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GAS CHROMATOGRAPHIC—MASS SPECTROMETRIC ANALYSIS OF POLYOLS IN URINE AND SERUM OF UREMIC PATIENTS

IDENTIFICATION OF NEW DEOXYALDITOLS AND INOSITOL ISOMERS

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SUMMARY

A gas chromatographic—mass spectrometric method was applied to a study of polyols in urine and serum of normal subjects and uremic patients. 4-Deoxythreitol, 4-deoxyerythritol, 5-deoxyxylitol, 5-deoxyarabitol, 2-deoxyribitol, 6-deoxymannitol, 6-deoxygalactitol, neoinositol and chiroinositol were identified in normal urine as well as in uremic urine for the first time. In uremia the urinary excretion of myoinositol and chiroinositol was significantly increased. The serum levels of myoinositol, chiroinositol and scylloinositol were increased in the uremic patients, whereas the serum level of 1-deoxyglucose (1,5-anhydroglucitol) was significantly decreased in the uremic patients as compared with the normal subjects. These findings suggest the altered metabolism of chiroinositol and 1-deoxyglucose in the uremic state.

INTRODUCTION

Polyols in human physiological fluids and tissue have recently drawn attention, and the polyol concentrations have been reported to change in various

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diseases. Pitkänen [1] reported that the serum and urinary levels of myo-inositol were increased in the uremic state, and that the urinary excretion of mannitol and myoinositol was increased in diabetes mellitus. Servo et al. [2] reported that the 1-deoxyglucose level in the cerebrospinal fluid was decreased in uremia and in diabetes mellitus. The derangements of the polyol metabolism were considered as possible causes of clinical symptoms. For example, retention of myoinositol was considered to be a cause of the uremic polyneuropathy [3, 4]. The increased production of sorbitol in the lens causes cataracts in diabetes mellitus [5], and sorbitol also plays an important role in the formation of diabetic complications in nervous tissue [6].

Detailed studies of polyols in urine and serum were performed to clarify the exact derangement of the polyol metabolism in uremia using high-resolution gas chromatography—mass spectrometry. In our study several new deoxyalditols were demonstrated to be present in human urine, and the abnormal metabolism of chiroinositol and scylloinositol was also demonstrated in the uremic state.

MATERIALS AND METHODS

Chemicals

Erythritol, xylitol, arabitol, L-arabinose, 2-deoxyribose, L-rhamnose and L-fucose were the products of Tokyo Kasei Kogyo Co. (Tokyo, Japan). Ribitol, mannitol, sorbitol, myoinositol, D-fructose, D-arabinose, D-glucose and D-galactose were the products of Yoneyama Chemical Industries Ltd. (Osaka, Japan). Threitol, xylulose and 6-deoxyglucose were obtained from Sigma Chemical Co. (St. Louis, MO, U.S.A.).

4-Deoxythreitol was synthesized by the sodium borohydride reduction of 4-deoxythreose, which was synthesized from D-xylose according to the methods of Leven and Compton [7] and Hough and Taylor [8]. 4-Deoxyerythritol was synthesized by the sodium borohydride reduction of 4-deoxyerythrose, which was synthesized from D-arabinose according to the method of Sugimoto and Matsuura [9]. 5-Deoxyxylitol was synthesized by the sodium borohydride reduction of 5-deoxyxylose, which was synthesized from D-xylose according to the method of Leven and Compton [7]. 5-Deoxyarabitol was synthesized by the sodium borohydride reduction of 5-deoxyarabinose, which was synthesized from D-arabinose according to the method of Zinner et al. [10]. 2-Deoxyribitol was synthesized by the reduction of 2-deoxyribose with sodium borohydride. 6-Deoxymannitol was synthesized by the reduction of L-rhamnose with sodium borohydride, 6-deoxysorbitol, by the reduction of 6-deoxyglucose with sodium borohydride, and 6-deoxygalactitol by the reduction of L-fucose with sodium borohydride.

Samples

Twenty-four-hour urine samples were obtained from five healthy adults and ten patients with chronic renal failure. Four of ten uremic patients were on 5-h hemodialysis three times a week. The serum creatinine level of ten uremic patients averaged 8.3 ± 3.7 mg/dl, ranging from 3.1 to 16.2 mg/dl.

Serum samples were obtained from eight healthy adults and twelve patients

with chronic renal failure. Nine of twelve uremic patients were on hemodialysis treatment. The serum creatinine level of the twelve uremic patients was 10.7 ± 4.0 mg/dl, ranging from 4.9 to 15.4 mg/dl.

The urine and serum samples were kept at −20°C prior to analysis.

Sample preparation

Serum was filtered through a cone membrane filter (CF 25, Amicon, Lexington, MA, U.S.A.). One milliliter of serum ultrafiltrate, or a volume of urine equivalent to 1 mg of creatinine, was applied to a Dowex 50W-X8 (H^+) column (5 cm × 0.8 cm I.D.) after the addition of 50 μg of ribitol as an internal standard. Anion and neutral substances were eluted with 30 ml of distilled water. The eluate was applied to Amberlite IRA 400 ($HCOO^-$) column (5 cm × 0.8 cm I.D.). Neutral substances were eluted with 30 ml of distilled water. The eluate was dried on a lyophilizer. The neutral substances were dissolved with 9 ml of hot methanol, then transferred to a test tube, and concentrated into about 2 ml with a nitrogen stream. The concentrate was transferred to a sample glass vial and dried with a nitrogen stream. The sample was then trimethylsilylated with 90 μl of N,O-bis(trimethylsilyl)trifluoroacetamide and 10 μl of trimethylchlorosilane at 60°C for 20 min; 2 μl of the sample were subjected to gas chromatography—mass spectrometry.

