Supplementary Table 1. Characteristics of Normal Subjects and Hemodialysis Patients

	Normal Subjects Clearance Studies (n=5)	Hemodialysis Patients (n=6)	Normal Subjects Compared to Patients (n=6)
Age (yrs)	40 ± 13	73 ± 12	46 ± 17
Gender (f/m)	1/4	0/6	2/4
BMI (kg/m^2)	24 ± 3	25 ± 3	27 ± 4
Dialysis Vintage (yrs)	-	4 ± 4	-
Treatment Durations (hrs)	-	3.0 ± 0.4	-
Blood Flow Rate (ml/min)	-	400	-
Dialysate Flow Rate (ml/min)	-	800	-
Monthly $spKt/V_{urea}$	-	1.50 ± 0.24	-

Values are mean ± sd. Plasma and urine was obtained from a first group of normal subjects for solute clearance measurements. Studies comparing plasma solute levels in hemodialysis patients and normal subjects were done subsequently with plasma obtained pre-treatment from hemodialysis patients and from a second set of normal subjects because normal plasma used in the original clearance studies was depleted. This second group of normal subjects included 3 subjects who had been included in the original clearance studies. Dialyzers used in hemodialysis patients were Revaclear (n=3) and Revaclear Max (n=3).

Supplementary Table 2 – Mass Spectrometric Features Potentially Representing Solutes Efficiently Cleared by the Kidney and Their Accumulation in Hemodialysis Patients

Neutral Mass	Ion Mode	$Clearance_{free}$ (ml/min/1.73m^2)	$Clearance_{total}$ (ml/min/1.73m^2)	Free Fraction (%)	Reagent Standards Obtained		Hemodialysis/Normal	
					Matched	Not Matched	Free	Total
205.0738	neg	7343 ± 567	294 ± 71	4 ± 1	Cinnamoylglycine	Indolelactic acid	121 [e]	39 [e]
303.1248[a]	pos	7023 ± 3219	121 ± 25	2 ± 1			*	*
466.2571	neg	4366 ± 1325	65 ± 9	2 ± 1			39 [e]	25 [e]
186.0893	neg	4205 ± 1421	748 ± 148	24 ± 6			217 [e]	25 [e]
396.0728[a]	neg	3994 ± 2046	885[b]	68[b]			6 [e]	7 [e]
229.0046[a]	neg	3762 ± 2591	564 ± 296	17 ± 10			391 [e]	84 [e]
288.0307	neg	3668 ± 1631	415 ± 121	13 ± 5			*	*
195.0531	neg	3617 ± 3618	1137 ± 957	35 ± 6	3-OH Hippuric acid	2-OH Hippuric acid 4-OH Hippuric acid	46 [e]	33 [e]
214.1207	neg	3242 ± 1009	98 ± 10	3 ± 1			14 [e]	7 [e]
457.1942[a]	pos	3085 ± 544	485 ± 140	17 ± 5			175 [e]	86 [e]
213.0096	neg	3023 ± 533	59 ± 12	2 ± 1	Indoxyl sulfate		85 [e]	26 [e]
180.0532	pos	2984 ± 1166	697 ± 239	24 ± 7		Nicotinuric acid	58 [e]	35 [e]
440.1687[a]	neg	2921 ± 755	470 ± 146	17 ± 6			243 [e]	112 [e]
210.0753	neg	2896 ± 1117	236 ± 40	9 ± 3	1,3,7-Trimethyluric acid		5 [e]	2
199.1209	neg	2850 ± 737	410 ± 52	16 ± 4		Ecgonine methyl ester	16 [e]	6 [e]
200.0144[a]	neg	2789 ± 590	4 ± 0.5	0.2 ± 0.05			64 [e]	9 [e]
169.0376	neg	2733 ± 1282	903[b]	49[b]	2-Furoylglycine		86 [e]	64 [e]
332.1841	neg	2471 ± 1426	335 ± 157	14 ± 4			100 [e]	29 [e]
160.0736	neg	2456 ± 578	186 ± 63	8 ± 5	[d] *see legend*		43 [e]	7 [e]
325.0801[a]	neg	2441 ± 1123	870 ± 191	56 ± 30			395 [e]	201 [e]
194.0690	pos	2368 ± 655	423[b]	34[b]		4-Aminohippuric acid	108 [e]	81 [e]

