

Probiotics as alternative medical treatment in gastrointestinal diseases

Probiotika als alternative medizinische Behandlungsmethode bei Gastrointestinalerkrankungen

M. HANDSCHUR, J. ZWIELEHNER, A.G. HASLBERGER, V. ABRATT, S. REID

Summary

In the late 19th century, microbiologists identified microflora in the gastrointestinal tracts of healthy individuals that differed from those found in diseased individuals. The beneficial microflora found in the gastrointestinal tract was termed probiotics. Probiotics are living microorganisms proven to exert health-promoting influences in humans and animals. Interest continues today as recent technological advances have enabled microorganisms to be isolated and colonised to determine their specific therapeutic properties. The World Health Organization deems probiotics to be the next-most important immune defence system when commonly prescribed antibiotics are rendered useless by antibiotic resistance. The use of probiotics in antibiotic resistance is termed microbial interference therapy. With increasing understanding that beneficial microbes are required for health, probiotics may become a common therapeutic tool used by health-care practitioners in the not too distant future. This review illuminates the use of probiotics as therapeutic treatment in gastrointestinal-associated diseases.

Keywords:

Gastrointestinal tract, probiotics, gut flora

Zusammenfassung

Ende des 19. Jahrhunderts fanden Mikrobiologen heraus, dass sich die Darmflora von gesunden Personen deutlich von jener kranker Personen unterscheidet. Keime dieser nützlichen Mikroflora des Gastrointestinaltraktes wurden als Probiotika bezeichnet. Probiotika sind lebende Mikroorganismen, welche einen nachweislichen gesundheitsfördernden oder -erhaltenden Effekt auf den Menschen oder Tiere ausüben.

Das Interesse an diesen Organismen ist bis heute ungebrochen, neue Techniken wurden entwickelt, um diese Keime zu isolieren, zu kolonisieren und ihr therapeutisches Potential zu bestimmen. Die Weltgesundheitsorganisation erachtet Probiotika als das nächstwichtigste Verteidigungssystem des Immunsystems, wenn gewöhnlich verschriebene Antibiotika durch Resistenzbildung unwirksam sind. Die Anwendung von Probiotika gegen Antibiotikaresistenz wird als mikrobielle Interferenztherapie bezeichnet. Mit wachsendem Verständnis, dass nützliche Mikroorganismen für die menschliche Gesundheit erforderlich sind, werden Probiotika mehr und mehr ein therapeutisches Instrument in naher Zukunft. Dieser Artikel beleuchtet die Verwendung von Probiotika als therapeutische Maßnahme bei Gastrointestinalerkrankungen und -problemen.

Schlüsselwörter:

Gastrointestinaltrakt, Probiotika, Darmflora

Introduction

The assemblages of bacteria resident in the gastrointestinal tract provide a first line of defence that can exclude invading pathogens, reduce the proliferation of opportunistic pathogens already resident in the gastrointestinal tract (GIT), and reduce the availability, carcinogenicity, or toxicity of noxious chemicals. The mucosa of the GIT is a second, multilayered line of defence that includes the mucous and other secretions, the epithelial cells, and immune-associated cells

scattered within and under the epithelium. The final line of defence contends with pathogens or noxious chemicals that transcend the mucosal barrier and enter the host and consists of the innate and acquired components of the systemic immune system and the xenobiotic metabolizing enzymes. The lactic acid producing bacteria (LAB) are considered to be immunomodulatory and directly or indirectly influence the GIT and systemic defence functions [1, 2].

