

Development of a synergistic synbiotic for *Lactobacillus plantarum* LP-LDL targeting cholesterol reduction



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Introduction and Aims

Lactobacillus plantarum LP-LDL is a probiotic selected from 4000 bacterial strains for its high bile salt hydrolase (BSH) and *in vitro* cholesterol reduction activities. Its efficacy in lowering cholesterol and systemic blood pressure, both contributing factors for the development of coronary heart disease, has been shown *in vivo* in mildly hypercholesterolaemic adults.

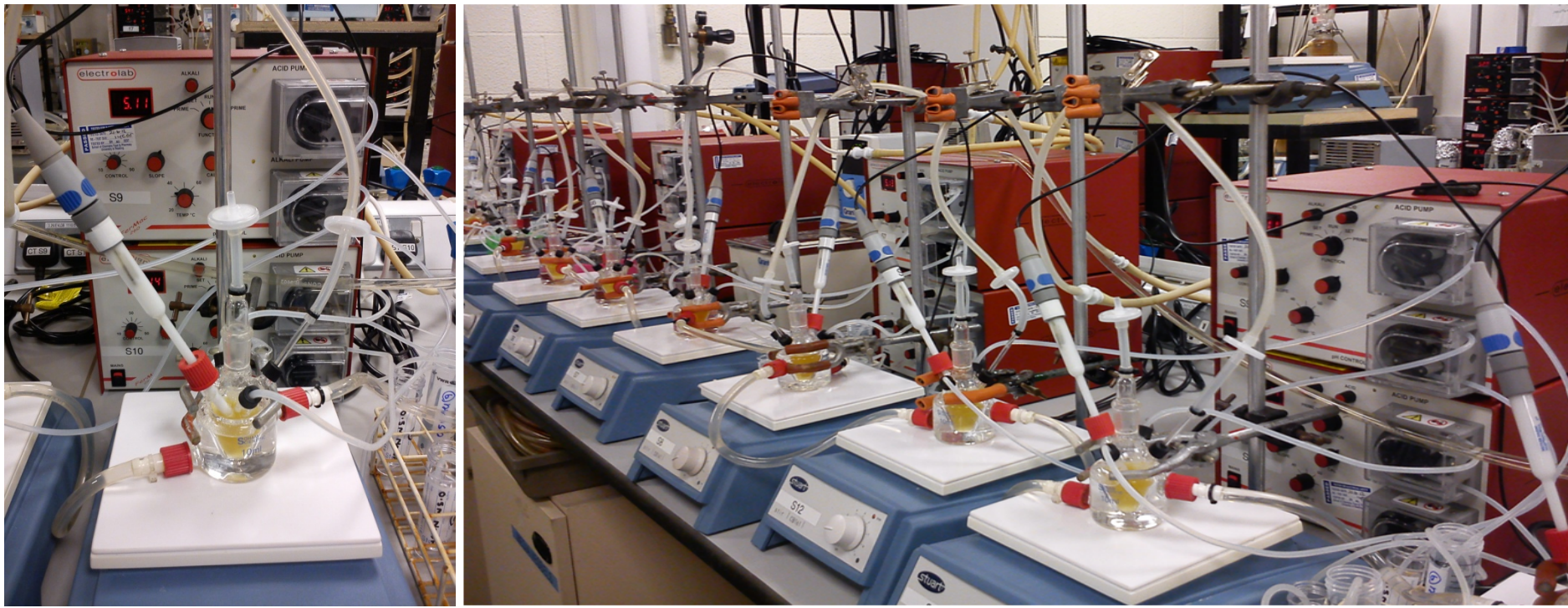
The aim of this work was to use reverse enzyme technology to synthesize galactooligosaccharides (GOS) that will selectively enhance the growth and cholesterol lowering activity of *Lactobacillus plantarum* LP-LDL.

Methods

A systematic approach was used to identify bacterial strains with high *in vitro* BSH activity and cholesterol reducing activity. *L. plantarum* LP-LDL was further tested for its β -galactosidase hydrolytic activity using the ONPG test.

Crude cell extracts of *L. plantarum* LP-LDL were used to synthesize GOS (LPGOS) from lactose.

