Electronic Supplementary Material (ESI) for Analyst.

SUPPLEMENTARY INFORMATION

Sensitive mass spectrometric analysis of carbonyl metabolites in human urine and fecal samples using chemoselective modification

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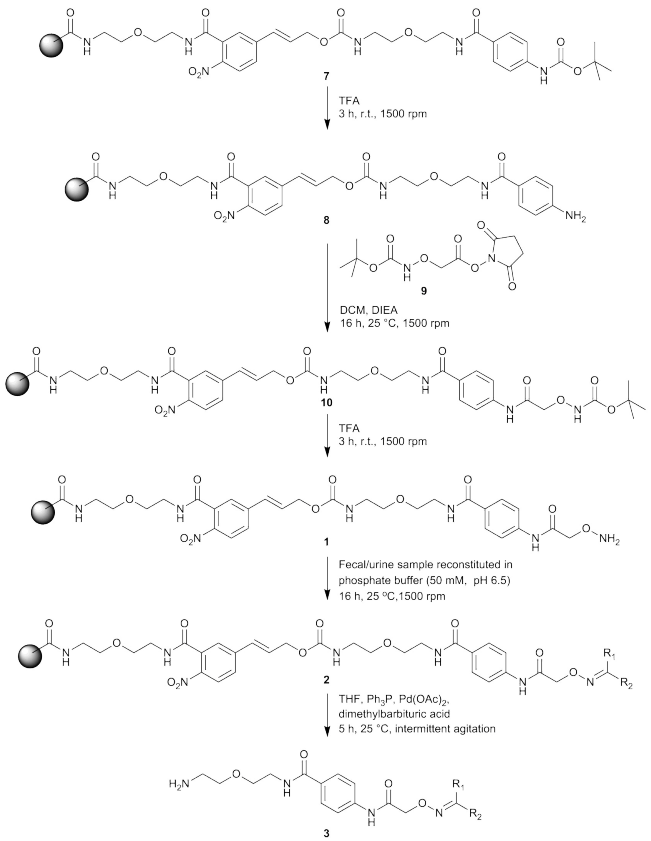
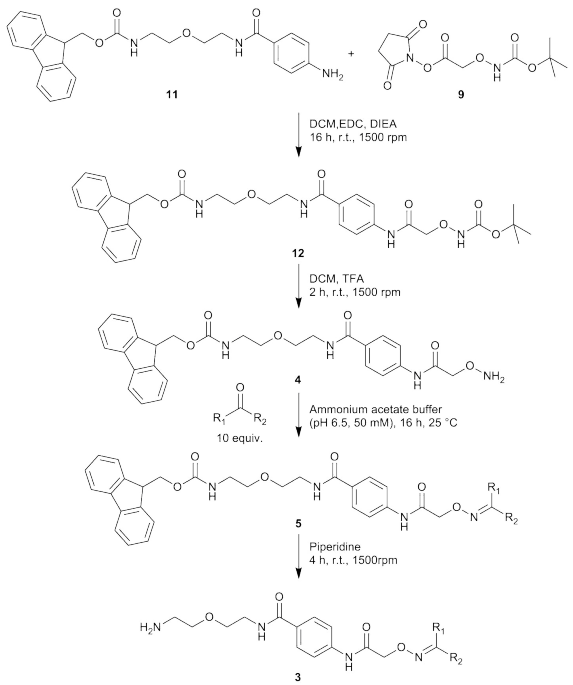
1. Supporting Schemes



Scheme S1: Preparation of immobilized chemoselective probe activated for carbonyl conjugation.



Scheme S2: Preparation of metabolite conjugates for carbonyl-containing metabolites library construction.

