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Validity of plasma phenyl-γ-valerolactones as novel biomarkers of dietary (poly)phenols: Preliminary analysis from the VALID project

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Diets rich in (poly)phenols are recognised as having potentially beneficial roles in health and the prevention of chronic diseases[(1)]. However, linking (poly)phenols with health outcomes is problematic because of their transient appearance in plasma[(2)], which limits the development of robust biomarkers of dietary exposure. Measures of phenyl-γ-valerolactones, products of colonic bacterial metabolism of the (poly)phenols (epi)catechin and procyanidin, offer the advantage of being more stable in plasma[(3)], and may represent novel biomarkers of dietary intake of (epi)catechin and procyanidin-rich foods such as tea, cocoa, grapes, nuts, red wine and berries. The aim of this analysis was to develop and validate plasma phenyl-γ-valerolactones as biomarkers of (epi)catechin and procyanidin-rich diets in a subsample of older adults from the island of Ireland.

This preliminary investigation was conducted as part of the multi-centred VALID project (www.jpi-valid.com) on 346 participants who provided a blood sample and completed an interviewer led (poly)phenol focused food frequency questionnaire. Plasma phenyl-γ-valerolactones were quantified using UHPLC-ESI-MS[(3)] at the University of Parma, while Phenol-Explorer® was used to estimate dietary intakes of (epi)catechin and procyanidin at Ulster University.

Analysis showed that 3 of a total of 11 phenyl-γ-valerolactones metabolites investigated, namely 5-(3′,4′-dihydroxyphenyl)-γ-valerolactone-3′-O-sulfate (3′4’-DiOH-VL-3′-O-Sulph), 5-(3′,4′-dihydroxyphenyl)-γ-valerolactone-3′-O-glucuronide (3′4’-DiOH-VL-3′-O-Gluc) and 5-(3′,5′-dihydroxyphenyl)-γ-valerolactone-3′-O-glucuronide (3′5’-DiOH-VL-3′-O-Gluc), were detectable in ≥52% of plasma samples and these were examined in relation to corresponding dietary (poly)phenol intake. Participants were classified into tertiles of low, medium and high (poly)phenol intake and the two most predominant phenyl-γ-valerolactones metabolites (3′4’-DiOH-VL-3′-O-Sulph and 3′4’-DiOH-VL-3′-O-Gluc, detected in 95% and 77% of samples, respectively) showed markedly higher concentrations in participants reporting the highest dietary (poly)phenol intakes (Table 1).

Table 1. Relationship of (poly)phenol intake with plasma phenyl-γ-valerolactones status of participants

		Dietary (poly)phenol intake[1]						
		Low (n = 115) 0–120 mg/d		Medium (n = 116) 121–168 mg/d		High (n = 115) ≥169 mg/d		
% of population detected in (n = 346)		x̃	Percentiles	x̃	Percentiles	x̃	Percentiles	*P*
Age (years)		76·7	74·1, 80·1	77·2	74·2, 80·7	77·6	73·9,79·6	0·798
Dietary (poly)phenol(mg/d)[1]		77[a]	44, 102	143[b]	132, 155	204[c]	181, 235	**<0·001**
Valerolactone(s)(nM)								
3′4′-DiOH-VL-3′-O-Sulph	95	8·0[a]	2·9, 17·3	7·2[a]	2·5, 23·9	13·4[b]	4·5, 41·0	**<0·001**
3′4′-DiOH-VL-3′-O-Gluc	77	8·3[a]	3·9, 18·3	7·9[a]	0·0, 14·0	15·8[b]	4·9, 30·5	**<0·001**
3′5′-DiOH-VL-3′-O-Gluc	52	3·2	0·0, 7·6	3·4	0·0, 7·3	0·0	0·0, 7·3	0·674

Data presented as median (x̃, 25th and 75th percentiles). Values within a row with different superscript letters are significantly different (ANOVA, followed by Games-Howell post hoc test). [1]Dietary (poly)phenol intake is the sum of (epi)catehin and procyanidins.

These preliminary results indicate that plasma phenyl-γ-valerolactones are potential biomarkers of (epi)catechin and procyanidin rich diets. Their use to monitor dietary (poly)phenols (and change in intake in response to intervention), and thus the potential protective effects of (poly)phenol rich diets on cognitive function in ageing, warrants further investigation.

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