The human gut is colonised by 10^{12} cells by 1 g dry weight, which is a complex ecosystem. It contains

about 1.2 kg bacteria and a smattering of yeasts. In utero the intestine ought to be sterile, but at birth the baby acquires bacteria from the maternal birth canal. Babies delivered by caesarean section are initially colonised by bacteria picked up from the hospital environment, thereby affecting the overall composition of their microflora. There is some evidence to suggest that babies delivered by natural birth benefit from their intestinal microflora by a reduced risk of necrotising enterocolitis. One explanation may be that vaginally delivered children are sooner colonised by Enterobacteria like *E. coli*; these bacteria prepare the environment for other beneficial microbiota [3]. The ratio of different groups of microorganisms is relatively constant, but different between human beings. An important change in diversity of microbial flora occurs in immune-compromised patients and people with gut and metabolism problems. Exogenous and endogenous factors like nutrition and medication influence the flora diversity [4]. Lactobacilli are known to produce bacteriocines and have an immune-relevant, health supporting function against potential pathogenic species [5, 6].

The distribution of mucosa-associated bacteria, bifidobacteria and lactobacilli and closely related lactic acid bacteria, were analysed in biopsy samples from the ascending, transverse, and descending parts of the colon. Denaturant Gradient Gel Electrophoresis (DGGE) profiles obtained with lactobacillus group-specific primers were complex and varied with host and sampling site in the colon. The overall bacterial community varied with host but not sampling site [7] and observed host-specific DGGE profiles of the mucosa-associated bacterial community in the colon support the hypothesis that host-related factors are involved in the determination of the GIT microbial community [8].

Colonisation

The protective and immune barrier of the human GIT is diverse. It includes the epithelial layer, the mucous layer, the mechanics of peristalsis and desquamation, and actions of secretory IgA, all of which impact bacterial attachment. After attachment, colonic bacteria are prevented from mixing with the host's eukaryotic cells by the epithelial layer, which acts as a vital barrier to invasion [7]. The barrier's healthy structure and proper functioning are essential for the health of the human host. In these complex systems the delicate balance between the GIT and the microflora is cooperatively maintained.

Before birth, the human GIT is sterile and the first colonisation takes place while birth by the bacterial communities of the birth canal and then by breast

feeding [9]. The gut flora of breast-fed children has a higher lactobacilli diversity and a higher amount of bifidobacteria than bottle-fed children and a lower risk for gastrointestinal diseases like diarrhea. The breast-fed infant contains a colon population of 90 % bifidobacteria with some Enterobacteriaceae and enterococci present, but virtually no bacteroides, staphylococci, lactobacilli, or clostridia [9].

After weaning, uptake of bacteria with foods may contribute to the population of commensal bacteria in the GIT and their immune functions [10].

The type and number of indigenous microflora increase distally along the length of the GIT. Favourable characteristics found in probiotics colonising the human gut are exhibited by *Lactobacillus plantarum*, *L. rhamnosus*, *L. reuteri*, and *L. agilis*. However, these lactobacilli species are scarce in people living in industrialised nations. *L. plantarum* is carried by 25% of the general population in the United States, whereas nearly 100% of the population in Africa and Asia are colonised with favourable lactobacillus species. The most significant reason is that a western diet contains drastically decreased amounts of lactobacilli [11].

Overgrowth of one bacterial species or imbalances in microflora resulting from a disturbed mucosal layer can alter digestive function, intestinal products, and/or immunological function [7]. In addition, a defective epithelial layer can allow bacteria to gain entry into the human host. This breach can arouse an inflammatory response in the host that has the potential to further alter normal function.

Function of the gut

Colonisation of the gut with appropriate microflora contributes to its ability to function normally. Commensal microflora by-products contribute to the health of the intestinal tract and include short-chain fatty acids (SCFAs), polyamines, vitamins, antioxidants, and amino acids [8].

Probiotics modulate not only the endogenous flora of the GIT, but also the immune system. Lactobacilli augment both cellular and humoral immunity [12]. Lactic acid-producing bacteria stimulate various aspects of the immune system, including phagocytic function of macrophages, natural killer cells, monocytes, and neutrophils.

Another example of a probiotic enhancing the immune response can be seen in the activation of the reticuloendothelial system and complement cascade by *Saccharomyces boulardii* [9]. Clearly, interaction of commensal gastrointestinal flora with the gut-associated immune system is an important key in maintaining normal immune function.

