

Lactobacillus casei strain Shirota (Yakult)

Research Update for Healthcare Professionals

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Lactobacillus casei strain Shirota – Research Update

IMPROVEMENT IN INTESTINAL HEALTH

1. A probiotic fermented milk drink containing *Lactobacillus casei* strain Shirota improves stool consistency of subjects with hard stools.

Tilley L *et al* (2014) *Int J Probiotics Prebiotics* 9(1): 31.

Summary

The aim of this study was to investigate the effect of a fermented milk drink containing *Lactobacillus casei* Shirota (LcS) on the bowel habit (with emphasis on stool consistency) of subjects suffering from hard stools. The ability of the probiotic strain (LcS), to survive throughout the gastrointestinal tract was also evaluated.

A double-blind, placebo-controlled, randomized study was carried out over an eight-week period in subjects with symptoms of constipation (n=120). All subjects received 65 ml/day of a probiotic fermented milk drink containing LcS or a placebo. Patients completed a questionnaire to assess the consistency of their stools. Half the study population was also evaluated for the survival of the probiotic strain (LcS) using (i) culture and (ii) LcS specific monoclonal antibody to identify the cultured colonies as LcS (ELISA).

There was a significant decrease in stool hardening during the probiotic intervention period (fermented milk drink containing LcS). The benefit in clinical effect was paralleled with the microbiological effect as the number of viable LcS bacteria in the faeces increased during the probiotic consumption period and decreased during the wash-out period.

2. Perioperative symbiotic therapy in elderly patients undergoing gastroenterological surgery: A prospective, randomized control trial.

Okazaki M, Matsukuma S *et al* (2013) *Nutr* 29:1224-1230.

Summary

Forty-eight patients completed the trial that includes 25 in the Synbiotic group (S group patients received Biolactis powder containing living *Lactobacillus casei* strain Shirota and BBG-01, a live *Bifidobacterium breve* strain Yakult as well as galacto-oligosaccharides) and 23 in the Control group

(C group). Synbiotic therapy significantly maintained the status of *Bifidobacterium* and *Lactobacillus* and the number of *Enterobacteriaceae*, *Staphylococcus* and *Pseudomonas* was significantly decreased. The total organic acid and short-chain fatty acid concentrations were increased and the pH was markedly decreased in the S group compared to the C group. The incidence of postoperative infectious complications was 12% in the S group and 36% in the C group, however, the difference did not reach statistical significance (P=0.06).

This study concludes that synbiotic therapy improved the intestinal microbial environment, and might decrease the incidence of infectious complications in elderly subjects.

3. Maintenance of healthy intestinal microbiota in women who regularly consume probiotics.

Tsuji H, Chonan O, Suyama Y *et al* (2014) *Int J Probiotics Prebiotics* 9(1/2):31-38.

Summary

Lactobacillus casei strain Shirota (LcS) and *Bifidobacterium breve* strain Yakult (BbrY) are probiotics that are found to have beneficial effects on human health.

The intestinal microbiota of 91 staff working in Yakult was compared with 98 women from the general population who were not in the habit of consuming probiotics. It was observed that

- a) Frequency of detection of LcS and BbrY in the feces was higher in the staff than in the general group of women;
- b) Counts of bacteria, including *Bifidobacterium*, *Clostridium coccooides* group, *Bacteroides fragilis* group, *Enterococcus* and *Lactobacillus* was significantly higher in the staff than in the general group, whereas the frequency of detection and counts of *Prevotella*, *Staphylococcus*, and *C.perfringens* was significantly lower in the staff than in the general group;
- c) Stools of the staff were significantly softer than those of the general group.

This study shows that regular consumption of probiotics improves the intestinal microbiota and bowel habit in these staff.

4. Effect of probiotics on human blood urea levels in patients with chronic renal failure.

Miranda Alatrister PV, Urbina Arronte R *et al* (2014) *Nutr Hosp Mar* 1:29(3):582-90.

Summary

Patients with Chronic Kidney Disease (CKD) show an increase in bowel aerobic bacteria that produce uremic toxins and decreased anaerobic bacteria such as *Bifidobacteria* and *Lactobacillus*. This study was conducted to evaluate the effectiveness of two different *Lactobacillus casei* strain Shirota (LcS) doses in achieving a decrease in urea concentrations in at least 10% in patients with KDOQI stage 3 and stage 4 CKD.

A simple randomized, controlled clinical trial was conducted on outpatients treated at the National Institute of Medical Sciences and Nutrition Salvador Zubirán in México D.F.

Patients were provided LcS as follows: Group A: 8×10^9 Colony-Forming Units (CFU) and Group B: 16×10^9 CFU. Patients visited every 15 days to obtain 15 or 30 bottles of LcS during two months. Patients were followed-up for eight weeks; baseline and final samples were obtained to calculate the basal and final concentrations of blood urea and serum creatinine (CrS). During the follow-up both groups consumed a diet of 30 kcal/kg/weight and 0.8 g/kg/weight of protein.

