, a small cell size for optimal binding capacity

Structure and characterization of the yeast cell as well as the cell wall, are crucial to understanding their functionality. *Pichia guilliermondii* yeast cells are smaller compared to *Saccharomyces cerevisiae*.

As such they provide a greater surface area per unit of weight added to the feed (Peisker et al. 2017). They are more hydrophobic, which promotes an even distribution in the gut and attracts lipophilic pathogens (Oh et al. 2018). CitriStim showed its ability to bind potential pathogenic bacteria. The yeast's passage through gastric digestion further improved the effect of CitriStim (Figure 1).

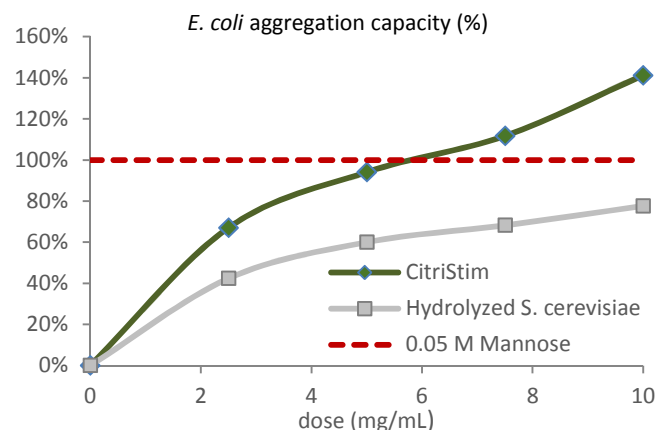


Figure 1: Effect of digested yeast products on aggregation capacity of broiler strains of *E. coli* (mannose set as positive control)

The binding ability of the product was confirmed for broiler chickens, swine and ruminant strains of *E. coli* and *Salmonella enterica*.

If potentially pathogenic bacteria are bound to CitriStim, then a lower proportion should adhere to the intestinal epithelium. Indeed, *in vitro* and *in vivo* trials confirmed the efficacy of CitriStim in reducing the adhesion of *E. coli* and *S. enterica* to mucus lining the host's intestinal epithelium.

Besides the binding of potential pathogenic bacteria, CitriStim has a powerful ability to bind endotoxins such as LPS from *E. coli* (lipopolysaccharide; Peisker et al. 2019). This may limit systemic inflammation caused by luminal translocation of their endotoxins (LPS) into systemic circulation, a phenomenon typically observed in sub-acute ruminal acidosis.

### CitriStim, a potent immune modulator

Yeast components can modulate immune responses and impact the composition of microbiota (Kim et al. 2011). In particular the number of regulatory T-cells (T-reg), interleukins and the activity of macrophages are responsive to dietary manno-proteins and  $\beta$ -glucans. In a non-challenging situation, it has been found that CitriStim positively increases the number of T-reg and anti-inflammatory cytokine IL-10. Thus the energy expenditure of the host towards unwanted and unnecessary immune reactions is minimized.

The immune effect of CitriStim was different however, when animals were placed into a challenging situation. In turkeys injected with *E. coli* lipopolysaccharide (LPS), CitriStim enhanced macrophage activity by increasing nitric oxide production. In addition, the number of T-reg was reduced since the immune system should not be suppressed under challenge (Figure 2). Concomitantly IL-10 decreased