Microflora and antibiotics

Antibiotics were found to influence on the microflora mainly in three ways: They can disrupt the ecological balance and allow overflow of species with potential pathogenicity such as enterococci, *Clostridium* sp. or yeasts. A second consequence is the development of antibiotic resistances among bacteria in the normal flora, the third effect is the reduction of colonisation resistance, i.e. the resistance of host against implantation of new, possible pathogenic microorganisms. Meropenem and Cefpirom were shown to decrease the number of *Escherichia coli* species (*E. coli* sp.) and to increase *Enterococcus* sp. and *Candida* sp. significantly. The use of probiotics in antibiotic resistance is termed microbial interference therapy. With increasing understanding that beneficial microbes are required for health, probiotics may become a common therapeutic tool used by healthcare practitioners in the not too distant future [13].

Diarrhea is a well-known complication of antibiotic therapy caused by quantitative and qualitative changes in the intestinal flora. Estimates of the risk of antibiotic-associated diarrhea vary between 5 and 30%, depending on the antibiotic administered, and beta-lactams are associated with a somewhat higher risk than other antibiotic classes [14, 15].

For animal breeding, antibiotics were added as fed additive for fattening and prophylactic as well as therapeutic therapy. Since 2006 all antibiotics for fattening and prophylactic use are prohibited in the European Union (EU) [16]. Probiotics are an attractive and "natural" alternative for fattening, prophylaxis as well as for therapy to restore the disordered gut flora after and while a medical necessary antibiotic treatment.

The effect of probiotics on pathogenic bacteria

Colonisation and growth of pathogenic and toxin-producing bacteria in the human gut results in various clinical problems: the most common are diarrhea, mucosal inflammation, bacterial translocation and the efflux of bacterial toxins in the bloodstream. This may lead to serious consecutive diseases and the need of an intensive antibiotic treatment that in turn affects the non-pathogenic, "healthy" gut flora too [17, 18]. Probiotics have been shown as prophylactic and therapy supporting additive to prevent or silent colonisation and growth of pathogens [19].

Probiotics reduce plasma levels of bacterial endotoxin concentrations, at least in part, by inhibiting trans-

location of bacteria across the gastrointestinal lumen into the bloodstream [20]. Administration of *Lactobacillus* sp. to Interleukin-10 knockout mice decreased translocation of bacteria to extra intestinal sites and reduced myeloperoxidase concentrations, often associated with inflammation in the bowel [21].

There are several ways probiotic microflora can prevent pathogenic bacteria from adhering and colonising gut mucosa. Probiotics disallow colonisation by disease-provoking bacteria through competition for nutrients, immune system up-regulation, production of antitoxins, and up-regulation of intestinal mucin genes [22]. Increased mucous production prevents adherence and colonisation by competing microflora, thereby preventing imbalances.

The inhibition of pathogenic bacteria by probiotics is an orchestrated combination of structure and function. Probiotic bacteria produce a variety of substances that are inhibitory to both gram-positive and gram-negative bacteria. These inhibitory substances include organic acids, hydrogen peroxide and bacteriocins against other, potentially pathogenic bacteria. Therefore, the practice of combining probiotics needs to include beneficial bacteria that do not inhibit other included strains [23].

Animal experiments showed that an oral-fed probiotic *E. faecium* colonises the gut and alters the gut flora qualitative and quantitative. Potential pathogenic strains disappeared while "healthy" strains appeared [24].

Studies have shown that *S. boulardii* protects animals against *C. difficile* intestinal disease by degradation of the toxin receptor on the intestinal mucosa [25, 26].

Helicobacter pylori have recently been shown to be an important etiologic agent of chronic gastritis as well as gastric and duodenal ulcers. It has also been postulated that chronic *H. pylori* infection leads to stomach carcinoma. *Lactobacillus* has been shown to be antagonistic to *H. pylori* both *in vitro* and in a gnotobiotic murine model [20, 27].

