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EFFECT OF *LACTOBACILLUS* STRAINS AND *SACCHAROMYCES BOULARDII* ON PERSISTENT DIARRHEA IN CHILDREN

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Abstract The efficacy of probiotics on persistent diarrhea remains uncertain. The purpose of this study was to evaluate the effect of *Lactobacillus* sp and *Saccharomyces boulardii* on persistent diarrhea in children. In a double-blind trial eighty-nine children, aged 6-24 months were randomly distributed to receive pasteurized cow milk containing 2 viable lyophilized strains *Lactobacillus casei* and *Lactobacillus acidophillus* strains CERELA, (10^{10}-10^{12} colony-forming units per g) (n =30), or lyophilized *S. boulardii,* (10^{10}-10^{12} colony forming units per g) (n =30) or pasteurized cow milk as placebo (n =29); on each diet 175 g was given twice a day for a 5 day period. Number of depositions, duration of illness and frequency of vomiting were considered. Enteric pathogens were isolated from stools in 40% of the patients, 27% had rotavirus. *Lactobacillus* and *S.boulardii* significantly reduced the number of depositions ($p < 0.001$) and diarrheal duration ($p < 0.005$). Similarly both significantly ($p < 0.002$) reduced vomiting as compared with placebo. There was no difference between treatments depending on rotavirus status. In conclusion, *L. casei* and *L. acidophillus* strains CERELA and *S. boulardii* are useful in the management of persistent diarrhea in children.

Key words: persistent diarrhea, probiotics, *Lactobacillus* sp*, Saccharomyces boulardii*, rotavirus

Resumen ***Efecto de cepas de* Lactobacillus *y* Saccharomyces boulardii *sobre la diarrea persistente en niños.*** La eficacia de los probióticos sobre la diarrea persistente en niños aún no ha sido comprobada. Este trabajo controlado doble ciego tuvo como propósito evaluar ese efecto usando *Lactobacillus* sp y *Saccharomyces boulardii.* Ochenta y nueve niños entre 6 meses y 2 años de edad fueron distribuidos al azar para recibir leche pasteurizada conteniendo cepas liofilizadas de *Lactobacillus casei* y *Lactobacillus acidophillus* desarrolladas por CERELA (Centro de Referencia para Lactobacilos (10^{10}-10^{12} CFU por g), n=30, o cepas liofilizadas de *S. boulardii* (10^{10}-10^{12} CFU por g), n = 30, o placebo, n =29. Cada niño recibió 175 g dos veces por día durante 5 días. Se evaluó el número de deposiciones/día, la duración de la diarrea y la duración de los síntomas. Se aislaron gérmenes patógenos en las heces en el 40% de los casos: 27% eran rotavirus. *Lactobacillus* sp y *S. boulardii* redujeron significativamente el número de deposiciones ($p < 0.001$), la duración de la diarrea y el número de vómitos ($p< 0.005$) y ($p< 0.002$) respectivamente, comparado con placebo. No hubo diferencias entre los tratamientos en pacientes con rotavirus-positivo o rotavirus-negativo. En conclusión, este trabajo demuestra que cepas de *L. casei* y *L. acidophillus* desarrolladas por CERELA y de *S. boulardii* son similarmente efectivas en el tratamiento de la diarrea persistente en niños.

Palabras clave: diarrea persistente, probióticos, *Lactobacillus* sp*, Saccharomyces boulardii,* rotavirus

The vast majority of young children with acute diarrhea and mild or no dehydration who are managed according to appropriate treatment protocols such as that promoted by World Health Organization (WHO)[1] can be successfully treated with lactose-containing diets or with lactose- free ones[2]. Besides, available evidence indicates that undiluted non human milks and breast milk are well tolerated during diarrhea and may in fact reduce the severity and duration of the illness and prevent the nutritional status deterioration[3, 4], *Lactobacillus* included in probiotics can also limit the course of acute diarrhea[4,5] especially rotavirus diarrhea[6, 7], although variable results can be found according to the use of diverse species and subspecies[8] or to the number of colony forming units[9](CFU).

