



Abstract Book

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Oral Presentations



Bioavailability, absorption and metabolism

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Circulating (poly)phenol metabolites blood-brain barrier transport and brain availability

Rafael Carecho^{1,2}, Daniela Marques¹, Diogo Carregosa^{1,3}, Domenico Masuero⁴, Mar Garcia-Aloy⁴, Federica Tramer⁵, Sabina Passamonti⁵, Urska Vrhovsek⁴, Rita Ventura², Maria Alexandra Brito^{6,7}, Cláudia N. Santos^{1,3,2}, Inês Figueira¹

¹*CEDOC, NOVA Medical School, Faculdade de Ciências Médicas, Universidade NOVA de Lisboa, Campo dos Mártires da Pátria, Lisboa, Portugal.* ²*Instituto de Tecnologia Química e Biológica António Xavier, Universidade NOVA de Lisboa, Avenida da República, Oeiras, Portugal.* ³*iBET, Instituto de Biologia Experimental e Tecnológica, Avenida da República, Apartado 12, Oeiras, Portugal.*

⁴*Department of Food Quality and Nutrition, Research and Innovation Centre, Fondazione Edmund Mach (FEM), via E. Mach 1, San Michele all'Adige, Italy.* ⁵*Department of Life Sciences, University of Trieste, via L. Giorgieri 1, Trieste, Italy.* ⁶*iMed.Ulisboa—Research Institute for Medicines, Faculty of Pharmacy, Universidade de Lisboa, Av. Prof. Gama Pinto, Lisboa, Portugal.* ⁷*Department of Pharmaceutical Sciences and Medicines, Faculty of Pharmacy, Universidade de Lisboa, Av. Prof. Gama Pinto, Lisboa, Portugal*

Objectives/Background: (Poly)phenols have been extensively studied considering their beneficial brain-health effects, particularly regarding neurodegenerative disorders. Circulating metabolites resultant from colonic metabolism of dietary (poly)phenols are highly abundant in the bloodstream, though still marginally underexplored, particularly regarding their brain accessibility. Our goal is to disclose circulating (poly)phenol metabolites' capability of reaching the brain, *in silico*, *in vitro*, and *in vivo*.

Materials/Methods: For three selected (poly)phenol metabolites, *in silico* relevant molecular descriptors were obtained using Qikprop software. Metabolites' blood-brain barrier (BBB) transport and further metabolism were assessed in human brain microvascular endothelial cells (HBMEC) in transwells. Their fate towards brain, liver, kidney, urine, and blood, was also assessed in Wistar rats upon injection. Both UPLC-MS/MS and untargeted analysis were employed.

Results/Findings: The results from computational analysis indicate that all the studied metabolites can passively cross the BBB. Transport kinetics along time using HBMEC highlighted different BBB permeability rates of the (poly)phenol metabolites, with novel end-route metabolites appearing at the brain site. From *in vivo* experiments, we found that all the injected metabolites can almost immediately cross the BBB and reach the brain, though at distinct extents, presenting different tissue distribution rates.

Conclusion: Overall, we proved the ability of three circulating (poly)phenol metabolites to reach the brain, in circulating concentrations, with the ultimate potential to tackle neurodegeneration.

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Keywords

blood-brain barrier, circulating (poly)phenol metabolites, brain uptake