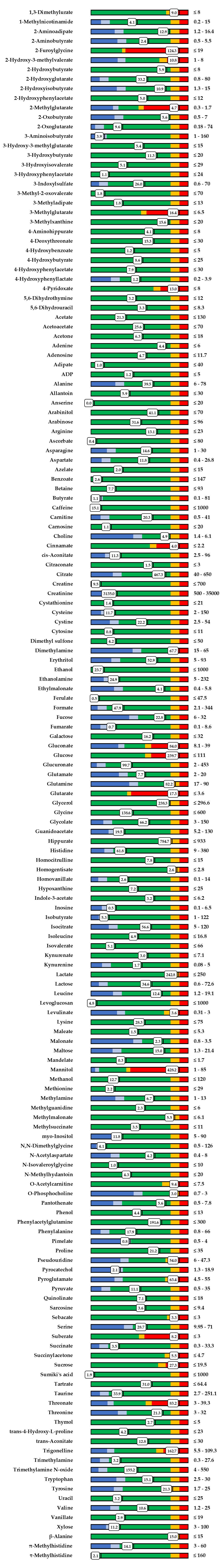
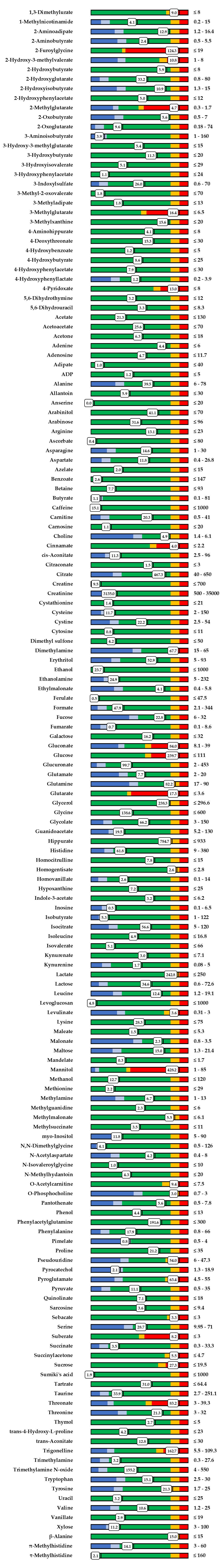
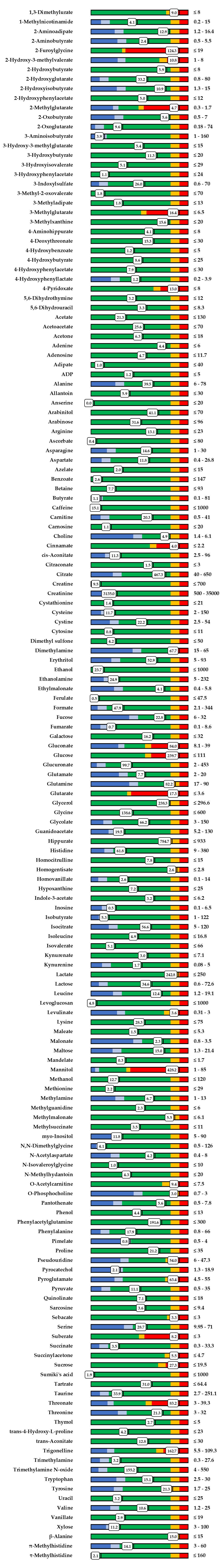
**Table S1**. List of the 165 metabolites identified and quantified by the SYNHMET approach. Correlation information include the number of points, the chemical shift used for NMR spectrum profiling, the identified HRMS hit, including chromatographic mode and retention time, the measured molecular weight and the correlation coefficient. For each of the three groups of subjects, the average, the minimun and maximum values are shown, together with the normal range estimated from the HMDB database.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Correlation** | | | | | **Results [M/mM creatinine]** | | | |  |
| **Compound** | **N**  **(NMR)a** | ****  **[ppm]** | **Hit** | **MW** | **R2** | **Control**  **(n=9)** | **Chronic Cystitis**  **(n=6)** | **Bladder Cancer**  **(n=31)** | **Normal Rangeb** | **Biochemical classification** |
| 1,3-Dimethylurate | 21 (21) | 3.3 3.4 | RP+/- (6.64)  HC+/- (2.20) | 196.0593 | 0.9932 | 1.2 (0.4-2.7) | 1.8 (0.3-5.0) | 1.9 (0.01-9.0) | ≤ 8 | Xanthine Metabolism |
| 1-Methylnicotinamide | 42 (44) | 4.5 8.2 8.9 9.0 9.3 | RP+ (0.89) | 136.0634 | 0.9848 | 3.7 (1.7-6.3) | 5.3 (1.8-10.2) | 3.3 (0.9-9.2) | 0.2 - 15 | Nicotinate and Nicotinamide Metabolism |
| 2-Aminoadipate | 31 (31) | 2.2 | RP+ (2.51) | 161.0685 | 0.9935 | 9.5 (5.8-14.7) | 10.3 (1.0-14.5) | 9.8 (2.7-19.1) | 1.2 - 16 | Lysine Metabolism |
| 2-Aminobutyrate | 31 (31) | 1.0 | HC+ (3.61) | 103.0634 | 0.9937 | 2.6 (1.4-4.4) | 1.9 (1.2-2.4) | 2.1 (0.6-5.3) | 0.5 - 5.5 | Methionine, Cysteine, SAM and Taurine Metabolism |
| 2-Furoylglycine | 27 (27) | 6.6 | RP+/- (5.50)  HC+/- (3.82) | 169.0372 | 0.9849 | 3.5 (1.6-6.4) | 6.3 (1.9-19.4) | 11.8 (0.7-124.3) | ≤ 19 | Food Component/Plant |
| 2-Hydroxy-3-methylvalerate | 20 (20) | 0.9 | HC- (2.30) | 132.0787 | 0.9986 | 3.8 (1.9-5.9) | 4.6 (2.9-6.2) | 3.9 (1.7-10.8) | 1 - 8 | Leucine, Isoleucine and Valine Metabolism |
| 2-Hydroxybutyrate | 8 (8) | 0.9 | HC+ (1.11) | 104.0475 | 0.9980 | 1.0 (0.6-2.0) | 3.6 (1.0-11.6) | 2.2 (0.6-7.3) | ≤ 8 | Methionine, Cysteine, SAM and Taurine Metabolism |
| 2-Hydroxyglutarate | 40 (40) | 2.2 2.3 | RP- (2.25) | 148.0376 | 0.9965 | 25.5 (19.1-30.8) | 24.7 (5.4-37.7) | 29.8 (13.4-64.3) | 0.8 - 80 | Fatty Acid Metabolism |
| 2-Hydroxyisobutyrate | 46 (46) | 1.3 | - | 104.0475 | - | 4.6 (3.7-6.0) | 5.3 (3.6-6.9) | 6.8 (2.9-12.3) | 1.3 - 15 | Chemical |
| 2-Hydroxyphenylacetate | 37 (40) | 3.5 6.9 | RP- (9.04) | 152.0476 | 0.9957 | 3.5 (2.7-5.0) | 4.5 (2.6-5.9) | 4.7 (1.5-10.9) | ≤ 5 | Phenylalanine and Tyrosine Metabolism |
| 2-Methylglutarate | 26 (26) | 1.1 | HC- (3.71) | 146.0584 | 0.9956 | 0.7 (0.3-1.4) | 0.7 (0.5-1.1) | 1.0 (0.4-4.7) | ≤ 2 | Fatty Acid Metabolism |
| 2-Oxobutyrate | 41 (41) | 1.1 | RP- (1.54) | 102.0318 | 0.9912 | 1.4 (1.0-1.7) | 3 (1.4-4.4) | 2.6 (0.8-5.6) | 0.5 - 7 | Leucine, Isoleucine and Valine Metabolism |
| 2-Oxoglutarate | 29 (34) | 2.4 3.0 | HC- (4.57) | 146.022 | 0.9967 | 13.2 (3.5-31.9) | 11.1 (1.1-16.5) | 8.8 (1.5-32.1) | ≤ 74 | Fatty Acid Metabolism |
| 3-Aminoisobutyrate | 38 (40) | 1.2 | RP+ (0.97)  HC+ (6.56) | 103.0631 | 0.9984 | 8.2 (5.9-10.6) | 35.3 (3.6-123.5) | 13.3 (1.0-98.5) | 1 - 160 | Pyrimidine Metabolism, Thymine containing |
