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Suppressive effect of frequent ingestion of *Lactobacillus johnsonii* La1 on *Helicobacter pylori* colonization in asymptomatic volunteers

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Keywords: *Helicobacter pylori*, *Lactobacillus johnsonii*, ¹³C-urea breath test, probiotic

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Sir,

Helicobacter pylori colonization occurs earlier and with a higher frequency in individuals from developing countries who live in conditions of inadequate sanitation than in individuals from industrialized countries. In Chile, for example, between 60% and 70% of the adolescents and >80% of the adults from the low socio-economic stratum are colonized by this pathogen.¹ This high prevalence may have important consequences as *H. pylori* is currently recognized as an aetiological factor of gastroduodenal ulcer and as a risk factor for the development of gastric adenocarcinoma, a highly prevalent cancer in Chile. In most people, however, the presence of *H. pylori* in the gastric mucosa remains asymptomatic during life, and in consequence it is neither possible nor ethical to eradicate the bacteria colonizing their gastric mucosa with antibiotics. Furthermore, treatment with antibiotics presents other problems related to its high cost for families from the low socio-economic stratum and to the appearance of resistance in *H. pylori* as well as in other species. For these reasons, it is important to develop low-cost, large-scale alternative solutions applicable to the at-risk population to prevent or decrease *H. pylori* colonization. In this sense, the use of dietary components capable of interfering with *H. pylori*, including some vegetables and probiotic microorganisms, appears attractive.²

Some specific strains of exogenous lactobacilli are resistant to the low pH of the stomach and may transiently adhere to the gastric mucosa, where they may exert functional effects. Some of them have been shown to exert *in vitro* and *in vivo* bactericidal effects against *H. pylori*, suggesting that they could possibly interfere with *H. pylori* colonization

in humans.³ This has recently been confirmed by clinical trials. Sakamoto *et al.*⁴ reported that *Lactobacillus gasseri* OLL2716 ingestion suppressed *H. pylori* infection in adults, but curiously the same strain had no effects in colonized children.⁵ Using a drinkable, whey-based, spent-culture supernatant of *Lactobacillus johnsonii* La1 (La1), Michetti *et al.*⁶ described decreased *H. pylori* colonization in adult volunteers; furthermore, we recently observed a significant but low suppressive effect in colonized children after 1 month of La1 ingestion (S. Cruchet, M. C. Obregon, G. Salazar, E. Diaz & M. Gotteland, unpublished data). On the basis of these findings, we proposed to carry out a clinical trial to test whether increasing the frequency of La1 ingestion might result in a higher antagonist effect against *H. pylori*.

Twelve asymptomatic volunteers (two males, 10 females; age: 39.7 ± 11.2 years) *H. pylori*-positive by ¹³C-urea breath test (¹³C-UBT), without previously diagnosed gastrointestinal pathologies or history of antibiotic, antacid or prokinetic drug treatments, were recruited for the study. The protocol was approved by the Ethics Committee of INTA and an 'informed consent' form was signed by the subjects who agreed to participate. Volunteers had to ingest 80 mL of a commercial product (Chamyto, Nestlé Chile, Santiago, Chile) containing >10⁷ La1/mL, every 2 h from 08:00 to 22:00 h (i.e. a total of 640 mL of product per day) for 2 weeks. The aim of this design was to increase the duration of the contact between La1, the gastric mucosa and *H. pylori*. After 1 and 2 weeks of ingesting the product, a second and third ¹³C-UBT were carried out with a commercial kit (Tau-Kit, Isomed, Madrid, Spain) using 75 mg ¹³C-urea. The excess δ¹³CO₂ over baseline (DOB) values expressed as ‰ were compared for the basal, 1 and 2 week periods.

One volunteer (8.3%) presented with diarrhoea during the first 3 days of the study and decided to withdraw. Results (Figure 1) show that DOB values decreased significantly during the course of the study (ANOVA for repeated measurements: $F = 4.18$, $P = 0.034$), reflecting a suppressive effect upon *H. pylori* colonization by La1; after 1 week, DOB2 values [28.92‰, 95%CI (21.67–36.17‰)] tended to be lower than DOB1 basal values [46.39‰; 95%CI (24.20–68.56‰), $P = 0.066$] and this decrease reached significance after the second week [DOB3 = 27.39‰, 95%CI (16.24–38.54‰), $P = 0.043$]. Results also showed that the higher the DOB1 basal values, the greater the decrease in DOB values when comparing the basal and 2 week periods (DOB3–DOB1) (Pearson correlation: $r = 0.88$, $P = 0.0015$). Our results indicate that continuous ingestion of a La1-containing product at

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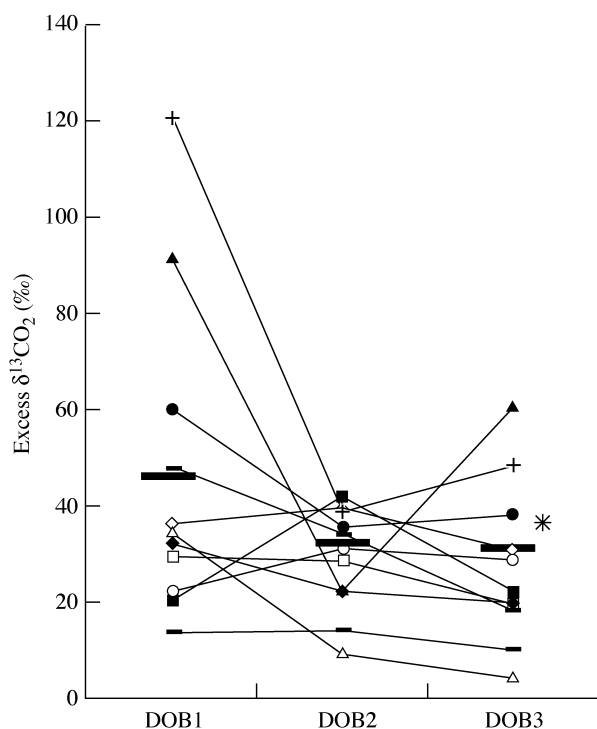


Figure 1. DOB values at the beginning of the study (DOB1) and after 1 (DOB2) and 2 (DOB3) weeks of ingesting the La1-containing product. Horizontal bars represent means for each time point. (ANOVA for repeated measurements, $F=4.18$, $P=0.034$; Tukey post-hoc test: DOB1 versus DOB2: $P=0.066$; DOB1 versus DOB3: $P=0.043^*$).

2 h intervals for a 14 h period every day results in a 40% decrease in DOB values after 2 weeks. This effect is higher than that observed by Sakamoto *et al.*⁴ with *L. gasseri* and comparable to that observed by Michetti *et al.*⁶ with a spent-culture supernatant of La1, i.e. a medium much more concentrated than was used in the present study. Whether this effect

is due to the higher frequency of product ingestion, or to the total amount of product ingested during the day, is difficult to elucidate. The study is interesting in that it suggests that it is possible to modulate *H. pylori* colonization in an at-risk population through the regular ingestion of a probiotic-containing dietary product widely available in the local market. However, it is important to note that the number of subjects participating in the study was small and that the follow-up was only short-term; in consequence, a larger clinical trial is necessary to confirm these preliminary results.

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