Parkinson's disease, a chronic neurodegenerative disorder characterized by a wide range of symptoms, poses a significant threat to modern society, particularly as its prevalence increases with age. There is no cure for the disease and the available treatments focus on symptom management and improving quality of life. Because of that, there is a constant search for better therapeutic strategies and preventive measures. Emerging evidence suggests that dietary polyphenols may play a beneficial role in neurodegeneration, especially urolithin A. It is a metabolite produced in the gut through the transformation of ellagitannins by colonic bacteria. Urolithin A is known for its anti-inflammatory, antioxidant, and anti-apoptotic properties, contributing to mitochondrial health and homeostasis.

Recent research has linked Parkinson's disease with gastrointestinal dysfunction, where issues such as altered gut microbiota composition, increased intestinal permeability and inflammation often precede neurological symptoms. This suggests a strong gut-brain connection in the pathogenesis of the disease. This project aims to investigate whether urolithin A can improve Parkinson's disease symptoms by enhancing intestinal integrity and modulating gut microbiota composition. Our previous study has shown that pomegranate extract, rich in ellagitannins, can improve postural stability, neuronal survival, and reduce oxidative damage in a Parkinson's disease rat model. These findings prompt further investigation into the potential mechanisms through which the compound exerts its neuroprotective effects, particularly focusing on the gut.

This study will conduct both in vitro and in vivo experiments to explore the impact of urolithin A on gut health and its potential to influence Parkinson's disease progression. In vitro experiments will analyze urolithin A-treated gut microbiota to observe changes in bacterial community structure. In vivo, experiments will use a genetic mouse model of Parkinsonism to assess the effects of the compound on gut microbiota composition, intestinal integrity, inflammatory markers, and brain pathology. Key research questions include whether the compound can decrease intestinal permeability, reduce inflammation, affect tight junction proteins in the gut, and subsequently translate these improvements to reduce the disease symptoms. Additionally, the study will examine how urolithin A alters gut microbiota diversity, richness, and bacterial metabolite production.

We believe that our study will contribute to deeper insights into early-stage neuroprotective strategies for Parkinson's disease and underscore the importance of gut health in neurodegenerative conditions. We assume that the administration of urolithin A will decrease intestinal permeability by reducing the level of pro-inflammatory cytokines and increasing the level of tight junction proteins. We also suppose that the compound will have a favourable effect on gut microbial composition, diversity and bacterial metabolite production. We hope to obtain a beneficial local impact on intestinal integrity that will affect the pathological changes in the central nervous system burdened by the Parkinson's disease model.

By bridging neuroscience, microbiology, and nutrition, this multidisciplinary research offers a novel approach to the management of Parkinson's disease. Understanding how urolithin A impacts both the gut and brain could lead to new dietary-based strategies for delaying the onset and progression of the disease. This project aims to contribute to global knowledge and pave the way for future therapies regarding intestinal health and microbiota alterations in neuroprotection.