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THE INFLUENCE OF DIETARY FACTORS ON THE RISK OF URINARY STONE FORMATION

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Abstract

The action of various beverages and foods on the composition of the urine in the circadian rhythm and in the 24-hour urine has been investigated under standardized conditions. Orange juice leads to a significant increase of urinary pH and citric acid excretion. Black tea leads to a raised excretion of oxalic acid by only 7.9%. In the short term, beer increases diuresis, but afterwards leads to a compensatory antidiuresis with increased risk of stone formation. Depending on their composition, mineral waters have very different effects on the urinary constituents. Milk as well as cocoa beverage significantly increase calcium excretion; moreover, cocoa causes an increase in the oxalic acid excretion. The leafy vegetable foods containing oxalate, e.g., spinach and rhubarb, lead to peaks of oxalate excretion of 300-400% in the circadian excretion curve. Cheese leads to a significant rise of calcium excretion with acidification of the urine and lowering of citrate excretion. Calcium excretion is increased by 30% by sodium chloride. Foods containing purine result in an increased uric acid excretion over several days. Depending on their phytic acid content, brans bind calcium, but lead to an increased oxalic acid excretion.

Analysis of the urine indicates that average diet in Germany entails a high risk of urinary stone formation. As a result of the change to a balanced mixed or vegetarian diet, according to the requirements, significant alterations in urinary pH, calcium, magnesium, uric acid, citric acid, cystine, and glycosaminoglycan excretion are measured, resulting in a drastic reduction in the risk of urinary stone formation.

Key Words: Dietary factors; urinary composition: pH, citric acid, calcium, magnesium, oxalic acid, uric acid, glycosaminoglycans, cystine; relative supersaturation.

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Introduction

After World War II, urolithiasis in Europe increased in parallel with the increasing prosperity of the population. The undernutrition in the last years of the war and afterwards led to lowering of the incidence of urinary stones [19]. Since the 1970's, an equally high prevalence of urolithiasis of 4-5% has been demonstrated in Germany [20], and this figure is probably representative for Western Europe. The correlation between the risk of urinary stone formation and overnutrition was recognized at a very early stage. A correlation could be established between income and expenditure on food [16, 17]. An increasing intake of animal protein, purine, fat, refined carbohydrates and sodium chloride with a simultaneous decrease in the intake of dietary fiber was associated with this. The high-energy food requires a higher drinking volume [10] to flush out and dilute the lithogenic substances which have to be excreted via the kidneys [10].

In view of the increase in the frequency of urolithiasis in Germany, nutrition is today one of the most important prerenal epidemiological risk factors for urolithiasis [1, 6, 9]. In our investigations, the determination of risk factors in calcium oxalate urolithiasis showed that a major effect of diet can be demonstrated especially in hyperuricosuria and hypocitraturia (Figures 1a and 1b). In administration of neutral beverages, a significant lowering of the risk of urinary stone formation is attained solely by the urinary dilution (Fig. 2).

In standardized investigations with healthy subjects, we have tested various effects of diet on the composition of the urine and the calculated risk of urinary stone formation.

Materials and Methods

Healthy subjects

All investigations were carried out in healthy subjects aged 25-35 years. The number of test subjects varied from trial to trial and is specified in the individual investigations.

