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Article

Impact of *Saccharomyces cerevisiae* DSM 34246 (Canobios-BL) var. *boulardii* Supplementation on Nutritional Status and Fecal Parameters in Healthy Breeding Adult Cats

Nicolò Lonigro, Elisa Martello, Natascia Bruni, Mauro Bigliati, Annalisa Costale, Ilaria Lippi, Giorgia Meineri and Francesca Perondi

veterinary sciences

https://doi.org/10.3390/vetsci12010044

Summary

This study tested *Saccharomyces cerevisiae* DSM 34246 (Canobios-BL) var. *boulardii* on adult Chartreux cats to evaluate its impact on gut health. Fourteen healthy cats (4 males, 10 females) were randomly assigned to a control (CTR) and treated (SACC) group. Both were fed a dry diet twice daily, with the additive given to the SACC group (5×10^9 CFU/kg) and a placebo to the CTR.
Over 35 days, body weight, condition scores, fecal parameters, and water intake were measured. Statistical analysis showed significant improvements in body condition, fecal parameters and IgA, **indicating that *S. boulardii* positively affected gut health in these cats.**

Table 2 (partial). Fecal score (FS) and fecal IgA (IgA) parameters measured in treated (SACC) versus untreated (CTR) cats at different time points during the study.

	t_0	t_1	t_2	t_3	t_4	t_5	Average	*p*-Value
FS (score ± SE)								
CTR	4.4 ± 0.5	4.1 ± 0.1	4.1 ± 0.1	4.3 ± 0.2	4.3 ± 0.2	4.6 ± 0.3	4.3 ± 0.1	0.85
SACC	**4.3 ± 0.4**	**4.3 ± 0.4**	**3.1 ± 0.1**	**3.3 ± 0.2**	**3.1 ± 0.1**	**3.0 ± 0.0**	3.5 ± 0.1	0.0006
IgA (mg/g ± SE)								
CTR	5.4 ± 0.3	5.9 ± 0.2	5.8 ± 0.2	5.6 ± 0.2	5.8 ± 0.2	5.5 ± 0.1	5.7 ± 0.1	0.64
SACC	**5.8 ± 0.2**	**5.5 ± 0.2**	**5.6 ± 0.2**	**5.9 ± 0.2**	**6.1 ± 0.2**	**6.6 ± 0.2**	5.9 ± 0.1	0.0084

Conclusions

The supplementation of *S. boulardii* at the recommended dietary dosage of 5.0×10^9 CFU/kg of feed used in adult healthy cats for 35 consecutive days significantly affected several parameters, including FS and IgA.

However, the supplementation did not cause a significant variation in BW in the animals. Based on the results obtained, ***S. boulardii* is a promising supplement for cat diet for stabilizing the gut flora.** Importantly, further exploration of the role of yeast products as probiotics in cats with intestinal diseases is necessary to improve feline intestinal health.

KEYPOINTS

- *S. boulardii*, as a strain of *S. cerevisiae*, has strong probiotic properties and antipathogenic abilities.
- Two studies in cats have confirmed the positive effects of yeast products (*S. cerevisiae*) on feline gut health by modulating gut microbes and improving microbiota.
- Dysbiosis can significantly impact intestinal health, and gut microbes are crucial for maintaining health and regulating the occurrence of various diseases in pets.
- **A significant increase in fecal IgA was observed in the group fed with *S. boulardii* after 35 days of treatment.**
- **Immunoglobulin levels can indirectly reflect an animal's ability to resist exogenous pathogens and are critical parameters for evaluating immunity.**
- IgA is crucial for the local anti-infection action of the body's mucosa.

Article

How Does *Saccharomyces cerevisiae* DSM 34246 (Canobios-BL) *var. boulardii* Supplementation Impact the Fecal Parameters of Healthy Adult Dogs?

Nicolò Lonigro, Francesca Perondi, Natascia Bruni, Mauro Bigliati, Annalisa Costale, Elena Pagani, Ilaria Lippi, Alice Melocchi, Lucia Zema, Giorgia Meineri and Elisa Martello

veterinary sciences

https://doi.org/10.3390/vetsci12010045

Summary

This study tested ***Saccharomyces cerevisiae* DSM 34246 (Canobios-BL) var. *boulardii* on adult dogs West Highland White Terrier (WT) and German Shepherd (GS) to evaluate its impact on gut health**. A total of 53 healthy adult dogs were randomly assigned to control (CTR: WT 14/28, GS 12/25) and treated (SACC: WT 14/28, GS 13/25) groups. Both were fed a dry diet twice daily, with the additive given to the SACC group (5×10^9 CFU/kg) and a placebo to the CTR. Over 35 days, body weight, body condition score, fecal parameters, and water intake were measured. Statistical analysis showed significant improvements in body condition, fecal parameters, and IgA, **indicating *S. boulardii* positively affected gut health in dogs.**

Table 2 (partial). Fecal Score (FS) and Fecal IgA (IgA) parameters measured in treated versus untreated West Highland White Terriers (WTs) and German Shepherds (GSs) at different times during the study.