Gas chromatography—mass spectrometry

Derivatized samples were analyzed with a Hewlett-Packard 5710A gas chromatograph combined with a double-focussing mass spectrometer (JMS D-300, JEOL). The data were stored and processed by a JMA 2000 data system of JEOL. The gas chromatograph was equipped with an OV-101 open-tubular glass capillary column (30 m × 0.25 mm I.D.) and a splitless injector. The column temperature was programmed from 120°C to 260°C at 3°C/min.

Electron-impact ionization (EI) mass spectra were recorded at an ionizing energy of 70 eV, an ionization current of 300 μA, and an accelerating voltage of 3 kV. Chemical ionization (CI) mass spectra were recorded with ammonia as a reactant gas. Ionizing energy was 260 eV and the other conditions were the same as for EI.

Quantitation of polyols in urine and serum

Standard curves were obtained with the OV-101 capillary column (30 m × 0.25 mm I.D.) using standard solutions with concentrations ranging from 1 μg to 1 mg per 1 ml of distilled water. After addition of 50 μg of ribitol as an internal standard, these solutions were processed as described in the section for sample preparation. Standard curves relating the concentrations of threitol, erythritol, xylitol, arabitol, mannitol, sorbitol and myoinositol to the ratios of peak area of the polyols to ribitol were obtained from the gas chromatograms. Since the concentration of ribitol in normal and uremic urine was less than 5 μg per urine volume equivalent to 1 mg of creatinine, and since ribitol was not detected in normal or uremic serum, 50 μg of ribitol were used as an internal standard.

To compare the daily urinary excretion of neoinositol, chiroinositol, epi- or cisinositol and scylloinositol in uremic patients with that in normal subjects,

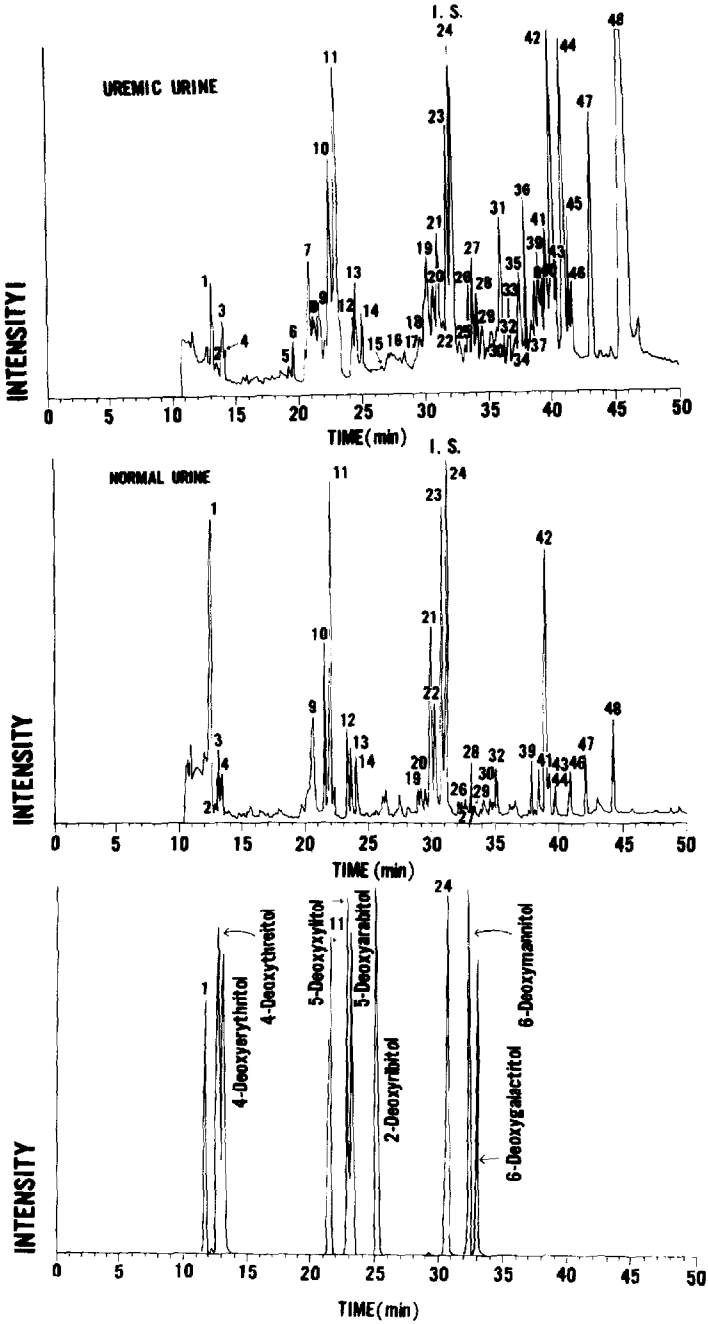

Fig. 1. Gas chromatograms of polyols in urine of a patient with chronic renal failure (upper chromatogram), a healthy subject (middle chromatogram) and of synthesized polyols (lower chromatogram). Peak identifications: 1 = glycerol, 3 = 4-deoxythreitol, 4 = 4-deoxyerythritol, 10 = threitol, 11 = erythritol, 12 = 5-deoxyxylitol, 13 = 5-deoxyarabitol, 15 = 2-deoxyribitol, 19 = xylulose, 22 = xylitol, 23 = arabitol, 24 = ribitol (internal standard), 26, 28 = isomers of 6-deoxyhexitol, 27 = 6-deoxymannitol, 29 = 6-deoxygalactitol, 30 = fructose, 31 = 1-deoxyglucose, 36 = α-glucose, 37 = β-galactose, 39 = neoinositol, 42 = mannitol, 43 = sorbitol, 44 = chiroinositol, 45 = β-glucose, 46 = epi- or cisinositol, 47 = scylloinositol, 48 = myoinositol.

peak area ratios of the inositol isomers to ribitol, corresponding to the concentrations per urine volume equivalent to 1 mg of creatinine, were obtained from the gas chromatograms and the values obtained were multiplied by the daily amount of creatinine excreted in the urine (mg/day).