The finding of rod-shaped bacteria attached to the small intestinal epithelium of some untreated and treated **celiacdisease** patients, but not to the epithelium of healthy controls, ignites the notion that bacteria may be involved in the pathogenesis of celiac disease [28].

Several probiotics have been examined for their ability to prevent **traveller's diarrhea**, including *Lactobacillus*, *Bifidobacterium*, *Streptococcus* and *Saccharomyces* [29].

The effect of probiotics on **antibiotic-induced diarrhea** was shown in several studies but may differ in order to given antibiotics. In general, good results have been shown by the oral treatment with

Bifidobacterium lactis, *Streptococcus thermophilis*, *Lactobacillus reuteri*, *Lactobacillus rhamnosus* and *Enterococcus faecium* [30, 31, 32].

Patients receiving **nasogastric tube feeding** frequently develop diarrhea. The mechanism of the diarrhea is not known, but investigators postulate that enteral feeding causes changes in normal flora that result in altered carbohydrate metabolism and subsequent diarrhea [33]. Two separate studies (both placebo-controlled and double-blind) demonstrated a significant reduction in diarrhea in these patients when they were given *S. boulardii* [34, 35].

Acute **rotavirus diarrhea** is associated with an enhanced immune response to rotavirus. In a double-blind study, *L. rhamnosus GG* has been shown as treatment for rotavirus-induced diarrhea and could reduce the morbidity by dehydration. Intervention with *L. rhamnosus* shortens the time of intravenous rehydration [36].

In patients suffering on **HIV**, the gut flora, which is a big part of the immune system, is often disturbed by the medical necessary treatment with antibiotics and the HI virus itself makes the gut mucosa more permeable. Both leads to heavy diarrhea and so to an enormous loss of body water and gut bacteria [37, 38]. Pathogenic bacteria and food-associated potential pathogenic microorganisms may colonise the compromised gut and lead to secondary infections. Studies with oral-fed probiotics (e.g. *L. reuteri* or *S. cerevisiae*) show that HIV and antibiotic-associated diarrhea can be silenced and the gut flora can be changed in a positive way [39]. Using modern molecular methods, a shift in the bacterial population of the gut flora and a higher diversity of lactobacilli was seen in HIV-associated diarrhea and clinical symptoms were silenced by the oral treatment with *L. reuteri* [40].

Pouchitis is a complication of ilea reservoir surgery occurring in 10 to 20% of the patients who undergo surgical treatment for chronic ulcerative colitis. Bacterial overgrowth in the pouch, resulting in degradation of the mucus overlaying the epithelial cells [41, 42, 43]. This results in inflammation and symptoms that include bloody diarrhea, lower abdominal pain and fever. Investigators have postulated that *Lactobacillus GG* may be an effective therapeutic agent for paucities because it does not demonstrate mucus-degrading properties [43].

Especially in the developed world, people suffer from a congenital deficiency of the enzyme β -Galactosidase. This deficiency results in an inability to digest

and absorb lactose and so to a **lactose intolerance**. Bacteria metabolise the lactose and the resulting by-products cause abdominal cramping, bloating, diarrhea and nausea. Lactase-positive strains of bacteria (e.g. lactobacillus, bifidobacterium and streptococcus) are commonly added to pasteurised dairy products to increase digestibility of the lactose present in the dairy product [44, 45, 46]. There are two probable mechanisms by which the addition of these bacteria is beneficial, i.e. the reduction of lactose in the dairy product through fermentation and the replication of the probiotic in the gastrointestinal tract, which releases lactase.

The group around *Haskey* reported a case of a paediatric **ulcerative colitis** patient who showed increased length of remission, resolution of symptoms, and improved quality of life following the administration of symbiotic therapy [47].