| 3-Hydroxy-3-methylglutarate | 44 (44) | 1.3 | HC- (3.69) | 162.0532 | 0.9888 | 3.8 (2.5-5.1) | 4.1 (2.0-8.5) | 4.6 (1.8-14.0) | ≤ 15 | Leucine, Isoleucine and Valine Metabolism |
| 3-Hydroxybutyrate | - (41) | 1.2 | - | 104.0475 | - | 4.7 (1.8-6.3) | 3.9 (0.9-5.5) | 5.9 (1.3-11.3) | ≤ 20 | Ketone Bodies |
| 3-Hydroxyisovalerate | 43 (43) | 1.3 2.4 | RP- (4.71)  HC- (2.06) | 118.0639 | 0.9886 | 8.2 (4.3-18.5) | 6.5 (3.4-8.5) | 4.3 (1.7-9.1) | ≤ 29 | Leucine, Isoleucine and Valine Metabolism |
| 3-Hydroxyphenylacetate | 33 (33) | 6.8 | RP- (8.54) | 152.0476 | 0.9889 | 4.2 (0.6-9.5) | 3.0 (0.7-5.8) | 3.0 (0.4-10.9) | ≤ 24 | Phenylalanine and Tyrosine Metabolism |
| 3-Indoxylsulfate | 43 (45) | 7.5 7.7 | HC- (0.63) | 213.0093 | 0.9937 | 22.3 (10.3-34.5) | 26.9 (18.1-34.1) | 28.2 (2.7-83.5) | 0.6 - 70 | Tryptophan Metabolism |
| 3-Methyl-2-oxovalerate | 28 (29) | 0.9 1.1 | RP+ (0.82) | 130.0627 | 0.9928 | 2.5 (1.3-4.2) | 5.6 (1.9-13.2) | 4.1 (1.8-10.4) | ≤ 5 | Leucine, Isoleucine and Valine Metabolism |
| 3-Methyladipate | 16 (16) | 0.9 | HC- (1.94) | 160.0738 | 0.9939 | 1.7 (0.7-3.3) | 1.7 (0.2-4.3) | 2.7 (0.1-12.4) | ≤ 13 | Lysine Metabolism |
| 3-Methylglutarate | 23 (23) | 0.9 | RP- (4.67) | 146.0584 | 0.9941 | 1.3 (0.4-3.2) | 1.1 (0.4-2.0) | 3.0 (0.2-16.4) | ≤ 8 | Leucine, Isoleucine and Valine Metabolism |
| 3-Methylxanthine | 37 (38) | 3.5 8.0 | HC+ (3.11) | 166.0488 | 0.9974 | 4.7 (1.9-10.0) | 4.7 (3.2-7.7) | 6.6 (1.9-16.2) | ≤ 20 | Xanthine Metabolism |
| 4-Aminohippurate | 39 (39) | 6.9 7.4 | HC+/- (3.24) | 194.0693 | 0.9971 | 2.9 (1.8-4.4) | 4.1 (3.4-5.2) | 3.3 (1.4-6.1) | ≤ 8 | Benzoate Metabolism |
| 4-Deoxythreonate | 31 (32) | 1.2 | RP- (1.51) | 120.043 | 0.9949 | 17.2 (9.5-28.9) | 22.0 (16.0-31.5) | 17.5 (5.6-44.4) | ≤ 30 | Glycine, Serine and Threonine Metabolism |
| 4-Hydroxybenzoate | 15 (15) | 7.8 | RP+ (6.81) | 138.0315 | 0.9962 | 0.9 (0.3-3.0) | 1.4 (0.1-4.5) | 1.5 (0.01-5.1) | ≤ 5 | Benzoate Metabolism |
| 4-Hydroxybutyrate | 45 (45) | 2.2 | - | 104.0475 | - | 8.4 (4.4-15.6) | 7.6 (5.1-9.3) | 8.0 (3.4-22.5) | ≤ 25 | Neurotransmitter metabolites |
| 4-Hydroxyphenylacetate | 21 (25) | 3.4 6.9 | HC- (1.92) | 152.0474 | 0.9974 | 5.0 (2.0-8.4) | 5.4 (0.8-12.5) | 7.6 (0.3-70.9) | ≤ 30 | Phenylalanine and Tyrosine Metabolism |
| 4-Hydroxyphenyllactate | 12 (12) | 6.8 7.2 | RP+/- (7.70) | 182.0576 | 0.9950 | 2.0 (0.6-4.5) | 1.2 (0.6-2.1) | 1.2 (0.2-2.8) | ≤ 4 | Phenylalanine and Tyrosine Metabolism |
| 4-Pyridoxate | 40 (40) | 2.4 7.9 | RP +/- (4.41) | 183.0528 | 0.9969 | 4.4 (2.5-8.2) | 3.9 (0.6-5.9) | 5.2 (1.9-14.4) | ≤ 8 | Vitamin B6 Metabolism |
| 5,6-Dihydrothymine | 43 (43) | 1.2 | HC+ (2.42) | 128.0583 | 0.9978 | 3.7 (2.1-4.6) | 4.1 (2.8-5.0) | 2.7 (0.4-4.7) | ≤ 12 | Pyrimidine Metabolism, Thymine containing |
| 5,6-Dihydrouracil | 23 (23) | 2.7 | RP+ (1.65) | 114.0428 | 0.9934 | 5.1 (2.1-7.7) | 4.7 (1.3-8.9) | 4.4 (1-16.8) | ≤ 9 | Pyrimidine Metabolism, Uracil containing |
| Acetate | - (38) | 1.9 | - | - | - | 26.4 (6.0-126.9) | 47.7 (5.2-172.1) | 55.0 (4.3-640.6) | ≤ 130 | Urinary tract infection markers |
| Acetoacetate | 38 (38) | 3.4 | RP+ (1.18) | 102.0316 | 0.9954 | 7.7 (1.9-16.6) | 14.1 (3.5-35.4) | 11.9 (1.6-101.7) | ≤ 70 | Ketone Bodies |
| Acetone | - (44) | 2.2 | - | - | - | 2.3 (1.1-4.0) | 2.1 (1.0-4.6) | 3.1 (0.8-13.0) | ≤ 18 | Ketone Bodies |