Standardization of the investigations

All test subjects received a standardized diet

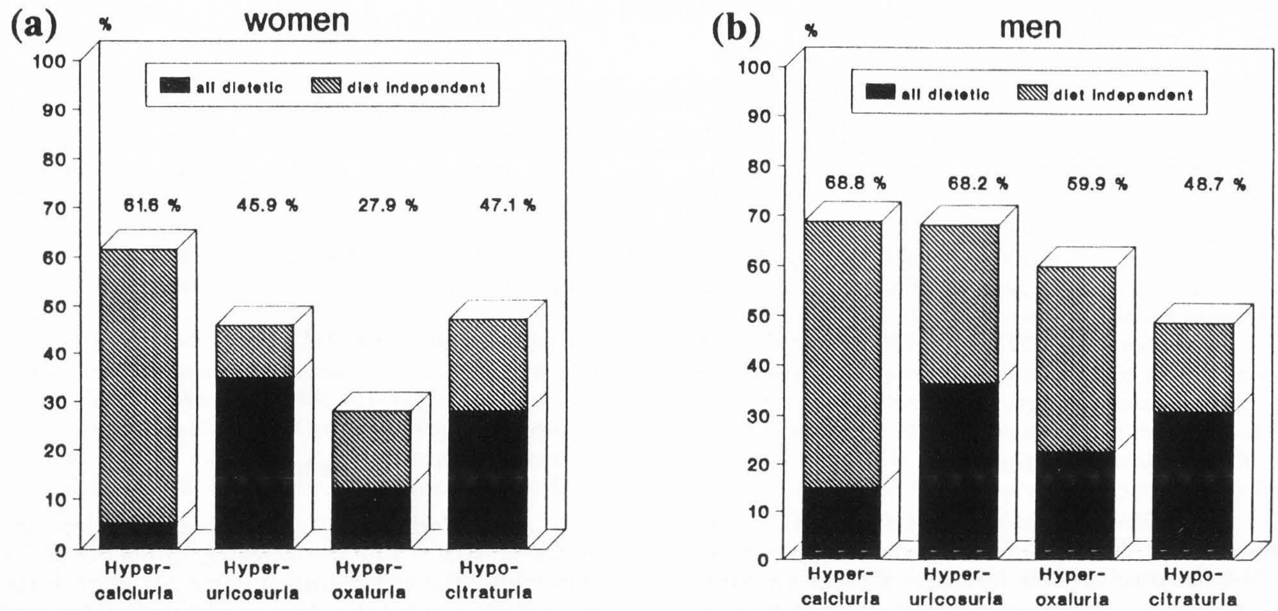

Figure 1. Risk factors in calcium oxalate urolithiasis (n = 486) and the importance of dietary factors for **(a)** women (n = 172) and **(b)** men (n = 314).

consisting of normal foods to ensure consistency of the investigation results. The same was eaten and drunk each day. Sport and other extreme exercise were ruled out in the experimental phase.

On the exposure/loading days, one beverage or one food was exchanged for the food to be tested. A two to five day phase of adaptation/habituation preceded each exposure phase.

The standard diet had the following composition:

Energy	2500 kcal
Total protein	95 g
Fat	82 g
Carbohydrate	370 g
Fiber	30 g
Sodium	3.8 g
Potassium	3.3 g
Phosphorus	1.3 g
Calcium	0.8 g
Magnesium	0.3 g
Vitamin C	74 mg

Drinks consisted of 2,400 ml of neutral beverages (fruit tea, apple juice, decaffeinated coffee).

The drinks and foods tested are listed in Table 1. To test various diets, standardized daily diet plans, which were fulfilled by the constituents, were drawn up (Table 2). The urine samples were collected in polyethylene receptacles and mixed with 5 ml/l of a 5% solution of thymol in isopropanol to preserve the urine. The individual urinary parameters were determined with the methods specified in Table 3 [8]. The relative supersaturation with calcium oxalate and other stone-forming components in the 24-hour urine was calculated with the EQUIL program [5, 21].

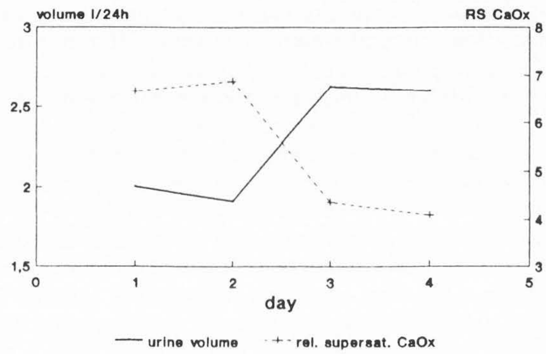

Figure 2. Relative supersaturation (--+--) with calcium oxalate (calculated by EQUIL) as a function of 24-hour urine volume (——).

The Wilcoxon matched-pairs signed-rank test was used to check for statistical significance between test pairs in bran studies. In all other investigations, U-test of Wilcoxon, Mann and Whitney was chosen. Significance level was at 5%.

Results

Urinary dilution

Orange juice: Immediately after the exposure/loading (500 ml at 9 AM and 11 AM), a significant rise in the urinary pH occurs in the course of the day which persists to the following day. In parallel to this, the citric acid excretion rises significantly; however, this already reaches the initial value by the evening. It is striking that the calcium excretion after intake of orange

Table 1. Overview of the assay arrangements of the tested beverages and foods.

beverages/foods	quantity	n
orange-juice	1 l	9
black-tea	1,5 l (21 g)	10
beer (regular)	1 l	7
soda-water A (HCO_3: 3388 mg/l)	1 l	12
soda-water B (HCO_3: 73 mg/l)	1 l	9
milk	1 l	9
cocoa-beverage	1 l	9
spinach	200 g	6
rhubarb	200 g	10
cheese (gouda)	100 g	11
sodium-chloride	13 g	10
purine	2 g	15
liver	150 g	11
herring	200 g	6
bran, rice	36 g	15
soy	36 g	15
wheat	36 g	15
diets, normal-mixed	3590 kcal	10
optimized-mixed	2544 kcal	10
ovo-lacto-vegetarian	2600 kcal	10

Table 2. Composition of the diets (main factors).

content	normal mixed diet	optimized mixed diet	ovo-lacto-vegetarian diet
energy (kcal)	3590	2544	2600
protein (g)	95	65	65
fat (g)	132	82	84
alcohol (g)	49	0	0
fiber (g)	24	28	52
purines (mg)	509	291	202
calcium (mg)	876	768	787
oxalic acid (mg)	66	74	129

juice falls significantly for several hours (Table 4), whereas the oxalic acid excretion remains unchanged. In the 24-hour urine, there is a fall of the relative supersaturation for calcium oxalate from 2.99 to 2.05 (-31%) on the day of exposure.

