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MEETING ABSTRACT

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Bioactivation of simvastatin by probiotic bacteria: *in vitro* study

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Background: Simvastatin is a lipid-regulating drug that acts as 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor that reduces cholesterol production by the liver. It is administered perorally as a prodrug in the form of lactone (SVL) and is hydrolysed in the human body chemically or enzymatically to its open acid form, simvastatin acid (SVA). Due to great metabolic capacity of gut microflora and probiotic bacteria and their role in drug response, the aim of the study was to examine if selected probiotic bacteria may transform SVL into its active form.

Methods: The study was performed *in vitro*. A suspension of probiotic bacteria, *Lactobacillus acidophilus* and *Bifidobacterium longum* (10⁸/ml), was incubated with SVL solution (50 µg/ml) for 24 h. In order to examine the intracellular, extracellular and total content of SVL and SVA after incubation, all samples were sonicated, centrifuged, processed and analysed by LC-MS/MS.

Results: The concentration of SVL decreased by 44% in total content (sum of extracellular and intracellular) after 24 h of incubation with selected probiotic bacteria. Semiquantitative and qualitative analysis of the incubation medium revealed a substantial amount of SVA. Regarding the distribution of compounds, the concentration of SVA after the incubation period was much higher in extracellular content while SVL accumulated to a greater extent intracellularly.

Discussion: The results of our study suggest that the selected bacterial strains, *L. acidophilus* and *B. longum*, lead to transformation of SVL into its active form SVA. This reaction may be mediated by hydrolytic enzymes that are present in selected bacterial strains. The distribution of compounds may be explained by their physico-chemical properties—the more hydrophilic properties of SVA do not make it a good candidate for transport through cell membrane compared to SVL, which is a highly lipophilic compound that accumulated predominantly intracellularly. Further *in vivo* studies are needed in order to provide more detailed insight into the effect of probiotic bacteria on the therapeutic response to simvastatin.

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