*Saccharomyces boulardii* – a key probiotic in clinical practice
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#optibacwebinar
• Introduction to *Saccharomyces boulardii*
• Methods of action
• The clinical research and use of *S. boulardii* in clinic
• Protocol

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Probiotics definition

**Pro** (pro) = « in favor of »

**Biotics** (biotic) = « life »

“Live microorganisms which when administered in **adequate amounts** confer a **health benefit** on the host”

Many bacteria species and strains

Only 1 yeast strain is a probiotic
Bacteria vs. Yeast

**Bacteria**
- Prokaryotic cells (DNA strands)
- Sensitive to antibiotics
- Replicate by division
- Divides every 20-30 min

**Yeast**
- Eukaryotic cell (nucleus)
- Insensitive to antibiotics
- Sensitive to anti-fungal agents e.g. garlic
- Replicates by budding

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*Division*

*Budding*
**S. boulardii**: the only ONE probiotic yeast

- Henri Boulard discovered it in 1923
- On tropical fruits peel (lychee) in Vietnam
- The peel was used by natives against diarrhea, especially in those afflicted with cholera
Taxonomy / Identity

• *S. cerevisiae* vs. *S. boulardii*
  – Can be sometimes confusing because they both have similar names
  – *S. cerevisiae* = Baker’s and Brewer’s yeast

• Complete scientific name are as follows:
  – *S. cerevisiae* = *Saccharomyces cerevisiae*
  – *S. boulardii* = *Saccharomyces cerevisiae var boulardii*

  *However there are many differences*
Survival in the gastrointestinal tract

- Achieve high concentration in the colon quickly
- **Transient** - does not permanently colonise the colon
- In human volunteers, the maximum stool concentration is reached 36-60 hours
- Eliminated within 2-5 days
- Naturally resistant to antibiotics
- Sensitive to non absorbable anti-fungi (e.g. Nystatine)

Mechanisms of action

1. Binding of enterohaemorrhagic *E. coli* and *Salmonella*
2. Protection against toxins in the gut lumen
3. Favour growth of lactic acid bacteria e.g. *Lactobacillus spp*
4. Reinforces the integrity of the mucosal lining
5. Increases surface area in the gut
6. Increases brush border enzymes
7. Stimulates increase in Secretory IgA
8. Acts against *Candida albicans*
1. Binding of harmful bacteria such as *E. coli* and *Salmonella*

*S. Boulardii* with D-mannose rich outer membrane, giving sticky surface.

Many harmful bacteria stick to one *S. boulardii*, and are removed from the gut.

D-mannose on the outer membrane of the SB sticks to Type I fimbriae of bacteria. Type I fimbriae is present on E. coli, Salmonella, Klebsiella and more...

Farah, 31/07/2013
2. Protection against toxins in the lumen

*Clostridium Difficile*

- *S. boulardii* inhibits the effects of *C. Diff* toxins A and B. *S. boulardii* releases a 54kDa protease which inactivates toxins A and B and lyses the colonic receptors (Castagliuolo, 1996)

*Cholera toxin*

- *Cholera* toxins A and B lead to the activation of cAMP which induces the opening of Cl- channels and closing of Na+/H+ channels and Cl-/HCO3-exchanges. This results in water and electrolyte secretion (Dias, 1995).
- *S. boulardii* releases a 120kDa protein which stimulates antisecretory factors resulting in a down-regulation of cAMP.

*E. Coli*

- *S. boulardii* produces a protein phosphatase. This dephosphorylates endotoxins such as *E. Coli* LPS, altering its binding site and partially inactivating cytotoxic effects (Buts, 2006).
3. Favour growth of lactic acid bacteria


Although SB itself just acts as a cleanse by removing harmful bacteria from the system there is less competition for the natural resident friendly bacteria, therefore they are seen to flourish:

This table shows upon supplementation with SB, lactobaccillus levels increased by 100 fold, bifidobacteria by 10 fold and E. coli decreased by around 100 fold.

Faran, 31/07/2013
4. Reinforces the integrity of the mucosal lining

*S. boulardii* maintains the integrity of the gut wall lining by preserving tight junctions. It does this preventing the phosphorylation of MLC (Myosin Light Chain). The phosphorylation of MLC is the first step in the cell signalling pathway when *E.coli* and other harmful bacteria attack tight junctions.