Beer: Regular beer ("Kölsch"-beer) leads to an increase of the urine volume and the specific gravity in the urine is lowered immediately after consuming beer (Table 4). However, this effect only persists for a short time. There is a reduction of urinary excretion (antidiuresis) as early as 2-3 hours after cessation of beer intake, and this persists for a long time with a raised specific gravity. Furthermore, a rise of the uric acid excretion and the fall of the urinary pH is measured. The relative supersaturation with calcium oxalate increases from 3.07 to 3.45 (12.4%) on consumption of 1 litre of beer.

Black tea: The extreme intake of 1.5 litre of tea from 21 g of tea-leaves over the day leads to an increase of the oxalic acid excretion by only 7.9% (from 0.305 to 0.329 mmol/24 h; Fig. 3). With the tea, 0.959 mmol (86.3 mg) of oxalic acid is ingested, so that 2.5% is excreted in the urine. In parallel to the increase of the

Table 3. Analytes and principles of analytical methods.

Analytes	Analytical methods	CV (%)
Volume of urine	gratuated cyliner	-
Density	urometer	-
pH	glass elctrode	-
Ammonium	selective electrode	1.5
Sodium	flame photometer	1.3
Potassium	flame photometer	1.3
Calcium	AAS	0.2
Magneisum	AAS	0.4
Chloride	coulometry	2.0
Inorg. phosphorus	molybdate reaction	< 5
Inorg. sulfate	nephelometry	< 5
Uric acid	enzymatic, uricase	< 5
Oxalic acid	ion chromatography	< 2
Citric acid	enzym., citrate lyase	1.6
Creatinine	Jaffé reaction	2.0

CV (%) = coefficient of variation in per cent.

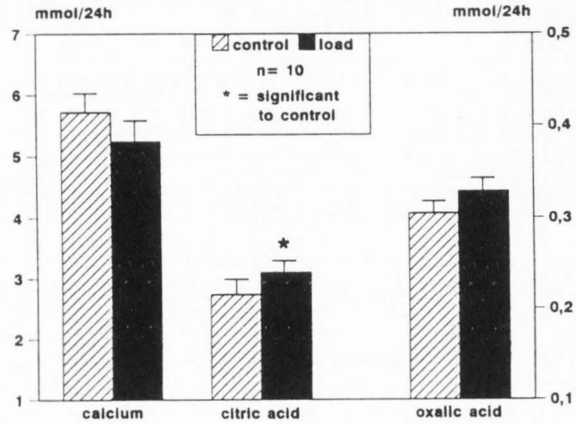

Figure 3. Urinary oxalic acid, calcium, and citric acid excretion [mean and standard error of mean (SEM); 24 hour] on black tea loading (n = 10).

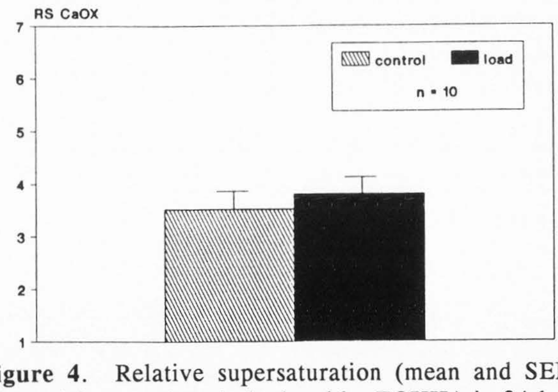

Figure 4. Relative supersaturation (mean and SEM) with calcium oxalate (calculated by EQUIL) in 24-hour urine on black tea loading (n = 10).

oxalic acid excretion, the calcium excretion falls slightly on black tea load. It appears to us to be important that although, the excretion of citric acid, an inhibitor in calcium oxalate lithiasis, is significantly raised by black tea, only a slight increase (7.4%) in the relative supersaturation with calcium oxalate is calculated (Fig. 4).

Table 4. Urinary composition on orange juice and beer loading.

time		orange juice (n=9)						beer (n=7)			
		pH		citric acid µmol/h		calcium µmol/h		volume ml/h		specific gravity	
		control	load	control	load	control	load	control	load	control	load
7-9	M	6.87	6.79	100	114	101	117	61.8	75.5	1010	1011
	SEM	0.25	0.25	16	19	26	18	17.5	27.0	1.9	2.1
9-11	M	6.42	6.67	126	212*	167	191	147.5	232.5	1006	1002*
	SEM	0.16	0.12	17	29	22	31	28.2	27.5	1.7	0.6
11-13	M	6.50	7.11*	161	274*	199	170	297.5	364.6	1002	1001
	SEM	0.22	0.10	41	30	20	23	22.5	25.1	0.4	0.3
13-16	M	6.24	6.86*	149	172	274	131*	131.2	64.5*	1007	1013*
	SEM	0.17	0.20	15	25	45	14	14.4	7.2	1.3	1.0
16-19	M	6.25	6.89*	139	160	196	150	116.7	58.8*	1007	1014*
	SEM	0.16	0.10	27	27	39	24	8.3	4.6	0.8	0.7
19-22	M	5.90	6.24	113	133	174	154	66.4	55.2	1012	1015
	SEM	0.18	0.21	23	22	37	32	11.2	7.6	2.0	1.2
22-7	M	6.05	6.32	71	74	94	85	46.3	46.7	1012	1012
	SEM	0.16	0.20	12	9	15	11	10.1	7.0	1.2	1.7

M = mean; SEM = standard error of mean. *Significant to control day.