Saccharomyces boulardii, a nonpathogenic yeast, has also been used empirically in the treatment of acute

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infectious diarrhea[10, 11]. *S. boulardii* adheres to human jejunal cells but it does not multiply in the gut and disappears from the stools once ingestion has stopped[12] Both probiotics, *Lactobacillu*s and *Sacharomyces boulardii* supposedly exert an important impact in either the small or large intestine but the exact nature by which they exert their protective effects is not known.

Persistent diarrhea in children is defined as the continuation of an acute diarrheal episode for at least two weeks[13]. The illness is associated with malnutrition, malabsortion and growth failure, and is widely prevalent in developing countries, where 8% of acute diarrheas turn into persistent type[14, 15].The cause of persistent diarrhea is not known, pathogenic mechanisms are not well-understood and satisfactory treatment is not available[15], so that many cases are refractory and death rates remain high, 45-70%[14]. A recent study[16] showed that green banana and pectin mediated through their bacterial conversion into short-chain fatty acids (SCFA) are useful in the dietary management of persistent diarrhea. Similar beneficial effect with bifidobacteria and lactobacilli has also been recognized in the management of persistent diarrhea in several studies[17,18]. Based on these data and others observed in controlled clinical trials, indicating that those microorganisms are effective in many intestinal disorders[19], and since *S. boulardii* has never been tested in persistent diarrhea, we assessed by a well-controlled study the efficacy of *Lactobacillus acidophillus* subsp CRL 730 and *Lactobacillus casei* subsp CRL 431 from the Cerela Culture Collection (CRL) and *S.boulardii* in the management of children with persistent diarrhea.

Material and Methods

Patients. This, randomized, double-blind, placebo-controlled study was implemented in the Departamento de Maternidad e Infancia del Hospital A. Posadas, situated in Moron, a community on the Northwestern outskirts of Buenos Aires city, from January 1996 to April 1998. The children were selected from the outpatients department and admitted into a special study ward.

Children of both sexes between 6 to 24 months of age who presented the following characteristics were admitted: (1) a history of frequent loose stools (> 3 per day) for the last consecutive 14 days or more, (2) not being breast fed, (3) no history of allergy to cow´s milk, or no history of treatment with antimicrobial or antidiarrheal agents within the preceding 7 days, (4) an absence of concurrent systemic illness, a weight for age < 60% of the value for the 50 th percentile according to the tables of the American National Center for Health Statistics Standard, or dehydration of more than 10% of body weight (severe), and (5) ability to take oral food. For each child, an informed written consent was required, either from their parents or legal guardian, and the study protocol was approved by the Ethical Review Committee of Hospital A. Posadas.

Patients evaluation. Each patient remained in the hospital for at least 5 days. A complete history was recorded, and physical examination including assessment of dehydration was performed by a physician on admission to hospital (LW). Patients with mild or moderate dehydration were rehydrated *ad libitum* orally or by gastric tube for 4 to 6 hours with the standard WHO/UNICEF sodium- glucose-based oral rehydration salt (ORS) solution before starting the study. The fluid deficit was corrected within four to six hours of admission. After rehydration and until diarrhea stopped, ORS solution was offered according to WHO recommendations as a maintenance therapy.

The patient´s body weight, the amount of oral rehydration solution, the average energy intake, the mean volume of formula consumed, as well as the number and type of stools, (liquid, soft or normal) and clinical symptoms such as vomiting, abdominal distention (abdominal circumference) or colic, were daily recorded by specially trained nursing staff every eight-hours until discharge. Urine was collected separately in urine bags and weighed. At the end of the study, patients who had been discharged from the hospital without a complete clinical recovery were followed up daily either in the hospital or at home via a chart filled out by their parents for 12 days after starting the study.