2. Supporting Figures

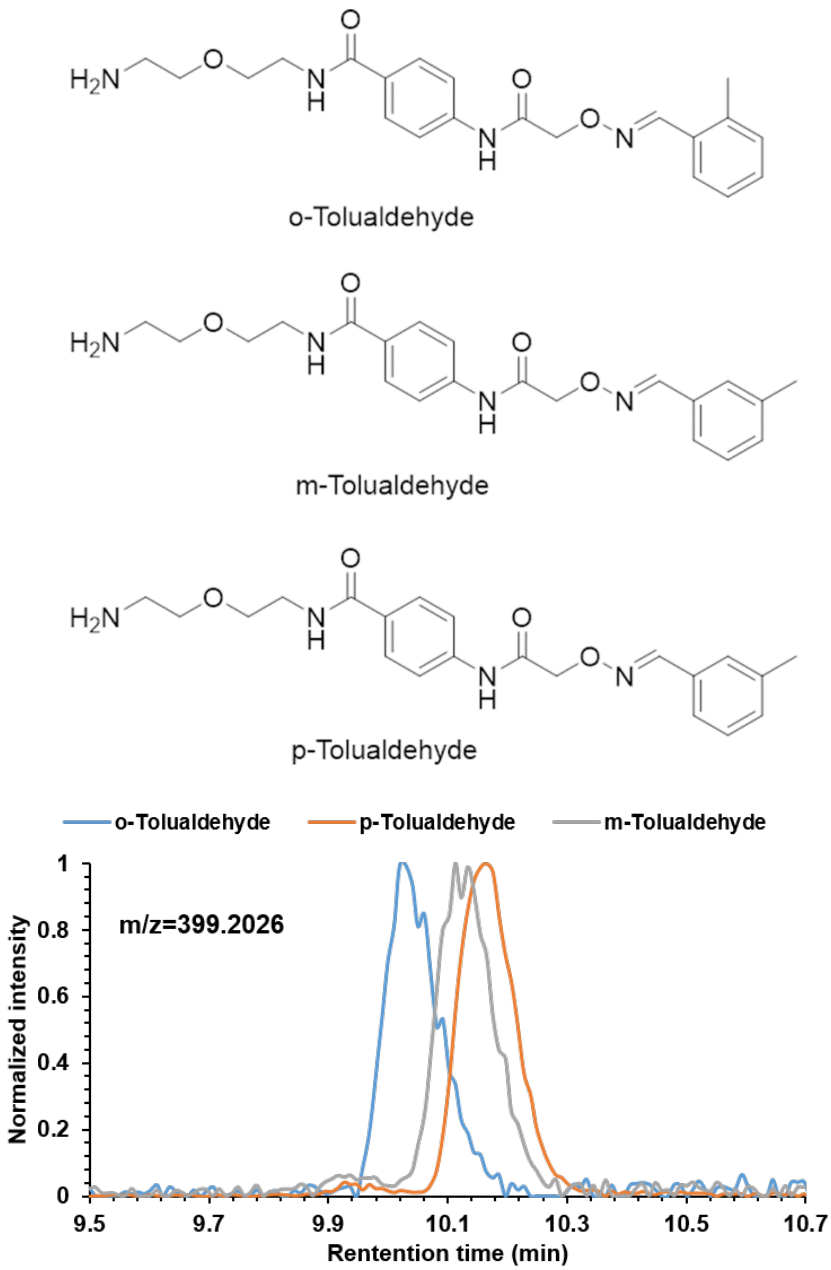


Figure S1: Examples of three extracted ion chromatograms of the LC-MS analysis of the three regioisomers of conjugated *o*-, *m*-, and *p*-tolualdehyde.

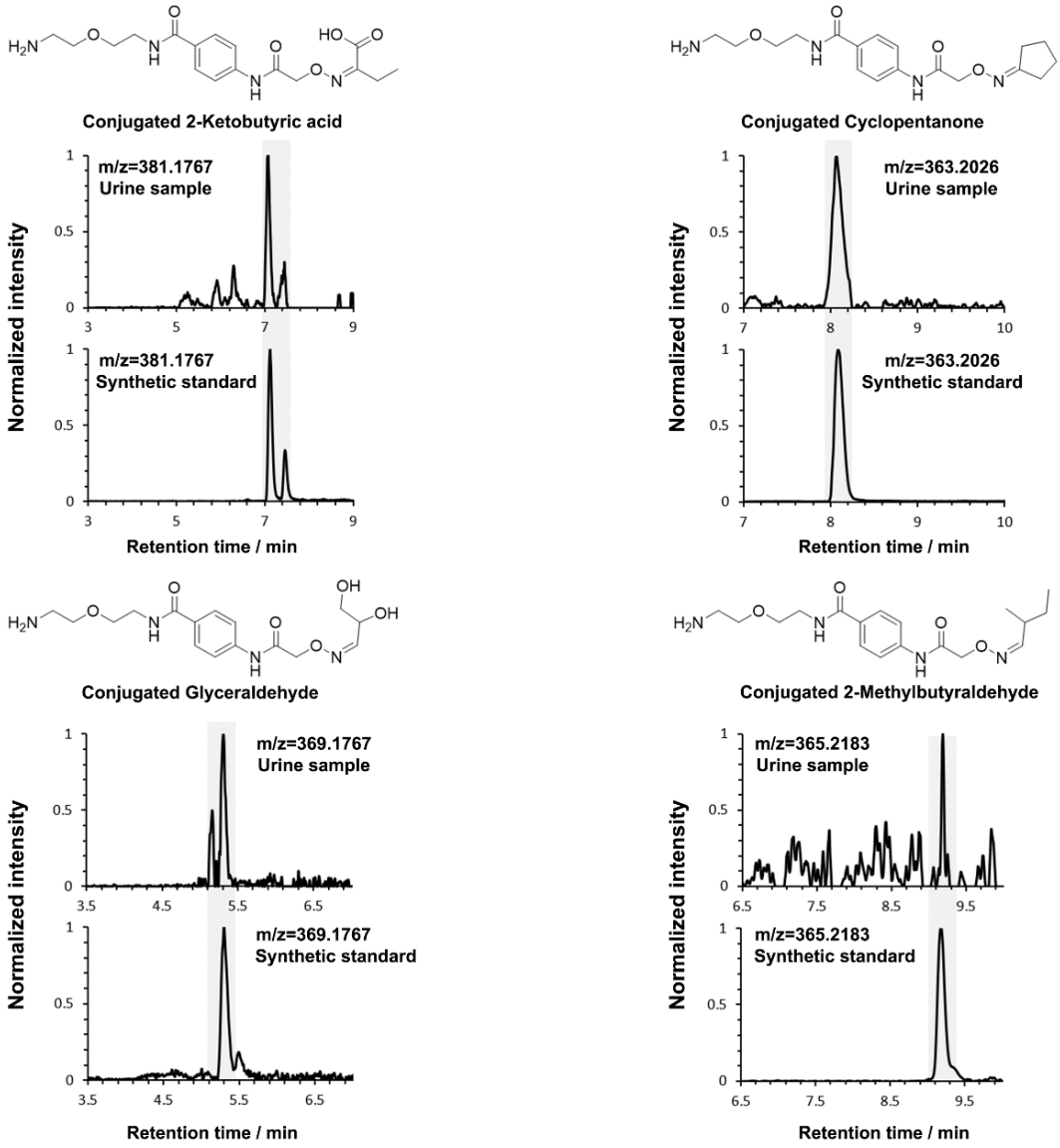


Figure S2: Representative extracted ion chromatograms of LC-MS co-injection experiments for validation of metabolites in urine samples.