| Adenine | 33 (33) | 8.2 | RP+ (0.78) | 135.0528 | 0.9924 | 2.1 (1.4-3.5) | 2.1 (1.4-2.7) | 2.2 (1.2-4.6) | ≤ 6 | Purine Metabolism, Adenine containing |
| Adenosine | 33 (33) | 6.1 8.2 8.3 | HC+ (2.61) | 267.0966 | 0.9912 | 1.1 (0.1-2.1) | 3.4 (0.9-9.1) | 1.6 (0.01-9.7) | ≤ 3 | Purine Metabolism, Adenine containing |
| Adipate | 13 (13) | 1.5 | HC- (1.97) | 146.0584 | 0.9936 | 2.5 (1.0-7.2) | 2.3 (0.6-4.9) | 1.5 (0.1-5.0) | ≤ 40 | Fatty Acid Metabolism |
| ADP | 37 (40) | 4.6 6.1 8.3 8.5 | RP- (4.83) | 427.0209 | 0.9893 | 1.5 (0.9-4.4) | 1.9 (0.9-5.3) | 1.6 (0.8-3.5) | ≤ 4 | Purine Metabolism, Adenine containing |
| Alanine | 44 (46) | 1.5 | RP+ (0.80)  HC+ (6.14) | 89.04755 | 0.9886 | 39.1 (26.0-59.1) | 27.3 (13.1-39.7) | 26.4 (10.4-108.8) | 6 - 65 | Alanine and Aspartate Metabolism |
| Allantoin | 46 (46) | 5.4 | RP+ (0.94)  HC+/- (1.57) | 158.0436 | 0.9831 | 11.1 (6.0-14.8) | 7.7 (4.3-12.6) | 10.2 (3.5-19.0) | ≤ 30 | Purine Metabolism, (Hypo)Xanthine/Inosine containing |
| Anserine | 5 (5) | 2.7 3.1 | HC+/- (9.44) | 240.1222 | 0.9988 | 1.9 (0.2-4.6) | 4.7 (0.03-27.5) | 1.0 (0.02-18.8) | ≤ 20 | Dipeptide Derivative |
| Arabinitol | 41 (41) | 3.6 3.7 | HC- (2.11) | 152.0688 | 0.9979 | 39.1 (30.1-52.2) | 44.5 (6.2-69.9) | 56 (11.6-207.0) | ≤ 70 | Pentose Metabolism |
| Arabinose | - (43) | 5.2 | - | 150.0525 | - | 16.3 (11.2-19.9) | 7.8 (5.3-12.8) | 17.0 (1.5-48.9) | ≤ 96 | Pentose Metabolism |
| Arginine | 22 (23) | 3.2 | RP+ (0.77) | 174.1114 | 0.9988 | 6.2 (4.0-9.7) | 3.8 (1.0-6.6) | 6.8 (2.5-38.7) | 1.1 - 20 | Urea cycle Arginine and Proline Metabolism |
| Ascorbate | 15 (16) | 4.0 4.5 | RP+/- (1.42) | 176.0318 | 0.9976 | 7.5 (0.1-31.2) | 1.6 (0.2-7.8) | 10.4 (0.1-260.9) | ≤ 80 | Ascorbate and Aldarate Metabolism |
| Asparagine | 41 (41) | 2.9 | RP+ (0.79) | 132.0533 | 0.9899 | 15 (7.3-26.4) | 6.5 (1.6-14.4) | 7.2 (2.9-17.2) | 1 - 30 | Alanine and Aspartate Metabolism |
| Aspartate | 15 (15) | 2.8 | RP+ (0.99) | 133.0372 | 0.9960 | 5.8 (4.7-7) | 6 (1.3-9.1) | 8.5 (3-22.2) | 1.5 - 22 | Alanine and Aspartate Metabolism |
| Azelate | 11 (11) | 1.3 1.5 2.2 | RP- (9.64)  HC- (1.39) | 188.1048 | 0.9998 | 3.5 (1.4-7.6) | 6.7 (1.3-27.6) | 2.6 (0.5-16.6) | ≤ 15 | Fatty Acid Metabolism |
| Benzoate | 19 (21) | 7.5 7.9 | RP+/- (7.24)  HC- (1.77) | 122.0377 | 0.9964 | 2.2 (0.5-6.2) | 2.3 (0.5-5.1) | 8.5 (0.1-128.6) | ≤ 15 | Benzoate Metabolism |
| Betaine | 38 (43) | 3.3 | RP+ (0.89) | 117.0787 | 0.9809 | 9.7 (5.5-12.2) | 30.5 (5.2-142.0) | 14.0 (3.2-68.5) | ≤ 25 | Glycine, Serine and Threonine Metabolism |
| Butyrate | 24 (24) | 0.9 | RP+ (0.79) | 88.05236 | 0.9959 | 2.1 (1.0-4.6) | 1.3 (0.8-1.9) | 2.1 (0.7-15.2) | ≤ 4 | Fatty Acid Metabolism |
| Caffeine | 16 (16) | 3.3 7.9 | HC+ (1.27) | 194.0805 | 0.9971 | 0.8 (0.1-2.0) | 2.1 (0.3-8.0) | 2.65 (0.03-15.1) | 0 – 1.2 | Xanthine Metabolism |
| Carnitine | 43 (44) | 3.2 | RP+ (0.88)  HC+ (8.02) | 161.1048 | 0.9835 | 7.8 (1.4-18.1) | 14.2 (1.2-24.7) | 15.9 (1.9-45.5) | 0.5 - 20 | Fatty Acid Metabolism |
| Carnosine | 14 (14) | 3.2 7.2\* 8.2\* | RP+ (0.77)  HC+/- (8.97) | 226.106 | 0.9882 | 8.9 (2.5-41.3) | 8.3 (0.7-27.6) | 5.1 (0.5-44.7) | £ 20 | Dipeptide Derivative |
| Choline | 32 (32) | 3.2 | RP+ (0.82)  HC+ (5.68) | 103.0995 | 0.9824 | 4.3 (3.6-5.3) | 4.2 (1.9-9.2) | 4.2 (1.6-17.2) | 1.4 - 7 | Glycero/Phospholipid Metabolism |