		West Highland White Terrier (WT *n*=28)			German Shepherd (GS *n*=25)		
		CTR	SACC	*p*-Value	CTR	SACC	*p*-Value
FS (±SE) (1–7)	T_0	4.3 ± 0.2	4.3 ± 0.2	0.9	4.3 ± 0.4	4.2 ± 0.3	0.9
	T_1	4.3 ± 0.2	4.1 ± 0.2	0.4	4.4 ± 0.2	**3.8 ± 0.2**	<0.1
	T_2	4.3 ± 0.2	**3.6 ± 0.2**	<0.1	4.0 ± 0.2	**3.4 ± 0.1**	<0.1
	T_3	4.1 ± 0.3	3.8 ± 0.2	0.4	4.6 ± 0.4	**3.3 ± 0.2**	<0.1
	T_4	4.3 ± 0.3	**3.6 ± 0.2**	<0.1	4.8 ± 0.3	**3.5 ± 0.1**	<0.1
	T_5	4.1 ± 0.2	**3.4 ± 0.1**	<0.1	4.3 ± 0.2	**3.2 ± 0.1**	<0.1
IgA (±SE) (mg/g)	T_0	0.6 ± 0.1	0.69 ± 0.1	0.3	0.57 ± 0.08	0.58 ± 0.04	0.8
	T_1	0.6 ± 0.1	0.68 ± 0.1	0.2	0.51 ± 0.07	0.62 ± 0.04	0.3
	T_2	0.6 ± 0.1	0.74 ± 0.1	0.2	0.51 ± 0.08	**0.71 ± 0.06**	<0.1
	T_3	0.6 ± 0.1	**0.8 ± 0.1**	<0.1	0.50 ± 0.08	**0.78 ± 0.07**	<0.1
	T_4	0.6 ± 0.1	**0.9 ± 0.1**	<0.1	0.52 ± 0.08	**0.85 ± 0.07**	<0.1
	T_5	0.5 ± 0.1	**1.0 ± 0.1**	<0.1	0.50 ± 0.07	**0.92 ± 0.08**	<0.1

Conclusions

The supplementation of ***S. boulardii*** for 35 days, at the recommended dietary dosage of 5.0×10^9 CFU/kg of feed in healthy dogs of different breeds (WH and GS), significantly improved the FS and Fecal IgA, and other parameters. Based on the results obtained**, feed supplementation with the above-mentioned yeast product could also be recommended in clinical settings for an improvement in the fecal parameters of healthy dogs, also promoting an enhanced mucosal immunity**. Further studies are recommended in dogs and cats suffering from gastrointestinal diseases.

KEYPOINTS

- **The administration of *S. boulardii* led to a significant increase in fecal IgA in the treated group.**
- Fecal IgA is a biomarker for intestinal immunity or inflammation in dogs and puppies and has been recently proposed as a non-invasive marker of canine intestinal health.
- Secretory IgA is the most important humoral protective immune factor in the intestine. It inhibits the adhesion, colonization, and penetration of microorganisms, as well as the absorption of food antigens.
- **The use of supplementation with yeast products in dogs increases ileal and Fecal IgA, indicating enhanced mucosal immunity and immunomodulatory properties.**

Review

Saccharomyces boulardii: What Makes It Tick as Successful Probiotic?

Pedro Pais, Vanda Almeida, Melike Yılmaz and Miguel C. Teixeira

Journal of Fungi

doi:10.3390/jof6020078

Summary

Several bacteria have been identified as probiotics and their modes of action scrutinized to some extent, but yeasts may also exhibit probiotic properties. The baker's yeast *Saccharomyces cerevisiae* does not seem to present significant advantageous attributes for human health. On the other hand, the closely related ***Saccharomyces boulardii* is effective in complementing the treatment of acute gastrointestinal diseases such as diarrhea or chronic diseases such as inflammatory bowel disease (IBD). To date, this is the only yeast used as a probiotic.**

In this review, **current knowledge on *S. boulardii* traits that support its probiotic nature** and the correlation with distinctive features when **compared with the non-probiotic *S. cerevisiae* will be explored.**

Table 1 (partial). Metabolic and physiologic features of *S. cerevisiae* and *S. boulardii*.