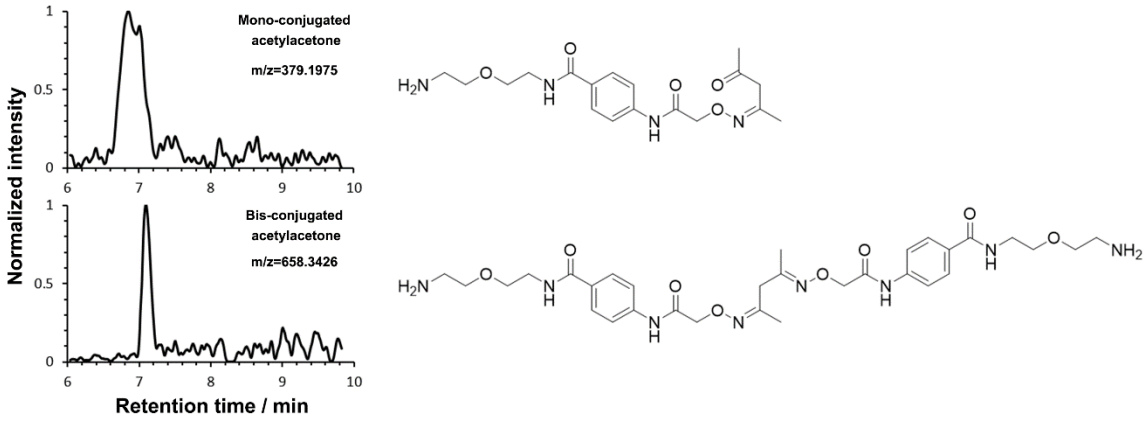


Figure S3: Mono- and bis-conjugated adducts of acetylacetone.

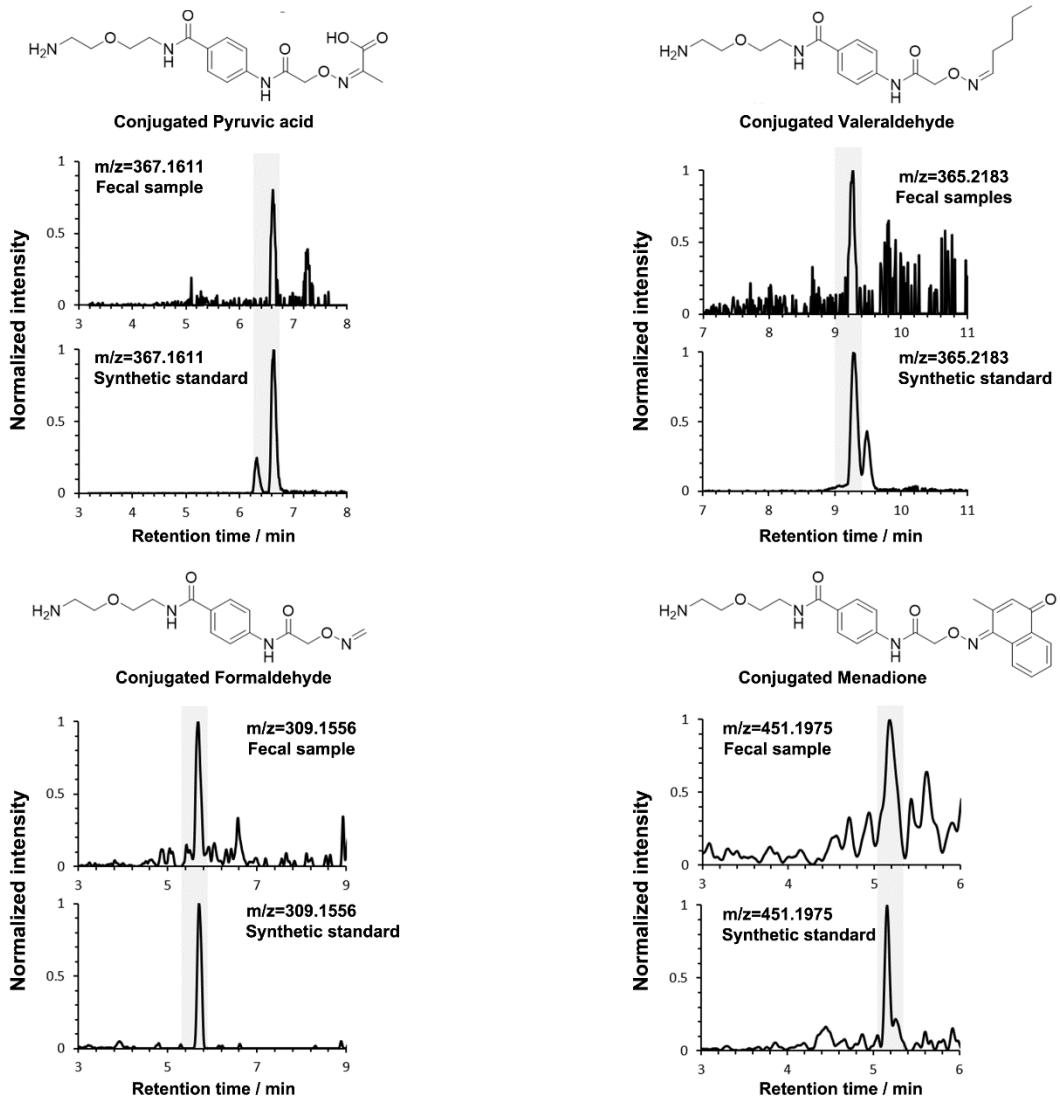


Figure S4: Representative extracted ion chromatograms of LC-MS co-injection experiments for validation of metabolites in fecal samples.

