Dietary intake and urinary excretion of lignans in Finnish men

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Intake of lignans has been assessed in different study populations, but so far none of the studies has compared the daily intake of lignans and the urinary excretion of plant and enterolignans. We assessed the intake of lariciresinol, pinoresinol, secoisolariciresinol and matairesinol in 100 Finnish men consuming their habitual omnivorous diet, and measured the 24 h urinary excretion of plant and enterolignans to compare the intake and metabolism. Dietary determinants of lignan intake and their urinary excretion were also determined. The mean intake of lignans was 1224 (SD 539) μg/d, of which lariciresinol and pinoresinol covered 78 %. Almost half (47 %) of the intake of lignans was explained by the intake of rye products, berries, coffee, tea and roots. The urinary excretion of plant lignans corresponded to 17 % and enterolignans to 92 % of the intake of lignans. The urinary excretion of plant lignans was explained 14 % by the intake of rye products and intake of coffee, and consequently 3–7 % by the intake of water-insoluble fibre. The urinary excretion of enterolactone was explained 11 % by the intake of vegetables and rye products, 14 % by the intake of water-soluble fibre and only 4 % by the intake of lariciresinol. Although the assessed intake of lignans corresponded well with the urinary excretion of lignans, the enterolactone production in the human body depended more on the dietary sources of lignans than the absolute intake of lignans.

Lignans: Enterolactone: Diet: Urine

Lignans are phenolic compounds widely distributed in the plant kingdom[1]. It has been long assumed that only two plant lignans, secoisolariciresinol and matairesinol, are the dietary precursors of enterolactone and enterodiol (enterolignans), lignan metabolites that are produced after intestinal fermentation in humans[2]. It is now known that secoisolariciresinol and matairesinol are not the only dietary precursors of enterolignans[3,4], and other plant lignans, such as lariciresinol and pinoresinol, are converted to enterolignans[5]. High serum enterolactone concentrations have been associated with a reduced risk of breast cancer[6] and CVD[7], but also several studies have not observed any associations[8,9], which has caused debate on the role of enterolactone[10].

Dietary intake of lignans was first assessed by using the data only for secoisolariciresinol and matairesinol[11–13], and the intake varied from 175 to 991 μg/d[13–18]. After an analytical method was developed to measure also lariciresinol and pinoresinol in foods[19], an updated database was developed for lignans in different Dutch foods[20], and subsequently intakes of lariciresinol and pinoresinol in addition to secoisolariciresinol and matairesinol were for the first time reported in a Dutch study population[21]. The mean or median intake of the four lignans has been approximately 1000 μg/d in the Dutch, French and Canadian studies[6,21,22]. Analytical methods for

measuring food lignans are usually developed so that they give the highest possible yield for each analyte[19,23], which may lead to overestimation of the lignan intake.

Correlation between daily grain product intake (kJ/d) and 24 h urinary excretion of enterolactone has been calculated to be 0·996, indicating that cereal foods are important sources of plant lignans, which can be metabolised to enterolactone[24]. Several studies have reported the intake of whole-grain products to be the most important determinant of serum enterolactone[25–27], but also coffee, tea and alcohol affect the serum enterolactone concentrations[21,26]. The urinary excretion of enterolignans has been reported as 2·0 and 17·7 μmol/d in American omnivores and macrobiotics, respectively[24]. More recently the urinary excretion of enterolactone has been reported to be 18·4 μmol/d in Danish women[28], 23·9 μmol/d in French women and men[29], and 2·5 μmol/d in Finnish women and men[24,30]. The urinary excretion of different plant lignans has been reported, after they were identified[31]. Quantitative results for urinary plant lignans have been reported only for matairesinol[32], except in the method development paper[33]. So far none of the studies has reported the daily intake of plant lignans and the urinary excretion of plant and enterolignans. Therefore it is unclear how well the calculated intake of plant lignans

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corresponds to the urinary excretion, and on the other hand it is not known whether the intake of lignans would explain the production of enterolignans.

The aim of the present study was to assess the intake of lariciresinol, pinoresinol, secoisolariciresinol and matairesinol in Finnish men, to compare the intake of lignans with the urinary excretion of plant and enterolignans, and to study the dietary determinants of lignan intake and their urinary excretion.

