

MINUTES ON BIOCODEX TRAIN THE TRAINERS PARIS FRANCE JULY 10TH 2015

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SUMMARY

The purpose of Train the Trainers Workshops was to learn about the specific properties and physiopathology, mode of action and uses of *Saccharomyces boulardii* CNCM I-745 in the treatment of different diseases through the latest clinical papers published. The sessions focused on the treatment of acute diarrhea, antibiotic associated diarrhea, traveler's diarrhea, chronic idiopathic diarrhea, *Clostridium difficile* associated diarrhea and *Helicobacter pylori* (Hp) eradication.

Key words: *Train the trainers, Workshops, Saccharomyces boulardii, Children*

INTRODUCTION

The content of each session presented by the scientific committee was not affected by any conflict of interest. The workshop was chaired by Prof. Henry Cohen, Past President of World Gastroenterology Organization, Secretary General at The Uruguayan Academy of Medicine, in Uruguay and co-chaired by Prof. Carlos Velasco Benitez, University of Valle Cali, Colombia, Prof. Yvan Vandenplas, Head of pediatric gastroenterology department at University children's hospital Brussels, Belgium was the distinguished guest as well as Prof. Wilfrido Coronel From Department of Microbiology, Cartagena University, Colombia and Prof. Jorge Palacios Associate Professor of Pediatrics San Carlos de Guatemala Medical University in Guatemala.

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RESUMEN

El objetivo del *Train the Trainers Workshops* es aprender acerca de las propiedades específicas y fisiopatológicas, el modo de acción y uso del *Saccharomyces boulardii* CNCM I-745 en el tratamiento de las diferentes enfermedades a través de la evidencia clínica. Las diferentes secciones se enfocan en la enfermedad diarreica en cuanto a su tratamiento, la asociada a los antibióticos, la del viajero, la idiopática crónica, la asociada a *Clostridium difficile* y la erradicación de la infección por *Helicobacter pylori*.

Palabras claves: *Train the trainers, Grupo de trabajo, Saccharomyces boulardii, Niños*

HOW TO DELIVER A MEDICAL PRESENTATION

Prof. Henry Cohen from Uruguay, conducted the first session. His lecture provided tools to build and deliver a good scientific presentation. The outline of this session included preparation, materials, skills, techniques, evaluation and summary. Contents included an overview on how adults learn, the educational pattern to improve teaching skills

Prof. Cohen highlighted that the involvement of the audience in the subject of teaching and training relevance are very important points in the learning process.

Marco educativo

- Evaluar las necesidades
- Establecer metas y objetivos
- Determinar el método de enseñanza
- Preparar material de enseñanza
- Enseñar
- Evaluar el programa/currículum

WGO

Train the Trainers



conferences, small group sessions, case presentations, interaction with the instructor, teaching at the side of the patient's bed, electronic resources, etc. Conferences are more suitable for reviewing important subjects, specifying topics, comparing different points of view and communicating new material. While only 5% of all information presented in a conference will be remembered as much as 80% of it can be learned by practicing it or teaching it to others.

In order to succeed in delivering a medical presentation, it is important to master the subject, to prepare the teaching subject in advance, to select adequate learning materials and to use appropriate skills and techniques to deliver the presentation. It is also crucial to be aware of the attention period for adults, to deliver clear and specific messages and to keep the audience's attention. A presentation should have an introduction, a discussion and a conclusion.

Formato de una presentación

- **Introducción**
Inicio sólido, foco/objetivos
- **Discusión**
Puntos principales, ordénalos de manera lógica
- **Conclusión**
Revisión, finalizar a tiempo, con estilo

The starting statement should be solid (start with a question, interesting facts, anecdotes, hypothetical situations, shared point of view), the presentation body should be precise and the conclusion should state the purpose of the presentation and the key-points.

