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MEETING ABSTRACT

A2.1

Exploring simvastatin bioaccumulation and biotransformation in probiotic bacteria for enhanced insight into drug–microbiota interactions

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Background: The considerable challenge faced in clinical practice is the variability in drug response among individuals, primarily resulting from differences in drug pharmacokinetics. The factors contributing to these differences between individuals are sometimes challenging to attribute solely to genetic factors. It is suggested that these variations may be influenced, at least in part, by the effects of the intestinal environment. Within the intestinal lumen, the presence of microbiota can alter the absorption and pharmacokinetic profile of numerous drugs [1,2,3]. The potential involvement of gut microbiota in the response to simvastatin, which exhibits significant inter-individual variations, has received insufficient attention so far. To gain a deeper understanding of the underlying mechanisms and their impact on clinical outcomes in patients receiving simvastatin therapy, our study aimed to investigate the bioaccumulation and biotransformation of simvastatin in probiotic bacteria under *in vitro* conditions.

Methods: Simvastatin samples with probiotic bacteria were incubated under anaerobic conditions at 37°C for 24 hours. Extracellular and intracellular samples were collected at predetermined time intervals and prepared for analysis with liquid chromatography–mass spectrometry (LC–MS). Simvastatin concentrations were measured using LC–MS/MS. Potential biotransformation pathways were explored using a bioinformatics approach in conjunction with experimental assays.

Results: During the incubation, simvastatin was transported into bacterial cells, resulting in increased drug bioaccumulation over time. A decrease in total drug levels during the incubation period suggests partial biotransformation of the drug by bacterial enzymes. Bioinformatics analysis indicated that the lactone ring of simvastatin was most susceptible to metabolic changes, with ester hydrolysis followed by hydroxylation being the most likely reactions.

Discussion: Our findings reveal that the bioaccumulation and biotransformation of simvastatin by intestinal bacteria may underlie the altered bioavailability and therapeutic effects of the drug. Since our study focused on selected bacterial strains *in vitro*, further comprehensive research is necessary to fully understand the complex interactions between drugs and the microbiota in influencing the overall clinical response to simvastatin. Such insights could lead to novel approaches for personalized lipid-lowering therapy.

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Keywords: gut microbiota – drug metabolism – drug pharmacokinetics

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