Materials and methods

Study settings and population

The present study population was a subset of the participants in the Antioxidant Supplementation in Atherosclerosis Prevention (ASAP) study[34]. The ASAP study is a balanced 2×2 factorial double-masked placebo-controlled randomised clinical trial to study the effects of vitamin C and E supplementation on oxidative stress, lipid peroxidation and atherosclerotic progression in human subjects. The present study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Research Ethics Committee, Hospital District of Northern Savo. Written informed consent was obtained from all subjects. From 256 male participants, a subsample of 100 consecutive men aged 58·6 (SD 6·5) years was selected for the lignan intake study[35]. All data and samples used for the present study were collected at the baseline visit between April and October 1995 before any vitamin supplementation. Subjects collected 24 h urine sample during the preceding day of the study visit. One of the subjects took antibiotics in the preceding 6 months. The total volume of the urine sample was determined and samples were stored first at $-70^{\circ}C$ and later at $-20^{\circ}C$ until lignans were analysed.

Assessment of food and nutrient intake

The consumption of foods was assessed at the study baseline with an instructed 4 d food recording by household measures. The instructions were given and the completed food records were checked by a nutritionist. Subjects were asked to abstain from alcohol for 1 week before the laboratory visit, and alcohol consumption was recorded from a questionnaire inquiring year-round consumption. The intakes of nutrients were calculated using NUTRICA® software (version 2.5; National Public Health Institute, Turku, Finland)[36]. The contents of lariciresinol, pinoresinol, secoisolariciresinol and matairesinol in foods were entered into the database. The assessment of lignan intake was mainly based on the lignan contents of foods reported by Milder *et al.* [20] for The Netherlands. For flours we used the values published by Smeds *et al.* [37] and the lignan contents of different berries were analysed from frozen berry samples (Table 1). Values for foods containing lignans less than 10 μg/100 g fresh weight were not considered. Altogether the lignan contents of 110 foodstuffs (twenty-nine cereal foods, fifty-six vegetables, fruits and berries, and twenty-five other foods, for example, coffee and tea) commonly consumed by the Finnish population were entered into the database. On the basis of these values, the lignan content of mixed dishes was calculated.

The above-mentioned foods containing lignans were grouped as: wholegrain products (including rye products), rye products, rice, pasta, vegetables, roots, potatoes, pulses, nuts, fruits, berries, fruit juices, berry juices, jam, coffee, and tea. In more detail, the wholegrain products included different breads, flakes, bran, germ and muesli products, excluding refined flour products. The rye products contained different rye breads, rye flour, flakes, bran and malt. The rice and pasta groups included both wholegrain and refined products, and they were not included in the wholegrain products. The vegetable group included all fresh and frozen vegetables, excluding pickled and canned vegetables. The roots (most commonly consumed in Finland are carrots, Swedish turnip (swede), turnip and beetroot) included all roots, except potatoes which were grouped into a separate variable. The fruits included fresh, canned and dried fruits and fruit nectars, while other juices were included in the fruit juices. The berries included all fresh and frozen berries, crushed lingonberries and lingonberry jam, which in Finland are usually prepared without sugar. Other preserved berry and fruit products were grouped into the jam variable and berry juices into their own variable. The coffee and tea variables included these drinks, and the lignan content of a drink was entered as that in the brewed drink.

Lignan analyses of berries and breads

Lignans in Finnish berries and rye breads were analysed with HPLC using coulometric electrode array detection. The sample pretreatment for berries and breads was modified

Table 1. Lignan content of different berries (μg/100 g fresh weight)

Berries	Lariciresinol	Pinoresinol	Secoisolariciresinol	Matairesinol	Total
Strawberry (Dutch) (*Fragaria × ananassa*)	117	212	5	nd	334*
Bilberry (*Vaccinium myrtillus*)	41	59	14	nd	114
Raspberry (*Rubus idaeus*)	13	142	11	nd	166
Lingonberry (*Vaccinium vitis-idaea*)	19	586	140	nd	745
Cranberry (*Vaccinium oxycoccus*)	69	122	193	nd	384
Cloudberry (*Rubus chamaemorus*)	166	54	12	nd	232
Redcurrant (*Ribes rubrum*)	20	0	36	nd	56
Blackcurrant (*Ribes nigrum*)	0	0	109	nd	109
Gooseberry (*Ribes uva-crispa*)	10	30	82	nd	122
Sea buckthorn (*Hippophae rhamnoides*)	33	0	6	nd	39

nd, Not detected.
* From Milder *et al.* [20].