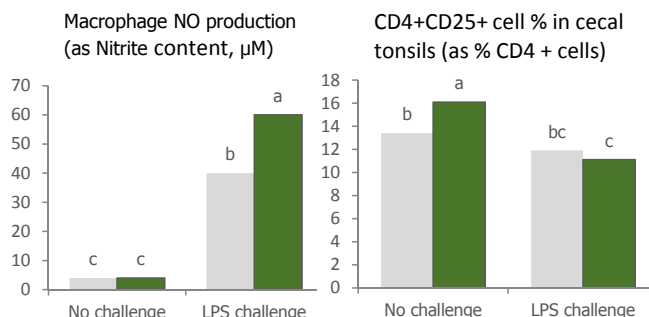
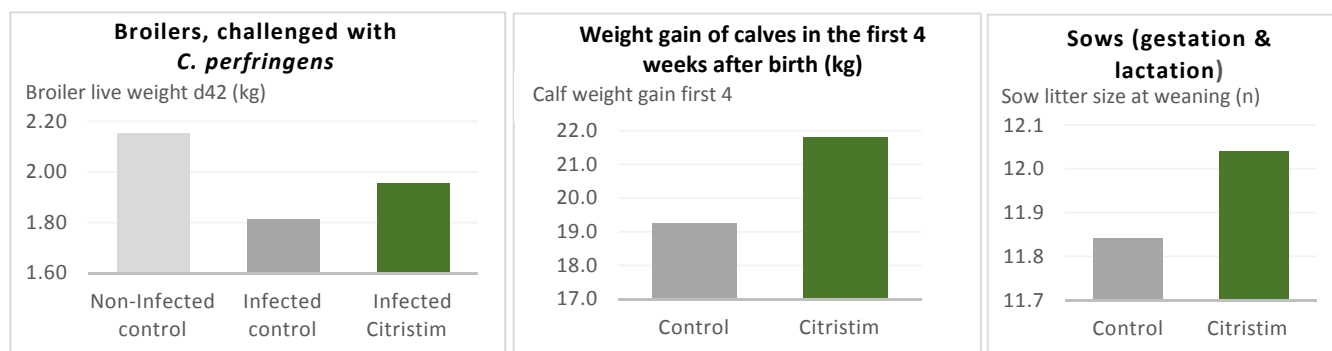


Figure 2: Impact of CitriStim on immunity parameters in 6-week-old turkeys, whether or not challenged with *E. coli* LPS

(■ Control, ■ CitriStim; a, b, c, p < 0.05)

– adapted from Shanmugasundaram et al. 2014)



**Figure 3: Effect of Citristim on performance in different animal species**

as well and IL-1 increased due to the mediatory effect of Th17 cells that constantly receive the input of the product components.

A similar pattern on immune response was observed in broiler chickens fed with CitriStim and experimentally challenged with coccidia (Shanmugasundaram et al. 2013), suggesting that the mode of action of this product on the immune system is independent of the type of pathogen.

CitriStim could be regarded as an adaptogenic substance since it may stabilize physiological processes and promote homeostasis. The concept of adaptogens was already developed in 1947 to describe a substance that may increase resistance to biological stress, e.g. microbial challenge. CitriStim would fulfil the adaptogen criteria that it must be nontoxic, nonspecific, and believed to affect the physiology of the organism.

### CitriStim enhances the resilience of animals

Farm animals are constantly subject to stressful situations. In this context, CitriStim improves the resilience of animals, by promoting their resistance, enabling them to recuperate faster. CitriStim helps the animals to more easily face typical challenges occurring on farms. Animals receiving this proprietary whole inactivated yeast supplement, responded with improved productivity.

Amongst examples, feeding CitriStim limited the reduction in performance of broiler chickens challenged with *Clostridium perfringens* and promoted the growth of newborn calves. Feeding CitriStim to sows during gestation and lactation increased the number of piglets weaned per litter (see Figure 3).

CitriStim is a unique, original and innovative tool to secure productive performance of farm animals raised in commercial operations, strengthening production and providing proven benefits.

### Want to know more? Contact the authors

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### About Pancosma

A Swiss company headquartered in Rolle, Switzerland, Pancosma is a global leader in developing, manufacturing and distributing a wide range

of innovative feed additives. The company is present in more than 75 countries. Its portfolio consists of phytonutrient-based technologies, organic trace minerals, palatants, yeast and organic acids. Pancosma continually strives to deliver innovative solutions for animal nutrition through its commitment to research, development and sustainability. Pancosma is a brand of ADM, a global leader in human and animal nutrition and the world's premier agricultural origination and processing company. For more information, visit [www.adm.com](http://www.adm.com).

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