| Cinnamate | 12 (12) | 6.5 | HC+ (6.25) | 148.0526 | 0.9945 | 0.3 (0.04-0.4) | 0.3 (0.05-1.0) | 0.6 (0.02-4.0) | ≤ 2.5 | Food Component/Plant |
| cis-Aconitate | 44 (46) | 3.1 5.8 | RP+/- (2.91) | 174.0161 | 0.9855 | 15.8 (12.8-21.1) | 21.4 (12.8-34.0) | 19.7 (5.2-37.2) | 2.5 - 96 | TCA Cycle |
| Citraconate | 31 (31) | 5.5 | RP+ (2.25) | 130.0264 | 0.9952 | 1.1 (0.8-1.6) | 1.3 (1.2-1.4) | 1.3 (0.6-2.6) | ≤ 3 | Food Component/Plant |
| Citrate | 16 (46) | 2.5 2.7 | RP+/RP- (2.29) | 192.0266 | 0.9853 | 333.8 (25-522.2) | 293.8 (119.4-422.2) | 261 (14.2-737.7) | 10 - 650 | TCA Cycle |
| Creatine | 44 (46) | 3.0 3.9 | RP+/- (0.98)  HC+/- (6.91) | 131.0692 | 0.9643 | 53.8 (8.9-365.1) | 16.6 (5.7-35.7) | 11 (3.9-68.5) | ≤ 700 | Creatine Metabolism |
| Creatinine | 46 (46) | 3.0 4.0 | RP+ (0.92)  HC+/- (3.70) | 113.0587 | 0.9868 | 10-20 c | 2.3-17 c | 1.2-15 c | 2.5 – 23c | Creatine Metabolism |
| Cystathionine | 7 (7) | 2.7 3.1 | RP+ (0.78) | 222.0668 | 0.9981 | 4.1 (0.6-20.0) | 2.4 (0.2-5.4) | 1.7 (0.3-5.7) | ≤ 21 | Methionine, Cysteine, SAM and Taurine Metabolism |
| Cysteine | 20 (20) | 3.1 | RP+ (1.16) | 121.0197 | 0.9976 | 9.8 (3.7-32.2) | 10.2 (5.1-19.8) | 10.4 (5.0-23.5) | 2 - 150 | Methionine, Cysteine, SAM and Taurine Metabolism |
| Cystine | 10 (10) | 3.4 4.1 | RP+/RP- (0.78) | 240.0231 | 0.9969 | 8.7 (6.7-10.3) | 8.5 (2.8-15) | 7.9 (3.2-26.8) | 2.5 - 25 | Methionine, Cysteine, SAM and Taurine Metabolism |
| Cytosine | 22 (22) | 6.0 7.5 | HC+ (3.44) | 111.0434 | 0.9944 | 1.2 (0.4-4.2) | 1.8 (0.7-3.9) | 1.3 (0.3-4.7) | ≤ 11 | Pyrimidine Metabolism, Cytidine containing |
| Dimethylamine | - (45) | 2.7 | - | - | - | 38.1 (26.5-63.0) | 32.1 (24.6-50.7) | 48.1 (29.9-89.6) | 15 - 65 | Food Component/Plant |
| Dimethyl sulfone | 43 (44) | 3.1 | RP+ (1.40) | 94.00866 | 0.9865 | 4.8 (2.3-7.3) | 2.7 (1.7-4.5) | 5.5 (1.2-25.4) | ≤ 50 | Food Component/Plant |
| Erythritol | 12 (17) | 3.6 3.7 3.8 | HC- (1.77) | 122.0581 | 0.9954 | 37.5 (10.9-60.5) | 79.1 (25.9-154.1) | 89.3 (24-1148) | 5 - 80 | Food Component/Plant |
| Ethanol | - (42) | 1.2 | - | - | - | 6.5 (1.6-13.4) | 4.8 (1.7-8.1) | 37.8 (5.2-572.5) | 5–500 | Food Component/Plant |
| Ethanolamine | 42 (44) | 3.1 | RP+ (0.76)  HC+ (5.36) | 61.05295 | 0.9895 | 48.8 (37-57.7) | 45.7 (35-53) | 30.4 (3.5-51.6) | 5 - 60 | Glycero/Phospholipid Metabolism |
| Ethylmalonate | 11 (11) | 0.9 | RP+ (0.84) | 132.042 | 0.9926 | 2.8 (1.1-6.6) | 3.0 (1.3-5.8) | 3.0 (1.1-9.9) | 0.4 - 6.0 | Leucine, Isoleucine and Valine Metabolism |
| Ferulate | 12 (13) | 6.4 | HC+ (1.79) | 194.0582 | 0.9958 | 0.6 (0.1-1.9) | 0.4 (0.2-0.7) | 0.8 (0.1-5.4) | ≤ 10 | Food Component/Plant |
| Formate | - (45) | 8.5 | - | - | - | 26.1 (12.6-54.4) | 15.6 (8.4-31.9) | 19.7 (4.3-63.5) | 5 - 130 | Glycine, Serine and Threonine Metabolism |
| Fucose | 41 (41) | 1.2 5.2 | HC- (3.69) | 164.0689 | 0.9881 | 12.8 (6.2-18.7) | 15.3 (8.9-23.2) | 13.9 (7.3-34.0) | 6 - 26 | Pentose Metabolism |
| Fumarate | 32 (32) | 6.5 | RP- (2.50) | 116.0107 | 0.9844 | 0.6 (0.4-1.1) | 0.8 (0.5-1.1) | 1.2 (0.3-7.5) | 0.1 - 2 | TCA Cycle |
| Galactose | 11 (11) | 5.3 | HC- (5.34) | 180.0634 | 0.9987 | 2.2 (0.2-4.2) | 1.4 (0.01-5.6) | 2.7 (0.03-16.2) | ≤ 32 | Fructose, Mannose and Galactose Metabolism |
