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ABSTRACT BOOK

PP295. Unveiling the Intricacies of Simvastatin Bioaccumulation and Biotransformation in Probiotic Bacteria Model for Insightful Revelations on Drug-Microbiota Interplay

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Background: Addressing the considerable challenge encountered in clinical practice, the variability in drug response among individuals poses a significant hurdle. These differences, often challenging to attribute solely to genetic factors, are believed to be influenced, at least partially, by the effects of the intestinal environment. The presence of microbiota within the intestinal lumen has been recognized for its potential to modify the absorption and pharmacokinetic profile of numerous drugs [1]. Despite the significant interindividual variations observed in the response to simvastatin, there has been inadequate attention to the potential involvement of gut microbiota. To gain a more profound understanding of the underlying mechanisms and their impact on clinical outcomes in patients undergoing simvastatin therapy, our study aimed to explore the bioaccumulation and biotransformation of simvastatin in probiotic bacteria under in vitro conditions.

Methods: Simvastatin samples were subjected to anaerobic incubation with probiotic bacteria at 37°C for 24 hours. Extracellular and intracellular samples were systematically collected at predetermined time intervals and meticulously prepared for subsequent analysis through LC-MS. The concentrations were quantified utilizing LC-MS/MS. To elucidate potential biotransformation pathways, a comprehensive bioinformatics approach was employed, complemented by experimental assays.

Results: Throughout the incubation period, simvastatin was internalized into bacterial cells, leading to a progressive increase in drug bioaccumulation. The observed decline in total drug levels during incubation suggests the occurrence of partial biotransformation facilitated by bacterial enzymes. Bioinformatics analysis highlighted the lactone ring as particularly susceptible to metabolic alterations, with ester hydrolysis followed by hydroxylation identified as the most probable reactions.

Conclusion: Our findings point to the significance of bioaccumulation and biotransformation processes of simvastatin by intestinal bacteria, potentially influencing the drug's altered bioavailability and therapeutic effects. Given the in vitro focus on specific bacterial strains in our study, further comprehensive research is imperative to fully grasp the intricate interactions between drugs and the microbiota, ultimately influencing the overall clinical response to simvastatin. These insights may pave the way for innovative approaches in tailoring lipid-lowering therapy on an individualized basis.

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[1] Đanić, M., Pavlović, N., Lazarević, S., Stanimirov, B., Vukmirović, S., Al-Salami, H. & Mikov, M. (2023). Bioaccumulation and biotransformation of simvastatin in probiotic bacteria: A step towards better understanding of drug-bile acids-microbiome interactions. Frontiers in Pharmacology, 14, 1111115.