

Title: Different strategies of utilizing bioactive potential of natural products-derived postbiotic metabolites.

In recent years we have witnessed a significant increase in our understanding of the role of human gut microbiota and its metabolites in maintaining body homeostasis. Gut bacteria express a vast number of enzymes that transform compounds entering the gastrointestinal tract, often significantly changing their structure and biological properties. Postbiotic metabolites derived from natural products represent a niche of active substances and a rich reservoir of promising compounds for the development of new active pharmaceutical ingredients.

In my work, I have presented 3 research strategies on utilizing therapeutic potential of postbiotic metabolites. The first strategy, using as examples plant substances traditionally employed in the therapy of mild mood disorders, offers a new perspective on their mechanisms of action from the microbiota-gut-brain axis viewpoint, highlighting the role of emerging postbiotic metabolites in the efficacy of traditionally used natural products. The remaining two strategies involved urolithin A, a known postbiotic metabolite, as a lead molecule for further research. I proposed two innovative approaches to exploit its therapeutic potential related to its strong anti-inflammatory activity, which is limited *in vivo* by phase II metabolism: firstly, through chemical modification of the original compound's structure to enhance the bioavailability of its active form; and secondly, through topical application of the unchanged urolithin A, thus avoiding the action of detoxifying enzymes.

The results from *in vitro* studies on urolithin A derivatives have been published in the form of two original papers, and along with a review article focused on the activity of postbiotic metabolites derived from plant substances used in mood disorders, form part of a series of publications constituting the presented doctoral dissertation. Due to the implementation-oriented nature of the work on the semi-technical scale synthesis of urolithin A and development of formulations for topical application, the research findings are contained in the project reports and are briefly described in this work. The conducted studies outline promising approaches for utilizing postbiotic metabolites and represent innovative strategies, laying the groundwork for further research and implementation work on this rich world of gut metabolism products.

Keywords:

gut microbiota, inflammation, natural products, postbiotic metabolites, urolithin A