3. Supporting Tables

Table S1. 99 metabolites detected after analysis of urine samples using the carbonyl-specific chemical probe. Plausible metabolites were annotated using HMDB comparison.

Annotated Carbonyl conjugates	Predicted m/z		
	U8	U15	U20
4-Hydroxy-2-oxobutanoic acid; xi-3-Hydroxy-2-oxobutanoic acid	397.1707		
5.8-dihydroxy-2-(1-hydroxy-3-methoxy-4-oxocyclohexyl)-3.7-dimethoxy-4H-chromen-4-one;			659.2526
L-4-Hydroxyglutamate semialdehyde		426.1983	
L-4-Hydroxyglutamate semialdehyde		426.1978	
(+)-12a-Hydroxypachyrrhizone;		661.2162	
[2-ethyl-5-(3.5.7-trihydroxy-3.4-dihydro-2H-1-benzopyran-2-yl)phenyl]oxidanesulfonic acid			
(2E.11Z)-5-[5-(Methylthio)-4-penten-2-ynyl]-2-furanacrolein		511.2015	
Polyporusterone E; Polyporusterone D; Polyporusterone G		739.4612	
[(4-{3-[2-(2.4-dihydroxyphenyl)-2-oxoethyl]-4.6-dihydroxy-2-methoxyphenyl}- 2-methylbut-2-en-1-yl)oxy]sulfonic acid	733.2366	733.2355	733.2355
{2-[5.7-dihydroxy-2-(4-hydroxy-3-methoxyphenyl)-4-oxo-4H-chromen-6-yl]- 4-hydroxy-6-methyl-5-oxooxan-3-yl}oxidanesulfonic acid;	803.2059		
1.1-Dibromo-1-chloro-2-propanone	526.9680		526.9688
1.3-Diphenyl-1-propanone; 1.3-Diphenyl-2-propanone; Lactaroviolin		489.2516	
1-[4.9-Dihydro-2-(methylthio)-1.3-thiazino[6.5-b]indol-4-yl]-2-propanone			569.2010
14-hydroxy-E4-neuroprostane; 17-hydroxy-E4-neuroprostane; 20-hydroxy-E4-neuroprostane;		655.3669	
4-hydroxy-D4-neuroprostane; 7-hydroxy-D4-neuroprostane;Prehumulone; Macrophorin C;			
1-deoxy-1-(N6-lysino)-D-fructose		412.1823	412.1821
2-(dimethylamino)acetaldehyde; 4-Aminobutyraldehyde	366.2141		366.2139
2.3.4.5.6-Penta-O-acetyl-D-glucose; Monotropein	669.2641		
2.3-Dimethyl-2-cyclohexen-1-one; 6-Methyl-3.5-heptadien-2-one; (E.E)-2.4-Octadienal;			
trans. trans-3.5- Octadien-2-one; 1.5-Octadien-3-one; (E.E)-2.6-Octadienal;		403.2328	
3.5.5-Trimethyl-2-cyclopenten-1-one; Methyl-1-cyclopenten-1-yl)-ethanone;			
2-{[5.7-dihydroxy-2-(4-hydroxy-3-methoxyphenyl)-5H-chromen-3-yl]oxy}oxane-3.4.5-triol;			
Luteolinidin 3-O-glucoside; Pelargonidin 3-galactoside; Cyanidin 3-rhamnoside;	712.2549	712.2599	712.255
Peonidin 3-arabinoside; Petunidin 3-arabinoside; Pelargonidin 5-galactoside;			
Isopeonidin 3-arabinoside; Isopeonidin 3-xyloside; Peonidin 3-xyloside;			
2-Aminomuconic acid semialdehyde			420.1868
2-Decarboxybetanin	786.3025		786.3032
3-Oxoalanine		382.1714	
3-Phenylpropionylglycine			486.2345
3'-Sialyllactose; 6'-Sialyllactose		912.3558	
4-(2-Amino-3-hydroxyphenyl)-2.4-dioxobutanoic acid		502.1919	
4-(Methylthio)-2-butanone; 4-Mercapto-2-pentanone; S-Propyl thioacetate;			
3-Mercapto-2-pentanone; 2-Mercapto-3-pentanone; Tetrahydro-2-methylthiophen-3-ol;		397.1903	
Tetrahydro-2-methyl-3-furanthiol; 1-(Methylthio)-2-butanone; 4-(Methylthio)butanal;			
xi-2-Methyl-1.3-oxathiane; 3-(Methylthio)butanal; 3-(Methylthio)-2-butanone			
4-(Methylthio)-2-butanone; 4-Mercapto-2-pentanone; S-Propyl thioacetate;			
3-Mercapto-2-pentanone; 2- Mercapto-3-pentanone; Tetrahydro-2-methylthiophen-3-ol;		397.1907	
Tetrahydro-2-methyl-3-furanthiol; 1-(Methylthio)-2-butanone; 4-(Methylthio)butanal;			
xi-2-Methyl-1.3-oxathiane; 3-(Methylthio)butanal; 3-(Methylthio)-2-butanone			
4'.5.6-Trimethylscutellarein 7-glucoside	769.2956	769.2938	769.2948
4.6-Dihydroxy-2-quinolinecarboxylic acid		484.1809	
4-[(2-Furanylmethyl)thio]-2-pentanone		477.2164	
4-[(2-Furanylmethyl)thio]-2-pentanone		477.2178	
4-Acetylimidazo[4.5-c]pyridine		440.2053	
4-Mercapto-4-methyl-2-pentanone; 4-(Methylthio)-2-pentanone;	411.2052		411.2057
3-Mercapto-2-methylpentanal;			
5.7-Dihydroxy-3'.4'-dimethoxy-8-(3-hydroxy-3-methylbutyl)- isoflavone 7-glucoside		841.3455	
5-Chloro-4-(2-imidazolin-4-on-2-ylamino)-2.1.3-benzothiazdiazole		532.1634	
5-Hydroxyindoleacetaldehyde; Hydroxymethyl indol-3-yl ketone;			454.2079
1-Methoxy-1H-indole-3-carboxaldehyde			
5-Methyl-2.5-di-1-pyrrolidinyl-2-cyclopenten-1-one	513.3169		
6-[(5-acetyl-1-benzofuran-4-yl)oxy]-3.4.5-trihydroxyoxane-2-carboxylic acid		631.2223	
6-[4-(2-carboxy-2-oxoethyl)-2-methoxyphenoxy]-3.4.5-trihydroxyoxane-2-carboxylic acid		665.2338	
7-methoxy-3-(3-methoxyphenyl)-4H-chromen-4-one;			
2-(3.5-dimethoxyphenyl)-4H-chromen-4-one;			
5.7-Dimethoxyisoflavone;		561.2324	
5.6-Dimethoxyflavone; 5.7-Dimethoxyflavone; 5-Hydroxy-			
7-methoxy-6-methylflavone			
Acetaldehyde			323.1710
Alloxan			421.1472
Anisindione; 7-Hydroxy-2-methylisoflavone	531.2236	531.2238	531.2226
Apigenin 4'-O-glucoside	711.2529	711.2529	711.2525
Apigenin 4'-O-glucoside		711.2543	
Artonin T; Cajaisoflavone; Dihydrocycloartomunin; Dihydroisocycloartomunin; Cycloaltilisin		729.3100	
$C_{15}H_{12}O_6S$		631.1735	
$C_{20}H_{18}O_7$			649.2521
$C_{21}H_{22}O_{10}$		713.2637	