Feeding was started as soon as children were considered to be fully rehydrated. Subjects were given soft foods from hospital according to their ages, including milk containing lactose, and milk products usually consumed by the child (fermented dairy products were excluded to avoid the effects of substances produced during fermentation process). Children under one year, received jelly, boiled mashed vegetables, potatoes with meat, as well as cooked cereal (rice, maize powder) and vegetable oil. The older children received an ordinary mixed diet. Diets and usual drink were freely given to the children by their mothers and under the supervision of nurses.

When an unformed stool was followed by 2 stools that retains its shape and does not stick to the container (formed stool), diarrhea was considered stopped.

An increase in fecal motion for 3 consecutive 8 hours periods; a recurrence of dehydration of more than 5% of body weight during maintenance oral rehydration therapy, or a recurrence or starting of gastrointestinal symptoms such as vomiting, abdominal distention and colic at any time during the treatment period, indicated a treatment failure.

Tolerability was assessed during each clinical evaluation, and all adverse events were recorded.

Study medication. After admission, children were allocated to receive one of three dietary treatments. Group 1 received pasteurized cow milk, as placebo, group 2 received lyophilized *S. boulardii,* and group 3 received pasteurized cow´s milk containing lyophilized *Lactobacillus casei, and Lactobacillus acidophillus* sp strains CERELA (10^{10}-10^{12} CFU per g). The yeast was reconstituted in sterile distilled water at a concen-tration of 0.1 g/mL (1 g of powder per mL contained 10^{10} CFU of *S. boulardii*) in order to be suspended in pasteurized cow´s milk.

Treatments were given twice daily, at a dose of 175 g during 5 days. Each formula with the same consistence and appearence was supplied in opaque bottles and were given to the children by their mothers under the direct supervision of nursing staff. All study formula were given to children for 5 days. None of the staff had access to the randomization codes.

Laboratory determination. On admission, a fresh stool sample or occasionally a rectal swab was obtained from each of the patients to identify rotavirus and adenovirus by genus-specific enzyme-linked immunosorbent assay (*ELISA* kit, Abbott laboratories) and a standard microbiological culturing was performed for *Escherichia coli, Salmonella, Shigella, Campylobacter and Yersinia*[20]. Specimens were transported in Cary-Blair medium to the microbiology laboratory (Hospital A. Posadas). After reception, they were inmediatly frozen and stored at –20° C until they were assayed (within 10 days). Stools specimens were examined microscopically for the presence of ova and parasites, and a special test for *Giardia lamblia* measured by enzyme-linked immunosorbent assay was performed. The presence of reducing substances in the stools were tested by *Clinitest* (Ames) on admission and on every alternate stool. A pH measurement of every stool was done with pH paper. The osmotic gap was calculated from electrolyte concentration on every stool water during the first 48 hours of study, using the following formula: 290-2([Na+]+[K+]), and stool fat was evaluated by means of a Sudan stain.

Anal swabing was cultivated in a LAPT soft agar medium[20] in order to examine the implantation of lactobacilli in the intestine on admission, after stopping treatment, and even seven days after discontinuing each formula (Cerela).

Venous blood was obtained for determination of electrolytes (Na+, K+, Cl-, HCO3-), glucose, proteins, hematocrit and total and differencial white cell count.

Statistical analysis. Data of the 3 treatment groups were analyzed by means of the non-parametrical U tests of Mann-Whitney and Kruskal- Wallis. To compare the differences between the curves, the Log Rank test was calculated. The sample size was estimated with reference to previous studies, with an assumption of a 50% reduction in stool frequency, a power of 80% and a P value of less than 0.05. (R.Q.).

Results

Patients. Of the 93 children enrolled, 4 were excluded before the final analysis: 2 due to vomiting (both receiving placebo) and 2 due to urinary tract infection (1 receiving *S.boulardii* and 1 receiving *Lactobacillus)*. Five to 8 children were recruited each month.

