

Phenolic compounds as modulators of gut microbiota composition: An *in vitro* batch fecal fermentation approach

Adriana C. S. Pais,^{a,b} Tânia B. Ribeiro,^b Ezequiel R. Coscueta,^b Ana Sofia Salsinha,^b Maria Manuela Pintado,^b
Armando J. D. Silvestre,^a Sónia A. O. Santos^a

^a CICECO-Aveiro Institute of Materials, Chemistry Department, University of Aveiro, 3810-193 Aveiro, Portugal ^b Universidade Católica Portuguesa, CBQF - Centro de Biotecnologia e Química Fina – Laboratório Associado, Escola Superior de Biotecnologia, Rua Diogo Botelho 1327, 4169-005 Porto, Portugal

Email: a.c.p.s@ua.pt

The human diet comprises a variety of bioactive compounds, such as phenolic compounds which are widely present in vegetables and fruits that confer numerous health benefits.¹ However, the health benefits of these compounds appear to be directly influenced by a number of factors, including their bidirectional relationship with gut microbiota,^{1,2} as these compounds are metabolized by these microorganisms, and, simultaneously, modulate their composition.^{1,3} Nevertheless, knowledge about the impact of these dietary compounds have individually on human gut microbiota remains limited^{3,4}.

Three phenolic compounds (ellagic acid, naringenin, and phloroglucinol) were subjected to an *in vitro* batch fermentation with a pool of fresh human fecal samples collected from healthy donors. Subsequently, the samples were further analyzed by 16S amplicon metagenomics sequencing and their short-chain fatty acids (SCFAs) profile was determined by gas chromatography with a flame ionization detector (GC-FID).

Ellagic acid and phloroglucinol exhibited prebiotic properties, as evidenced by the production of specific SCFAs, including acetic, propanoic, and butyric acids. Furthermore, these compounds positively influenced the growth of beneficial genera of bacteria, such as *Lactobacillus* and *Bifidobacterium*. In contrast, naringenin exerted an influence on other genera with a pathogenic character, such as *Escherichia* and *Salmonella*.

These findings contribute significantly to our understanding of how these phenolic compounds influence the gut microbiota composition. As a future perspective, this knowledge could be relevant to the development of new formulations in the nutraceutical or pharmaceutical areas. Furthermore, studying of phenolic compounds in combination may be a crucial step in future research to achieve a more diverse and well-balanced gut microbiota ecosystem.

Acknowledgements: This work was developed within the scope of the project CICECO-Aveiro Institute of Materials, UIDB/50011/2020, UIDP/50011/2020 & LA/P/0006/2020, financed by national funds through the FCT/MCTES (PIDDAC). Thank the CBQF for its institutional support through the FCT project UIDB/50016/2020. Acknowledgments are also due to FCT/MCTES for the PhD grant to ACSP (SFRH/BD/143348/2019) and for the research contract under Scientific Employment Stimulus to S. Santos (2021.03348.CEECIND).

References:

1. L. Valdés, A. Cuervo, N. Salazar, P. Ruas-Madiedo, M. Gueimonde and S. González, *Food Funct*, **2015**, 6, 2424–2439.
2. A. Duda-Chodak, T. Tarko, P. Satora and P. Sroka, *Eur J Nutr*, **2015**, 54, 325–341.
3. M. Dueñas, I. Muñoz-González, C. Cueva, A. Jiménez-Girón, F. Sánchez-Patán, C. Santos-Buelga, M. V. Moreno-Arribas and B. Bartolomé, *Biomed Res Int*, **2015**, 1–15.
4. C. G. Fraga, K. D. Croft, D. O. Kennedy and F. A. Tomás-Barberán, *Food Funct*, **2019**, 10, 514–528.