Summary

Probiotics do have a prophylactic and therapeutic potential [48]. In patients ongoing an immune suppressive or antimicrobial therapy, the prophylactic intake of probiotics might prevent diarrhea, gut disorders, the overgrowth of one bacterial species, clinical complications caused by toxins and bacterial translocation. Probiotics are an attractive alternative to antibiotics in animal breeding and permanent or prophylactic treatment with antibiotics of patients as well as additional treatment against various diseases.

However, promising ongoing research is done in the field of probiotics as medical treatment and prophylaxis in gastrointestinal disorders, but more research is necessary in respect of microbial treatment in heavy underlying diseases as HIV infections and cancer.

References

- [1] *Isolauri E., Ouwehand A.C., Laitinen K.*: Novel approaches to the nutritional management of the allergic infant. *Acta Paediatr* 2005; 94: 110–114.
- [2] *Haller D., Serrant P., Granato D., Schiffrin E.J., Blum S.*: Activation of human NK cells by staphylococci and lactobacilli requires cell contact-dependent costimulation by autologous monocytes. *Clin Diagn Lab Immunol* 2002; 29 (3): 649–657.
- [3] *Reid G.*: When microbe meets human. *Clin Infect Dis* 2004; 15 (39): 827–830.
- [4] *Elmadfa I., Leitzmann C.*: Ernährung des Menschen. 3: Ulmer-Verlag, 1998.