from the method published by Peñalvo et al. [23], and modifications were described by Penttinen-Damdimopoulou et al. [38]. The lignan contents of the four above-mentioned lignans (lariciresinol, pinoresinol, secoisolariciresinol and matairesinol) in the Finnish rye breads were similar to those reported by Milder et al. [20], and therefore the Dutch values for breads were used for consistency. The Dutch values for strawberries were higher than those reported by others [39,40], but again the Dutch values were used to minimise the effects of different analytical methods on the results. For the other berries, lignan contents were determined in our laboratory (Table 1). Lower values have been previously published for the four lignans in raspberries, blackcurrants and blueberries [39]. In sea buckthorn only secoisolariciresinol and matairesinol have been determined [41], but their sum was close to our value, although we detected lariciresinol instead of matairesinol.

Analysis of urinary plant and enterolignans, and serum enterolactone

Analysed lignans were secoisolariciresinol, matairesinol, pinoresinol, lariciresinol, syringaresinol, isolariciresinol, enterolactone and enterodiol. Molecular structures and metabolic pathways of these lignans are presented in Fig. 1. The urinary lignans were analysed using HPLC with a coulometric electrode array detector (HPLC-CEAD). Sample pretreatment and chromatographic conditions for urinary lignans have been described in detail previously [33]. Serum enterolactone concentrations were determined with the time-resolved fluoroimmunoassay method as described previously in detail [42].

Statistical methods

Statistical analyses were carried out with SPSS statistical software (version 14.0 for Windows; SPSS, Inc., Chicago, IL, USA). The intake of lignans and the urinary excretion of lignans were logarithmically transformed to improve normality. A stepwise linear regression analysis was used to determine the foods explaining the intake of lignans, and foods and nutrients explaining the urinary excretion of lignans. Changes for R^2, adjusted R^2 values of the models and standardised regression β coefficients were reported for the determinants. The size of the study population was divided by the median urinary excretion of enterolactone, and the means between the groups were compared with ANOVA.

Results

Intake of lignans and their dietary determinants

The mean intake of the four plant lignans was 1224 (SD 539) µg/d (median 1162 µg/d; range 250–989 µg/d), of which lariciresinol represented 40 %, pinoresinol 38 %, secoisolariciresinol 14 % and matairesinol 7 % (Table 2). Almost half (47 %) of the intake of lignans was explained by the intake of rye products, berries, coffee, tea and roots (Table 3). More than half of the intake of lariciresinol (55 %) and pinoresinol (51 %) was explained by the intake of wholegrain products, coffee, berries, and tea, but the intake of secoisolariciresinol (57 %) was explained mainly by the intake of coffee and tea. Only 13 % of the intake of matairesinol was explained, and determinants were the intake of coffee and roots. The effects of rye products on the coefficients of explanation were tested separately. A few percent reduction of the coefficient of explanation for the intake of lariciresinol (−7 %) was observed, when the rye products were entered to the model, instead of the wholegrain products. The coefficients of explanation of the intake of pinoresinol, secoisolariciresinol or matairesinol were not affected. According to the results of the regression analysis, consuming daily more of
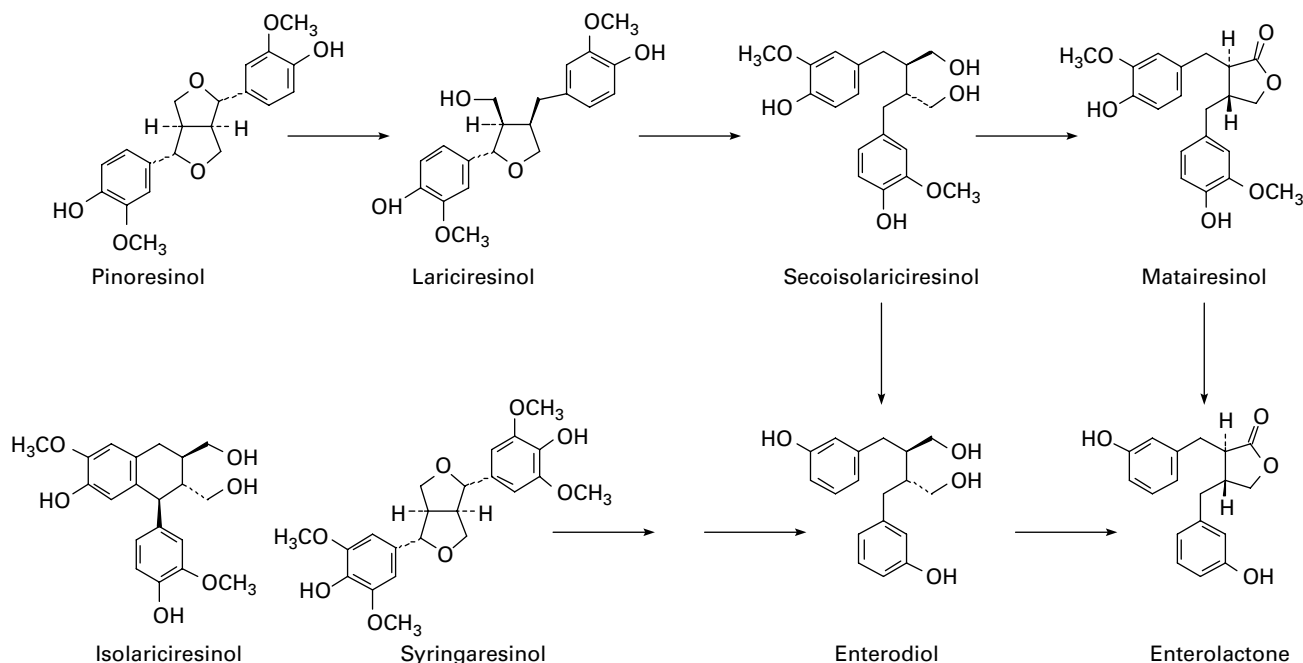