Thirty patients with CKD were evaluated. When analyzing the percentage change between the different doses, a decrease $> 10\%$ was found in the blood urea concentrations for patients treated with the 16×10^9 dose, which was significant with respect to the baseline measurement.

IMMUNE MODULATION

1. Probiotic modulation of dendritic cell function is influenced by ageing.

You J, Dong H, Mann ER *et al* (2014) *Immunobiology* 219(2):138-48.

Summary

Dendritic cells (DCs) are critical for the generation of T-cell responses and their function may be modulated by probiotics, which confer health benefits in immunocompromised individuals, such as the elderly.

This study investigated the effects of four probiotics, *Bifidobacterium longum* bv. infantis CCUG 52486, *B. longum* SP 07/3, *Lactobacillus rhamnosus* GG (L.GG) and *L. casei* Shirota (LcS), on DC function in an allogeneic Mixed Leucocyte Reaction (MLR) model using DCs and T-cells from young and older donors in different combinations.

All four probiotics enhanced expression of CD40, CD80 and CCR7 in both young and older DCs, but enhanced cytokine production (TGF- β , TNF- α) by old DCs only.

LcS induced IL-12 and IFN γ production by DC to a greater degree than other strains, while *B. longum* bv. infantis CCUG 52486 favoured IL-10 production. Stimulation of young T cells in an allogeneic MLR with DC was enhanced by probiotic pretreatment of old DCs, which demonstrated greater activation (CD25) as compared to untreated controls. However, pretreatment of young or old DCs with LPS or probiotics failed to enhance the proliferation of T-cells derived from older donors. In conclusion, this study demonstrates that ageing increases the responsiveness of DCs to probiotics, but this is not sufficient to overcome the impact of immunosenescence in the MLR.

CANCER

1. *Lactobacillus casei* Shirota enhances the preventive efficacy of soymilk in chemically induced breast cancer.

Kaga C *et al* (2013) *Cancer Sci* 104:1508-1514.

Summary

The habitual consumption of soy isoflavones in combination with the probiotic *Lactobacillus casei* Shirota (LcS) was shown to decrease the risk of breast cancer occurrence as demonstrated in a previous population-based case-controlled study among Japanese women.

The present study evaluated the cooperative prevention mechanism of soymilk and LcS using an animal carcinogenic model. Female Sprague-Dawley rats received a high-fat, AIN-76A diet containing soymilk, LcS, both soymilk and LcS, or none and were orally exposed to 2-amino-1-methyl-6-phenylimidazo [4,5-b] pyridine at a dose of 85 mg/kg bodyweight eight times for a period of 2 weeks. The development of palpable mammary tumors were monitored for 17 weeks. Tumor tissues were immunohistochemically examined for estrogen receptor (ER)- α , Ki-67 and CD34.

The incidence and multiplicity of mammary tumors was reduced after the consumption of soymilk alone and soymilk in combination with LcS, while tumor size was decreased by LcS alone and LcS in combination with soymilk as compared with the control group. An immunohistochemical analysis revealed that soymilk in combination with LcS more effectively reduced the numbers of ER- α positive and Ki-67-positive cells in tumors than soymilk alone and that both soymilk and LcS inhibited tumor angiogenesis.

The results demonstrate that soymilk prevents the development of mammary tumors and LcS suppresses tumor growth, potentially enhancing the preventive efficacy of soymilk. The habitual consumption of LcS in combination with soymilk might be a beneficial dietary style for breast cancer prevention.

OTHERS

1. In case of obesity, longevity-related mechanisms lead to anti-inflammation.

Kaya MS *et al* (2014) *Age (Dordr)* 36(2):677-87.

Summary

The exact mechanisms which contribute to longevity have not been figured out yet. The aim of this study was to find out a common way for prompting longevity by bringing together the well-known applications such as food restriction, exercise, and probiotic supplementing in an experimental obesity model.

Experimental obesity was promoted in a total of 32 young (2 months old) and 32 aged (16 months old) male Wistar albino rats through 8-week cafeteria diet (salami, chocolate, chips, and biscuits). Old and young animals were divided into groups each consisting of eight animals and also divided into four subgroups as obese control, obese food restriction, obese probiotic-fed and obese exercise groups.

Probiotic group diet contained 0.05 %w/total diet inactive and lyophilized *Lactobacillus casei* str. Shirota.

The exercise group was subjected to treadmill running 1 h/day, at 21 m/min and at an uphill incline of 15 % for 5 days a week. Food restriction group was formed by giving 40 % less food as compared to others. The control group was fed regular pellet feed ad libitum. This program was continued for 16 weeks.

Blood samples from all the groups were analyzed for fasting glucose, insulin, IGF-1, insulin-like growth factor binding protein 3 (IGFBP-3), interleukin (IL)-6, IL-12, malondialdehyde (MDA), fT3, TT3, fT4, TT4, and liver tissue MDA levels were measured. All applications showed anti-inflammatory effects through the observed changes in the levels of IGFBP-3, IL-6, and IL-12 in the young and old obese rats. While the interventions normally contribute to longevity by recruiting different action mechanisms, anti-inflammatory effect is the only mode of action for all the applications in the obesity model.