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Immunomodulatory properties of *Lactobacillus salivarius* are not limited to the intestine

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Previous studies have shown the beneficial effects exerted by probiotics on inflammatory bowel disease[(1)], an intestinal condition characterized by an altered intestinal immune response[(2)]. However, it would be interesting to know whether the immunomodulatory properties of probiotics are restricted to a local effect in the intestine or whether their effect can also be extrapolated to other systemic immune alterations. The aim of the present study was to test the effect of a probiotic, *Lactobacillus salivarius* CECT5713, in two experimental models of local or systemic altered immune response, i.e. the trinitrobenzenesulfonic acid (TNBS) model of rat colitis and the lipopolysaccharide (LPS)-induced septic shock in mice. For this purpose, mice or rats (n 10) were given the probiotic (5×10^8 colony-forming units/ml drinking water), starting 2 weeks before damage induction. A control group (n 10) without probiotic was also used for reference. Colitis was induced in rats by intracolonic administration of TNBS (10 mg) and after 1 week was evaluated both histologically and biochemically (myeloperoxidase activity, glutathione content, inducible NO synthase (iNOS) expression)[(3)]. Septic shock was induced in mice by administering LPS (40 mg/kg, intraperitoneally) and the mice killed 24 h later, when colon and spleen were removed. Colonic iNOS expression was determined by Western blot, and activated T-cells were obtained from spleens by concanavalin A incubation and the immune response evaluated by RT–PCR or ELISA for different cytokines (IL-2, -5, -6 and -10). The results showed that *L. salivarius* was able to ameliorate both the local and systemic altered immune response. The probiotic exerted intestinal anti-inflammatory activity, since it significantly reduced the extension of the colonic damage induced by TNBS in comparison with non-treated colitic rats; this effect was accompanied by a 42% reduction in myeloperoxidase activity ($P<0.05$), a 44% increase in glutathione content ($P<0.05$) and a reduction in colonic iNOS. Moreover, the probiotic treatment significantly prevented the increase in colonic weight (mg/cm) induced by septic shock (264 (SE 15) *v*. 322 (SE 15); $P<0.05$), without showing differences from normal mice (246 (SE 14)). Similarly, the LPS-induced colonic iNOS expression was lower in the probiotic-treated mice (30%). LPS also stimulated the expression of different cytokines assayed in the splenocytes, while the probiotic-treated mice showed a reduction in cytokine expression of 80% for IL-5 and 100% for both IL-2 and IL-6 (Figure 1). IL-10 secretion was reduced in control mice (603 (SE 102) pg/ml; $P<0.05$) in comparison with the normal group (1064 (SE 80) pg/ml), which was increased in probiotic-treated mice (1034 (SE 150 pg/ml; $P<0.05$) when compared with the LPS control group. In conclusion, the immunomodulatory properties of the probiotic *L. salivarius* are not restricted to the intestine, since it is also able to ameliorate the alteration in the systemic immune response derived from LPS administration to mice.

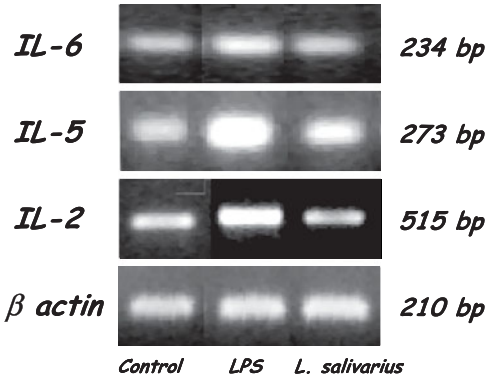

Figure 1. *Lactobacillus salivarius* administration reduced cytokine expression (RT-PCR) in LPS-induced septic shock in mice.

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