Fig. 1. Structures and metabolism of lignans.

Table 2. Dietary intake and urinary excretion of lignans

(Mean values and standard deviations)

Lignan	Proportion of lignan intake (%)	Intake from diet (μg/d)		Urinary excretion (μg/d)		Urinary excretion (μmol/d)		Proportion of intake (%)*
		Mean	SD	Mean	SD	Mean	SD	
Lariciresinol	40	494	197	85	63	0·23	0·17	17
Pinoresinol	38	467	220	22	46	0·06	0·13	5
Secoisolariciresinol	14	173	122	80	101	0·22	0·28	5
Matairesinol	7	91	81	17	26	0·05	0·07	19
Plant lignans		1224	539	204	175	0·81	0·69	17
Enterodiol		–	–	168	529	0·56	1·75	
Enterolactone		–	–	957	850	3·21	2·85	
Enterolignans				1125	999	3·77	3·35	92
Total lignans				1329	1064	4·34	3·48	109

* Percentage amount of urinary excretion of the dietary intake.

either 75 g of rye products, 45 g of berries, 273 ml of coffee or 132 ml of tea, corresponding to regular servings, would increase the intake of lignans approximately 200 μg/d, which is comparable with a 15–20 % increase in the daily intake of lignans.

Urinary excretion of lignans and their dietary determinants

The urinary excretion of the four plant lignans corresponded to 17 % of the total lignan intake, and the most extensively metabolised were pinoresinol and secoisolariciresinol, for which only 5 % of the intake was detected in the urine as such (Table 2). The urinary excretion of enterolignans represented 92 % of the intake of lignans. The total excretion of the four plant lignans

Table 3. Dietary determinants of lignan intake in a stepwise linear regression analysis

Dietary lignan	R^2 change	Determinants*	β
Plant lignans†	0·205	Rye products	0·321
	0·091	Berries	0·370
	0·073	Coffee	0·444
	0·108	Tea	0·355
	0·022	Roots	0·149
Adjusted R^2	0·472		
Lariciresinol	0·238	Wholegrain products	0·397
	0·114	Coffee	0·462
	0·082	Berries	0·359
	0·100	Tea	0·323
	0·028	Roots	0·165
	0·018	Pasta	0·138
Adjusted R^2	0·554		
Pinoresinol	0·306	Wholegrain products	0·497
	0·147	Berries	0·430
	0·025	Tea	0·275
	0·057	Coffee	0·268
Adjusted R^2	0·514		
Secoisolariciresinol	0·409	Coffee	0·732
	0·082	Tea	0·301
	0·050	Pasta	0·230
	0·026	Roots	0·167
	0·027	Berries	0·166
Adjusted R^2	0·572		
Matairesinol	0·103	Coffee	0·323
	0·039	Roots	0·198
Adjusted R^2	0·125		

* Intake of foods, *P* in 0·05 and out 0·10 in stepwise regression analysis.
† Sum of lariciresinol, pinoresinol, secoisolariciresinol and matairesinol.

and enterolignans represented 109 % of the intake of lignans. In addition to urinary plant lignans presented in Table 2, also syringaresinol and isolariciresinol were analysed. The mean urinary excretion of syringaresinol and isolariciresinol were 12 (SD 23) and 78 (SD 95) μg/d, respectively.