Annotated Carbonyl conjugates	Predicted m/z		
	U8	U15	U20
$C_{21}H_{24}O_6$		651.3061	
$C_{24}H_{26}O_{12}$	785.2907		785.2847
$C_{24}H_{34}O_{20}$	921.3119		
$C_{26}H_{28}O_{12}$		811.3043	
$C_{27}H_{34}O_{16}$		893.326	
$C_{31}H_{37}N_3O_{11}S$	938.3573		
Carbamazepine-O-quinone	545.2161		545.2168
Chlorosesamone	571.1957		
Chrycorin		499.2002	
Cinnamaldehyde; (Z)-3-Phenyl-2-propenal; Indanone; 2-Methylcumarone; Atropaldehyde		411.2033	
Cyclopassifloic acid D; 6beta-Hydroxyasiatic acid; Isothankunic acid; (3beta,19alpha)-3,19,23,24-Tetrahydroxy-12-oleanen-28-oic acid		783.4877	
Deoxyribose 5-phosphate; 1-Deoxy-D-xylulose 5-phosphate; Deoxyribose 1-phosphate; Deoxyribose 5-monophosphate; 5-Deoxyribose-1-phosphate		493.1689	
DHAP(18:0); LysoPA(0:0/18:1(9Z)); LysoPA(18:1(9Z)/0:0)		715.4006	
DHAP(6:0); Homolanthionine; Formononetin		547.2163	
DHAP(6:0); Homolanthionine; Formononetin		547.2155	
DHAP(8:0); Demethoxyegonol; Desmosflavone; Dimethylstrobochrysin; 4'-Hydroxy-R-phenprocoumon; 6-Hydroxy-R-phenprocoumon; 8-Hydroxy-R-phenprocoumon; 7-Hydroxy-R-phenprocoumon		575.2492	
Erythrose; L-Erythrulose	399.1863		
FAPy-adenine		432.2095	
FAPy-adenine		432.2093	
Genistein 4',7-O-diglucuronide		901.2606	
Glycolaldehyde	339.166	339.166	339.1658
Hydroxysepiapterin	532.2244		
Indolepyruvate		482.2046	
Isocarlinoside; Neocarlinoside; Kaempferol 3-[apiosyl-(1->2)-galactoside]; Rustoside; Quercetin 3-[rhamnosyl-(1->2)-alpha-L-arabinopyranoside]; Graveobioside A; Kaempferol 3-xylosylglucoside	859.2863		
Isolimonic acid		785.3637	
L-2-Amino-3-oxobutanoic acid; L-Aspartate-semialdehyde	396.187	396.1873	396.1869
Laccarin	473.2502		
Lactaldehyde; 3-Hydroxypropanal; Hydroxyacetone	353.1816	353.1816	353.1816
Lactaldehyde; 3-Hydroxypropanal; Hydroxyacetone	353.1822		
L-Furosine; Pyrraline		533.2709	
Luteolin 4'-glucoside 7-galacturonide		903.2754	
Mesoxalic acid		397.1355	
Musanolone F		597.2318	
N-(1-Deoxy-1-fructosyl)histidine	596.2656		
N-[[3-(b-D-Glucopyranosyloxy)-2,3-dihydro-2-oxo-1H-indol-3-yl]acetyl]aspartic acid; Silidianin	763.2822		
N-Acetyl-L-glutamate 5-semialdehyde		452.214	452.2145
Neoacrimarine K		838.3267	
Pefloxacin N-oxide		628.2912	
Polyporusterone B; Polyporusterone C		755.4551	
Pyridoxal; Isopyridoxal; 3alpha,4,5,7alpha-Tetrahydro-5-hydroxy-1H-isoindole-1,3(2H)-dione; 3alpha,4,7,7alpha-Tetrahydro-4-hydroxy-1H-isoindole-1,3(2H)-dione		446.203	
Pyroglutamylglycine		465.2087	
Pyroglutamylglycine		465.21	
Pyruvic acid; Malonic semialdehyde; Glucosereductone		367.1615	
Pyruvic acid; Malonic semialdehyde; Glucosereductone		367.1606	
Quercetin 3-O-(6\-malonyl-glucoside) 7-O-glucoside			991.2982
Shoyuflavone C		697.2004	
Suprofen; Tiaprofenic acid		539.1934	
Uridine diphosphate acetylgalactosamine 4-sulfate		966.1865	
Uridine; Pseudouridine		523.2133	
xl-Dihydro-2-methyl-3(2H)-thiophenone; Dihydro-5-methyl-2(3H)-thiophenone; xi-2-Acetylthietane	395.1737	395.1744	395.1743