Features	*S. cerevisiae*	*S. boulardii*
Optimal growth temperature	30° C	37° C
High temperature resistance (52 °C)	45% viability	65% viability
Acid pH resistance (pH=2 for one hour)	No - 30% viability	Yes - 75% viability
Tolerance to bile acids [>0.3%(w/v)]	No - Survival up to 0.15% (*w/v*)	No - Survival up to 0.10% (*w/v*)
Basic pH resistance (pH=8)	Yes	Yes

In vitro testing of probiotic formulations consisting of *S. boulardii* and bacterial probiotics (*Lactobacillus* spp. and *Bifidobacterium* spp.) highlighted **the ability of *S. boulardii* to survive GI tract conditions.**

S. boulardii was able to survive after incubation in a gastric-like environment and in an intestinal environment (bile salts, pancreatin, pH 7.0) for 3 h, whereas the viability of the bacterial probiotics was severely impaired.

S. boulardii is also more resistant to a gastric environment than *S. cerevisiae*, while the viability of both species in an intestinal environment (sodium chloride, pepsin, pancreatin, pH 8.0) is not affected after 1 h.

Accordingly, 1 h was enough to show that ***S. boulardii* is more resistant to low pH than *S. cerevisiae*, particularly at pH 2.0**

Main modes of action of *S. boulardii* probiotic activity



- **Modulation of the normal microbiome**: production of antimicrobial substances, immune modulation, improvement in the gut barrier function.
- **Antimicrobial activity**: exclusion of pathogens, modulation of metabolic and signaling pathways, production of inhibitory compounds or immune modulation.
- **Adhesion to the intestinal mucus membrane**, thus reducing the availability of binding sites for pathogens.
- **Ability to bind bacterial pathogens** due to the presence of mannose residue in the yeast cell wall.
- **Immune modulation**: modulation of inflammatory process increasing the levels of anti-inflammatory cytokines and decreasing pro-inflammatory cytokines; increase in secretory immunoglobulin levels IgA and IgM; interaction with dendritic cell monocytes, macrophages and lymphocytes.
- **Trophic effects**: stimulation of brush border membrane digestive enzymes and nutrient transporter activity; modulation of SCFAs synthesis (acetate and butyrate).

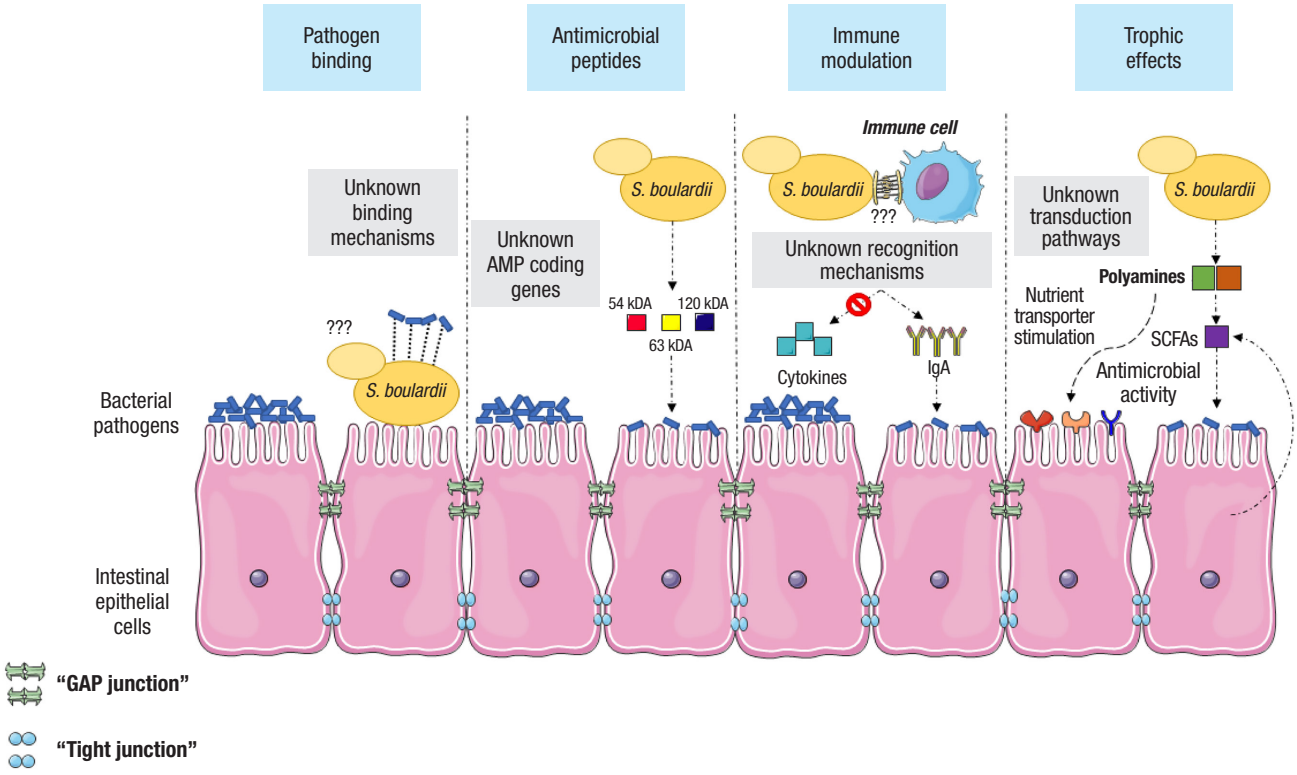

Figure 1. Overview of the main modes of action that support *S. boulardii* probiotic activity in the intestinal epithelium.

