Inter-individual variability in response to the intake of flavonols on blood lipid levels:a meta-analysis of randomized controlled human trials

Regina Menezes^{1,2}, Ana Rodriguez-Mateos³, Antonia Kaltsatou⁴, Antonio González-Sarrías⁵, Arno Greyling⁶, Christoforos Giannaki⁷, Cristina Andres-Lacueva⁸, Eileen R Gibney⁹, Julie Dumont¹⁰, Manuel Schär¹¹, Mar Garcia-Aloy⁸, Susana Durán¹², Tatjana Ruskovska¹³, Viktorija Maksimova¹³, *Emilie Combet¹², *Paula Pinto^{1,2,14}

¹iBET, Portugal; ²ITQB, Portugal; ³University of Düsseldorf, Germany; ⁴University of Thessaly, Greece; ⁵CEBAS-CSIC, Spain; ⁶Unilever R&D,Netherlands; ⁷University of Nicosia, Cyprus; ⁸University of Barcelona, Spain, ⁹University College Dublin, Ireland; ¹⁰University of Lille, France; ¹¹University of Reading, United Kingdom; ¹²University of Glasgow, United Kingdom; ¹³Goce Delcev University, Republic of Macedonia; ¹⁴Polythecnic Institute of Santarém, Portugal.

*corresponding authors: paula.pinto@esa.ipsantarem.pt, Emilie.CombetAspray@glasgow.ac.uk

Abstract

Cardiovascular diseases (CVD) continue to be the leading cause of morbidity and mortality in most developed countries [1]. Several epidemiological studies have linked flavonols with decreased risk of stroke [2] and CVD [3], whilst human intervention studies have shown improvements in several biomarkers of CVD risk after flavonol consumption [4]. However, some heterogeneity in the individual physiological responses to the consumption of these compounds has been identified. For example, age and stage of hypertension seem to be important factors influencing the blood pressure lowering effect of quercetin [5, 6]. This meta-analysis aims to analyse the effect of flavanol intake on blood lipids, one of the major biomarkers of CVD risk, and factors affecting the inter-individual variability.

A systematic search was conducted in PubMed, Web of Science, Scopus and trial registry platforms. Only human randomized controlled trials with measured cardiometabolic outcomes were selected for data extraction of the measured outcomes, individual factors of the participants, characteristics of the study, and study quality. From 671 screened references, 19 studies were selected for data extraction and 16 studies were used for meta-analysis on total cholesterol, LDL, HDL and triacylglycerides (TAG). Inter-individual variability was assessed by subgroup analysis on BMI, age, sex, country and health status. Estimated intervention/control standardized mean differences suggested that consumption of flavonols was associated with significant reductions in total cholesterol (-0.180 mmol/L, 95% CI -0.307, -0.053), LDL (-0.219 mmol/L, 95% CI -0.350, -0.088) and TAG (-0.280 mmol/L, 95% CI -0.408, -0.151) and a significant increase in HDL (0.235 mmol/L, 95% CI 0.104, 0.365). Subgroup analysis showed a more pronounced effect in Asian countries and in participants with normal baseline lipid levels, compared to borderline and high baseline values. Results suggest that ethnicity and health status may influence the effect of flavonol intake on blood lipid levels.

References

1) WHO, Global Health Observatory (http://www.who.int/gho/mortality_burden_disease/en/); 2) Hollman PC *et al.* J Nutr. 2010, 140:600-4; 3) Wang X *et al.* Br J Nutr. 2014,111: 1–11; 4) Toh JY *et*

al. Curr Atheroscler Rep, 2013; 15:368; 5) Egert S et al Br J Nutr. 2009, 102:1065-74; 6) Brüll V et al. Br J Nutr. 2015, 114:1263-77.

Acknowledgments

The present work was conducted within COST Action FA1403 – POSITIVe. AGS is holder of a 'Juan de la Cierva' contract from the Spanish Ministry of Economy and Competitiveness (MINECO). RM is supported by the BacHBerry project (FP7-613793). RM and PP are grateful to iNOVA4Health Research Unit (LISBOA-01-0145-FEDER-007344). University of Barcelona is grateful to MINECO for the JPI-HDHL-FOODBALL project (PCIN-2014-133-MINECO-Spain) and to the Generalitat de Catalunya's Agency AGAUR for the grant 2014SGR1566.