The urinary excretion of the four plant lignans was explained 14 % by the intake of rye products and coffee (Table 4). The highest intake of coffee (>750 ml/d) was observed in the present study among those subjects having also the highest intake of rye products (165 *v.* 105 g/d; *P*=0·005), and therefore the high intake of lignans (1817 *v.* 1127 μg/d; *P*<0·001). These subjects excreted in particular enterodiol (1·7 *v.* 0·37 μmol/d, *P*=0·054), while the urinary excretion of plant lignans was lower than among the others. Consequently, the standardised β was found to be negative for the intake of coffee as a determinant of the urinary excretion of plant lignans. The urinary excretion of lariciresinol was explained 16 % by the intake of rye products, coffee and pasta. A similar coefficient of explanation was obtained for urinary isolariciresinol, and determinants were the intake of rye products, coffee and vegetables. The urinary excretion of other plant lignans was explained only a few percent by the intake of rye products or tea, and the urinary excretion of pinoresinol had no food determinants. The urinary excretion of enterolactone was explained 11 % by the intake of vegetables and rye products and the urinary excretion of enterodiol by the intake of pasta. According to the results of the regression analysis, consuming daily either 64 g more vegetables or 75 g more rye products, corresponding to regular servings, would increase the urinary excretion of enterolactone approximately 0·75 μmol/d, which corresponds to a 23 % increase in the daily excretion.

Intake of fibre and lignans as determinants of the urinary excretion of lignans

The intake of vegetables and berries was significantly higher in the high-enterolactone group, and the intake of other fibre-rich foods, such as wholegrain products, rye products, and fruits, was also higher in the high-enterolactone group (Table 5). Although these differences were not significant, they were large enough to find significant discrepancies of fibre intake favourable to the high-enterolactone group. The intake of water-soluble fibre explained 14 % of the

Table 4. Dietary determinants of urinary lignan excretion in a stepwise linear regression analysis

Urinary lignan	R^2 change	Determinants*	β
Plant lignans†	0·101	Rye products	0·416
	0·055	Coffee	− 0·255
Adjusted R^2	0·139		
Lariciresinol	0·086	Rye products	0·410
	0·047	Coffee	− 0·276
	0·052	Pasta	0·230
Adjusted R^2	0·159		
Pinoresinol	–	No determinants	–
Secoisolariciresinol	0·050	Rye products	0·224
Adjusted R^2	0·040		
Matairesinol	0·126	Rye products	0·226
Adjusted R^2	0·041		
Syringaresinol	0·045	Tea	0·213
Adjusted R^2	0·035		
Isolariciresinol	0·085	Rye products	0·419
	0·060	Coffee	− 0·276
	0·035	Vegetables	0·189
Adjusted R^2	0·155		
Enterolactone	0·069	Vegetables	0·290
	0·058	Rye products	0·243
Adjusted R^2	0·109		
Enterodiol	0·039	Pasta	0·198
Adjusted R^2	0·029		

* Intake of foods, P in 0·05 and out 0·10 in stepwise regression analysis.
† Sum of lariciresinol, pinoresinol, secoisolariciresinol and matairesinol.

urinary excretion of enterolactone, while the intake of water-insoluble fibre explained 3–7 % of the urinary excretion of enterodiol and plant lignans secoisolariciresinol and isolariciresinol (Table 6). The intake of fibre, in general, explained 12 % of the urinary excretion of plant lignans, and 9 % of the urinary excretion of lariciresinol. The intake of lignans in the high-enterolactone group differed from that of the low-enterolactone group only by 176 μg/d, but the urinary excretion of enterolignans differed 1300 μg/d (4·02 μmol/d) (Table 5). Consequently, the intake of lariciresinol explained only 4 % of the urinary excretion of enterolactone, 6 % of the urinary excretion of lariciresinol, and 8 % of the urinary excretion of plant lignans, while the intake of matairesinol explained 5 % of the urinary excretion of pinoresinol (Table 6).