Table S2. Complete list of carbonyl-containing standard conjugates **3** sorted by molecular weight.

	HMDB ID	Compound	Monoisotopic Mass	Conjugated m/z	RT/min
1	HMDB0001426	Formaldehyde	30.0105	309.1556	5.70
2	HMDB0000990	Acetaldehyde	44.0262	323.1713	6.34
3	HMDB0001659	Acetone	58.0418	337.1869	7.07
4	HMDB0003366	Propanal	58.0418	337.1869	7.16
5	HMDB0003344	Glycolaldehyde	60.0212	339.1662	5.87
6	HMDB0001167	Pyruvaldehyde	72.0211	351.1662	10.57
7	HMDB0000474	Butanone	72.0575	351.2026	7.83
8	HMDB0003543	Butanal	72.0575	351.2026	8.06
9	HMDB0000119	Glyoxylic acid	74.0003	353.1454	5.77
10	HMDB0006961	Hydroxyacetone	74.0368	353.1819	6.32
11	HMDB0006458	DL-Lactaldehyde	74.0368	353.1819	6.56
12	HMDB0003453	3-Hydroxypropanal	74.0368	353.1819	6.86
13	HMDB0031407	Cyclopentanone	84.0575	363.2026	8.10
14	HMDB0003407	Diacetyl	86.0367	365.1818	7.28
15	HMDB0034235	2-Pentanone	86.0731	365.2182	8.67
16	HMDB0031526	2-Methylbutyraldehyde	86.0732	365.2183	9.19
17	HMDB0031206	Valeraldehyde	86.0732	365.2183	9.28
18	HMDB0006478	Isovaleraldehyde	86.0732	365.2183	9.12
19	HMDB0000243	Pyruvic acid	88.0160	367.1611	6.63
20	HMDB0003243	Acetoin	88.0524	367.1975	6.64
21	HMDB0001051	Glyceraldehyde	90.0316	369.1767	5.30
22	HMDB0001882	Dihydroxyacetone	90.0317	369.1768	5.71
23	HMDB0032914	Furfural	96.0211	375.1662	7.66
24	HMDB0003315	Cyclohexanone	98.0731	377.2182	8.98
25	HMDB0031496	trans-2-Hexenal	98.0731	377.2182	10.01
26	HMDB0031648	Acetylacetone	100.0524	379.1975	6.86
27		Acetylacetone (bis-conjugated)		658.3426	7.09
28	HMDB0031598	2.3-Pentanedione	100.0524	379.1975	8.13
29	HMDB0029599	Glutaraldehyde	100.0525	379.1975	7.17
30	HMDB0000753	3-Hexanone	100.0888	379.2339	9.62
31	HMDB0031578	2-Methylpentanal	100.0888	379.2339	9.76
32	HMDB0031220	2-Ethylbutyraldehyde	100.0888	379.2339	9.86
33	HMDB0002939	4-Methyl-2-pentanone	100.0888	379.2339	9.64
34	HMDB0005994	Hexanal	100.0888	379.2339	10.35
35	HMDB0005842	2-Hexanone	100.0888	379.2339	9.83
36	HMDB0000005	2-Ketobutyric acid	102.0316	381.1767	7.09
37	HMDB0000060	Lithium acetoacetate	102.0317	381.1768	7.12
38	HMDB0001352	β-Hydroxypyruvic acid	104.0109	383.1560	5.13
39	HMDB0006115	Benzaldehyde	106.0419	385.1870	9.36
40	HMDB0000720	Levulinic acid	116.0473	395.1924	7.18
41	HMDB0031522	Mesoxalic acid	117.9902	397.1353	5.09
42	HMDB0002649	Erythrose	120.0422	399.1873	5.10
43	HMDB0006293	Erythrulose	120.0422	399.1873	7.08
44	HMDB0033910	Acetophenone	120.0575	399.2026	9.47
45	HMDB0029636	o-Tolualdehyde	120.0575	399.2026	10.02
46	HMDB0029638	p-Tolualdehyde	120.0575	399.2026	10.11
47	HMDB0029637	m-Tolualdehyde	120.0575	399.2026	10.17