| Gluconate | 10 (10) | 4.1 | HC- (5.15) | 196.0584 | 0.9950 | 24.7 (8.2-45.4) | 20.1 (5.5-53.4) | 23.1 (9.1-84) | 6 - 50 | Food Component/Plant |
| Glucose | 32 (44) | 5.2 | HC- (2.14) | 180.0634 | 0.9942 | 27.6 (3.7-45.7) | 3412 (3.5-20153.2) | 107.8 (2.6-1996.6) | ≤ 60 | Glycolysis, Gluconeogenesis, and Pyruvate Metabolism |
| Glucuronate | 44 (44) | 5.2 | RP- (0.85)  HC- (5.34) | 194.0424 | 0.9904 | 14.4 (9.1-22.4) | 12.3 (2.8-18.8) | 28 (5.1-176.1) | 2 - 25 | Food Component/Plant |
| Glutamate | 15 (15) | 2.3 2.4 | HC- (4.89) | 147.0529 | 0.9958 | 7.5 (6.3-8.8) | 11.2 (4.7-18.4) | 8.3 (2.9-15.8) | 2 - 20 | Glutamate Metabolism |
| Glutamine | 44 (46) | 2.4 | RP+ (0.81)  HC- (6.58) | 146.0688 | 0.9817 | 64.5 (36.6-89.1) | 45.1 (17.7-67.9) | 39.5 (21.3-82.2) | 17 - 90 | Glutamate Metabolism |
| Glutarate | 27 (27) | 2.2 | RP- (0.94) | 132.0424 | 0.9920 | 1.4 (0.05-3.2) | 1.5 (0.4-3.0) | 3.3 (0.04-17.3) | ≤ 4 | Lysine Metabolism |
| Glycerol | 15 (19) | 3.5 | HC+ (3.14) | 92.04748 | 0.9939 | 11.2 (6.0-16.1) | 86.4 (2.9-307.4) | 15.6 (0.6-238.3) | ≤ 40 | Glycero/Phospholipid Metabolism |
| Glycine | 42 (46) | 3.6 | RP+ (0.78)  HC+ (6.29) | 75.03217 | 0.9800 | 197.3 (124.9-442.7) | 96.3 (49.8-194.3) | 84.2 (16.3-242.3) | 30 - 300 | Glycine, Serine and Threonine Metabolism |
| Glycolate | - (46) | 3.9 | - | - | - | 55.8 (36.7-126.3) | 40.2 (23.2-49.2) | 39.3 (18.0-75.3) | 3 - 150 | Chemical |
| Guanidoacetate | 35 (35) | 3.8 | RP+ (0.87) | 117.0537 | 0.9853 | 36.4 (19.0-75.5) | 26.3 (5.1-40.2) | 16.4 (3.4-37.9) | ≤ 130 | Creatine Metabolism |
| Hippurate | 39 (46) | 4.0 7.5 7.6 7.8 | RP+/- (8.21)  HC+/- (3.60) | 179.0581 | 0.9657 | 302.1 (76.5-815.3) | 308.8 (92.6-753.5) | 469.6 (15.5-1569.7) | ≤ 850 | Benzoate Metabolism |
| Histidine | 40 (40) | 3.2 3.3 4.0 7.2 8.2 | RP+/- (0.77) | 155.0693 | 0.9966 | 112.3 (50.3-218.8) | 54.6 (8.9-113.7) | 36.9 (9.8-77.2) | ≤ 120 | Histidine Metabolism |
| Homocitrulline | 9 (9) | 3.1 | HC+/- (7.21) | 189.1114 | 0.9946 | 7.0 (2.9-13.7) | 5.5 (3.6-7.8) | 6.4 (2.1-11.2) | ≤ 15 | Urea cycle Arginine and Proline Metabolism |
| Homogentisate | 17 (17) | 3.5 6.7 6.8 | HC- (1.93) | 168.0423 | 0.9892 | 0.7 (0.3-1.3) | 0.8 (0.4-1.2) | 0.9 (0.2-4.1) | ≤ 3 | Phenylalanine and Tyrosine Metabolism |
| Homovanillate | 25 (25) | 6.9 | RP- (7.24)  HC- (1.77) | 182.0578 | 0.9923 | 2.3 (0.5-5.5) | 2.3 (0.4-5.1) | 3.6 (0.1-11.4) | ≤ 14 | Phenylalanine and Tyrosine Metabolism |
| Hypoxanthine | 41 (43) | 8.2 | HC+ (2.36) | 136.0386 | 0.9862 | 4.6 (1.9-7.4) | 7.6 (1.7-16.0) | 4.6 (0.5-12.6) | ≤ 25 | Purine Metabolism, (Hypo)Xanthine/Inosine containing |
| Indole-3-acetate | 20 (20) | 7.2 | RP+ (9.83) | 175.063 | 0.9933 | 2.2 (0.5-5.0) | 1.5 (0.6-3.3) | 2.7 (0.2-10.5) | 1 - 8 | Tryptophan Metabolism |
| Inosine | 26 (26) | 6.1 8.2 8.3 | HC+ (2.37) | 268.0804 | 0.9902 | 0.7 (0.2-1.4) | 2.6 (0.2-10.7) | 0.7 (0.03-2.6) | 0.3 - 7 | Purine Metabolism, (Hypo)Xanthine/Inosine containing |
| Isobutyrate | - (45) | 1.1 | - | 88.05236 | - | 4.7 (3.0-7.5) | 4.9 (3.0-7.7) | 4.9 (2.1-11.8) | 1 - 10 | Food Component/Plant |
| Isocitrate | 18 (19) | 3.0 | RP- (1.30) | 192.0268 | 0.9969 | 23.1 (17.2-28.9) | 37.0 (19.3-64.3) | 30.6 (6.8-62.1) | 15 - 90 | TCA Cycle |