Table 5. Nutrient content of milk and cocoa beverages and influence on urine composition.

parameter	milk (1 litre) (n=9)					cocoa beverage (1 litre) (n=9)				
	content (mg/l)	control day mmol/24h-urine		loading day mmol/24h-urine		content (mg/l)	control day mmol/24h-urine		loading day mmol/24h-urine	
		M	SEM	M	SEM		M	SEM	M	SEM
sodium	480	150.60	8.50	166.50	7.80	504	127.80	8.00	169.60*	10.80
potassium	1570	49.80	4.10	62.80*	3.60	2390	43.20	3.50	66.10*	4.30
calcium	1200	3.48	0.37	4.70*	0.30	1246	2.85	0.46	3.35	0.43
magnesium	120	4.40	0.20	4.82	0.32	292	4.27	0.23	4.50	0.22
phosphate	920	17.60	1.90	24.40*	2.10	1304	14.60	2.20	19.90*	0.80
oxalic acid	7	0.49	0.05	0.41*	0.03	256	0.46	0.02	0.50	0.03
citric acid	-	2.61	0.18	2.85	0.26	-	2.18	0.25	2.51*	0.19
creatinine	-	12.00	0.70	12.00	0.70	-	10.50	0.70	11.30	0.90
RS CaOx		4.02	0.73	5.08	0.85		3.80	0.77	4.63	0.89

*significant to control day.

The urinary pH and all other measured parameters (Table 3) are not affected by black tea.

Mineral water: Mineral water is an ideal beverage to dilute the urine. However, the respective calcium content must be considered. Alkalization therapy can be supported with the high bicarbonate content of mineral water. In our investigations with the high-bicarbonate water A, an increase of urinary pH and citric acid excretion is attained over the entire day (Figs. 5 and 6). If the mineral water contains only little bicarbonate (B), the urinary pH and the citric acid excretion are not affected.

Water A contains relatively large amounts of minerals: 232 mg/l calcium, 337 mg/l magnesium and 365 mg/l sodium. Nevertheless, a reduction of the relative supersaturation with calcium oxalate by 12% is attained with the constant urine dilution. On the other hand, water B is completely neutral; the relative supersaturation remains unchanged.

Milk: After drinking milk, the potassium, calcium and phosphate excretion in the urine increases significantly. The oxalic acid excretion falls significantly, but the relative supersaturation with calcium oxalate rises from 4.0 to 5.1 (+ 29%; Table 5).

Cocoa beverage: A significant increase of sodium, potassium, phosphate and citric acid excretion in the urine is induced by cocoa. The calcium and oxalic

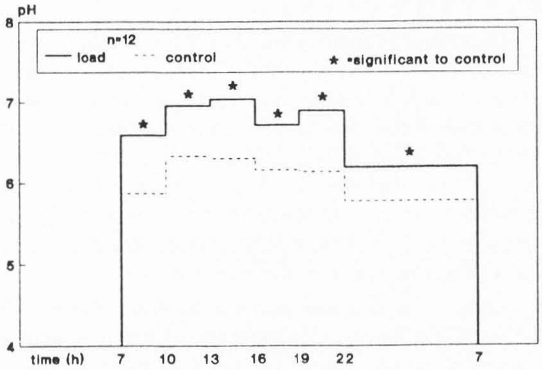

Figure 5. Circadian rhythm of urinary pH on soda water (A) loading (HCO_3^-: 3388 mg/l).

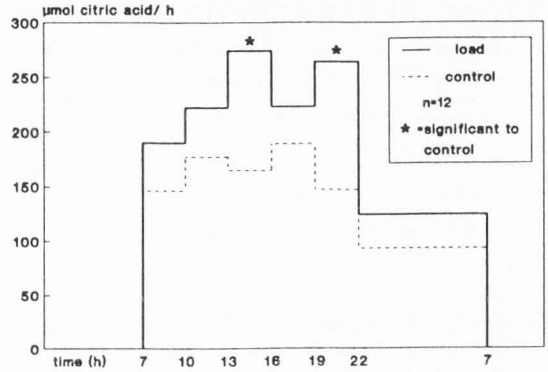

Figure 6. Circadian rhythm of urinary citric acid excretion on soda water (A) loading (HCO_3^-: 3388 mg/l).

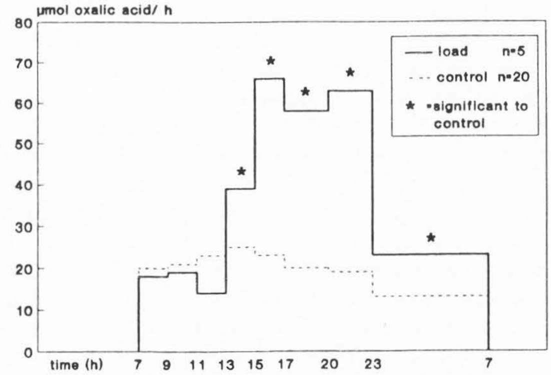

Figure 7. Circadian rhythm of urinary oxalic acid excretion on spinach loading (200 g).

acid excretion also rises (though not significantly). The relative supersaturation with calcium oxalate in the 24-hour urine rises by 22% after consumption of 1 litre of cocoa beverage (Table 5).