Discussion

The present study reported for the first time the intake of four plant lignans and their urinary excretion in the subjects consuming their habitual omnivorous diet. The intake of lignans obtained by dietary assessment corresponded well to the excreted amount of plant and enterolignans, indicating that the studied plant lignans in foods were the major enterolignan precursors in the Finnish diet. Major determinants of the lignan intake were wholegrain and rye products, berries, coffee, tea and roots. The intake of lignans was much better explained by the intake of particular foods than was explained the urinary excretion of plant and enterolignans. Major dietary determinants of the urinary excretion of lignans were the intake of rye products, coffee, vegetables and pasta. As well, the urinary excretion of plant and enterolignans was explained by the intake of fibre, but to a lesser extent by the intake of

lignans, meaning that the enterolactone production depended more on the dietary sources of lignans than on the absolute intake of lignans.

The median intake of lariciresinol, pinoresinol, secoisolariciresinol and matairesinol in the present study (1162 μg/d) was similar to that observed in French women (1112 μg/d)[6]. A slightly lower median intake of lignans has been observed in Dutch men and women (979 μg/d)[21] and in Canadian women (857 μg/d)[22]. The percentage contributions of lariciresinol, pinoresinol, secoisolariciresinol and matairesinol to the daily intake were very similar in the present study compared with those cited above[6,21], although in the Canadian women the major lignan was reported to be secoisolariciresinol[22], corresponding to flaxseed as a major source of lignans contributing as much as 88 % of the total intake.

Before the knowledge of other precursors, the intake of secoisolariciresinol and matairesinol was defined as 285 μg/d in Finnish men[13], corresponding well with our value (264 μg/d), indicating that previous results for secoisolariciresinol and matairesinol are well in line with the new values, although different study populations, methods for dietary data, and lignan contents for foods have been used. In the other studies much higher intakes for secoisolariciresinol and matairesinol have been reported, but those studies have used lignan content values of foods obtained after *in vitro* faecal fermentation[14,17], which overestimates the amount of secoisolariciresinol and matairesinol in foods.

The intake of plant lignans in the present study was explained by the intake of wholegrain or rye products, berries, coffee, tea, roots and pasta, and the intake of rye products covered 75 % of the daily intake of wholegrain products. The high intake of wholegrain products is a characteristic of the Finnish diet, as in the Dutch study tea and coffee contributed 30 % and vegetables 24 % to the intake of lignans[21], while in the French women fruits and vegetables contributed together 66 %, tea 11 %, but the cereal foods only 7 %[6]. In the present study the intakes of different lignans were also explained by the intake of tea and coffee, but only the intake of secoisolariciresinol was mainly determined by coffee. The intake of tea, although low in the present study, still partly explained the intake of all lignans except matairesinol. In the Dutch study, multigrain bread was reported to be a relevant source of lignans because of its potential content of flaxseed and sesame[21], by far the richest sources of lignans[21,43]. In the present study subjects did not eat nuts or seeds, and at the time of the study availability of breads containing flaxseed or sesame seed was limited in Finland. This aspect, however, deserves attention in future studies. In the previous studies the intake of berries was reported together with fruits, and the separate contribution of berries to the intake of lignans could not be discerned[6,21]. In the present study the intake of berries explained the intake of plant lignans, whereas the intake of fruits, twice as much as that of berries, had no clear effect on the lignan intake. The intake of berries was before recognised as a determinant of secoisolariciresinol and matairesinol intake in Finnish men[13], which has now been confirmed in the present study.

Although lignans have been detected in some amount almost everywhere[44,45], the present results support previous findings indicating that lariciresinol, pinoresinol, secoisolariciresinol

Table 5. Intake of foods, drinks and nutrients, and urinary excretion of lignans in Finnish men

(Mean values and standard deviations)