| Isoleucine | 35 (35) | 1.0 | RP+ (2.89) | 131.0945 | 0.9934 | 2.3 (1.2-3.4) | 1.8 (0.4-2.5) | 1.9 (0.3-5.1) | 0.4 - 6 | Leucine, Isoleucine and Valine Metabolism |
| Isovalerate | 15 (16) | 0.9 | HC- (1.96) | 102.0685 | 0.9933 | 1.4 (0.8-2.3) | 0.9 (0.2-2.2) | 1.1 (0.04-5.1) | ≤ 3 | Leucine, Isoleucine and Valine Metabolism |
| Kynurenate | 30 (30) | 6.9 8.2 | HC- (3.56) | 189.0425 | 0.9934 | 2.3 (1.0-3.4) | 2.7 (1.8-3.5) | 2.0 (0.5-4.8) | ≤ 7.1 | Tryptophan Metabolism |
| Kynurenine | 19 (19) | 6.8 6.9 7.8 | HC+ (5.14) | 208.0847 | 0.9927 | 1.9 (0.6-5.0) | 1.9 (0.9-3.3) | 1.1 (0.5-2.2) | 0.8 - 3 | Tryptophan Metabolism |
| Lactate | 12 (12) | 1.2 4.1 | RP- (1.57) | 90.03216 | 0.9969 | 13.1 (4.7-34.2) | 15.1 (5.1-31.0) | 53.2 (3.0-438.5) | 1.5 - 40 | Glycolysis, Gluconeogenesis, and Pyruvate Metabolism |
| Lactose | 38 (38) | 5.2 | HC+/- (3.89) | 342.1159 | 0.9960 | 6.0 (1.8-12.8) | 14.9 (2.8-54.0) | 6.8 (1.9-34.6) | 1 - 25 | Disaccharides and Oligosaccharides |
| Leucine | 34 (34) | 0.9 1.0 | RP+ (3.11) | 131.0945 | 0.9893 | 5.4 (2.0-7.1) | 4.1 (0.7-6.4) | 4.3 (0.5-12.4) | ≤ 9 | Leucine, Isoleucine and Valine Metabolism |
| Levoglucosan | 44 (44) | 5.4 | - | - | - | 3.3 (1.8-4.4) | 6.5 (3.6-12.7) | 6.5 (2.4-23) | 2.4 – 29.0 | Glycolysis, Gluconeogenesis, and Pyruvate Metabolism |
| Levulinate | 20 (20) | 2.2 2.4 | RP+ (1.11) | 116.0471 | 0.9958 | 2 (0.6-3.6) | 1.4 (0.8-2.3) | 1.8 (0.6-6.7) | 0.3 - 3 | Food Component/Plant |
| Lysine | 30 (30) | 3.0 | RP+ (0.69) | 146.1053 | 0.9948 | 14.8 (2.3-41.2) | 8.0 (1.9-16.8) | 7.6 (1.0-34.7) | ≤ 80 | Lysine Metabolism |
| Maleate | 39 (39) | 6.0 | HC- (0.76) | 116.0117 | 0.9843 | 0.2 (0.2-0.3) | 0.4 (0.2-0.7) | 0.5 (0.1-4.2) | ≤ 0.6 | Food Component/Plant |
| Malonate | 23 (23) | 3.1 | HC- (3.70) | 104.0121 | 0.9980 | 2.7 (1.6-4.1) | 2.4 (1.4-3.8) | 2.5 (1.0-5.3) | ≤ 4 | Fatty Acid Metabolism |
| Maltose | 34 (36) | 5.4 | HC+/- (3.37) | 342.1159 | 0.9943 | 5.8 (2.0-9.5) | 3.8 (0.4-9.8) | 4.6 (0.2-18.7) | ≤ 22 | Disaccharides and Oligosaccharides |
| Mandelate | 5 (5) | 5.0 7.4 | RP- (7.59) | 152.0477 | 0.9974 | 0.1 (0.1-0.2) | 0.2 (0.1-0.3) | 0.5 (0.04-11.2) | ≤ 2 | Benzoate Metabolism |
| Mannitol | 41 (41) | 3.7 3.8 3.9 | RP+/- (0.87)  HC+/- (2.51) | 182.0786 | 0.9869 | 24.0 (15.4-50.2) | 31.5 (12.6-63.2) | 72.0 (13.3-428.2) | 5 - 90 | Fructose, Mannose and Galactose Metabolism |
| Methanol | - (46) | 3.3 | - | - | - | 11.4 (6.8-18.3) | 13.5 (6.3-25.2) | 27.3 (10.2-105.2) | ≤ 120 | Food Component/Plant |
| Methionine | 26 (26) | 2.1 | RP+ (2.38) | 149.0508 | 0.9938 | 1.2 (0.6-1.8) | 1.4 (0.2-2.1) | 1.6 (0.6-2.8) | 0.5 - 8 | Methionine, Cysteine, SAM and Taurine Metabolism |
| Methylamine | - (44) | 2.6 | - | - | - | 4.0 (2.2-6.6) | 6.4 (1.6-14.4) | 4.7 (1.8-12.9) | 1 - 13 | Creatine Metabolism |
| Methylguanidine | 11 (11) | 2.8 | HC+ (4.71) | 73.06414 | 0.9988 | 2.0 (1.5-3.6) | 2.3 (0.9-7.1) | 2.9 (0.5-18.5) | 0.5 - 10 | Creatine Metabolism |
| Methylmalonate | 11 (11) | 1.2 | RP- (1.20) | 118.0267 | 0.9973 | 3.0 (1.8-4.3) | 4.2 (2.1-6.7) | 3.6 (1.2-6.5) | ≤ 4 | Leucine, Isoleucine and Valine Metabolism |
| Methylsuccinate | 38 (38) | 1.1 | RP- (5.25) | 132.0429 | 0.9937 | 2.4 (1.5-3.6) | 1.3 (0.1-3.1) | 1.6 (0.03-7.2) | ≤ 11 | Leucine, Isoleucine and Valine Metabolism |
| myo-Inositol | 38 (38) | 3.3 3.5 4.1 | HC- (3.04) | 180.0635 | 0.9849 | 8.4 (4.7-12.4) | 55.4 (7.5-227.9) | 44.1 (9.2-355.3) | 4 - 90 | Inositol Metabolism |