A total of 89 patients were evaluated: 29 received placebo (group 1), 30 received *S. boulardii* (group 2) and 30 received *Lactobacillus.* The three study groups were comparable in their demographic and clinical characteristics at admission. There were no significant differences among the groups in the distribution of the enteropathogens at admission.

An etiologic agent was isolated in 35 of the 89 (40%) patients evaluated, with rotavirus, with rotavirus in 24 patients (Table 1).

Clinical Results

Number of depositions. Children receiving *S. boulardii* or lactobacilli had a gradual reduction in the number of daily stools, more noticeable after the first day of treatment, compared to those in placebo group. On day 5, the number of daily stools decreased to 2.0 ± 2.0 in the *S. boulardii* and 1.5 ± 0.9 in the lactobacilli group, respectively, in comparison with placebo (5.2 ± 3.0), (p< 0.001) (Fig 1).

TABLE 1.– *Clinical characteristics of patients randomly assigned to receive a placebo-pasteurized milk with no microorganism (group 1),* Saccharomyces boulardii *–pasteurized milk (group 2) or Lactobacillus casei and* Lactobacillus acidophilus *strains Cerela –pasteurized milk (group 3) at admission*

Characteristic	Group 1 (n=29)		Group 2 (n=30)		Group 3 (n=30)	
	Mean	SD	Mean	SD	Mean	SD
Age (mo)	11.9	5.0	11.0	5.6	12.4	5.3
Sex (F/M)	13/14		14/16		13/19	
Weight /age Z score	- 3.1	1.5	-3.0	1.4	- 3.1	1.7
Height /age Z score	- 3.6	2.6	-3.6	2.5	- 3.5	2.4
Duration of diarrhea (d)	22.4	2.2	24.6	2.6	24.8	3.0
Stools passed in previous 24 h (No)	7.5	4.0	7.3	1.5	7.9	3.1
Severity of diarrhea in previous 24 h *	2.5	0.7	2.6	0.8	2.5	0.5
mild	4		4		5	
moderate	14		10		10	
severe	13		15		14	
Hydration status %						
Some dehydration	5.5	0.8	5.0	1.5	4.8	1.4
Malnutrition (No)	6		6		7	
Stool pathogens (No)						
Rotavirus	7		9		8	
E.coli,Salmonella,Shigella	4		4		3	
No isolation	18		17		19	

(mo)= months,(d)=day; (No)=number

**The degree of diarrhea: up to 3 unformed depositions=mild or grade 1; from 3 to 6 depositions=moderate or grade 2; more than 6 depositions= severe or grade 3.*

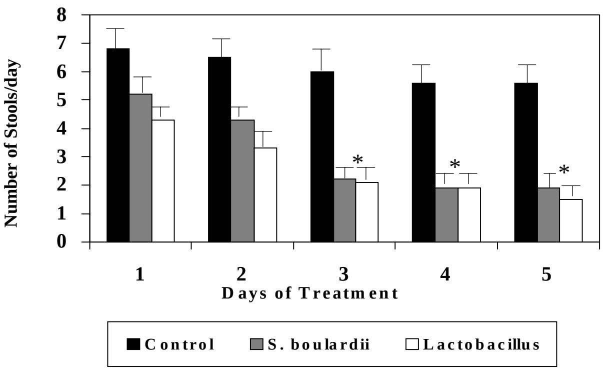

Fig.1.– Bar graphs showing effects of *Lactobacillus* strains Cerela and *Saccharomyces boulardii* treatment in reducing number of stools/day during 5 days in children with persistent diarrhea compared with control group. Results are mean ± SEM * p < 0.001