5. Increases surface area in the gut

*S. boulardii* increases the levels of polyamines – spermine and spermidine (Buts, 1994).

This leads to cell proliferation

As can be seen as an increase in villi height and crypt depth, which gives increased surface area in the small intestine for improved absorption of nutrients from the diet.

Polyamines = group of cell components that are important in the regulation of cell proliferation and cell differentiation. Polyamine deficiency results in an arrest of cell proliferation, which can be reversed by supplementation with external polyamines. Polyamine deficiency can also, under certain circumstances, result in programmed cell death or apoptosis.
“In weanling rats (d 20 to d 30), a daily dose of 100 mg of lyophilized *S. boulardii* produced significant (*p* < 0.025) increases in sucrase (157%) and maltase (47%) activities.” Buts JP et al (1994)

It’s thought this increase is mediated by *Saccharomyces boulardii* induced increase in spermine and spermidine.

*S. boulardii* has a trophic effect on the gut.
7. Stimulates increase in Secretory IgA

Secretory IgA is an immune factor found in the intestinal tract, which helps to protect against harmful pathogens.

Qamar et al (2001)
Upon supplementation with SB levels of sIgA are greatly increased

Farah, 31/07/2013
8. Acts against *Candida albicans*

How does it work?

- “Crowds out” the candida yeast
- Produces capric, caprylic, and caproic acids which inhibits the adhesion of the candida by destroying the hyphae, and also prevents the biofilm from forming (Murzyn et al, 2010)
Mechanisms of action - Overview

McFarland LV. *Saccharomyces boulardii* in adults

- **Toxins increase water secretion**
- **Bacteria destroy tight junction, invade mucosa**
- **Intestinal flora depleted by antibiotics**
- **Viral infection destroys mature enterocytes**
- **Decrease in disaccharidase causes osmotic diarrhea**
- **Decrease in IgA**
- **Inflammation**

**Luminal action**
1. Anti-toxin effect against
   - C. difficile toxins A and B (54 kDa protease)
   - Cholera toxin (120 kDa protein)
   - E. coli LPS (53 kDa protein phosphatase)
2. Antimicrobial activity
   - Preservation of tight junctions
   - Bacteria adhere to Sb, Sb decreases invasion
3. Modulation of intestinal flora
4. Metabolic activity: Sb increases short chain fatty acids, favors normal colonic function

**Trophic action**
5. Enzymatic activity
   - Polyamines favor enterocyte maturation
   - Increased disaccharidase levels - beneficial in viral diarrhea
6. Increased sIgA levels increases immune defense in the gut

**Mucosal action-anti-inflammatory effect**
7. Acts on the cellular signals and decreases synthesis of inflammatory cytokines
Clinical Applications of *S. boulardii*

- Diarrhoea
- Candida
- Pathogenic bacteria overgrowth
- *Clostridium difficle*
- IBD
- IBS
- *H. pylori*
Diarrhoea


- Review/Meta analysis of 31 randomised, placebo-controlled treatment arms in 27 trials, encompassing 5029 study patients
- Found *S. boulardii* to be significantly effective and safe in 84% of those treatment arms
- Can therefore be strongly recommended for prevention of AAD, as well as for traveller’s diarrhoea and the prevention of nutrition-related diarrhoea; also for the alleviation of *Helicobacter pylori* infection and related symptoms.
Diarrhoea

Diarrhoea

• Kurugol & Koturoglu (2005) - 200 children. Duration of diarrhoea reduced (4.7 vs 5.5).

• Wan et al (2017) 408 children. Incidence of diarrhoea less with SB than control 22 vs 57

• Zhang et al (2017) looked at 163 elderly hospitalised patients on antibiotics. 14.8% vs 28.0%

• Kabbani et al (2017)

• Das et al (2016)

• Tung et al. (2009) - *Clostridium difficile*

• Surawicz (2003) - *Clostridium difficile*

‘We know that the possible therapeutic mechanisms of probiotics in intestinal inflammatory disorders include: antagonism against enteric pathogens; strengthening of the gut mucosal barrier; inhibition of the local secretion of inflammatory mediators; and stabilisation of local immunological activity’ (Kelesidis T 2012).