	HMDB ID	Compound	Monoisotopic Mass	Conjugated m/z	RT/min
48	HMDB0011718	4-Hydroxybenzaldehyde	122.0368	401.1819	8.00
49	HMDB0034170	Salicylaldehyde	122.0368	401.1819	9.05
50	HMDB0030776	Maltol	126.0316	405.1767	4.92
51	HMDB0031294	2-Octanone	128.1201	407.2652	11.29
52	HMDB0001140	Octanal	128.1201	408.2725	11.58
53	HMDB0000695	alpha-ketoisocaproate	130.0629	409.2080	8.75
54	HMDB0000491	3-Methyl-2-oxovaleric acid	130.0629	409.2080	8.84
55	HMDB0000223	Oxalacetic acid	132.0058	411.1509	6.31
56	HMDB0003441	Trans-Cinnamaldehyde	132.0575	411.2026	10.18
57	HMDB0003224	2-Deoxy-D-ribose	134.0579	413.2030	5.57
58	HMDB0002818	Alloxan	142.0014	421.1465	11.01
59	HMDB0000646	L-Arabinose	150.0528	429.1979	5.21
60	HMDB0000283	Ribose	150.0528	429.1979	5.21
61	HMDB0036061	Safranal	150.1044	429.2495	10.99
62	HMDB0035089	R-Carvone	150.1044	429.2495	11.34
63	HMDB0035824	Carvone	150.1044	429.2495	11.68
64	HMDB0035250	Myrtenal	150.1045	429.2496	11.44
65	HMDB0012308	Vanillin	152.0473	431.1924	8.14
66	HMDB0000849	Rhamnose	164.0684	443.2135	5.42
67	HMDB0001545	Pyridoxal	167.0582	446.2033	5.99
68	HMDB0033713	2-Undecanone	170.1670	449.3121	12.81
69	HMDB0001892	Menadione	172.0524	451.1975	5.16
70	HMDB0003466	L-Gulonic acid γ-lactone	178.0477	457.1928	7.65
71	HMDB0000707	4-Hydroxyphenylpyruvic acid	180.0422	459.1873	9.24
72	HMDB0000169	D-Mannose	180.0633	459.2084	5.12
73	HMDB0001151	D-Allose	180.0633	459.2084	5.17
74	HMDB0000122	D-Glucose	180.0633	459.2084	5.08
75	HMDB0000660	D-Fructose	180.0633	459.2084	5.08
76	HMDB0001266	L-Sorbose	180.0633	459.2084	5.11
77	HMDB0033704	Galactose	180.0634	459.2085	5.11
78	HMDB0000684	L-Kynurenine	208.0847	487.2298	12.64
79	HMDB0032797	Jasmonic acid	210.1255	489.2706	10.14
80	HMDB0000803	N-Acetylglucosamine	221.0899	500.2350	5.41
81	HMDB0001548	D-Ribose 5-phosphate	230.0191	509.1642	5.37
82	HMDB0000296	Uridine	244.0695	523.2146	13.95
83	HMDB0003312	Daidzein	254.0579	533.2030	8.46
84	HMDB0001401	D-Glucose 6-phosphate	258.0151	537.1602	5.22
85	HMDB0001254	Glucosamine 6-phosphate	259.0457	538.1908	4.54
86	HMDB0015008	Suprofen	260.0507	539.1958	9.26
87	HMDB0001358	Retinal	284.2140	563.3591	14.35
88	HMDB0005800	Luteolin	286.0477	565.1928	7.58
89	HMDB0061073	Noroxymorphone	287.1158	566.2609	6.06
90	HMDB0000975	Trehalose	342.1162	621.2613	5.08
91	HMDB0000186	α-Lactose	342.1162	621.2613	5.10
92	HMDB0000163	Maltose	342.1162	621.2613	5.06
93	HMDB0000015	Cortexolone	346.2144	625.3595	11.38
94	HMDB0000163	Maltotriose	504.1690	783.3141	5.16

Table S3. An overview of captured metabolites has been compiled detailing metabolic sources and biological importance