Foods containing oxalate

Spinach: The oxalic acid excretion in the circadian rhythm increases to more than 300% even on consumption of normal amounts of spinach (200 g) for

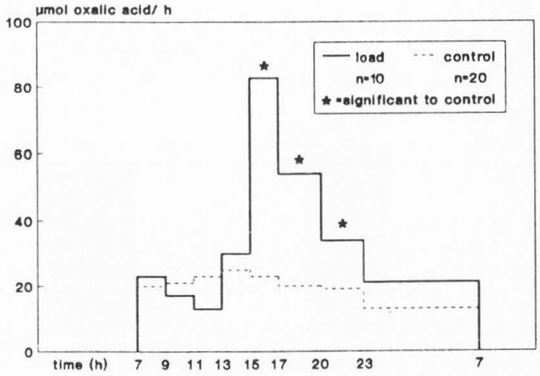

Figure 8. Circadian rhythm of urinary oxalic acid excretion on rhubarb loading (200 g).

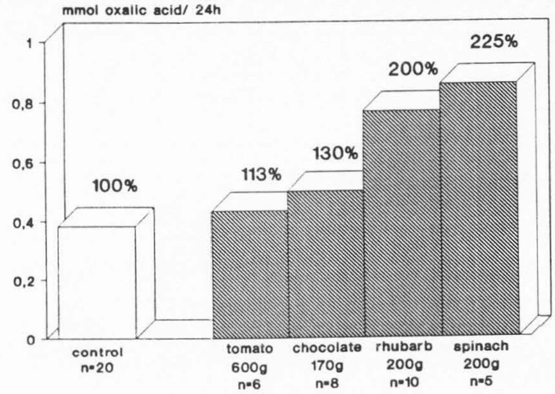

Figure 9. Urinary oxalic acid excretion (24 hours) on the intake of various foods.

lunch, and the excretion remains raised above the normal level until the earlier hours of the morning (Fig. 7).

Rhubarb: Consumption of 200 g boiled rhubarb leads to extreme oxalic acid excretion (more than 400%) in the urine after 2-4 hours. In the subsequent hours, the excretion falls again relatively rapidly (Fig. 8). It can be inferred from this that in the case of rhubarb, the oxalate ions are more available and are quickly absorbed via the intestine. After consumption of spinach, however, the oxalate ions are only released progressively from the cells in the course of passage through the intestine.

The comparison of foods with various oxalate contents: tomatoes (low), chocolate (moderate), rhubarb and spinach (high), shows (Fig. 9) that normal amounts of tomatoes are harmless, that the limit value of oxalate excretion in the urine (0.5 mmol/24 h) is exceeded after regular consumption of chocolate and that rhubarb as well as spinach lead to a pronounced hyperoxaluria in the 24-hour urine.

Foods and calcium

Cheese: Intake of 800 mg calcium with gouda cheese leads to a significant rise of calcium and magnesium excretion in the urine (Fig. 10). At the same time, the urinary pH, citric acid and oxalic acid excretion decrease. Regular consumption of cheese always entails a risk of urolithiasis.

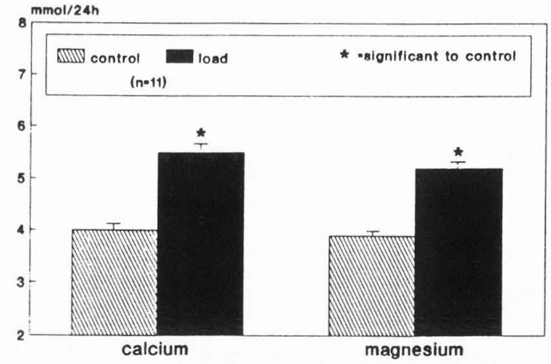

Figure 10. Calcium and magnesium excretion (mean and SEM) in 24-hour urine on cheese loading (n = 11).

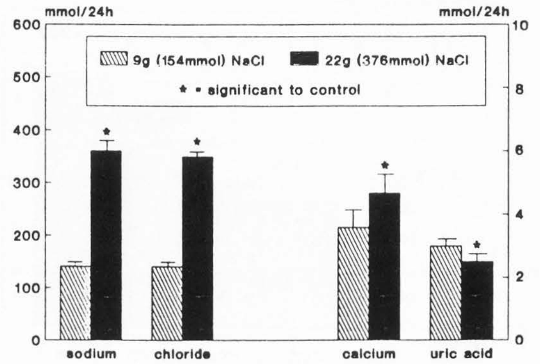

Figure 11. Influence of sodium chloride on the urinary excretion (mean and SEM; 24 hours) of sodium, chloride, calcium and uric acid (n = 10).

