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Comparing alkylresorcinols and mammalian lignans as biomarkers of wholegrain wheat or wholegrain rye intake in a dose-response intervention trial: the Grain Mark Study

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Observational studies indicate that wholegrain foods are beneficial for health. However, these findings are restricted by difficulties in accurate assessment of wholegrain food intake in populations due to poor definitions of wholegrain foods, limited information on portion/ serving sizes and lack of detail on the wholegrain content of individual foods. Thus, there is a need to identify biomarker(s) for wholegrain foods, which can be used to accurately assess intake for better correlation with health outcomes and to give strength to observational and intervention studies.

Sixty-eight non-smoking healthy volunteers (48% male), mean age 54.5 years, participated in the study. After a wash-out period of 4 weeks during which volunteers avoided all wholegrain foods, they were randomly allocated into two groups; a wholegrain wheat group and a wholegrain rye group. The volunteers were asked to consume 3 servings (48 g) of either whole grain per day for 4 weeks (Dose 1) from a selection of foods provided. After this period, they were asked to double their intake of the same foods (Dose 2) for further 4 weeks. At the end of each period, volunteers provided fasting blood and 24 h urine samples for the measurement of plasma alkylresorcinols and plasma/24 h urine mammalian lignans; enterolactone (ENL) and enterodiol (END).

Biomarker (concentration, unless stated otherwise)	Regression statistics for mean wholegrain rye intake			Regression statistics for mean wholegrain wheat intake		
	Slope (ln)	R ²	P value	Slope (ln)	R ²	P value
Plasma AR C17:0	+ 0.015	0.454	<0.0001	+ 0.006	0.480	<0.0001
Plasma AR C19:0	+ 0.015	0.435	<0.0001	+ 0.015	0.578	<0.0001
Plasma AR C21:0	+ 0.012	0.406	<0.0001	+ 0.015	0.607	<0.0001
Plasma AR C23:0	+ 0.014	0.431	<0.0001	+ 0.013	0.629	<0.0001
Plasma AR C25:0	+ 0.018	0.417	<0.0001	+ 0.013	0.517	<0.0001
Plasma total AR	+ 0.015	0.444	<0.0001	+ 0.015	0.612	<0.0001
Plasma ENL	+ 0.002	0.020	0.0301	–	–	NS
Plasma END	–	–	NS	–	–	NS
Plasma total lignans	–	–	NS	–	–	NS
24 h urine ENL excretion	+ 0.003	0.046	0.0004	+ 0.003	0.028	0.0048
24 h urine END excretion	–	–	NS	–	–	NS
24 h urine total lignan excretion	+ 0.003	0.043	0.0005	+ 0.003	0.031	0.0031

Using linear mixed effects models, adjusting for age, gender and BMI, there were significant linear dose-response trends between wholegrain intake and all plasma alkylresorcinol homologues in both rye and wheat groups (all $P < 0.0001$). However, wholegrain intake was only weakly associated with plasma ENL concentration in the rye group ($P < 0.05$), and not at all in the wheat group. Twenty-four hours urine ENL excretion was significantly associated with wholegrain intake in both rye ($P < 0.001$) and wheat ($P < 0.01$) groups.

These results demonstrate that plasma alkylresorcinol concentrations are more accurate biomarkers of both wholegrain rye and wholegrain wheat intake than mammalian lignans.

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