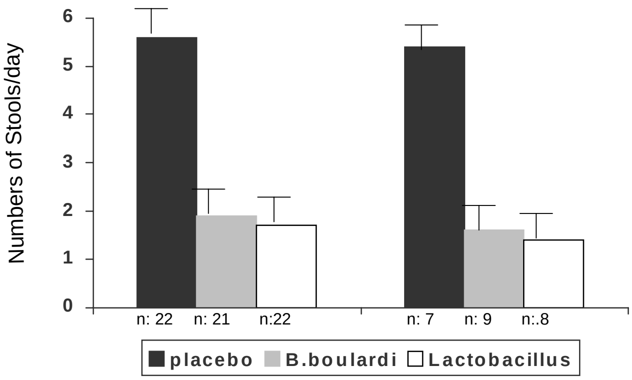

Fig. 2.- Mean SEM number of stools at day 5 of treatment for rotavirus-negative and rotavirus-positive patients. Treatment effect P=0.1

Duration of diarrhea. In a similar way the duration of diarrhea (days mean ± SD) did not differ significantly between children receiving *S. boulardi* (3.8 ± 1.5) or lactobacilli (3.7 ± 1.3) compared with placebo (8.5 ± 4.2); p< 0.005 respectively.

The analysis of patients whose diarrhea did not stop within the 5-day study period were 17% in *S. boulardii* (5/30), 10% in lactobacilli (3/30) and 90% (26/29) in placebo, respectively. In the placebo group most children continued manifesting diarrhea up to 12 days.

With regard to the duration of symptoms the results showed that patients treated with *S. boulardii* or *Lactobacillus* had a significant faster recovery compared with those receiving placebo (days, mean ± SD: 2.4 ± 1.6, 1.5 ± 1.4, 3.2 ± 2.0, p< 0.025 and p< 0.002 respectively) without a significant difference between both groups.

There was no difference between treatments depending on rotavirus status concerning recovery rates. *Saccharomyces boulardii* and *Lactobacillus* versus placebo were found to be similarly effective (p= 0.1) in both rotavirus-positive and rotavirus-negative (Fig 2).

The presence of *Lactobacillus casei* was investigated in the feces of 30 patients from group 3 on day-5 and was detected in 28 patients with a mean fecal count of 10^7 CFU/g. Nineteen of those patients (68%) still showed persistence of lactobacilli in the feces (10^5-10^6 CFU/g), seven days after discharge.

The presence of reducing substances in stools was measured in all patients and there was no significant association between the presence of reducing substances and lack of efficacy of treatments. Stool pH mostly showed values of > 5.6, and the fecal osmotic gap was of 60.6 mOsm/kg (mean SD), suggesting that electrolytes account for most of stools osmolarity (secretory diarrhea) without substantial variation by feeding effects. The presence of excessively large and numerous fat globules by stain were only observed in a few cases (15%).There were no treatment failures neither appearance of symptoms possibly related to treatment.

Discussion

Childhood diarrhea accounts for substantial morbidity and mortality worldwide especially among children from developing countries who are more susceptible as a result of poor nutrition, impaired immune status or frequent exposure to infectious agents[1].

The results of our study established the efficacy of *L. casei and L. acidophillus* strains Cerela and *S. boulardii* in the management of persistent diarrhea in children. Both therapies significantly reduced the number of daily stools, shortened the duration of illness and produced a significant clinical recovery compared with those who received placebo. Within 5 days of starting *Lactobacillus and S. boulardii*, most children recovered completely from their illness and were discharged from the hospital. Only a few patients paid a return visit to hospital within 3 months after hospital discharge, probably indicating a low recurrence of diarrhea at home.

Lactobacillus and *S. boulardii* were found to be similarly effective to decrease the duration of diarrhea in both rotavirus-positive and rotavirus-negative patients although statistical significance for reduction of symptoms may be doubtful probably due to the small number of children with rotavirus being studied. Further studies should be done to ascertain the precise role of these organisms on the gastroenteritis caused by rotavirus and other pathogens.

Rotavirus is a common cause of non-bloody diarrhea in children, accounting for 50-75% of episodes of acute diarrhea in children below 3 years referred to the hospital[21], but it is unknown if this percentage is always present in persistent diarrhea. In our study only 27% of patients had rotavirus. Rotavirus were observed continually on the time course of study.

Exactly how *Lactobacillus* and *S. boulardii* exert their protective effects has not yet been established.