SACCHAROMYCES BOULARDII CNCM I-475 IN ACUTE DIARRHEA: FROM SCIENCE TO CLINICAL PRACTICE

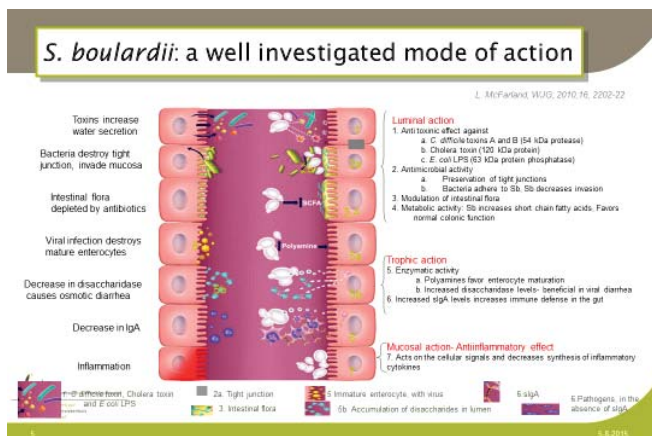
In this session, Prof. Vandenplas from Brussels University Children's Hospital presented the history of *Saccharomyces boulardii* CNCM I-745, its clinical indications and its efficacy together with key features of *Saccharomyces boulardii* CNCM I-745 including the fact that *Saccharomyces boulardii* CNCM I-745 is larger than bacteria, its effects and differences between a yeast and a bacteria: ideal growth conditions in terms of temperature and pH, antibiotic resistance, genetic material transmission.

The lecture addressed *Saccharomyces boulardii* CNCM I-745 luminal, trophic and mucosal mode of action.

The latest clinical studies using *Saccharomyces boulardii* acute diarrhea in children, the effectiveness and safety of *Saccharomyces boulardii* for acute infectious diarrhea, the clinical efficacy of *Saccharomyces boulardii* and Metronidazole in children with acute bloody diarrhea caused by amebiasis, the clinical efficacy of *Saccharomyces boulardii* and Metronidazole in symptomatic children with *Blastocystis hominis* infection.

	Bacteria	Yeast	Probiotic characteristic
Presence in human microbiota	99%	<1%	
Cell size	1 µm	10 µm	
Cell wall	Peptidoglycan LPS (gram -) LTA (gram +)	Mannose chitin, Glucans (PPM, PLM)	Immune response through TLRs
Ideal growth conditions			
> pH	> 6,5-7,5	> 4,5-6,5	Different actions sites on GIT
> Temperature (°C)	> 10-80	> 20-30	
Antibiotic resistance	No	No	Safe to associate with antibiotics
Genetic material transmission	Yes	No	

Cernicka, et al. *Abstract Pharmacol Ther* 2007;20:167-74



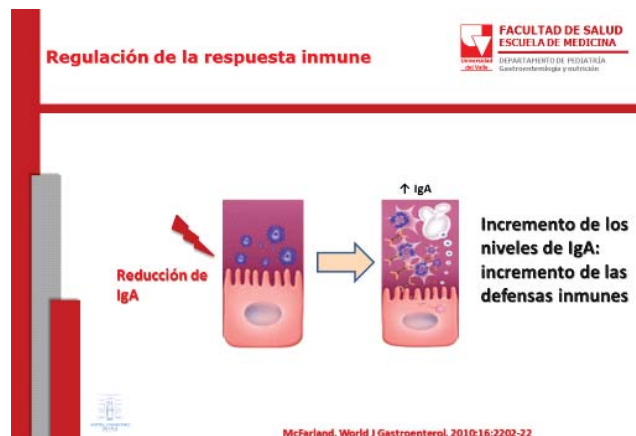
Pr. Vandenplas emphasized the fact that *Saccharomyces boulardii* is effective in the treatment and prevention of acute diarrhea in children, decreasing the duration and incidence of new episodes of diarrhea at 1 and 2 months by 59% and 43% respectively.¹ He also commented on several meta-analyses confirming the efficacy of *Saccharomyces boulardii* for the treatment of antibiotic associated diarrhea in children and as a supplementation for the eradication of *Hp* infection.

The lecture concluded that not all probiotic strains are equal, that *Saccharomyces boulardii* CNCM I-745 is a unique microorganism with an identified mechanism of action, backed up by a lot of clinical evidence in the treatment and prevention of acute diarrhea, antibiotic associated diarrhea and *Hp* infection.

SACCHAROMYCES BOULARDII CNCM I-745 A UNIQUE PROBIOTIC

Prof. Carlos Velasco Benitez from University of Valle Cali, Colombia; started his session by an overview on the clinical evidence on the use of *Saccharomyces boulardii* in medical publications. 259 publications among them, more than 70 clinical studies which indicates the growing scientific interest in *Saccharomyces boulardii* over the past years. The lecturer specified that 27% of all clinical studies were related to infectious diarrhea, 13% to antibiotic associated diarrhea, 11% to *Helicobacter pylori* and 10% to *Clostridium difficile*.