KEYPOINTS

- Despite the close correlation between *Saccharomyces boulardii* and *Saccharomyces cerevisiae* from the point of view of molecular phylogeny and typing, *S. boulardii* has identifiable distinctive characteristics, making it physiologically and metabolically different from *S. cerevisiae*.
- ***S. boulardii* is able to survive GI tract conditions, such as gastric acidity, better than *S. cerevisiae*.**
- *S. cerevisiae* is not considered as probiotic.
- *S. boulardii* is a probiotic yeast **with proven efficacy in the treatment of GI conditions, especially when used as an adjuvant to antibiotic treatment.**
- There is a **reduced translocation risk** in the treatment with *S. boulardii* when compared with *S. cerevisiae*.
- Present data indicate that the benefits of *S. boulardii* appear to be transient and independent of host gut colonization, differentiating its mode of action from other widely used bacterial probiotics.

Effect of *Saccharomyces boulardii* in dogs with chronic enteropathies: double-blinded, placebo-controlled study

Simona D'Angelo, Federico Fracassi, Francesca Bresciani, Roberta Galuppi, Alessia Diana, Nikolina Linta, Giuliano Bettini, Maria Morini, Marco Pietra

Vet Record

doi: 10.1136/vr.104241

Summary

Saccharomyces boulardii is used to treat acute and chronic enteropathies in humans, but to date, no studies have evaluated the use of this yeast in dogs. The current study, a prospective non-randomised, double-blinded, placebo-controlled study, evaluated the effects of *S. boulardii* in healthy dogs and dogs with chronic enteropathies (CE). Four healthy dogs and 20 dogs with CE were included. In healthy dogs, *S. boulardii* was administered for 10 days. Possible short-term adverse effects were recorded, and quantitative stool cultures for yeasts were performed. In dogs with CE, *S. boulardii* or a placebo was administered in addition to standard treatment protocols. Canine Chronic Enteropathy Clinical Activity Index, abdominal ultrasonography, gastroenteroscopy and histology were performed at the time of diagnosis and after 60 days of treatment. In healthy dogs, *S. boulardii* reached a steady state in five days and was completely eliminated on day 4 after administration. No short-term side effects were seen. Clinical activity index, stool frequency, stool consistency and body condition score improved significantly in dogs with CE receiving *S. boulardii* versus the placebo. In conclusion, ***S. boulardii* can be safely used in dogs with CE and seems to achieve better control of clinical signs than standard therapy alone.**

Results

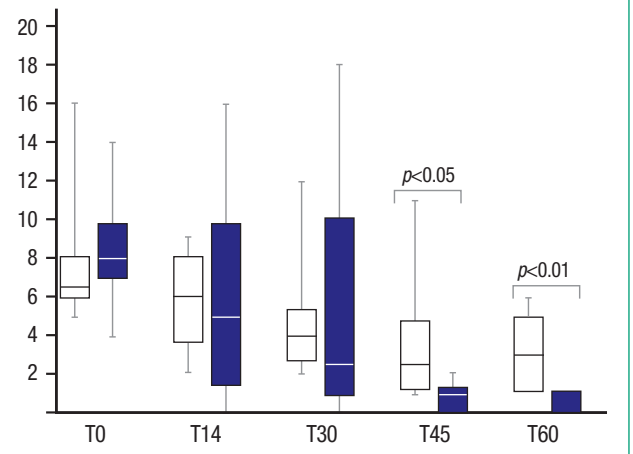

Figure 1. Canine Chronic Enteropathy Clinical Activity Index (CCECAI) score in dogs receiving *Saccharomyces boulardii* (blue boxes) or a placebo (white boxes) during treatment. Differences in CCECAI scores were significant between groups at T45 ($p<0.05$) and T60 ($p<0.01$). Values are represented as minimum and maximum (edges of the bars), median, and IQR (boxes).