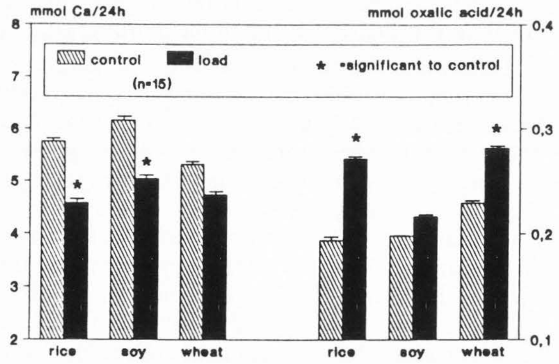

Figure 12. Calcium and oxalic acid excretion (mean and SEM) in 24-hour urine on bran (rice, soy, wheat) loading (n = 15).

Sodium chloride: The increased consumption of sodium chloride leads consecutively to an increased calcium excretion in the urine. In our experiments with an additional sodium chloride intake of 13 g (222 mmol), the calcium excretion is raised significantly (30%). Uric acid excretion falls concomitantly with the rise in calcium excretion (Fig. 11).

Foods containing purine

Guanine/adenine mixture: This synthetic purine mixture is used to carry out the purine loading test to determine a latent hyperuricemia [7]. On the loading day, and especially on the day after loading, there is a significant increase in uric acid excretion in the 24-hour urine. On the third day, the uric acid excretion returns to the initial values. On the other hand, the urinary pH, the oxalic acid, and citric acid excretion are not changed by the purine mixture (Table 6).

Liver: A normal portion of liver (150 g) for lunch leads to a significant increase of the uric acid excretion in the urine which still persists even on the following day. It is striking here that the pH value rises and that a significant increase in the potassium and citric acid excretion occurs in the 24-hour urine. The oxalic acid excretion is once more not affected (Table 6).

Herring: This kind of purine intake also leads to a significantly higher uric acid excretion in the 24-hour urine. Owing to the concomitant increase of sodium chloride, the 24-hour urine volume is significantly reduced. The oxalic acid and citric acid excretions remain unchanged (Table 6).

Foods containing bran

Bran products bind calcium in consequence of their phytic acid content. Hence, after intake of various brans, there is a reduced calcium excretion in the urine (Fig. 12). However, there is a concomitant increase in the oxalic acid excretion in the urine, so that specific therapeutic administration is only appropriate in hyperabsorption of calcium.

Diets

The testing of three different diets takes into consideration on one hand all the unfavorable dietary habits and on the other hand all the health-promoting recommendations without particular attention being paid to urolithiasis in establishing the composition of the foods. The normal mixed diet corresponds exactly to the average composition and amount determined in the "Nutritional Survey" in Germany [3], whereas the optimized and vegetarian diets are isoenergetic. With a volume of 1.5 litres, the fluid intake in the normal diet likewise corresponded to the average, whereas the two optimized diets comprised 2.5 litres of fluids per day. The risk of dietetic urinary stone formation can thus be inferred directly from the urine parameters measured. The two dietary switches alone give rise to a significant increase in the **urinary pH** in each case (Table 7), and the excretion of **uric acid** falls significantly. Whereas the excretion of **calcium** in the urine decreases significantly, there is a significant increase in the excretion of **magnesium**. It is very interesting that the **citric acid** excretion is significantly raised by the optimized mixed diet or also the vegetarian diet. On the other hand, the **oxalate** excretion is not affected by the optimized mixed diet: more oxalate (highly significant) is excreted on the vegetarian diet. This effect is especially remarkable

Table 6. Urinary composition on purine loading with guanine/adenine mixture, liver and herring.

parameter	guanine/adenine - mixture (2g) (n=15)				liver (150g) (n=11)			herring (200g) (n=6)		
	day 0 control M SEM	day 1 loading M SEM	day 2 M SEM	day 3 M SEM	day 0 control M SEM	day 1 loading M SEM	day 2 M SEM	day 0 control M SEM	day 1 loading M SEM	day 2 M SEM
uric acid (mmol/24h)	0.50 0.09	4.11 0.04	5.02* 0.09	3.63 0.07	2.80 0.07	3.67* 0.08	3.36 0.08	2.50 0.13	2.90* 0.18	2.68 0.13
pH	6.11 0.03	6.02 0.05	6.04 0.02	6.23 0.03	6.02 0.03	6.25 0.04	6.07 0.05	6.57 0.11	6.39 0.11	6.43 0.11
citric acid (mmol/24h)	3.80 0.11	4.02 0.12	3.92 0.11	3.81 0.09	2.44 0.11	3.66* 0.09	3.96* 0.13	3.35 0.31	3.32 0.31	3.43 0.40
oxalic acid (mmol/24h)	0.498 0.007	0.433 0.008	0.361 0.004	0.359 0.006	0.416 0.008	0.422 0.011	0.402 0.011	0.323 0.024	0.306 0.027	0.267 0.022
potassium (mmol/24h)	45.6 1.03	51.0 1.29	47.2 3.9	45.9 0.91	25.6 1.08	36.5* 0.78	39.5* 1.50	78.6 6.0	79.2 7.3	62.2* 2.7

*significant to day 0.