The effect of purified LPGOS alone and in combination with *L. plantarum* LP-LDL (LP) on the human faecal microbiome was evaluated in pH-controlled, micro scale batch cultures in the presence of cholesterol. Purified, commercially available bifidobacterial GOS (BGOS) was used as control.



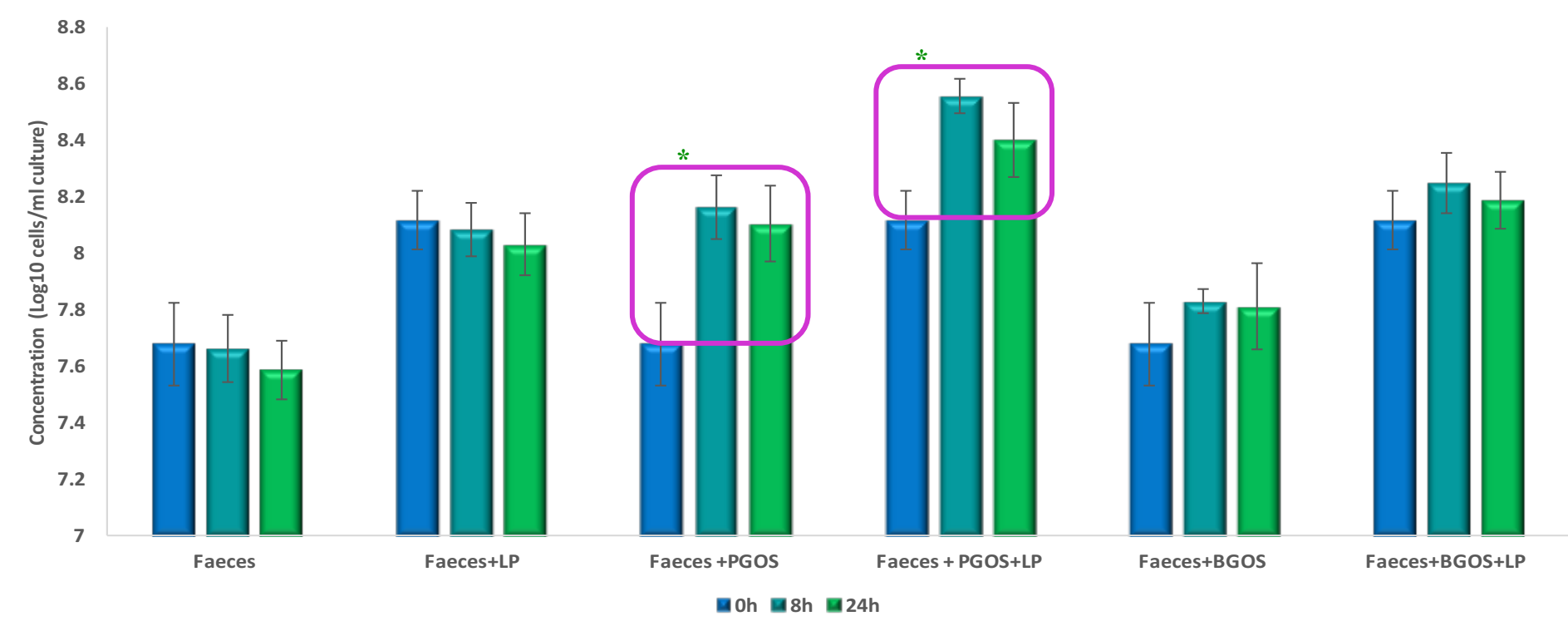
Micro scale faecal batch cultures (10ml) testing in parallel:

- Faeces
- Faeces + LP
- Faeces + LPGOS
- Faeces + LPGOS + LP
- Faeces + BGOS
- Faeces + BGOS + LP

Cultures (24h) were run in triplicate, using faeces from each of three healthy adults. Samples were obtained for bacteriology (FISH), metabolite, BSH activity and cholesterol reduction determination.