| N,N-Dimethylglycine | 44 (44) | 2.9 | RP+ (0.85) | 103.0631 | 0.9881 | 4.4 (2.2-7.1) | 5.0 (2.1-8.8) | 6.6 (1.4-21.4) | 0.5 - 12 | Glycine, Serine and Threonine Metabolism |
| N-Acetylaspartate | 38 (38) | 2.0 | RP+/- (1.82) | 175.0478 | 0.9884 | 5.8 (2.8-7.2) | 4.1 (0.4-7.1) | 3.6 (2-5.4) | 1.2 - 8 | Alanine and Aspartate Metabolism |
| N-Isovaleroylglycine | 29 (29) | 0.9 | RP+/- (7.08) | 159.0892 | 0.9896 | 1.3 (0.9-1.9) | 1.4 (0.5-1.8) | 1.0 (0.4-2.4) | ≤ 10 | Leucine, Isoleucine and Valine Metabolism |
| N-Methylhydantoin | 24 (24) | 2.9 | RP+ (2.93) | 114.0428 | 0.9936 | 1.9 (0.2-10.4) | 0.7 (0.4-1.3) | 3.1 (0.3-19.4) | ≤ 20 | Creatine Metabolism |
| O-Acetylcarnitine | 39 (39) | 2.1 3.2 | RP+ (1.79)  HC+ (7.72) | 203.1153 | 0.9940 | 2.5 (0.2-5.4) | 4.5 (0.3-10.5) | 5.3 (0.2-14.9) | ≤ 8 | Fatty Acid Metabolism |
| O-Phosphocholine | 44 (44) | 3.2 | RP+ (8.25) | 184.0733 | 0.9920 | 1.0 (0.7-1.6) | 1.4 (0.8-2.1) | 1.5 (0.4-3.0) | 0.5 - 3.5 | Glycero/Phospholipid Metabolism |
| Pantothenate | 41 (41) | 0.9 0.9 | HC+ (7.07) | 219.1107 | 0.9970 | 1.7 (0.7-3.1) | 3.2 (1.8-4.0) | 2.9 (0.9-6.5) | 0.5 - 5 | Pantothenate and CoA Metabolism |
| Phenol | 25 (25) | 6.9 | RP+ (8.21) | 94.04172 | 0.9941 | 1.7 (0.5-4.1) | 1.5 (0.3-4.9) | 2.3 (0.1-5.8) | ≤ 13 | Phenylalanine and Tyrosine Metabolism |
| Phenylacetylglutamine | 44 (46) | 7.3 7.4 | RP+/- (8.31)  HC+/- (4.78) | 264.1102 | 0.9940 | 124.6 (64.1-206.1) | 88.1 (41.4-123.6) | 103.4 (5.8-343.2) | ≤ 300d | Phenylalanine and Tyrosine Metabolism |
| Phenylalanine | 37 (37) | 7.3: 7.4 | RP+/- (4.89)  HC+/- (5.17) | 165.0788 | 0.9981 | 11.7 (6.3-14.6) | 11.4 (7.3-16.6) | 7.5 (2.6-17.8) | 2.5 - 12 | Phenylalanine and Tyrosine Metabolism |
| Pimelate | 6 (6) | 1.3 1.5 2.2 | RP- (8.37) | 160.0739 | 0.9981 | 0.8 (0.4-1.4) | 1.1 (0.6-1.6) | 1.4 (0.4-7.5) | 0.5 - 4.1 | Fatty Acid Metabolism |
| Proline | 5 (5) | 3.3 3.4 | RP+ (0.99)  HC+ (6.09) | 115.0632 | 0.9999 | 2.3 (1.1-3.7) | 3.3 (1.6-7.3) | 12.3 (0.7-270.7) | ≤ 35 | Urea cycle Arginine and Proline Metabolism |
| Propylene glycol | - (35) | 1.1 3.4 | - | - | - | 5.9 (3.6-14.4) | 5.7 (4.1-9.6) | 15.7 (3-56.8) | 1 - 45 | Glycolysis, Gluconeogenesis, and Pyruvate Metabolism |
| Pseudouridine | 44 (46) | 7.7 | RP+/- (1.88) | 244.0688 | 0.9935 | 26.2 (20.2-30.6) | 33.2 (24.1-43.6) | 34.4 (19.4-67.5) | 6 - 50 | Pyrimidine Metabolism, Uracil containing |
| Pyrocatechol | 31 (31) | 6.9 | HC+ (2.33) | 110.0369 | 0.9965 | 2.4 (1.4-4.1) | 3.5 (1.7-6.3) | 2.4 (0.9-5.4) | 2 - 9 | Benzoate Metabolism |
| Pyroglutamate | 40 (45) | 2.4 | RP+/- (2.48) | 129.0424 | 0.9954 | 27.8 (19.2-35.7) | 26.1 (4.2-45.6) | 34.4 (16.9-63.5) | 10 - 55 | Glutamate Metabolism |
| Pyruvate | - (46) | 2.4 | - | - | - | 7.1 (3.8-21.6) | 6.7 (4.5-9.9) | 6.1 (3.0-16.7) | 0.5 - 35 | Glycolysis, Gluconeogenesis, and Pyruvate Metabolism |
| Quinolinate | 35 (40) | 8.4 | RP+ (2.03) | 167.0215 | 0.9895 | 3.3 (2.7-4.3) | 3.7 (0.8-9) | 4.6 (1.5-11.7) | ≤ 18 | Nicotinate and Nicotinamide Metabolism |
| Sarcosine | 41 (41) | 2.7 | HC+ (2.48) | 89.0478 | 0.9914 | 2.5 (1.9-3.2) | 2.7 (1.1-7.3) | 2.1 (0.7-6.7) | ≤ 6 | Glycine, Serine and Threonine Metabolism |