Table 7. Urinary composition on three different diets.

parameter	normal diet		optimized diet		ovo-lacto-vegetarian diet	
	M	SEM	M	SEM	M	SEM
pH-value	5,86	0.15	6.42*	0.08	6.76*o	0.09
uric acid (mmol/24h)	3.66	0.17	3.14*	0.15	2.84*	0.16
calcium (mmol/24h)	4.53	0.57	3.36*	0.49	2.84*o	0.49
magnesium (mmol/24h)	4.31	0.31	5.51*	0.27	5.91*	0.39
citric acid (mmol/24h)	2.52	0.19	3.27*	0.25	4.59*o	0.36
oxalic acid (mmol/24h)	0.28	0.02	0.30	0.02	0.41*o	0.03
cystine (µmol/24h)	131.0	17.8	106.9	9.2	105.2	14.8
GAG (µmol/24h)	21.3	1.42	16.7	1.07	12.0*	1.55
RS CaOx	4.96	0.98	2.10*	0.28	1.98*	0.42
RS uric acid	3.30	1.03	0.48*	0.09	0.19*o	0.04

*significant to normal diet. °significant to optimized diet.

since vegetarian nutrition is generally recommended as a prophylactic diet against urolithiasis. A change in diet can also lower the excretion of **cystine**. In view of the simultaneous increase of urine volume in cystine urolithiasis, this result is of exceptional importance. On the other hand, we were also able to confirm in this study that the excretion of **glycosaminoglycans** in the urine falls significantly with dietary optimization. The calculation of the relative supersaturation, considering all ionic urinary parameters measured, shows a highly significant fall for the **relative supersaturation** both with calcium oxalate and with uric acid.

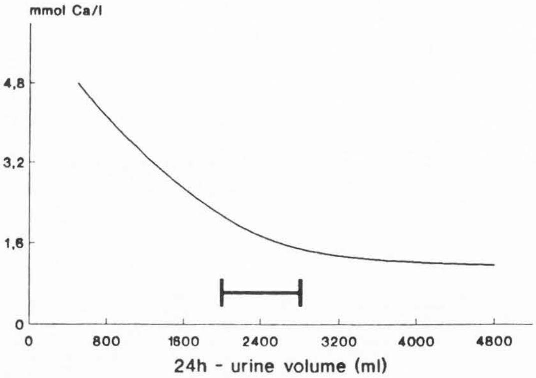

Figure 13. Dependance of calcium concentration in 24-hour urine on urine volume (n = 1677).

Discussion and Conclusions

Dietetic modification of the risk of urinary stone formation solely comprising recommendations for an adequate urine dilution is frequently regarded as sufficient. However, major mistakes can already be made with the choice of drinks. Provided that it does not entail any hygienic problems, water is a very good agent for urine dilution. Mineral water should be taken specifically for certain kinds of urinary stones depending on their mineral content and their acidifying or alkalizing effect. Thus, an alkalizing effect due to the high bicarbonate content of mineral water is desired in uric acid, calcium oxalate, and cystine stones, whereas, it is contraindicated in struvite stones. The regular intake of calcium with milk, or oxalate with cocoa, can increase the risk of calcium oxalate crystallization in the urine. Normal amounts of black tea (2-3 cups per day) do not affect the risk of urinary stone formation. Only large amounts of tea and a regular intake can increase the risk. For this reason, the intake of neutral beverages such as fruit teas and selected mineral waters is of particular importance in urinary dilution. The objective must be to obtain an even flow of urine over the entire day and to attain a 24-hour urine volume of 2-2.5 litres. An increase in excess of 3 litres of urine per 24 hours is very irksome and according to our investigation of urine dilution this is unnecessary (Fig. 13).

Foods high in oxalate always entail a raised risk of urolithiasis [2, 4, 13]. The oxalate excretion in the urine increases very rapidly. The circadian rhythm curve shows the very high concentrations in the first 4-6 hours. A hyperoxaluria continues over 20 hours especially with spinach, since a proportion of the oxalate is only released by cell breakdown in the intestine. Delayed excretion of uric acid is detected in purine loads. All three agents tested (synthetic, liver, herring), even when used at normal portions recommended in conventional nutrition, already raise excretion of uric acid in the 24-hour urine on the day after loading.

Dietary fiber may be very effective in binding calcium from foods. In particular, phytic acid in roughage is responsible for the binding capacity. Rice bran has already been used for treatment of hypercalciuria [11, 15]. Our investigations show different calcium binding capacities for different brans. The experimental conditions were chosen in such a way that a lowering of the calcium excretion in the urine was attained even with a high calcium intake. However, a rise of the oxalic acid excretion was also measured with all brans, so that a tendency to an increase of risk of urinary stone formation was observed in the calculation of relative supersaturation [11]. In pronounced intestinal hyperabsorption of calcium, an increased intake of brans may be a good prophylactic measure to prevent recurrences. However, such a therapy should not be administered in normocalciuria.

Changing the diet with consideration of individual risk factors is very important. However, the patient's overall behavior with regard to daily food and fluid intake is crucial. Investigations with various standardized diets provide a representative picture of the extent by which the risk of urolithiasis can be drastically decreased by a diet tailored to needs.