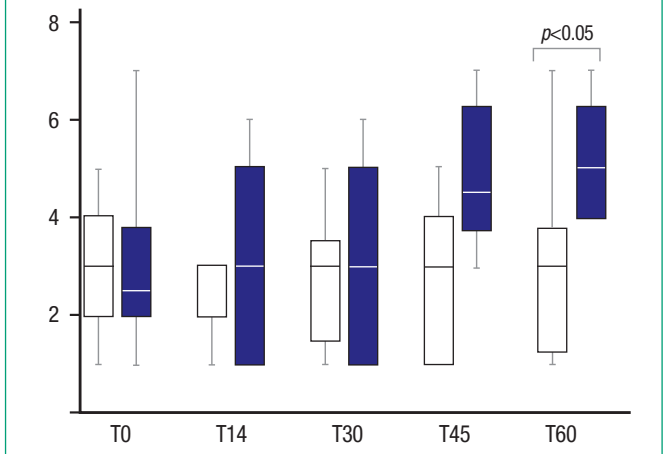

Figure 2. Body condition score (BCS) in dogs receiving *Saccharomyces boulardii* (blue boxes) or placebo (white boxes) during treatment. Differences in BCS score were significant between the groups at T60 ($p<0.05$). Values are represented as minimum and maximum (edge of the bars), median, and IQRs (boxes).

Conclusions

The results of the current study suggest that ***S. boulardii* can be safely used in dogs because its administration did not cause short-term adverse effects.** In dogs with CE treated with diet, antibiotics and immunosuppressive drugs, *S. boulardii* can be added to achieve better control of clinical signs. Further studies are needed to evaluate the mechanism of action of this probiotic to modify intestinal microflora and invoke an inflammatory response.

KEYPOINTS

- Dogs that received *S. boulardii* had **significant fewer or no clinical signs of CE (stool frequency and consistency, CCECAI score)** with respect to controls.
- Dogs that received *S. boulardii* showed a **significant increase of BCS** with respect to placebo; this could be due to improvement of GI functions, interference with pathogenic adherence, modulation of normal microbiota, restoring of normal fatty acid balance, release of secretory immunoglobulins, immune regulation of cytokine levels.

Effects of broad-spectrum antibiotics on the colonisation of probiotic yeast *Saccharomyces boulardii* in the murine gastrointestinal tract

Karl Alex Hedin, Vanessa Emily Rees, Hongbin Zhang, Vibeke Kruse, Ruben Vazquez-Uribe & Morten Otto Alexander Sommer

nature portfolio

Scientific Reports

https://doi.org/10.1038/s41598-022-12806-0

Summary

The probiotic yeast, *Saccharomyces cerevisiae* var. *boulardii*, a subspecies of the commonly used baker's yeast, *Saccharomyces cerevisiae,* has caught the attention within the field of probiotics and AMTs (advance microbial therapeutics).

S. boulardii taken as a probiotic supplement has been reported to ameliorate certain antibiotic-associated disorders, such as *Clostridium difficile* infections, inflammatory bowel disease and other gastrointestinal disorders.

Regrettably, *S. boulardii* has not been considered an efficient coloniser in conventional rodents with an intact microbiome due to its low abundance and short residence time in the gastrointestinal tract.

For instance, in conventional mice *S. boulardii* was completely washed-out after two days, even though it can survive the low pH of the stomach and harsh conditions of gastrointestinal tract.

In this study, **we characterised the effect of an antibiotic cocktail to build a robust mouse model for colonisation of *S. boulardii*.**