*Lactobacillu*s have traditionally been thought to work by competitive exclusion inhibiting the attachment and growth of pathogenic organisms, restoring the microbial balance in the gastrointestinal tract[22]*. Lactobacillus* may also enhance the immune-modulating effect on the host through Ig A response, or modifying mucosal IL-10 and Th1,Th2 lymphocytes thereby altering the cytokine profile[23]. Moreover, produce a proteinaceous factor(s) that alters epithelial permeability inhibiting bacterial translocation[24] and may also influence the levels of gut mucin glycoproteins[25].

Although any of the postulated mechanisms may lead to a shorter duration of acute or chronic diarrhea, several issues should be kept in mind when *Lactobacillus* have to be used in controlled trials. Those unresolved issues are: 1) strain selection, because not every strain shows efficacy and not every strain has efficacy in each disease[8], 2) dosage[9], 3) frequency of administration, 4) optimal delivery vehicle[6], 5) time passed to develop formed stool and 6) single strain or combinations[26]. Thus it is important to select a well-characterized strain from a well known supplier.

The effect of *Lactobacillus* on diarrhea duration is not modifiable by country of study neither is modifiable when comparing preparations containing living or killed microorganism[9].

Taken orally it does not persist in the gut, so continuous dosing is required[27, 28]. Respect *Lactobacillus* combinations, although the properties and activities of the individual bacterial constituents should be well established, the choice of proved combinations with presumed synergistic activities, used in controlled studies, may offer superior efficacy[26].

In several reports *Lactobacillus casei* and *L. acidophillus* strains CERELA in a fixed combination, have proved to have better efficacy than placebo in randomized, double-blind, clinical trials of patients with various intestinal disorders, and this efficacy has been combined with a similar profile regarding the number of vomiting compared to placebo[20, 28-31].

The protective effect of *S. boulardii* on acute diarrhea has been proposed, based mainly on results from animal studies[32,33], but based on the data of Potholaulakis et al[11] the effect of it on diarrhea appears to be manifested by a secreted product of the yeast, possibly a protease able to remove toxin receptors or brush border glycoproteins involved in adhesion of pathogens to the mucosa.

Green bananas and pectin also seem to be potential therapeutic agents for persistent diarrhea[16]. The underlying mechanism of actions of both, banana and pectin are postulated to be mediated by its high content of amylase-resistant starch which on reaching the colon is fermented by resident bacteria into SCFA. In the colon, SCFA provide energy and induce a trophic effect on the colonic as well as on small bowel mucosa. Similar observations consistent with this hypothesis have been reported by other investigators using other dietary fibers[34].

Nutrition of colonic epithelial cells (colonocytes) is maintained in health by luminal SCFA chiefly by *n*-butyrate[35] and its oxidation by colonocytes is involved in the regulation of sodium and water absorption from colon[36]. Hence, the malnutrition of colonocytes has been linked mainly with a diminished oxidation of SCFA or its luminal absence, supporting the concept that malnutrition of colonocytes plays a part in the pathogenesis of different forms of diarrhea[37]. *Lactobacillus* are also involved in the production of essential mucosal nutrients such as SCFA and amino acids such as arginine, cysteine and glutamine so that they may also participate in the regulation of intestinal functions[38]. Thus, the high luminal concentration of *Lactobacillus casei* in stool recovered from our patients on the seventh day of the discharge could be an important determining factor for the overall clinical course of diarrhea disease. These quality of *Lactobacillus* in addition to well-known trophic effects of *S. boulardi* on intestinal mucosa mediated by the release of polyamine[33] are strongly giving support to further new investigation on these agents in diarrhea.

In conclusion our data show that *L. casei* and *L. acidophillus* strains CERELA and *S. boulardii* significantly reduce the number of depositions, shorten the duration of diarrhea and duration of symptoms in children with persistent diarrhea.