Serum levels of 1-deoxyglucose, chiroinositol and scylloinositol were obtained from the mass chromatograms, because the peaks of these compounds were difficult to separate from the peaks of glucose furanoside, β-glucose and an unknown substance, respectively, in the gas chromatograms. The ion 259, $(M - 193)^+$, was used for 1-deoxyglucose. The ion 318, $(M - 294)^+$, was used for chiroinositol, scylloinositol and other inositol isomers. The ion 422, $(M - 90)^+$, was used for ribitol. Peak height ratios of 1-deoxyglucose, chiroinositol, and scylloinositol to ribitol were obtained from the mass chromatograms to compare the serum levels of the compounds in uremic patients with those in normal subjects.

Recoveries of polyols

Quintuplicate estimations of recoveries were carried out using 50-μg amounts of polyols, which were added to 1 ml of distilled water. The solution was applied to Dowex 50W-X8, the eluate then applied to Amberlite IRA-400, the polyols were subsequently eluted with distilled water and quantitated. Recoveries of threitol, erythritol, xylitol, arabitol, mannitol, sorbitol and myoinositol were as follows: 104.4 ± 3.0% (mean ± S.D., $n = 5$), 105.4 ± 8.5%, 94.7 ± 13.7%, 109.6 ± 6.8%, 96.7 ± 9.5%, 92.1 ± 8.7%, and 89.3 ± 14.8%, respectively.

EXPERIMENTAL RESULTS

Polyol profiles of uremic urine and serum

Fig. 1 shows the gas chromatograms of polyols in urine of a patient with chronic renal failure (upper chromatogram) and in normal urine (middle chromatogram). Identification of the peaks was performed by comparing their mass spectra and retention times with those of authentic compounds or from reference to the literature. In the uremic urine the peaks of chiroinositol, scylloinositol and myoinositol were higher than in normal urine.

Fig. 2 shows the gas chromatograms of polyols in the serum of a patient with chronic renal failure (upper chromatogram) and in normal serum (lower chromatogram). In the uremic serum the peaks of threitol, erythritol, arabitol, mannitol, sorbitol, chiroinositol, scylloinositol and myoinositol were higher than in normal serum.

Identification of deoxyalditols in urine

EI mass spectra of peaks 3 and 4 presented similar spectra, as shown in Figs. 3 and 4 (lower spectra), respectively. Molecular ions of the two compounds were found to be 322 by recording CI mass spectra. The intense peaks at m/z 117 and m/z 219 in addition to the peaks at m/z 103 and m/z 205 suggested the structure of 4-deoxytetriol by comparison with the mass spectrum of glycerol (M^+ 308). Since the trimethylsilyl (TMS) derivative of 4-deoxythreitol and peak 3 showed identical EI mass spectra (Fig. 3) and identical relative retention times (Fig. 1), peak 3 was identified as 4-deoxythreitol.

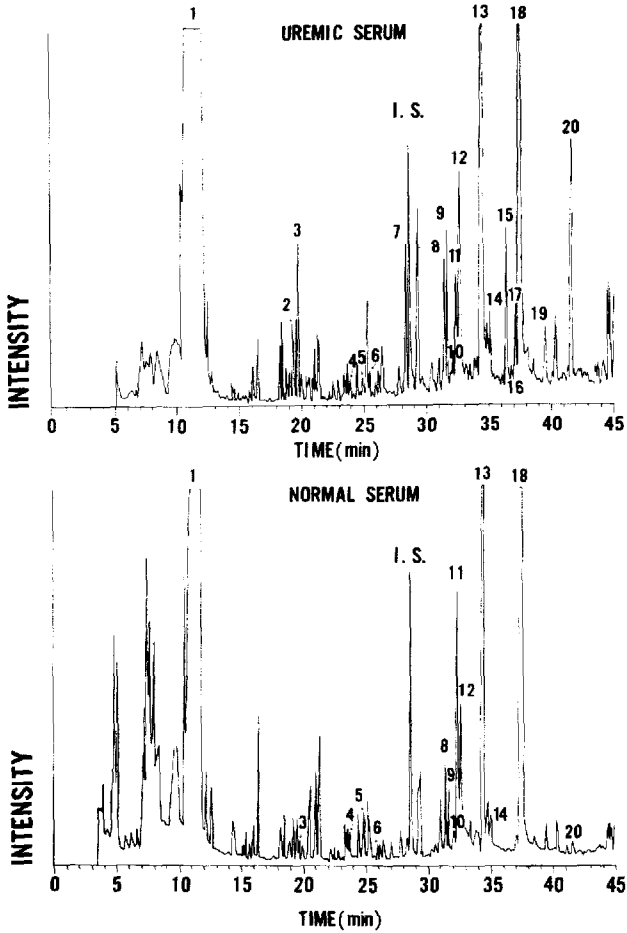

Fig. 2. Gas chromatograms of polyols in the serum of a patient with chronic renal failure (upper chromatogram) and a healthy subject (lower chromatogram). Peak identifications: 1 = glycerol, 2 = threitol, 3 = erythritol, 4, 5 = arabinose, 7 = arabitol, 8, 9, 10 = fructose, 11 = 1-deoxyglucose, 12 = glucose furanoside, 13 = α-glucose, 14 = β-galactose, 15 = mannitol, 16 = sorbitol, 17 = chiroinositol, 18 = β-glucose, 19 = scylloinositol (minor component), 20 = myoinositol.