Metabolite	Fecal	Urine	Source	Biological relevance
Formaldehyde			Endogenous & food	
Acetaldehyde			Endogenous & food	
Acetone			Endogenous & food	Derived from microbiome-metabolism
Propanal			Endogenous & food (celeries, sourdocks, tartary buckwheats, arrowhead, mango, and deerberries)	
Glycolaldehyde			Endogenous & food	
Butanone			Endogenous & food (dills, star fruits, napa cabbages, gooseberries, and pot marjorams)	
Butanal			Endogenous & food (white lupines, jerusalem artichokes, citrus, agars, and prairie turnips)	A biomarker for oxidative damage to lipids, proteins and DNA
Glyoxylic acid			Endogenous & food	Be associated with primary hyperoxaluria
Hydroxyacetone			Endogenous & food (bog bilberries, cardoons, amaranths, black salsifies, and komatsuna)	
Lactaldehyde			Endogenous	
Cyclopentanone			Endogenous & food (potato and tomato, butter, meats, coffee, roasted peanut)	
Diacetyl			Endogenous & food (nances, tartary buckwheats, tamarinds, pineapples, and celeriacs)	Be associated with several diseases such as crohn's disease, ulcerative colitis, and nonalcoholic fatty liver disease
2-Methylbutyraldehyde			Endogenous & food (sugar apples, horned melons, hyacinth beans, persian limes, and root vegetables)	Be associated with several diseases such as ulcerative colitis and nonalcoholic fatty liver disease
Valeraldehyde			Endogenous & food (black walnuts, milk (cow), and safflowers, garden tomato, alcoholic beverages, cauliflowers, sweet bay, and fruits.)	
Pyruvic acid			Endogenous & food (chickpea, pea, sweet trefoil)	
Acetoin			Food (cocoa and cocoa products, evergreen blackberries, orange bell peppers, tortilla chips, and pomes)	Be associated with several diseases such as eosinophilic esophagitis and ulcerative colitis
Glyceraldehyde			Endogenous	Cause chromosome damage to human cells in culture and is mutagenic in the Ames bacterial test
Furfural			Food (coffee, calamus, matsutake mushroom, pumpkin, malt, peated malt, Bourbon vanilla, Lamb's lettuce, pimento leaf and various fruits, e.g. apple, apricot, sweet cherry, morello cherry, orange, grapefruit, Chinese quince and a common consit of essential oils.)	
Cyclohexanone			Endogenous & food	The development of anosmia (an olfactory disorder) and rhinitis

Metabolite	Fecal	Urine	Source	Biological relevance
Glutaraldehyde			Endogenous & food	
Hexanal			Endogenous & food (milk)	
2-Ketobutyric acid			Endogenous & food (mamey sapotes, peachs, amaranths, lotus, and pepper)	
Hydroxypyruvic acid			Endogenous & food (alcoholic beverages, cocoa and cocoa products, and milk and milk products)	Hydroxypyruvic acid is involved in the metabolic disorder called the dimethylglycine dehydrogenase deficiency pathway
Benzaldehyde			Endogenous & food	
Erythrose			Food	Be associated with schizophrenia
o/m/p-Tolualdehyde			Endogenous & food (sweet cherries, alcoholic beverages, garden tomato, coffee and coffee products, and tea)	
Maltol			Endogenous & food (milk and milk products, nuts, soy beans, pepper (c. annuum), and coffee and coffee products)	
3-Methyl-2-oxovaleric acid			Endogenous & food	Chronically high levels of 3-methyl-2-oxovaleric acid are associated with maple syrup urine disease
Ketoisocaproate			Endogenous & food	Chronically high levels of ketoleucine are associated with maple syrup urine disease
Acetophenone			Food	
4-Hydroxybenzaldehyde			Endogenous & food (cardoons, colorado pinyons, oyster mushrooms, common chokecherries, and potato)	
Cinnamaldehyde			Food	
Arabinose			Endogenous & food (sweet basils and tamarinds)	Derived from microbiome-metabolism
Ribose			Endogenous & food (small amounts of ribose can be found in ripe fruits and vegetables)	
Myrtenal			Endogenous & food	
Pyridoxal			Endogenous & food (sourdoughs, lichee, arctic blackberries, watercress, and cottonseeds)	
2-Undecanone			Food (bananas, cloves, ginger, guava, strawberries, and wild-grown tomatoes)	
Rhamnose			Endogenous & food	Derived from microbiome-metabolism

Metabolite	Fecal	Urine	Source	Biological importance
Menadione			Endogenous & food	
4-Hydroxyphenylpyruvic acid			Endogenous & food (nanking cherries, maitakes, pineapples, bitter gourds, and wakames)	Be associated with several diseases such as deafness, onychodystrophy, osteodystrophy, mental retardation, and seizures syndrome, attachment loss, and colorectal cancer
Fructose			Endogenous & food (Honey, tree fruits, berries, melons, and some root vegetables, such as beets, sweet potatoes, parsnips, and onions)	An important contribution to senescence and many age-related chronic diseases
Allose			Endogenous	
L-Sorbose			Endogenous & food	
D-Mannose			Endogenous & food	
Daidzein			Food (soy beans and other soy products)	
D-Glucose 6-phosphate			Endogenous	
Retinal			Endogenous & food	
Luteolin			Food (food plants)	
α-Lactose			Endogenous & food (milk)	
Trehalose			Endogenous & food	Derived from microbiome-metabolism
Maltose			Endogenous & food (yellow pond-lilies, sunflowers, spinachs, cetacea (dolphin, porpoise, whale), and common octopus)	
Cortexolone			Endogenous & food	

Table S4. Peak areas of the butanone-conjugate and two different internal standards in urine and blank samples were analyzed by UPLC-MS in positive ionization mode. EIC for each compound: Benzoic acid-$^{13}C_6$ (*m/z* = 129.0642); Phenylalanine-$^{13}C_9$ (*m/z* = 176.1135); and butanone-conjugate (*m/z* = 351.2026).

Experiment	A [Conjugated butanone]	A [Internal standard 1 (Benzoic acid-$^{13}C_6$)]	Ratio (Conj-butanone/IS 1)	A [Internal standard 2 (Phenylalanine-$^{13}C_9$)]	Ratio (Conj-butanone/IS 2)
Urine sample	11,053	1,059	10.44	499,589	0.0221
H_20 (1)	18,659	771	24.20	474,115	0.0394
H_20 (2)	18,333	905	20.26	502,336	0.0365
Mean(H_20):	18,496	838	22.23	488,256	0.0380
		Recovery rate:	47.0%		58.2%