• Guslandi et al (2000) – 32 patients with Crohn’s disease – 38% relapsed in control group compared to the 6% relapse in intervention group
Candida

Candida is becoming less responsive to some of the antifungals as the biofilm is resistant to them

*Saccharomyces boulardii* is becoming a commonly used probiotic used to combat *Candida*.

*S. boulardii* secretes capric, caprylic, and caproic acids which inhibit the hyphae formation. It also reduces Candidial adhesion and biofilm formation. Murzyn et al., (2010)

- Matsubara VH., et al (2016) – A review which discusses the use of SB for Candidais
- Ducluzeau & Bensaada (1982) observed a 90% decrease in *Candida albicans* when treated with *S. boulardii*
- Berg et al (1993) found *S. boulardii* decreased the incidence of *C. albicans* translocation
- Jawhara, S. & Poulain, D. (2007) found *S. boulardii* decreased inflammation and *C. albicans* colonisation
IBS can be caused by several of the imbalances that *Saccharomyces boulardii* can help combat – such as pathogenic bacteria overgrowth, inflammation, candida. *S. boulardii* may therefore be applicable for IBS
**H. Pylori**

- *S. boulardii* as a useful adjuvant to antibiotics.
- Protects against side effects and therefore improves compliance.
- Increases eradication rate.

Homan & Orel (2015) found *S. boulardii* to be an effective adjuvant to antibiotic treatment of *H. Pylori*.

Namkin et al., (2016) looked at *S. boulardii* eradication of *H. Pylori* in 28 children in Iran – helped increase the eradication of *H. Pylori* but not as a single therapy.

Product specifications

- 5 billion per capsule
- Dairy free
- Free of excipients
- Packs of 14, 40, 80
- 8 mechanisms of action
- Can be taken alone, or in combination
Saccharomyces boulardii protocol

• 1-6 capsules a day depending on severity of symptom.
• Severe diarrhoea – start with 6 then reduce as symptoms clear
• Candida – start with 2, increase to 4 or 6 until symptoms clear
• Additionally, take a regular probiotic (such as For every day EXTRA Strength) to repopulate gut as it’s being cleared
• Take away from any other anti-microbial
• Consult doctor if pregnant or breast-feeding
• General diet – especially with IBS, IBD and Candida
Probiotics Database

Saccharomyces boulardii

- Non-pathogenic transient yeast
- Broad anti-pathogenic function
- Particularly researched for candida and diarrhoea

Saccharomyces boulardii is unique in this database of the world's best probiotic strains, in that it is a non-pathogenic transient (non-colonising) yeast rather than a bacteria. It is important to note, however, that it is genetically and functionally different from the well-known pathogenic Candida family of yeasts. It was originally classified as a separate species but, after much laboratory testing, it was shown to have certain generic and structural similarities to Saccharomyces cerevisiae and so is now classified as part of this species. That being said, S. boulardii is a unique microorganism and has vastly different strain-specific properties to other yeasts in the same S. cerevisiae species. In the same way that different strains of bacteria may have completely different actions and properties to other strains within the same species.

https://www.probioticsdatabase.co.uk
Thank you for your attention
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 References


Noteworthy Reviews/ Meta-analyses

• **McFarland 2010**: Systematic review and meta-analysis of *Saccharomyces boulardii* in adult patients
  – 27 RCT / 5029 patients
  – Prevention of AAD, TD, CDD recurrences

• **Doron 2008**: Probiotics for prevention of antibiotic-associated diarrhoea
  – 5 meta-analysis performed on AAD and probiotics
  – Overall reduction in the risk of AAD when probiotics co-administered with antibiotics

• **McFarland 2007**: Meta-analysis of probiotics for prevention of traveler's diarrhoea
  – Probiotics including *S. boulardii* had significant efficacy in prevention of TD

• **McFarland 2006**: Meta-analysis of probiotics for the prevention of AAD and the treatment of *C. difficile* Disease
  – Probiotics significantly reduced the relative risk of AAD

• **Szajewska 2005**: Meta-analysis: non-pathogenic yeast *Saccharomyces boulardii* in the prevention of antibiotic-associated diarrhoea
  – 5 RCT were included / 1076 participants
  – Boulardii reduced significantly the risk of diarrhea from 17.2% to 6.7%, No side effects were reported