The TMS derivative of 4-deoxyerythritol and peak 4 also showed identical mass spectra (Fig. 4) and identical relative retention times (Fig. 1). Peak 4 was then identified as 4-deoxyerythritol.

EI mass spectra of peaks 12 and 13 presented similar spectra as shown in Figs. 5 and 6 (lower spectra), respectively. CI mass spectra of the peaks indicated the molecular ions at *m/z* 424. The intense peaks at *m/z* 117 and *m/z* 219 in addition to the peaks at *m/z* 103 and *m/z* 205 suggested the structure of 5-deoxypentitol by comparison with the mass spectrum of erythritol (M^+ 410). Since the TMS derivative of 5-deoxyxylitol showed identical EI mass spectra (Fig. 5) and identical relative retention times (Fig. 1), peak 12 was identified as 5-deoxyxylitol. The TMS derivative of 5-deoxyarabitol and peak 13 also showed identical mass spectra (Fig. 6) and identical relative retention times (Fig. 1). Peak 13 was then identified as 5-deoxyarabitol.

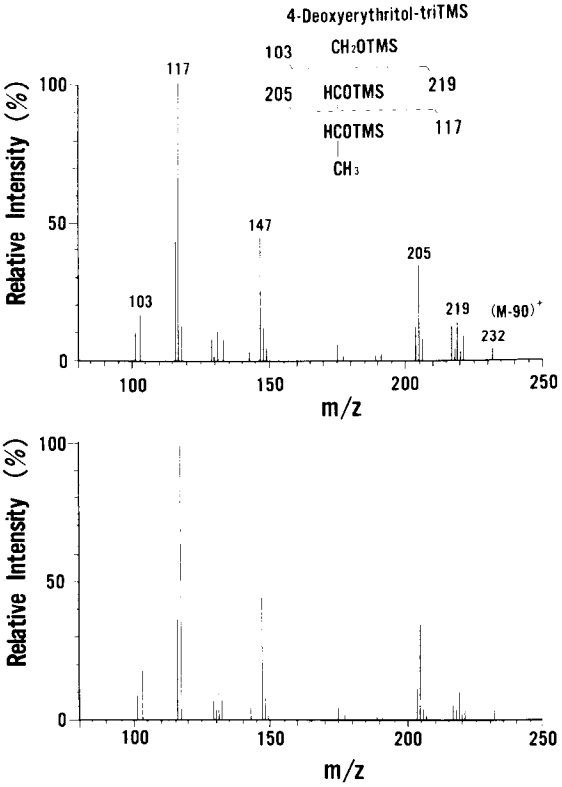

Fig. 3. EI mass spectra of TMS derivative of 4-deoxythreitol (upper spectrum) and of peak 3 (lower spectrum) in the gas chromatograms of Fig. 1.

The EI mass spectrum of peak 15 is shown in Fig. 7 (lower spectrum); the CI mass spectrum of the peak indicated the molecular ion at *m/z* 424. The intense peak at *m/z* 219, the low peak at *m/z* 117 and the base peak at *m/z* 103 suggested the structure of 2-deoxypentitol by comparison with the mass spectrum of erythritol (M^+ 410). Peak 15 was identified as 2-deoxyribitol since the TMS derivative of 2-deoxyribitol and peak 15 showed identical mass spectra (Fig. 7) and identical relative retention times (Fig. 1).

The EI mass spectrum of peak 27 is shown in Fig. 8 (lower spectrum). The molecular ion was found to be 526 by recording the CI mass spectrum. The base peak at *m/z* 117 and the intense peak at *m/z* 219 together with the peaks at *m/z* 103, 205 and 307 suggested the structure of 6-deoxyhexitol by comparison with the mass spectrum of ribitol (M^+ 512). Synthesized 6-deoxymannitol showed an identical EI mass spectrum (Fig. 8) and identical relative retention time (Fig. 1) with those of peak 27. Although synthesized 6-deoxysorbitol showed an almost identical relative retention time with that of peak 27, the mass spectrum of 6-deoxysorbitol-penta-TMS revealed a ten-fold increase in the intensity of the *m/z* 409 ion as compared with that of 6-deoxymannitol-penta-TMS. Peak 27 was then identified as 6-deoxymannitol.