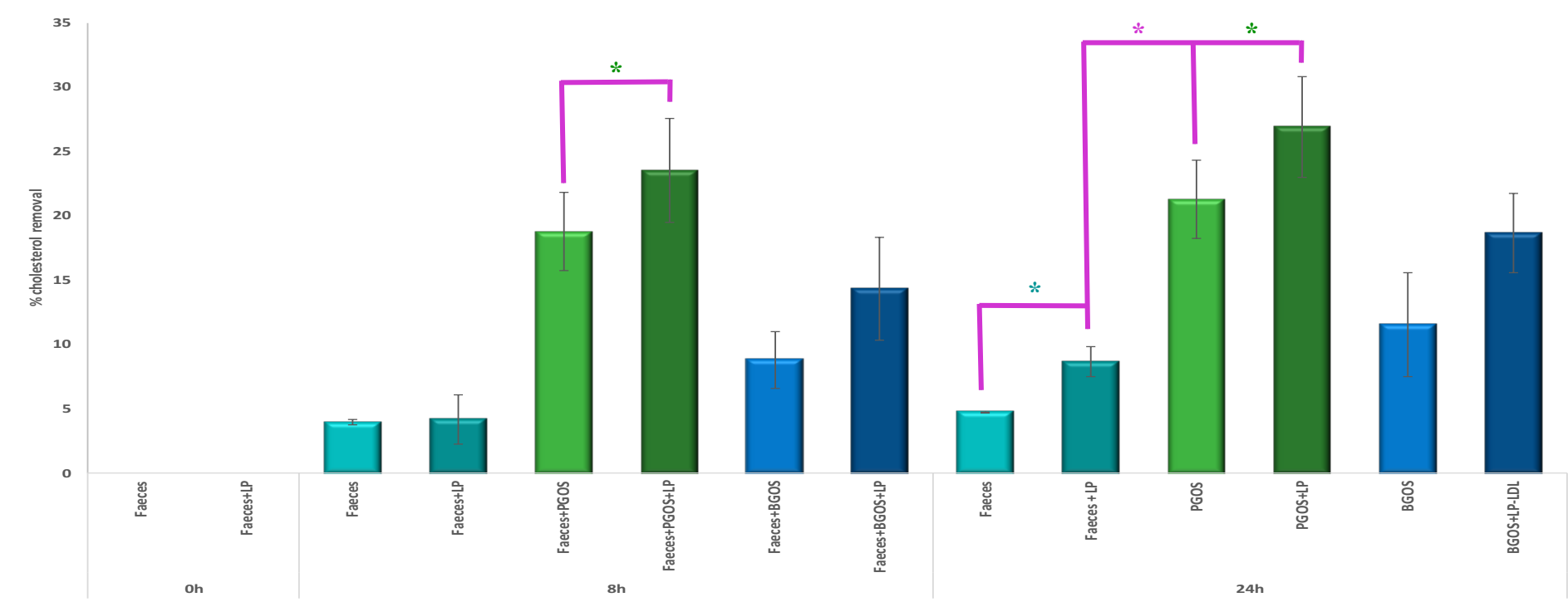
Results

LPGOS significantly and selectively increased *Lactobacillus* populations, BSH and cholesterol reducing activities. The effect was further enhanced by combining LPGOS with *L. plantarum* LP-LDL.



Average *Lactobacillus* concentrations (\pm SD) in faecal batch culture (n=3) enumerated using the Lab158 FISH probe

The effect on metabolic activity correlated with *Lactobacillus* concentrations indicating a true synergistic effect that was not observed when LP-LDL was used in combination with BGOS. BGOS did not have an impact on cholesterol reduction.



Average cholesterol reduction (\pm SD) in faecal batch culture (n=3). LP-LDL significantly reduces cholesterol even in the absence of carbohydrate source. Effect is significantly enhanced in the presence of PGOS.

Conclusions

We have used a systematic approach to select a probiotic, *L. plantarum* LP-LDL, targeting cholesterol reduction. Using β -galactosidases expressed by *L. plantarum* LP-LDL we achieved the synthesis of GOS that works in true synergy with the parent strain, not only increasing its population but also impacting on the biological activity the probiotic was selected for. This is the first time true synergy is demonstrated for a synbiotic in faecal culture.

Study Highlights

Selecting a probiotic to target a specific health biomarker and using its enzymatic artillery to generate GOS, resulted in the formulation of a true synergistic synbiotic enhancing:

- BSH activity
- Cholesterol reduction potential