	All		<2·5 μmol/d*		≥2·5 μmol/d†		
	Mean	SD	Mean	SD	Mean	SD	P‡
Foods and drinks							
Wholegrain products (g/d)	152	76	140	61	164	87	0·122
Rye products (g/d)§	114	75	101	62	127	84	0·086
Pasta (g/d)	12	26	11	22	13	30	0·719
Rice (g/d)	7	9	5	6	8	12	0·112
Vegetables (g/d)	92	64	77	48	107	74	0·021
Roots (g/d)	23	27	21	27	25	26	0·442
Fruits (g/d)	76	145	55	65	96	193	0·163
Berries (g/d)	38	45	28	44	47	45	0·031
Coffee (ml/d)	488	273	440	254	535	285	0·083
Tea (ml/d)	65	132	67	117	64	147	0·910
Fruit juices (ml/d)	34	98	28	94	40	102	0·521
Berry juices (ml/d)	82	189	74	208	89	171	0·687
Alcohol (g/week)	102	103	108	103	97	104	0·597
Nutrient intakes							
Lignans (μg/d)‖	1224	539	1136	453	1312	603	0·104
Fibre (g/d)	24	9	21	7	27	10	0·001
Water-soluble fibre (g/d)	5	2	5	1	6	2	0·001
Water-insoluble fibre (g/d)	12	5	10	4	13	6	0·001
Lignans in serum and urine							
Serum enterolactone (nmol/l)	16·6	14·4	7·13	6·28	26·0	14·0	<0·001
Urinary enterolactone (μmol/d)	3·21	2·85	1·20	0·76	5·22	2·76	<0·001
Urinary enterodiol (μmol/d)	0·56	1·75	0·37	0·42	0·74	2·40	0·299
Urinary lariciresinol (μmol/d)	0·23	0·18	0·23	0·20	0·24	0·14	0·675
Urinary pinoresinol (μmol/d)	0·06	0·13	0·05	0·06	0·07	0·17	0·382
Urinary secoisolariciresinol (μmol/d)	0·22	0·28	0·19	0·23	0·25	0·32	0·344
Urinary matairesinol (μmol/d)	0·05	0·07	0·04	0·07	0·05	0·08	0·617
Urinary syringaresinol (μmol/d)	0·03	0·05	0·03	0·04	0·03	0·06	0·661
Urinary isolariciresinol (μmol/d)	0·22	0·26	0·20	0·23	0·23	0·30	0·610
Urinary plant lignans (μmol/d)‖	0·57	0·49	0·52	0·46	0·61	0·51	0·317

* Low-enterolactone group in the text.
† High-enterolactone group in the text.
‡ P for ANOVA.
§ Included in wholegrain products.
‖ Sum of lariciresinol, pinoresinol, secoisolariciresinol and matairesinol.

and matairesinol are the main enterolignan precursors in a regular, non-supplemented diet. Even though syringaresinol and medioresinol have been found in high concentrations in cereals, in particular rye[23,37], the present results suggest that a minor fraction of them is metabolised to enterolactone. Otherwise, a larger difference between the intake and 24 h urinary excretion of lignans would have been observed, because the amount of syringaresinol alone in rye is almost as high as the amount of plant lignans included to the assessment of intake. Indeed, the metabolism of syringaresinol to enterolactone has been shown to be ineffective[5], but a possible biological action of this abundant lignan deserves further investigation.

The urinary excretion of plant lignans and enterolactone was explained by the intake of rye products, but not by wholegrain products, although rye products represented 75 % of the intake of wholegrain products. The highest intake of rye products was observed among the heavy coffee drinkers, and they also excreted more enterodiol, but not enterolactone. The high urinary excretion of enterodiol might occur due to a high intake of fibre shortening the transit time, and thus decreasing the effective fermentation time reported to increase serum

enterolactone[25], although the coffee itself does not decrease the transit time[46]. The urinary excretion of enterolactone and isolariciresinol was explained by the intake of vegetables, which has been found to be a determinant of serum enterolactone concentration[25–27] and to contribute to the lignan intake[6,21]. The urinary excretion of pinoresinol had no food determinants at all, and it was one of the most extensively metabolised plant lignans. This observation was in line with the previously suggested metabolic pathway (Fig. 1)[5] later confirmed[47].