The EI mass spectrum of peak 29 is presented in Fig. 9 (lower spectrum). Peak 29 and peak 27 showed similar mass spectra, suggesting an isomeric

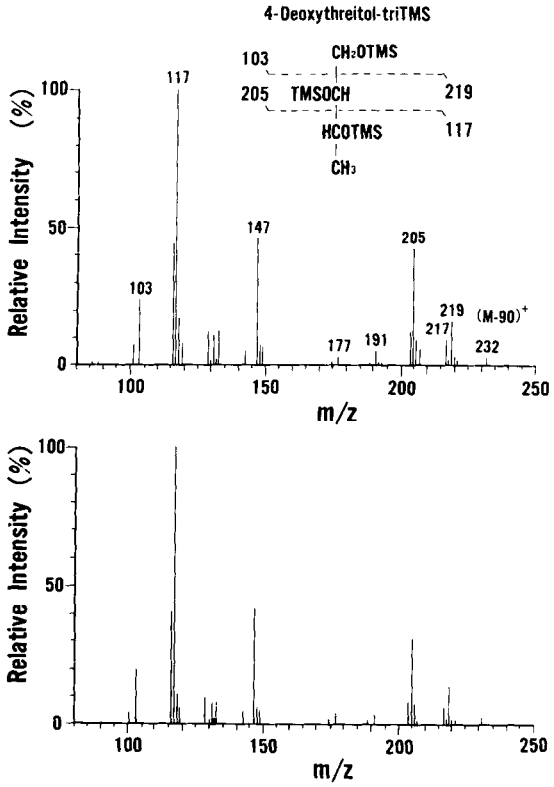

Fig. 4. EI mass spectra of TMS derivative of 4-deoxyerythritol (upper spectrum) and of peak 4 (lower spectrum) in the gas chromatograms of Fig. 1.

relationship. The molecular ion of peak 29 was 526 from the CI mass spectrum. Since the TMS derivative of 6-deoxygalactitol and peak 29 showed identical EI mass spectra (Fig. 9) and identical relative retention times (Fig. 1), peak 29 was identified as 6-deoxygalactitol.

Peaks 26 and 28 showed EI mass spectra similar to that of peak 27, suggesting that these peaks are isomers of 6-deoxyhexitol.

4-Deoxythreitol, 4-deoxyerythritol, 5-deoxyxylitol, 5-deoxyarabitol, 6-deoxymannitol, and 6-deoxygalactitol were identified in normal urine as well as in uremic urine for the first time.

Identification of inositol isomers in urine and serum

Five inositol isomers were found in normal and uremic urine (Fig. 1). The EI mass spectra of the five isomers are shown in Table I. Each relative intensity (%) indicated represents the mean of five measurements. Peak 48 was identified as myoinositol by comparing the EI mass spectrum and the relative retention time with those of the authentic compound.

Peak 39 in the gas chromatogram of Fig. 1 had a base peak at *m/z* 318. The relative intensity of the *m/z* 305 ion was as low as 30% and the relative intensities of *m/z* 432 and 433 were as high as 29% and 16%, respectively. By

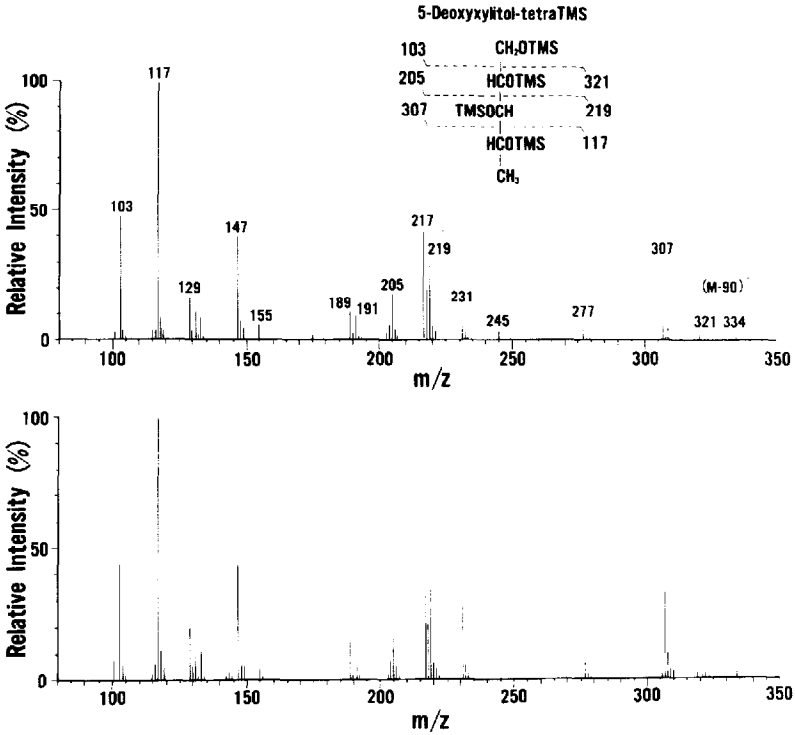

Fig. 5. EI mass spectra of TMS derivative of 5-deoxyxylitol (upper spectrum) and of peak 12 (lower spectrum) in the gas chromatogram of Fig. 1.