- [5] *Montalto M.* et al.: Probiotics: history, definition, requirements and possible therapeutic applications. *Ann Ital Med Int* 2002; 17 (3): 157–165.
- [6] *Bernbom N., Licht T.R., Saadbye P., Vogensen F.K., Norrung B.*: Lactobacillus plantarum inhibits growth of *Listeria monocytogenes* in an in vitro continuous flow gut model, but promotes invasion of *L. monocytogenes* in the gut of gnotobiotic rats. *Int J Food Microbiol* 2006; 15 (108): 10–14.
- [7] *Walker W.A.*: Role of nutrients and bacterial colonization in the development of intestinal host defense. *J Pediatr Gastroenterol Nutr* 2000; 30: 2–7.
- [8] *Pryde S.E., Duncan S.H., Hold G.L., Stewart C.S., Flint H.J.*: The microbiology of butyrate formation in the human colon. *FEMS Microbiol Lett* 2002; 17 (2): 133–139.
- [9] *Vanderhoof J.A., Young R.J.*: Use of probiotics in childhood gastrointestinal disorders. *J Pediatr Gastroenterol Nutr* 1998; 27: 323–332.
- [10] *Lu L., Walker A.W.*: Pathologic and physiologic interactions of bacteria with the gastrointestinal epithelium. *Am J Clin Nutr* 2001; 73 (6): 1124–1130.
- [11] *Bengmark S.*: Colonic food: pre- and probiotics. *Am J Gastroenterol* 2000; 95: 5–7.
- [12] *Vanderhoof J.A.*: Probiotics: future directions. *Am J Clin Nutr* 2001; 73: 1152–1155.
- [13] *Morte D.*: Antibiotic resistance. *Bioforum Europe* 2003; 3: 1–3.
- [14] *Ledergerber U., Regula G., Bissig G.B., Stärk K.D.C.*: Risk factors for antibiotic resistance from raw poultry meat in Switzerland. *BMC Public Health* 2003; 3: 1–9.
- [15] WHO: Antimicrobial resistance. Fact sheet N° 194 2002.
- [16] *Collignon P.*: Antibiotics resistance. *Med J Aust* 2002; 16 (177): 325–329.
- [17] *Park J.H.* et al.: Enteroendocrine cell counts correlate with visceral hypersensitivity in patients with diarrhoea-predominant irritable bowel syndrome. *Neurogastroenterol Motil* 2006; 18: 539–546.
- [18] *Quigley E.M.*: Bacterial flora in irritable bowel syndrome: role in pathophysiology, implications for management. *J Dig Dis* 2007; 8: 2–7.
- [19] *Quigley E.M., Quera R.*: Small intestinal bacterial overgrowth: roles of antibiotics, prebiotics, and probiotics. *Gastroenterology* 2006; 130 (2): 67–69.
- [20] *Aiba Y., Suzuki N., Kabir A.M., Takagi A., Koga Y.*: Lactic acid-mediated suppression of *Helicobacter pylori* by the oral administration of *Lactobacillus salivarius* as a probiotic in a gnotobiotic murine model. *Am J Gastroenterol* 1998; 93 (11): 2097–2101.
- [21] *Madsen K.L., Doyle J.S., Jewell L.D., Tavernini M.M., Fedorak R.N.*: Lactobacillus species prevents colitis in interleukin 10 gene-deficient mice. *Gastroenterology* 1999; 116 (5): 1107–1114.
- [22] *Mack D.R., Michail S., Wei S., McDougall L., Hollingsworth M.A.*: Probiotics inhibit enteropathogenic *E. coli* adherence in vitro by inducing intestinal mucin gene expression. *Am J Physiol Gastrointest Liver Physiol* 1999; 276: 941–950.
- [23] *Percival R.S., Marsh P.D., Challacombe S.J.*: Age-related changes in salivary antibodies to commensal oral and gut biota. *Oral Microbiol Immunol* 1997; 12 (1): 57–63.
- [24] *Handschr M., Jusek C., Jölli D., Haslberger A.G.*: Beeinflussung der Darmflora durch Probiotika – Analyse mittels molekularer Methode. *ernährung/nutrition* 2005; 29 (12): 497–501.
- [25] *Castagliuolo I., LaMont J.T., Nikulasson S.T., Pothoulakis C.*: *Saccharomyces boulardii* protease inhibits *Clostridium difficile* toxin A effects in the rat ileum. *Infect Immun* 1996; 64 (12): 5225–5232.
- [26] *Castagliuolo I., Riegler M.F., Valenick L., LaMont J.T., Pothoulakis C.*: *Saccharomyces boulardii* protease inhibits the effects of *Clostridium difficile* toxins A and B in human colonic mucosa. *Infect Immun* 1999; 67 (1): 302–307.
- [27] *Kabir A.M.* et al.: Prevention of *Helicobacter pylori* infection by lactobacilli in a gnotobiotic murine model. *Gut* 1997; 41 (1): 49–55.
- [28] *Sollid L.M., Gray G.M.*: A role for bacteria in celiac disease? *Am J Gastroenterol* 2004; 99 (5): 905–906.
- [29] *Hilton E., Kolakowski P., Singer C., Smith M.*: Efficacy of *Lactobacillus GG* as a Diarrheal Preventive in Travelers. *J Travel Med* 1997; 4 (1): 41–43.
- [30] *Schröder O., Gerhard R., Stein J.*: Antibiotic-associated diarrhea. *Z Gastroenterol* 2006; 44 (2): 193–204.
- [31] *Lindo J.F.* et al.: Intestinal parasitic infections in human immunodeficiency virus (HIV)-positive and HIV-negative individuals in San Pedro Sula, Honduras. *Am J Trop Med Hyg* 1998; 58: 431–435.