182.0580	neg	2264 ± 1075	[c]	[c]		Homovanillic acid 3-(4-Hydroxyphenyl)lactate	4 [e]	3 [e]
158.0578	neg	2241 ± 420	472 ± 98	21 ± 4		Succinylacetone	211 [e]	16 [e]
218.0249	neg	2107 ± 721	12 ± 4	0.5 ± 0.2			8 [e]	2 [e]
278.1296	pos	2032 ± 854	19 ± 2	1 ± 0.3			*	*
270.1939[a]	pos	2031 ± 1399	14 ± 21	0.9 ± 1.5			11 [e]	4 [e]
132.0424	neg	1988 ± 447	242 ± 127	11 ± 4	Methylsuccinic acid	Glutaric acid	119 [e]	6 [e]
150.0539	pos	1985 ± 610	284 ± 59	15 ± 3			48 [e]	23 [e]
196.0595	neg	1977 ± 2238	489 ± 293	39 ± 30	1,7-Dimethyluric acid	1,3-Dimethyluric acid	8 [e]	7 [e]
250.0698[a]	pos	1937 ± 702	434 ± 24	20 ± 5			33 [e]	26 [e]
273.1758[a]	pos	1906 ± 476	31 ± 17	1 ± 0.9			*	*
188.0687[a]	neg	1891 ± 283	219 ± 100	13 ± 7			*	*
101.0113[a]	neg	1885 ± 709	360 ± 86	19 ± 4			174 [e]	69 [e]
384.1613	neg	1882 ± 1658	5 ± 4	0.3 ± 0.2			3 [e]	2
179.0583	neg	1868 ± 1312	502 ± 397	27 ± 5	Hippuric acid		53 [e]	31 [e]
189.9936[a]	neg	1805 ± 1222	349[b]	11[b]			*	*
323.1938[a]	pos	1794 ± 1337	25 ± 26	3 ± 4			*	*
218.1156	neg	1737 ± 1076	468[b]	57[b]			10 [e]	8 [e]
247.1603[a]	pos	1692 ± 776	190 ± 89	12 ± 6			*	*
270.1575[a]	pos	1691 ± 413	568 ± 143	34 ± 4			14 [e]	11 [e]
268.1313	neg	1675 ± 1517	1 ± 1	0.07 ± 0.03			*	*
303.1215	pos	1648 ± 535	[c]	[c]			96 [e]	70 [e]
482.2526	neg	1602 ± 797	74 ± 26	6 ± 4			87 [e]	46 [e]
166.0488	pos	1594 ± 1825	342 ± 182	43 ± 35		1-Methylxanthine 3-Methylxanthine 7-Methylxanthine	17 [e]	9 [e]
278.9832[a]	neg	1529 ± 1802	134 ± 45	18 ± 2			20 [e]	13 [e]
159.0892	pos	1498 ± 324	436 ± 38	30 ± 6	Isovalerylglycine	2-Methylbutyrylglycine	46 [e]	9 [e]

222.0893	neg	1497 ± 1695	217 ± 227	18 ± 4			10 [e]	5 [e]
282.1210	pos	1488 ± 386	[c]	[c]			53 [e]	20 [e]
338.1460[a]	neg	1479 ± 312	408[b]	44[b]			*	*
453.1996[a]	pos	1473 ± 326	198 ± 15	15 ± 6			*	*
231.0201[a]	neg	1469 ± 594	232 ± 37	17 ± 6			3 [e]	1
336.1681[a]	pos	1436 ± 943	[c]	[c]			*	*
309.0164[a]	neg	1425 ± 1931	96 ± 34	17 ± 2			14 [e]	8 [e]
122.0369	neg	1424 ± 582	335 ± 202	26 ± 15			40 [e]	9 [e]
426.1535	neg	1391 ± 474	127 ± 14	10 ± 4			174 [e]	67 [e]
198.0750	pos	1378 ± 576	460 ± 35	56 ± 31			100 [e]	46 [e]
283.0543[a]	pos	1378 ± 550	[c]	[c]			34 [e]	5 [e]
171.0896[a]	neg	1373 ± 516	435[b]	23[b]			67 [e]	30 [e]
244.1312	neg	1360 ± 452	512 ± 301	53 ± 7			15 [e]	11 [e]
238.1313[a]	pos	1294 ± 573	[c]	[c]			132 [e]	32
256.1418[a]	pos	1284 ± 362	538 ± 260	44 ± 22			185 [e]	135 [e]
329.2202	pos	1255 ± 388	523 ± 164	43 ± 13			22 [e]	27 [e]
352.0776[a]	neg	1247 ± 197	457 ± 51	40 ± 9			57 [e]	71 [e]
289.1459[a]	pos	1237 ± 591	195 ± 47	17 ± 4			*	*
223.1206[a]	pos	1225 ± 422	50 ± 13	4 ± 1			6 [e]	2 [e]
246.1468	neg	1220 ± 722	247 ± 67	28 ± 12			2 [e]	1
374.1219	neg	1219 ± 84	[c]	[c]			*	*
232.0039	neg	1219 ± 1463	99 ± 96	10 ± 7			103 [e]	64 [e]
320.1113[a]	neg	1180 ± 112	285 ± 30	25 ± 3			167 [e]	48 [e]
204.0093[a]	neg	1174 ± 405	38 ± 11	3 ± 1			8	3
346.1633	neg	1169 ± 855	812[b]	67[b]			304 [e]	161 [e]
265.0945[a]	pos	1161 ± 404	[c]	[c]			403 [e]	220 [e]
337.1367	pos	1151 ± 156	[c]	[c]			90 [e]	42 [e]
157.0737	pos	1148 ± 235	575 ± 190	52 ± 19	Tiglylglycine		59 [e]	36 [e]