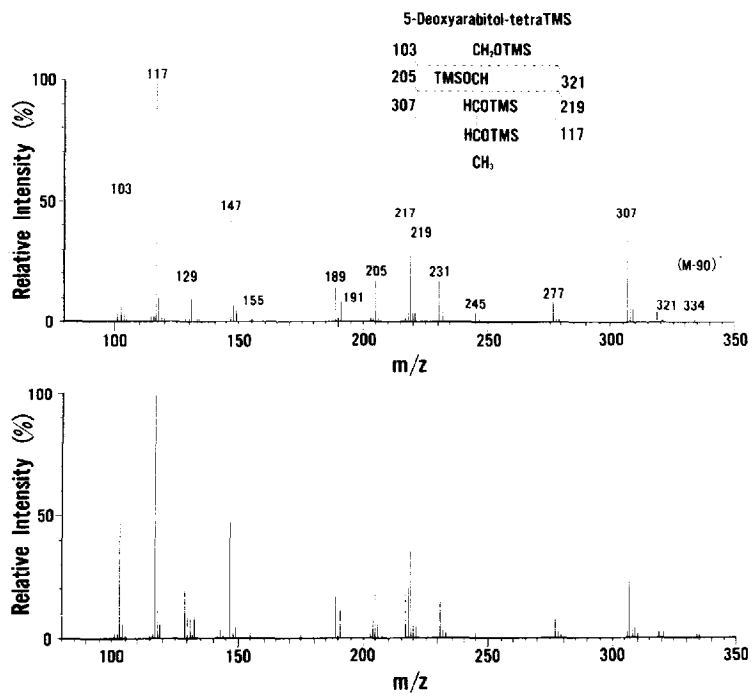

Fig. 6. EI mass spectra of TMS derivative of 5-deoxyarabitol (upper spectrum) and of peak 13 (lower spectrum) in the gas chromatogram of Fig. 1.

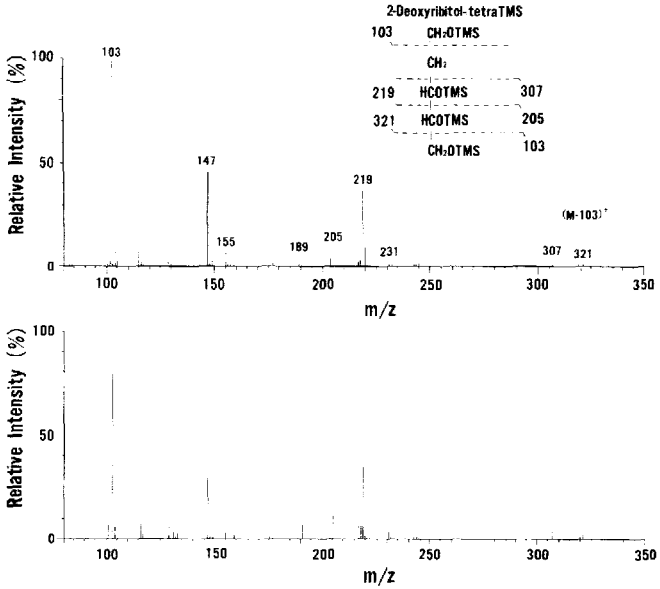

Fig. 7. EI mass spectra of TMS derivative of 2-deoxyribitol (upper spectrum) and of peak 15 (lower spectrum) in the gas chromatogram of Fig. 1.

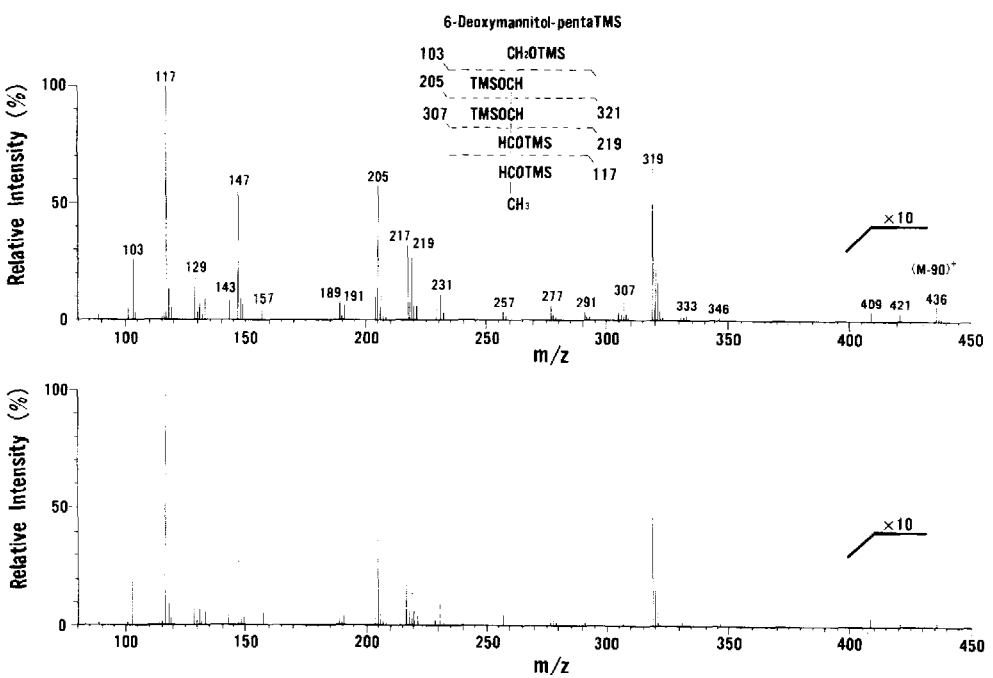

Fig. 8. EI mass spectra of TMS derivative of 6-deoxymannitol (upper chromatogram) and of peak 27 (lower spectrum) in the gas chromatograms of Fig. 1.