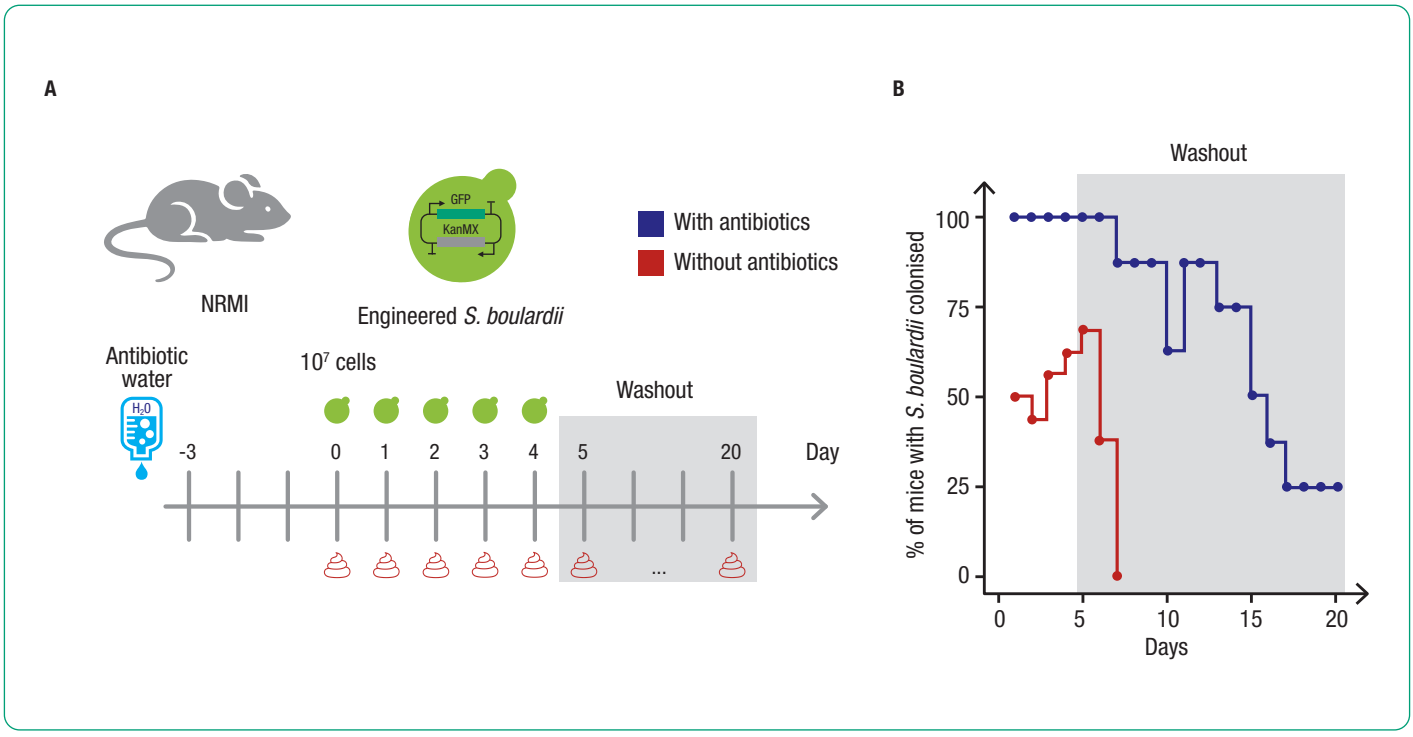

Figure 1 (partial). Assessment of *Saccharomyces boulardii* colonisation in antibiotic-treated mice.
(A) Graphical scheme of the experimental design. Mice were orally administered approximately 10^7 cells of *S. boulardii* daily for five consecutive days, followed by a 15-day washout period (grey-shaded area). The mice were divided into two cohorts, one of which received a combination of antibiotics dissolved in the drinking water.
(B) The step plot shows the time-course of the percentage of mice with detectable levels of *S. boulardii* in the antibiotic-treated cohort (blue) compared with the non-antibiotic-treated cohort (red). Furthermore, a more than 1,000-fold increase in the viable counts of *S. boulardii* was observed in the feces of antibiotic-treated mice compared with the non-antibiotic-treated cohort.

(continues)