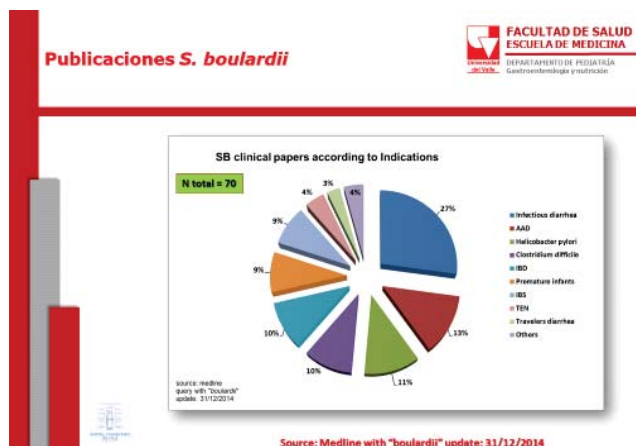
Prof. Velasco highlighted *Saccharomyces boulardii* CNCM I-745 mode of action, its luminal, trophic and mucosal action, its taxonomy and its specific properties that confers beneficial effects such as anti-



inflammatory, immunological, anti-toxin, antimicrobial effect.

An emphasis was given on the luminal action of *Saccharomyces boulardii* CNCM I-745 as an antitoxin and antimicrobial agent, supported by clinical evidence from scientific studies. *Saccharomyces boulardii*'s trophic mode of action including its beneficial enzymatic activity on viral diarrhea and its action as an intestinal microbiota modulator enhancing normal colonic function. To conclude, on *Saccharomyces boulardii* mode of action, Prof. Velasco Benitez highlighted data on *Saccharomyces boulardii* effects as an immune response regulator by reducing the IgA levels and therefore increasing the immune defenses and inflammation.

The session concluded with the statement that *Saccharomyces boulardii* CNCM I-745 the best known and studied probiotic strain with proven effectiveness in different clinic conditions. It has a well-established action mode for its trophic, luminal and immunological



action. These claims are based on clinical studies and meta-analyses published in worldwide scientific journals.

SACCHAROMYCES BOULARDII CNCM I-745 IN THE TREATMENT OF INFECTIOUS DIARRHEA

Prof. Wilfrido Coronell from Cartagena University, Colombia started the session *Saccharomyces boulardii* CNCM I-745 in the treatment of infectious diarrhea by mentioning the main causes of mortality among infants worldwide and the fact that diarrhea is the 7th leading cause of death among infants in Latin America, Africa, Caribbean and South Asia, indicating a global epidemiology on infectious diarrhea.² He focused on Latin America and Caribbean epidemiology indicating that according to the WHO objectives for 2015, a small progress is being made in treatment and prevention of children's diarrhea.

He backed his statements with clinical evidence showing that *Saccharomyces boulardii* CNCM I-745 reduces the duration of diarrhea caused by different etiologic factors. Several clinical studies confirmed that acute diarrhea caused by rotavirus and other agents in infants treated with *Saccharomyces boulardii* CNCM I-745 diminished within two days and stopped completely after 5 days of treatment, also after 5 days the rotavirus was no longer present in stools.

CNCM I-745 has proven its effectiveness for the treatment of acute infectious diarrhea as it is shown in clinical studies and confirmed by several meta-analyses.

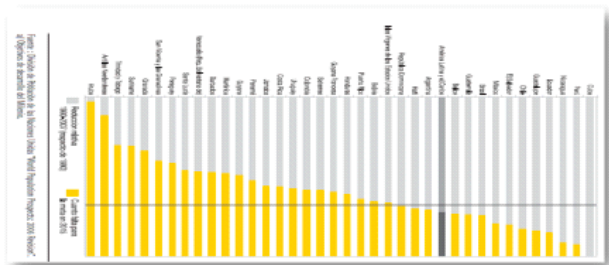
THERAPEUTIC ROLE OF SACCHAROMYCES BOULARDII CNCM I-745 IN GASTROENTEROLOGY

Prof. Jorge Palacios from The Guatemala Medical University presented a lecture on the therapeutic role of *Saccharomyces boulardii* CNCM I-745 in gastroenterology including antibiotic associated diarrhea (AAD), traveler's diarrhea, chronic idiopathic diarrhea, *Clostridium difficile* and *Helicobacter pylori* infections.