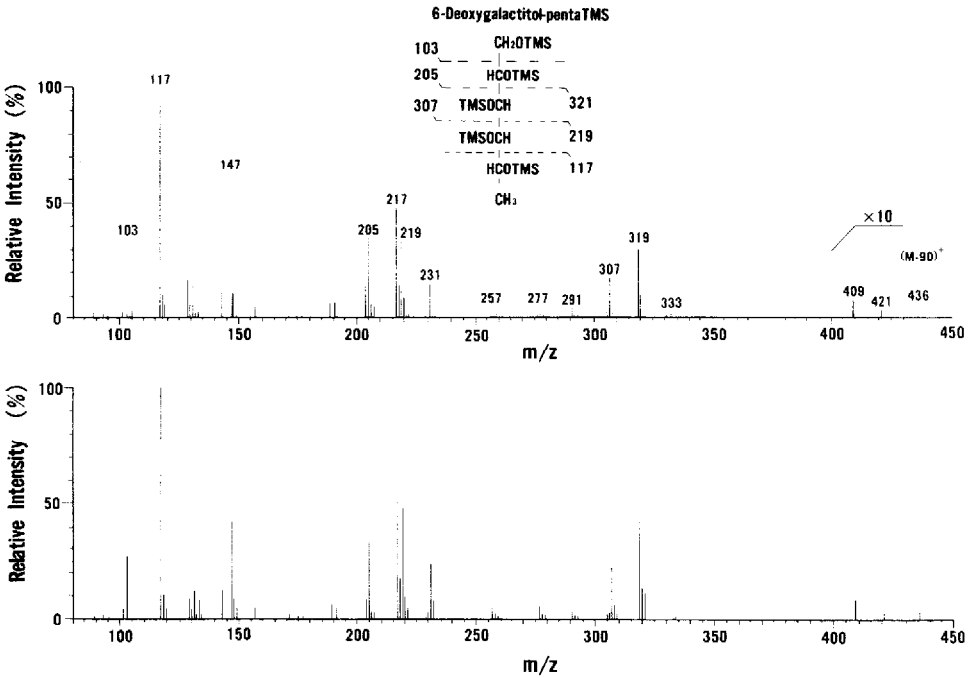

Fig. 9. EI mass spectra of TMS derivative of 6-deoxygalactitol (upper spectrum) and peak 29 (lower spectrum) in the gas chromatograms of Fig. 1.

comparison with the reference spectra [11] these characteristics of peak 39 indicated that this peak is the TMS derivative of neoinositol.

Peak 47 had a base peak at *m/z* 318. The relative intensities of *m/z* 265 and 367 were as low as 7% and 3%, respectively. By comparison with the reference spectra [11], these characteristics indicated that peak 47 is the TMS derivative of scylloinositol.

Peak 44 had a base peak at *m/z* 318. The relative intensity of *m/z* 305 was 82%. The relative intensities of *m/z* 432 and 433 were 9% and 10%, respectively. By comparison with the reference spectra [11], these characteristics indicated that peak 44 is chiroinositol.

Peak 46 had a base peak at *m/z* 217. The relative intensity of *m/z* 305 is higher than that of *m/z* 318. By comparison with the reference spectra [11], these characteristics suggested that peak 46 is epiinositol or cisinositol.

In normal serum only one inositol isomer, myoinositol, was detected, whereas in uremic serum chiroinositol, scylloinositol and myoinositol were detected (Fig. 2). Neoinositol and epi- or cisinositol could not be detected in normal serum or in uremic serum.

Urinary polyol excretion in uremic patients

Table II shows the daily urinary excretion of polyols in patients with chronic renal failure and of healthy adults. The daily urinary excretion of creatinine in uremic patients was 0.61 g, which was 44% of the daily creatinine excretion in healthy adults. The daily urinary excretion of erythritol, xylitol and arabitol

TABLE I

EI MASS SPECTRA OF INOSITOL ISOMERS IN THE GAS CHROMATOGRAMS OF FIG. 1

Each relative intensity (%) indicated represents the mean of five measurements.

m/z	Peak No.				
	39 Neoinositol	44 Chiroinositol	46 Epi- or cisinositol	47 Scylloinositol	48 Myoinositol
103	12	12	22	13	12
129	18	17	20	11	21
133	13	13	41	11	18
147	75	70	82	70	74
189	3	2	2	2	3
191	32	41	46	48	52
204	20	22	28	41	34
217	64	83	100	81	100
221	6	5	6	6	10
265	22	27	10	7	25
291	12	7	4	6	13
293	4	5	5	6	5
305	30	82	57	74	96
318	100	100	30	100	60
343	2	2	2	1	2
367	10	11	5	3	11
393	5	6	2	8	7
417	0.5	2	0.2	0.4	1
419	0.5	2	0.4	0.8	1
432	32	9	2	3	18
433	18	10	7	3	14
507	4	8	0.5	4	6
612	0.1	0.7	0.1	0.5	2

TABLE II

DAILY URINARY EXCRETION OF POLYOLS IN UREMIC PATIENTS

	Normal (n=5)	Uremic (n=10)	Uremic/normal
Threitol (mg/day)	5.7 ± 3.3	4.0 ± 3.3	0.70
Erythritol (mg/day)	66 ± 15	20 ± 13***	0.33
Xylitol (mg/day)	6.9 ± 4.8	2.0 ± 2.4**	0.29
Arabitol (mg/day)	46 ± 9.5	16 ± 12***	0.35
Mannitol (mg/day)	81 ± 37	94 ± 85	1.2
Sorbitol (mg/day)	8.6 ± 2.1	12 ± 14	1.4
Myoinositol (mg/day)	100 ± 71	430 ± 290**	4.3
Neoinositol*	55 ± 44	29 ± 36	0.53
Chiroinositol*	130 ± 140	750 ± 270***	5.8
Epi- or cisinositol*	44 ± 53	23 ± 48	0.52
Scylloinositol*	200 ± 140	290 ± 260	1.5
Creatinine (g/day)	1.4 ± 0.3	0.61± 0.28***	0.44

*Peak area ratio to internal standard (ribitol 50 μg) per day.
**$p < 0.05$.
***$p < 0.01$.

in uremic patients was significantly decreased compared with healthy subjects. However, the daily urinary excretion of myoinositol, chiroinositol and scyllo-inositol was increased in uremic patients compared with healthy subjects. The increase of myoinositol and chiroinositol in uremic urine was especially noticeable.