185.1048	pos	1147 ± 547	[c]	[c]			7 [e]	7 [e]
348.1787	neg	1146 ± 413	[c]	[c]			440 [e]	176 [e]
581.1344[a]	neg	1146 ± 371	[c]	[c]			*	*
258.1576[a]	pos	1142 ± 295	329[b]	51[b]			*	*
327.2042[a]	pos	1133 ± 367	[c]	[c]			*	*
258.0313[a]	pos	1131 ± 1108	123 ± 49	19 ± 4			13 [e]	8 [e]
283.1797[a]	pos	1126 ± 701	14 ± 7	0.9 ± 0.9			*	*
272.1629[a]	neg	1105 ± 309	30 ± 29	4 ± 2			2 [e]	1
146.0580	neg	1100 ± 304	42 ± 10	4 ± 1	Adipic acid	2-Methylglutaric acid 3-Methylglutaric acid	25 [e]	16 [e]
268.1419[a]	pos	1083 ± 358	[c]	[c]			35 [e]	18
280.1055	pos	1065 ± 611	347 ± 17	68 ± 31		L-Aspartyl-L-phenylalanine	260 [e]	178 [e]
260.1262	neg	1062 ± 252	[c]	[c]			*	*
311.1224	pos	1060 ± 384	458 ± 49	50 ± 26			25 [e]	13 [e]
300.1315[a]	pos	1059 ± 204	360[b]	46[b]			342 [e]	57 [e]
188.0144	neg	1055 ± 148	20 ± 3	2 ± 0.5	p-Cresol sulfate		38 [e]	10 [e]
174.0892	neg	1041 ± 147	69 ± 13	7 ± 2	Suberic acid		43 [e]	5 [e]

The table includes 90 features identified by high resolution mass spectrometry as representing solutes efficiently cleared by the native kidney. Values are mean±sd. [a] indicates features for which HMDB (http://www.hmdb.ca) did not contain a compound with mass within 3ppm of the observed feature's mass. Free fraction is the level in plasma ultrafiltrate as a percent of the total plasma level. [b] indicates peak areas in deproteinized plasma samples were too small to obtain more than one value for the $clearance_{total}$ and the free fraction. [c] indicates peak areas in deproteinized plasma samples too small to measure in all subjects. Standards matched indicates features matched to reagent compounds by accurate mass, retention time, and mass spectrometric fragmentation. Standards not matched are candidate reagent compounds that did not match retention time and/or mass spectrometric fragmentation with features having similar exact mass values. [d] 3-Methyladipic acid and pimelic acid were run as standards and both had retention

times and MS/MS product ions with *m/z* 97.0664 and 115.0769 in negative mode which were indistinguishable from those of the feature with exact mass 160.0736. In 71 of 90 cases, corresponding features were identifed in dialysis patients. Hemodialysis/Normal ratios were obtained by comparing peak areas corresponding to individual solutes in pre-treatment plasma from 6 hemodialysis patients and plasma from 6 normal subjects. In 19 of 90 cases, features corresponding to solutes identified as efficiently cleared in normal subjects were not identified in a second LC/MS run comparing dialysis patients and controls, as indicated by an * in the "Hemodialysis/Normal" columns. [e] indicates $q < 0.05$ for elevation of the solute concentration in hemodialysis patients above the level in normal subjects.

Supplementary Table 3 – Tandem Mass Spectrometry (MS/MS) of Features Chemically Identified as Solutes Efficiently Cleared by the Kidney

Solute	Mass (*m/z*)	Ion Mode	Collision Energy (eV)	Product Ions (*m/z*)
Cinnamoylglycine	204.0666	Neg	30	160.0771 117.0715
3-Hydroxy hippurate	194.0458	Neg	30	150.0564
Indoxyl sulfate	212.0023	Neg	30	80.9658 132.0459
1,3,7-Trimethyluric acid	209.0681	Neg	30	194.0447
2-Furoylglycine	168.0303	Neg	30	124.0409 67.0196
Methylsuccinic acid	131.0352	Neg	30	87.0458 113.0250
1,7-Dimethyluric acid	195.0522	Neg	30	180.0289
Hippuric acid	178.0510	Neg	30	134.0615
Isovalerylglycine	160.0965	Pos	35	75.9 142.0

Tiglylglycine	158.0810	Pos	35	82.9 140.0
Adipic acid	145.0507	Neg	30	83.0508 101.0613
p-Cresol sulfate	187.0071	Neg	30	107.0508 79.9580
Suberic acid	173.0819	Neg	30	111.0821 129.0926