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La más sana lógica indica que donde caben cuatro no pueden entrar veinte, criterio que rige para todas las instituciones de enseñanza del mundo y para todas las de la República Argentina, menos para su Universidad. Admitir en las aulas universitarias a más alumnos de los que puedan educarse, es algo que oscila entre la farsa y la estafa (1956).

Eduardo Braun Menéndez (1903-1959)

Lactobacillus reuteri (L. reuteri) is a well-studied probiotic bacterium that can colonize a large number of mammals. In humans, L. reuteri is found in different body sites, including the gastrointestinal tract, urinary tract, skin, and breast milk.Â Several beneficial effects of L. reuteri have been noted. First, L. reuteri can produce antimicrobial molecules, such as organic acids, ethanol, and reuterin.Â In children with atopic dermatitis, where the impairment of intestinal barrier function has been positively correlated with disease pathogenesis (De Benedetto et al., 2011), treatment with L. reuteri DSM 12246 (and L. rhamnosus 19070-2) significantly reduced the frequency of GI symptoms while decreasing the lactulose to mannitol ratio (Rosenfeldt et al., 2004), which reflects the reversal of a. Open access peer-reviewed chapter. Saccharomyces cerevisiae var. boulardii â€“ Probiotic Yeast. By Marcin Åukaszewicz.Â For example, Cheplin and Rettger (1920)[1] demonstrated that Metchnikov's strain, today called Lactobacillus delbrueckii subsp. bulgaricus, could not live in the human intestine. A scientific discussion to be constructive needs to forge and define new argued ideas.Â In developing countries, mortality due to acute diarrhea, especially in children, is alarmingly high. In contrast, in developed countries, mortality caused by diarrheal diseases may be considered marginal, yet these disorders are burdensome and widespread, having important economic impact on the society.Â 4. Effect of Sb on the virulence factors of Candida albicans. Saccharomyces boulardii is a tropical species of yeast first isolated from lychee and mangosteen fruit in 1923 by French scientist Henri Boulard. Although early reports described distinct taxonomic, metabolic, and genetic properties,[1] S. boulardii is a strain of S. cerevisiae, sharing >99% genomic relatedness, giving the synonym S. cerevisiae var boulardii. A type strain is Hansen CBS 5926.[2][3][4].Â that S. boulardii is effective in reducing the risk of AAD in children and adults.[15] Lactobacillus rhamnosus or Saccharomyces boulardii at high doses (more than 5 billion colony-forming units/day) is moderately effective (with no serious side effects) for the prevention of AAD in children and might also reduce the duration of diarrhea.[16]. Clostridium difficile infection[edit]. Saccharomyces boulardii is POSSIBLY SAFE for children when taken by mouth appropriately. However, diarrhea in children should be evaluated by a healthcare professional before using Saccharomyces boulardii. Pregnancy and breast-feeding: There is not enough reliable information about the safety of taking Saccharomyces boulardii if you are pregnant or breast feeding. Stay on the safe side and avoid use.Â AS, B. and LP, S. Effect of probiotic containing Saccharomyces boulardii on experimental ochratoxicosis in broilers: hematobiochemical studies. J Vet.Sci 2004;5(4):359-367. View abstract. (2003) Effect of Lactobacillus strains and Saccharomyces boulardii on persistent diarrhea in children. Medicina (B Aires) 63, 293â€“298.Google Scholar PubMed. 20Tjon, WE, Ten, A & Wolters, M (2004) Infant crying diary: a useful aid in distinguishing between normal and excessive crying behavior (article in Dutch). Ned Tijdschr Geneeskd 148, 257â€“260.Google Scholar. 21Herngreen, WP, van Buuren, S, van Wieringen, JC, et al. (1994) Growth in length and weight from birth to 2 years of a representative sample of Netherlands children (born in 1988â€“89) related to socioeconomic status and other backgr...Â Safety and persistence of orally administered human Lactobacillus sp. strains in healthy adults. Beneficial Microbes, Vol. 2, Issue. 1, p. 79.