Serum polyol levels in uremic patients

Table III shows the serum concentrations of polyols in patients with chronic renal failure and healthy adults. In uremic serum the concentrations of threitol, erythritol, arabitol, mannitol, sorbitol, myoinositol, chiroinositol and scyllo-inositol were increased as compared with normal serum. Xylitol, neoinositol and epi- or cisinositol could not be detected in uremic serum or in normal serum. The serum concentration of 1-deoxyglucose in uremic patients was significantly decreased compared with that in healthy subjects.

TABLE III

SERUM POLYOL LEVELS IN UREMIC PATIENTS

	Normal (n=8)	Uremic (n=12)	
Threitol (mg/dl)	0	0.099 ± 0.092	
Erythritol (mg/dl)	<0.1	0.98 ± 1.4	
Xylitol	0	0	
Arabitol (mg/dl)	0	1.5 ± 0.90	
Mannitol (mg/dl)	0	2.6 ± 2.5	
Sorbitol (mg/dl)	0	0.31 ± 0.21	
Myoinositol (mg/dl)	<1.0	9.4 ± 6.9	
Neoinositol	0	0	
Chiroinositol*	0	0.79 ± 0.74	
Epi- or cisinositol	0	0	
Scylloinositol*	0	0.28 ± 0.30	
1-Deoxyglucose**	1.0 ± 0.75	0.32 ± 0.34	$p < 0.05$

*Peak height ratio of m/z 318 to m/z 422 (ribitol 50 μg).
**Peak height ratio of m/z 259 to m/z 422 (ribitol 50 μg).

DISCUSSION

In the present profiling analysis, 4-deoxythreitol, 4-deoxyerythritol, 5-deoxyxylitol, 5-deoxyarabitol, 2-deoxyribitol, 6-deoxymannitol, and 6-deoxy-galactitol were identified in normal urine as well as in uremic urine for the first time. Although the metabolism of these deoxyalditols is not yet known, the endogenous reduction of 2-deoxyribose and fucose is a possible cause of the formation of 2-deoxyribitol and 6-deoxygalactitol. The metabolic origin and the physiological significance of these deoxyalditols should be determined.

Neoinositol and chiroinositol were also identified in normal and uremic urine for the first time, and the increased urinary excretion and elevated serum levels of chiroinositol and scylloinositol were first demonstrated in uremic patients. The urinary excretion of neoinositol and epi- or cisinositol was, however, decreased in uremic patients compared with normal subjects. Scyllo-

inositol was detected in the urine of mammals and in human urine following oral administration of myoinositol. Myoinositol, myoinose-2 and scylloinositol were detected in organs of rat and rabbit [12]. Scylloinositol is considered to be formed by the reduction of myoinose-2 which originates from the dehydrogenation of myoinositol. The increased urinary excretion and increased serum level of scylloinositol in the uremic patients in our study may be due to the increased formation of scylloinositol from myoinositol. The increased urinary excretion and increased serum level of chiroinositol as well as myoinositol in the uremic patients suggests that chiroinositol is formed from myoinositol or that the catabolism of chiroinositol takes place exclusively in the kidneys as myoinositol. The decreased urinary excretion of neoinositol and epi- or cisinositol in the uremic patients suggests that the metabolism of these inositols has no relation with myoinositol and that the catabolism of these inositols does not take place in the kidneys.

Myoinositol is an essential growth factor for human cell lines in tissue culture. It is a constituent of phosphoinosides, such as phosphatidylinositol, phosphatidylinositol monophosphate and phosphatidylinositol diphosphate, which may be linked to neural activity in neural tissue. Myoinositol is demonstrated to be synthesized from glucose. Urinary myoinositol excretion is normally a minor mechanism for the disposition of endogenously synthesized myoinositol or dietary intake (300—900 mg/day in man) of myoinositol [13]. The major catabolic pathway for myoinositol requires its initial oxidation to D-glucuronate in the renal cortex [14]. The complete pathway is referred to as the glucuronate—xylose—pentose phosphate pathway [15]. After nephrectomy the production of respiratory $^{14}CO_2$ from ^{14}C-labelled myoinositol injected into rats is virtually abolished [14]. The impaired renal oxidation of myoinositol in uremic patients is thus a major factor for the increased urinary excretion and increased serum level of myoinositol. Retention of myoinositol has been considered a possible cause of uremic polyneuropathy [3, 4].

The urinary excretion of erythritol, xylitol and arabitol was decreased in the uremic patients. This result is in accordance with an earlier study [1]. In the uremic patients the serum levels of threitol, erythritol, arabitol, mannitol and sorbitol were elevated. Since the urinary excretion of threitol, erythritol, and arabitol is decreased it seems likely that these polyols were retained in the blood due to the impaired renal function. The elevated serum levels of mannitol and sorbitol accompanied by the slightly increased urinary excretion suggest that the endogenous production of mannitol and sorbitol is increased in the uremic state. Sorbitol can be converted to mannitol through fructose [16]. The similar behavior of mannitol and sorbitol in the uremic state supports the interrelated metabolism of these two polyols.

The serum level of 1-deoxyglucose in the uremic patients was significantly decreased as compared with that in the normal subjects. 1-Deoxyglucose was first detected in the cerebrospinal fluid by Pitkänen [17]. The level of this compound in the cerebrospinal fluid was reported to be low in diabetic patients and in uremic patients.

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