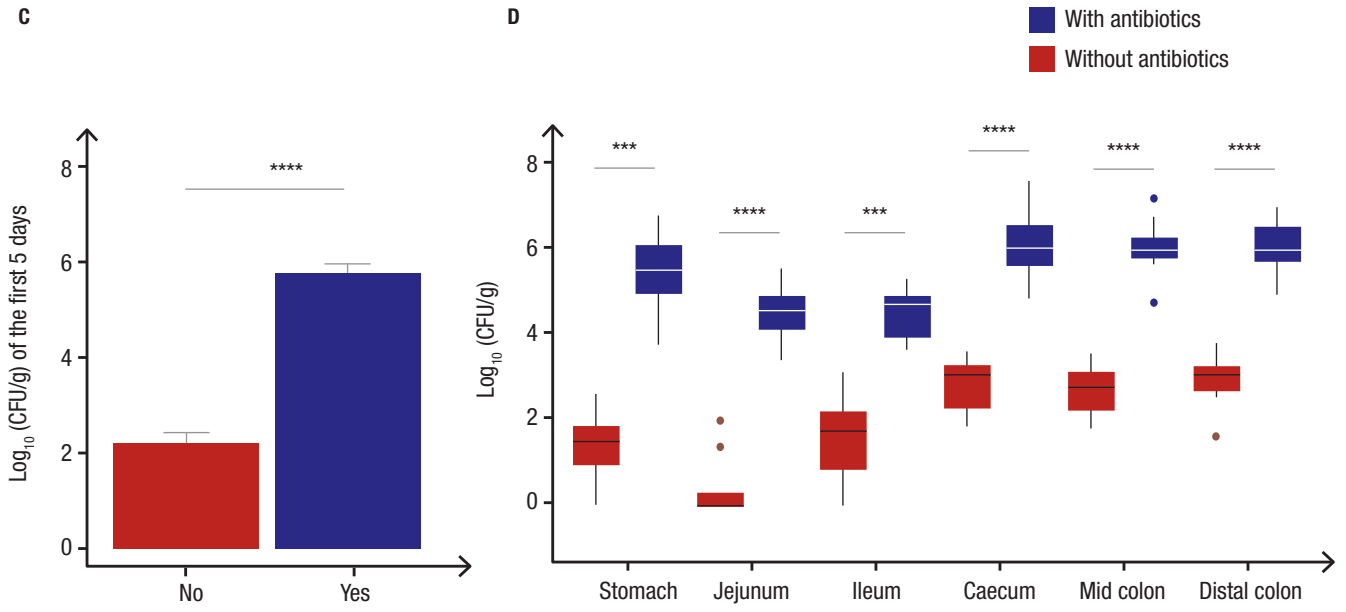

Figure 1 (partial). Assessment of *Saccharomyces boulardii* colonisation in antibiotic-treated mice. (*continuation*)
(C) Bar plot of the mean CFU/g of *S. boulardii* assessed in the faeces over the first five days.
(**D**) Box plot of the assessed CFU/g of *S. boulardii* in the gastrointestinal tract from the nonantibiotic-treated and antibiotic-treated mice sacrificed on the fifth day.
***$p<0.01$; ****$p<0.001$.
All samples were analysed by a dependent sample t-test.

Conclusions

The study demonstrated that **treating mice with a cocktail of antibiotics (ampicillin, kanamycin, metronidazole, vancomycin) enabled *S. boulardii* to remain in 75% of mice for 10 days and 25% of mice for 15 days (Fig. 1B) following the last oral administration.** This was in stark contrast to the colonisation observed in the nonantibiotic-treated mice that demonstrated complete washout of *S. boulardii* after two days.

KEYPOINTS

- *Saccharomyces boulardii* is not a common inhabitant of the mouse gastrointestinal tract.
- After 5 days oral administration in nonantibiotic-treated mice *Saccharomyces boulardii* was completely washed-out after 2 days.
- The treatment with a combination of broad-spectrum antibiotics would eliminate gut bacteria competing with *S. boulardii,* allowing for more robust colonisation and better reproducibility throughout the gastrointestinal tract.

Efficacy and safety of the probiotic *Saccharomyces boulardii* for the prevention and therapy of gastrointestinal disorders

Theodoros Kelesidis and Charalabos Pothoulakis

Therapeutic Advances in Gastroenterology

doi: 10.1177 / 1756283X11428502

Summary

Several clinical trials and experimental studies strongly suggest a place for *Saccharomyces boulardii* as a biotherapeutic agent for the prevention and treatment of several gastrointestinal diseases. *S. boulardii* mediates responses resembling the protective effects of the normal healthy gut flora. The multiple mechanisms of action of *S. boulardii* and its properties may explain its efficacy and beneficial effects in acute and chronic gastrointestinal diseases that have been confirmed by clinical trials. Caution should be taken in patients with risk factors for adverse events. This review discusses the evidence for efficacy and safety of *S. boulardii* as a probiotic for the prevention and therapy of gastrointestinal disorders in humans.

Table 1 (partial). Mechanisms of action of *Saccharomyces boulardii*.

LUMINAL ACTION
• Antimicrobial activity
• Antitoxic effect
• Cross-talk with normal microbiota
TROPHIC ACTION ON THE INTESTINAL MUCOSA
REGULATION OF IMMUNE RESPONSE
• By acting as an immune stimulant
• By reducing pro-inflammatory responses and promoting mucosal anti-inflammatory signaling effects

Table 3 (partial). Properties of *Saccharomyces boulardii* that can determine the efficacy of *S. boulardii*.

1. Survives passage to its target organ (most commonly the colon).
2. Survives at body temperature (37°C): unique advantage of being one of the few yeasts that do best at human body temperatures.
3. In lyophilized form, *S. boulardii* survives gastric acid and bile.
4. As is the case with all yeasts, *S. boulardii* is naturally resistant to antibiotics.
5. *S. boulardii* is resistant to proteolysis.
6. *S. boulardii* exists in the competitive milieu of the intestinal tract.
7. *S. boulardii* levels are higher in patients with disturbed intestinal microbiota (due to antibiotic exposure) compared to patients without antibiotic exposure.
8. When given orally, achieves steady-state concentrations within three days and is cleared within 3–5 days after it is discontinued.
9. Some types of fiber (psyllium) increased *S. boulardii* levels by 22%, while other types of fiber (pectin) showed no effect.

Article

Effects of *Saccharomyces boulardii* Supplementation on Nutritional Status, Fecal Parameters, Microbiota, and Mycobiota in Breeding Adult Dogs

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veterinary sciences

https://doi.org/10.3390/vetsci9080389

Summary

The aim of this study was to evaluate the effect of the administration of *Saccharomyces boulardii* on the nutritional, immunological, inflammatory, stress status, and the gut composition in 25 healthy adult American Staffordshire Terrier dogs. **Supplementation with *S. boulardii* significantly improved the intestinal status and induced a reduction of stress, a common condition affecting animals managed in a breeding environment.**

Table 1. Nutritional parameters and laboratory analytes of the dogs depending on the group (G) they belong to (CRT=control; TRT=treated), time (T), and their interaction (G × T).