The mean urinary excretion of enterolactone in the present study (3·2 μmol/d) was between the values observed before in Finnish omnivorous and lacto-vegetarian women[24], but lower than the mean urinary excretion in French men and women (23·9 μmol/d)[29], despite the similar lignan intake in both studies. The intake of lignans in the present study was mainly due to a high intake of cereal products containing water-insoluble fibre in contrast to vegetables, fruits and beverages which were major sources of lignans in the French and Dutch populations[6,21]. Indeed, in the present study the urinary excretion of enterolactone was explained by the intake of water-soluble fibre, while the urinary

Table 6. Intake of fibre and different lignans as determinants of the urinary excretion of lignans in a stepwise linear regression analysis

Urinary lignan	R^2 change	Determinants*	β
Plant lignans†	0·126	Fibre	0·355
Adjusted R^2	0·117		
Plant lignans†	0·090	Lariciresinol	0·302
Adjusted R^2	0·082		
Lariciresinol	0·101	Fibre	0·318
Adjusted R^2	0·092		
Lariciresinol	0·071	Lariciresinol	0·266
Adjusted R^2	0·061		
Pinoresinol	0·058	Matairesinol	0·241
Adjusted R^2	0·048		
Secoisolariciresinol	0·083	Water-insoluble fibre	0·287
Adjusted R^2	0·073		
Secoisolariciresinol	0·061	Plant lignans†	0·248
Adjusted R^2	0·052		
Matairesinol	–	No determinants	–
Syringaresinol	–	No determinants	–
Isolariciresinol	0·080	Water-insoluble fibre	0·284
Adjusted R^2	0·071		
Enterolactone	0·151	Water-soluble fibre	0·388
Adjusted R^2	0·142		
Enterolactone	0·054	Lariciresinol	0·232
Adjusted R^2	0·044		
Enterodiol	0·042	Water-insoluble fibre	0·204
Adjusted R^2	0·032		

* Intake of fibre or lignans, P in 0·05 and out 0·10 in stepwise regression analysis.
† Sum of lariciresinol, pinoresinol, secoisolariciresinol and matairesinol.

excretion of enterodiol and different plant lignans was explained by the intake of water-insoluble fibre, or fibre in general. According to these observations the urinary excretion of enterolactone, i.e. lignan metabolism, depends to some extent on the absolute intake of lignans, but more strongly on the dietary sources of lignans. The conversion of enterodiol to enterolactone was less efficient in the low-enterolactone group in contrast to the high-enterolactone group, indicating the lower activity, or lack of appropriate colon microflora[47]. Antibiotics, which have been shown to affect enterolactone production for several months[48,49], were taken before the study only by one of the subjects who excreted enterodiol, but hardly any enterolactone.

Although the intake of lignans and their urinary excretion corresponded well, there are some limitations in the present study. The intake of lignans in Finnish men was calculated by using mainly the lignan contents for Dutch foods. In addition to geographical differences in foods, lignan contents of foods are also affected, for example, by climate, site of growth and plant variety[20]. However, we compared the lignan content of Finnish rye breads with the values presented for the Dutch breads[20], and observed similar concentrations in both products. The assessment of lignan intake was carried out by using 4 d food recording, the content of which may depend on the season in Finland. For example, intake of berries and vegetables might be higher during the summer season in contrast to winter, and the present study population included subjects only from April till October. However, this possible overestimation of the intake of lignans does not seem to be relevant, since the intake of secoisolariciresinol and matairesinol corresponded to the values presented before for Finnish men[13]. The urine samples in the present study were stored 12 years before the lignan analyses.

Separate data on the stability of lignans in urine have not been published, but plant and enterolignans are quite stable at least at high temperature, in acid, and base, which are regularly applied for the sample pretreatment in food lignan methods[19,23,37,44]. In addition to the possible effects of storage time and conditions, urinary excretion of lignans varies from day to day, depending on diet and variations in the activity of colon microflora[30]. Food recording and 24 h urine sample collection in the present study were not matched by time, which might cause some discrepancy to the present results. Despite all of these above-mentioned methodological limitations, the intake of lignans corresponded well to the urinary excretion of lignans, which we believe cannot be pure coincidence.

In the present study the intake of lignans (lariciresinol, pinoresinol, secoisolariciresinol and matairesinol) in Finnish men compares to the urinary excretion of plant and enterolignans, and consumed plant lignans undergo extensive metabolism in the body resulting in mainly one compound, enterolactone. A relevant fraction of plant lignans, however, is absorbed intact or only partially metabolised. The urinary excretion of enterolactone, indicating the efficiency of lignan metabolism, depended more on the dietary sources of lignans than on the absolute intake of lignans. In the future, the associations between the intake of lignans or the body enterolactone concentrations and a risk of chronic diseases should be studied in the same study population to find out whether enterolactone production as such has relevance or does the diet alone count more.

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