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Abstract

Anti-Obesity Properties of a *Latilactobacillus sakei* Strain in *C. elegans* and Diet-Induced Obese Rats †

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Abstract: Introduction: In the last few years, several studies have described the beneficial effects of the supplementation of diets with certain probiotic strains and different obesity-related disturbances, including metabolic syndrome. New research lines aim to characterize and understand the strain-specific mechanisms of action and their effects on the host's health. The use of animal models is necessary to understand how probiotics interact with the gut microbiota and exert beneficial activities, which would allow us gain insight into potential new strategies against obesity-related diseases. Objective: we aim to characterize the effects of a novel probiotic strain of *Latilactobacillus sakei* (*L. sakei*) in two different animal models with adiposity excess. Methods: *Caenorhabditis elegans* was used as a starting in vivo model to analyse how the probiotics affect fat accumulation, oxidative stress, senescence, and lifespan when exposed to high-glucose conditions. Then, the effects of *L. sakei* oral administration (10^9 CFU/day) were evaluated in diet-induced obese (DIO) Wistar rats, and biochemical, transcriptomic, metagenomics, and metabolomics analyses were performed. Results: Supplementation with *L. sakei* in *C. elegans* counteracted the deleterious effects of glucose by reducing fat accumulation, enhancing the oxidative stress response, and extending lifespan by directly regulating the carbohydrate- and lipid metabolism-related genes *acox-1*, *maoc-1*, and *daf-16*. Following the same trend, DIO rats supplemented with *L. sakei* showed lower proportions of mesenteric and subcutaneous fat, improved glucose tolerance, and an ameliorated inflammatory marker profile, partly by regulating the expression levels of key metabolic genes like adiponectin, leptin, and *Acox1*. The oral administration of *L. sakei* modulated faecal microbiota composition and induced the production of novel plasma metabolites. Conclusions: our results unveil new strain-specific mechanisms of action through which *L. sakei* exerts health-promoting effects in *C. elegans* and DIO adiposity models, as well as further describe how these probiotics could potentially be useful for the prevention and treatment of metabolic syndrome-related diseases.

Keywords: microbiota; probiotics; obesity; lactic acid bacteria; inflammation; adiposity; insulin; metabolomics

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