	Group (G)		Time (T)						SEM		*p*-Value		
Laboratory analytes (unit)	**CTR**	**TRT**	**T_0**	**T_1**	**T_2**	**T_3**	**T_4**	**T_5**	**G**	**T**	**G**	**T**	**G×T**
pH	6.51	6.50	6.50	6.54	6.50	6.52	6.46	6.50	0.06	0.05	0.982	0.152	0.161
Calprotectin (µg/g)	**5.95**	**5.57**	**5.99^{ab}**	**6.04^{a}**	**5.94^{b}**	**5.63^{cd}**	**5.64^{c}**	**5.32^{d}**	**0.85**	**0.60**	**0.753**	**<0.001**	**0.108**
Lactoferrin (µg/g)	1.53	1.32	1.45	1.45	1.31	1.38	1.49	1.44	0.22	0.16	0.489	0.260	0.330
Zonulin (ng/mL)	52.51	50.36	49.58	52.35	49.84	53.79	50.18	52.96	0.77	1.16	0.046	0.250	0.710
Cortisol (pg/mg)	**0.61**	**0.55**	**0.60**	**0.65**	**0.57**	**0.60**	**0.53**	**0.54**	**0.02**	**0.02**	**0.090**	**0.100**	**<0.001**
Immunoglobulin A (mg/g)	47.71	48.17	48.87	48.68	48.33	47.40	47.66	46.75	1.70	1.23	0.849	0.100	0.116
Short chain fatty acids (µmol/g)	143.56	146.96	148.11	145.94	139.55	146.24	145.04	146.77	21.39	15.54	0.912	0.112	0.180
Indole/skatole (µmol/g)	**1.76**	**1.60**	**1.67**	**1.73**	**1.63**	**1.66**	**1.69**	**1.68**	**0.04**	**0.06**	**<0.001**	**0.937**	**0.001**

Means with superscript letters [a,b,c,d] identify significant differences among the sampling times ($p<0.05$).

A significant correlation between calprotectin levels and inflammatory states such as inflammatory bowel disease or chronic inflammatory enteropathies has been reported. Therefore, the decrease in fecal calprotectin levels assessed in dogs treated in this study could indicate a reduction in inflammation and a more stable intestinal environment. **Cortisol was found in several matrices**, such as blood, saliva, hair, urine, and feces. A lower production of cortisol could be correlated to a better ability of the animals to cope with the breeding environment, thus indicating a decrease in stress levels in the treated dogs.

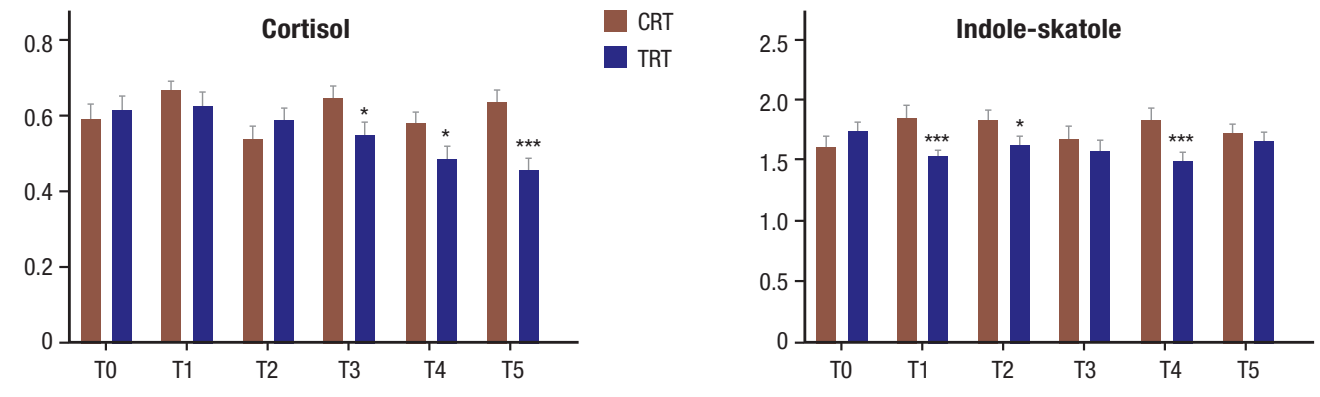

Figure 1. Concentration of cortisol (pg/mg) and indole/skatole (µmol/g) in the control (CRT) and treated (TRT) groups at each time point (T0 to T5). Graph bars with asterisks indicate significant differences between the dietary treatments within each sampling time; *=$p<0.05$, and ***=$p<0.001$.

KEY POINTS

- The 35 days administration of ***Saccharomyces boulardii* was well tolerated** by the dogs and showed positive effects on some fecal parameters.
- ***Saccharomyces boulardii* could be used to counter intestinal inflammation and psycho-physical stress in animals.**

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