Clinical evidence was shown on drug induced diarrhea, including the fact that not only antibiotics can cause AAD, but other drugs such as laxatives, NSAID's, chemotherapy, antacids, iron medication, cholinesterase inhibitors as well which can cause diarrhea. Other risk factors that can trigger AAD are age, previous history of AAD, other underlying diseases, chronic gastro enteropathy, immune deficiency, long term hospitalization, surgery, catheter and gastrointestinal procedures. All the factors mentioned above can cause dysbiosis and swelling.

AAD occurs in 17, 5% of hospitalized adults and from 5% to 39% of children. A severe case of AAD may force the patient to discontinue antibiotic therapy, therefore worsening the symptoms and increasing the risk of developing antibiotic resistance and being hospitalized, as well an increase of the risk of *C. difficile* associated diarrhea and higher cost of treatment in general. A clinical study evidenced a decrease of 57% in diarrhea episodes when *Saccharomyces boulardii* was introduced within the 48

América Latina Y EL Caribe: progreso en la reducción de la mortalidad infantil de 1990 a 2007 y reducción pendiente hasta 2015 respecto de la meta 5 de los ODM



Desafíos Número 6, diciembre de 2007, ISSN 1816-7527. La reducción de la mortalidad infantil en América Latina y el Caribe: avance dispar que requiere respuestas variadas. Boletín de la infancia y adolescencia sobre el avance de los objetivos de desarrollo del Milenio

Diarrea Asociada a Antibióticos (DAA's)



Boletín - Gut Microflora: Digest. Psyclo/Patol. Eje: Pimentel et al. 2000-181-97

Prevención de DAA's

- Estudio Prospectivo, doble-ciego, placebo-controlado en 180 pacientes hospitalizados, recibiendo antibióticos.
- S. boulardii* CNCM I-745 iniciado en 1as. 48h de Tx ATB y continuado por 2 semanas después de última dosis de ATB.



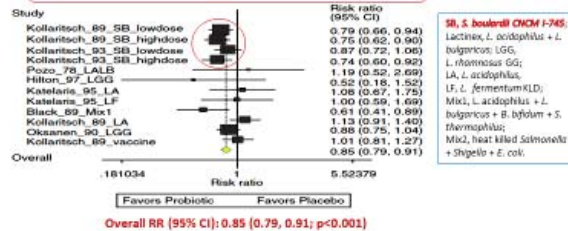
Surawicz, et al. Gastroenterology 1989;96:981-8

hours after antibiotic therapy intake and continued for 2 weeks after the last antibiotic dose. In addition, the introduction of *Saccharomyces boulardii* in combination with antibiotics in the treatment of *C. difficile* reduces its recurrence rate up to 70%.

It is estimated that each year from 20% to 50% of international travelers develop a case of traveler's diarrhea. Meta-analysis show that *Saccharomyces boulardii* CNCM I-745 is effective for prevention of traveler's diarrhea.

Meta-análisis: Probióticos en Prevención de DV

- 12 RCT's; no reporte de eventos adversos



Sb. S. boulardii CNCM I-745; Lactinex, *L. acidophilus* + *L. bulgaricus* LG6; *L. rhamnosus* GG; *L. L. acidophilus*; *L. L. fermentum* KLD; *Mix1, L. acidophilus* + *L. bulgaricus* + *B. bifidum* + *S. thermophilus*; *Mix2*, heat killed *Salmonella* + *Shigella* + *E. coli*.

When looking at chronic idiopathic diarrhea (CDI), a clinical study performed in 2008 confirmed that the use of *Saccharomyces boulardii* CNCM I-745 leads to an improvement of CDI and restoration of gut microbiota in all cases. As for *Helicobacter pylori* (*Hp*) infection, there is clear evidence that the use of *Saccharomyces boulardii* CNCM I-745 combined with triple therapy increase the eradication rate substantially and decrease the global side effects of *Hp* treatment.

- Biloo et al. World Journal of Gastroenterology. 2006;12(28):4557-4560
- www.thelancet.com Vol 380 December 15/22/29, 2012
- McFarland LV. Dig Dis 1998; 16: 292-307
- Surawicz, et al. Gastroenterology 1989; 96: 981-988