The average diet as determined in the "Nutritional Survey" [3] contains too much protein, purine, fat, sodium chloride, and alcohol. Overall, the energy content is too high. In consequence of this, excretion of uric acid and calcium in the urine is relatively high. Furthermore, a low urinary pH and a low excretion of citric acid and magnesium is measured. All the urine parameters specified can be significantly modified in a favorable way by switching to a diet appropriate to needs (both an optimized mixed diet and ovo-lacto-vegetarian diet) in the same test subjects. This results in a significant lowering of the calculated relative supersaturation with calcium oxalate and uric acid. It is to be particularly noted that the vegetarian diet brings about a further significant increase of the urinary pH and the citric acid excretion as well as a significant fall of calcium excretion compared to the optimized mixed diet. On the other hand, the alteration in oxalic acid excretion in the urine is contrary to expectations. The decrease of animal protein intake by 30% in the optimized mixed diet does not lead to any change in oxalic acid excretion. On increasing the protein intake from 50 to 84 g, Robertson *et al.* [18] observed a rise of oxalic acid excretion in the urine. On the other hand, Kok *et al.* [12] did not find any alteration in the oxalate excretion in the urine with a protein supplementation of 100% (1 g to 2 g/kg body weight).

Furthermore, the significant increase of oxalate excretion by 40% in the urine as a result of a switch to an ovo-lacto-vegetarian diet observed in our study is noteworthy. A protein intake (plant and egg protein) remains unchanged compared to the optimized mixed diet, but 75% (see Table 2) more oxalic acid was consumed owing to the plant food constituents. In the literature, a decreased oxalate excretion has been described in vegetarians with an animal protein intake of 20 g [18]. Marangella *et al.* [14] were able to demonstrate a significantly raised oxalic acid excretion in healthy vegetarians compared to a control group. The calculation of the relative supersaturation with calcium oxalate does not differ between optimized mixed diet and vegetarian diet under the experimental conditions described here. However, the relative supersaturation with uric acid was further lowered by the vegetarian diet.

The investigations with standardized diets in healthy subjects have shown that the risk of urinary stone formation can be lowered significantly and effectively by a diet appropriate to need with adequate fluid intake.

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Discussion with Reviewers

W.G. Robertson: Can you explain the differences in the urinary risk factors for men and women on the basis of differences in the diets of the two sexes?
Authors: During the present studies, we did not investigate a sex-dependent effect of dietary factors. A higher incidence of urolithiasis in men may refer to habitual overnutrition, e.g., a higher intake of energy, protein and purine, as well as alcohol.

W.G. Robertson: How important, do you think, are the diurnal fluctuations in the various urinary risk factors in terms of initiating new stone-formation?
Authors: Diurnal fluctuations in the urine composition are effected by dietary and drinking habits. Varying pH-values and concentrations of lithogenic and inhibitory urine factors can promote initiation of new stone formation.

H. Ito: Is two days of adaptation/habituation period adequate?
Authors: The two days of adaptation period is a practical compromise. According to our experiences, subsequent investigation resulted in relatively constant values.

D.J. Kok: Are the changes in pH (significantly down with beer with constant citrate) and citrate excretion (significantly up with tea with constant pH) truly dissociated with these regimens?
Authors: The investigation with beer was effected by an acute load with 1 litre beer: pH-value decreased, whereas citrate excretion did not respond to the load. By the beer intake, potassium is supplied in addition, so that a low citrate excretion is presumably compensated. At present, we cannot explain the increased citrate excretion on black tea load.

J.R. Asplin: What is the mechanism of the fall in urinary glycosaminoglycan excretion with the optimized diet? Is this a response to a change in one particular dietary component, or does the excretion rate of glycosaminoglycans (GAG) vary with the stone forming potential in the urine?
Authors: Since GAG excretion decreased simultaneously with the decreased protein intake, the induction of increased GAG excretion by animal protein can be inferred.

J.R. Asplin: Although the urine supersaturation as calculated by the EQUIL program fell on the optimized diet, the simultaneous fall in urine glycosaminoglycans may promote stones. Were any studies such as measurements of "Formation Product Ratios" performed to help assess stone forming risk on these diets?
Authors: There are many questions to be answered about GAG. For example, it is unclear whether there is a difference in GAG excretion between healthy subjects and stone patients, or which GAG are inhibitors and which are promoters of calcium oxalate stone formation.

R. Tawashi: Table 6 shows that 200 g herring reduced potassium in a significant way on the second day. Is this due to the reduction in urine volume or to concomitant effect of Na or both?
Authors: Reduction of potassium excretion on the ingestion of 200 g herring is certainly a consequence of the increased sodium intake during acute load.

Editor: Please provide more information about the EQUIL program?
Authors: The risk of crystallization of calcium oxalate and other common stone-forming components can be calculated from potential thermodynamic mass-action equilibrium constants. EQUIL is based on thermodynamic considerations and calculates how far the urine is from equilibrium with respect to the solid phases found in kidney stones. The relative supersaturation of the different stone forming salts is calculated from urinary pH and the analyzed concentrations (moles/litre) of a number of urinary parameters.