- [32] *Gaukel V., Spieß W.E.L.*: 3rd Karlsruhe Nutrition Symposium European Research towards Safer and Better Food Review and Transfer Congress. Berichte der Bundesforschungsanstalt für Ernährung. 1998.
- [33] *Guenter P.A.* et al.: Tube feeding-related diarrhea in acutely ill patients. *JPEN J Parenter Enteral Nutr* 1991; 15 (3): 277–280.
- [34] *Bleichner G., Blehaut H., Mentec H., Moyse D.*: *Saccharomyces boulardii* prevents diarrhea in critically ill tube-fed patients. A multicenter, randomized, double-blind placebo-controlled trial. *Intensive Care Med* 1997; 23 (5): 517–523.
- [35] *Tempe, J.D.* et al.: Prevention of diarrhea administering *Saccharomyces boulardii* during continuous enteral feeding. *Sem Hop* 1983; 59: 1409–1412.
- [36] *Oksanen P.J.* et al.: Prevention of travellers' diarrhoea by *Lactobacillus GG*. *Ann Med* 1999; 22 (1): 53–56.
- [37] *Beaugerie L.*: Assigning the cause of diarrhea and enterocolitis to drugs. Current approach and outlook for improvement. *Gastroenterol Clin Biol* 1998; 22 (10): 773–777.
- [38] *Rolfe R.D.*: The role of probiotic cultures in the control of gastrointestinal health. *J Nutr* 2000; 130 (2): 396–402.
- [39] *Herbrecht R., Nivoix Y., Fohrer C., Natarajan-Ame S., Letscher-Bru V.*: Management of systemic fungal infections: alternatives to itraconazole. *J Antimicrob Chemother* 2005; 56 (1): 39–48.
- [40] *Handschr M., Reid S., Abratt V., Haslberger A.G.*: Molecular investigation of the influence of oral fed *Lactobacillus reuteri* on the gut microbiota of HIV infected infants – a pilot study. *JFAE* 2007 Vol. 5 (3&4): 43–47.
- [41] *Madden M.V., Farthing M.J., Nicholls R.J.*: Inflammation in ileal reservoirs: 'pouchitis'. *Gut* 1990; 31 (3): 247–249.
- [42] *Mortensen N.*: Restorative proctocolectomy – the pouch operation: good or bad? *Scand J Gastroenterol* 1992; 192: 130–135.
- [43] *Ruseler-Van Embden J.G., van Lieshout L.M., Gosselink M.J., Marteau P.*: Inability of *Lactobacillus casei* strain GG, *L. acidophilus*, and *Bifidobacterium bifidum* to degrade intestinal mucus glycoproteins. *Scand J Gastroenterol* 1995 Jul; 30 (7): 675–680.
- [44] *Gilliland S.E., Kim H.S.*: Effect of viable starter culture bacteria in yogurt on lactose utilization in humans. *J Dairy Sci* 1984; 67 (1): 1–6.
- [45] *Kim H.S., Gilliland S.E.*: *Lactobacillus acidophilus* as a dietary adjunct for milk to aid lactose digestion in humans. *J Dairy Sci* 1983; 66 (5): 959–966.
- [46] *Pettoello M.M., Guandalini S., Ecuba P., Corvino C., di Martino L.*: Lactose malabsorption in children with symptomatic *Giardia lamblia* infection: feasibility of yoghurt supplementation. *J Pediatr Gastroenterol* 1989; 9: 295–330.
- [47] *Haskey N.D.W.*: Synbiotic therapy: a promising new adjunctive therapy for ulcerative colitis. *Nutr Rev* 2006; 64 (3): 132–138.
- [48] *Pessi T., Sutas Y., Marttinen A., Isolauri E.*: Probiotics reinforce mucosal degradation of antigens in rats: implications for therapeutic use of probiotics. *J Nutr* 1998; 128 (12): 2313–2318.

Address of the authors:

Michael Handschr^{1,2 *}
 Jutta Zwieler²
 Alexander G. Haslberger²
 Vallery Abratt³
 Sharon Reid³

¹ Ludwig-Boltzmann Institute for Leukemia research and Haematology Hanusch Hospital Vienna

² Dep. nutritional science University Vienna

³ Dep. Molecular and Cell Biology University Cape Town

* corresponding author
 michael.handschr@univie.ac.at



SOS-PATEN GESUCHT!

Ja, ich will Pate werden!

Helfen Sie den Kindern, werden Sie SOS-Kinderdorf-Pate!

Mit freundlicher Unterstützung von Coca-Cola, INTERSPAR, Marionnaud und NIVEA. Danke!

Rufen Sie uns an – Sylvia Fink und Hans Gregoritsch informieren Sie gerne unter unserer kostenlosen Tel.-Nr. 0800 / 80 80 81 oder unter www.sos-kinderdorf.at