| Sebacate | 7 (7) | 1.3 1.5 2.2 | RP+/- (8.82) | 202.1201 | 0.9976 | 1.9 (1.2-3.1) | 1.4 (0.4-2.8) | 1.5 (0.6-3.3) | ≤ 3 | Fatty Acid Metabolism |
| Serine | 20 (20) | 3.9 4.0 | RP+ (0.79)  HC+ (6.10) | 105.0424 | 0.9987 | 38.4 (25.8-55.2) | 15.5 (1.4-26.3) | 16.2 (1.2-29.1) | 11 - 55 | Glycine, Serine and Threonine Metabolism |
| Suberate | 9 (9) | 1.3 1.5 2.2 | RP+/- (9.06) | 174.0891 | 0.9991 | 2.4 (1.8-3.6) | 4.8 (1.8-14.6) | 2.7 (1.4-8.2) | ≤ 3 | Fatty Acid Metabolism |
| Succinate | 43 (45) | 2.4 | RP+/- (2.91)  HC- (1.95) | 118.0275 | 0.9997 | 4.8 (1.1-11.2) | 2.4 (1.5-5.5) | 10.2 (0.5-201.6) | 0.3 - 55 | TCA Cycle |
| Succinylacetone | 16 (16) | 2.3 2.4 | RP+ (0.80) | 158.0575 | 0.9919 | 2.7 (1.4-5.7) | 2.6 (1.1-3.8) | 3.6 (1.8-6.0) | ≤ 5 | Phenylalanine and Tyrosine Metabolism |
| Sucrose | 40 (40) | 5.4 | RP+/- (1.18) | 342.1165 | 0.9902 | 5.2 (1.2-10.0) | 3.5 (1.4-9.9) | 6.5 (0.9-27.3) | ≤ 20 | Disaccharides and Oligosaccharides |
| Sumiki's acid | 5 (5) | 7.0 | RP+/- (5.17)  HC- (3.86) | 142.0265 | 0.9988 | 0.7 (0.3-1.9) | 2.7 (0.3-10.8) | 1.0 (0.2-3.5) | 1.7 | Food Component/Plant |
| Tartrate | 19 (25) | 4.3 | RP- (0.97) | 150.0166 | 0.9846 | 0.6 (0.2-2.2) | 8.1 (0.2-44.0) | 58.4 (0.2-448.8) | ≤ 70 | Food Component/Plant |
| Taurine | 38 (42) | 3.3 3.4 | RP+ (0.80)  HC+/- (3.64) | 125.0144 | 0.9891 | 104 (29.1-212.4) | 79.4 (37.2-118.6) | 62.4 (3.2-143.3) | 4 - 260 | Methionine, Cysteine, SAM and Taurine Metabolism |
| Threonate | 15 (16) | 3.7 4.0 | RP- (0.90) | 136.0369 | 0.9985 | 14.5 (7.6-27.8) | 16.3 (4.9-29.1) | 21.1 (5.7-85.7) | 3 - 40 | Ascorbate and Aldarate Metabolism |
| Threonine | 40 (42) | 1.3 3.6 | HC+ (6.05) | 119.0584 | 0.9921 | 27.6 (14.8-55.0) | 12.2 (8.7-13.7) | 12.8 (4.3-34.7) | 4 - 32 | Glycine, Serine and Threonine Metabolism |
| Thymol | 43 (44) | 1.2 6.8 7.2 | RP+ (9.85) | 150.1043 | 0.9959 | 3.6 (2.0-6.0) | 3.7 (2.1-9.0) | 3.8 (2.3-6.0) | ≤ 5 | Food Component/Plant |
| trans-4-Hydroxy-L-proline | 3 (3) | 2.1 4.3 | RP+ (0.83) | 131.058 | 0.9998 | 1.4 (1.0-2.1) | 1.5 (1.0-2.5) | 3.8 (0.5-64.4) | 1.5 - 13 | Urea cycle Arginine and Proline Metabolism |
| trans-Aconitate | - (43) | 6.6 | - | 174.0162 | - | 5.0 (3.7-5.8) | 4.0 (2.6-6.5) | 5.6 (1.7-12.8) | ≤ 30 | TCA Cycle |
| Trigonelline | 36 (46) | 4.4 8.1 8.8 9.1 | RP+ (1.01)  HC+ (6.59) | 137.0474 | 0.9916 | 19.6 (5.2-38.5) | 22.9 (6.9-41.7) | 43.3 (2.8-162.7) | 3 - 110 | Nicotinate and Nicotinamide Metabolism |
| Trimethylamine | - (45) | 2.9 | - | - | - | 2.4 (0.9-9.3) | 5.3 (1.1-22.5) | 1.7 (0.9-3.3) | ≤ 20 | Urinary tract infection markers |
| Trimethylamine N-oxide | 26 (46) | 3.3 | RP+ (0.87)  HC+ (7.33) | 75.0683 | 0.9935 | 52.8 (13.6-276.8) | 47.4 (4.0-103.1) | 59.2 (3.5-297.7) | 4 - 550 | Food Component/Plant |
| Tryptophan | 41 (42) | 7.7 | HC+/- (5.08) | 204.0899 | 0.9940 | 10.9 (6.3-15.5) | 10.4 (5.6-15.8) | 6.5 (2.9-15.1) | 2.5 - 30 | Tryptophan Metabolism |
| Tyrosine | 39 (41) | 6.9 7.2 | RP- (3.39)  HC+/- (5.38) | 181.0738 | 0.9925 | 16.8 (7.7-23.9) | 18 (11.4-26.2) | 11.8 (2.0-25.1) | 3 - 25 | Phenylalanine and Tyrosine Metabolism |
| Uracil | 36 (38) | 5.8 | RP+ (1.74) | 112.0271 | 0.9917 | 5.2 (2.8-8.3) | 3.8 (0.5-11.3) | 3.2 (0.1-6.4) | 2 - 25 | Pyrimidine Metabolism, Uracil containing |
| Valine | 40 (41) | 1.0 | RP+ (1.36) | 117.0787 | 0.9927 | 5.1 (2.3-7.1) | 4.2 (1.2-6.2) | 4.4 (0.2-10.6) | 2.1 - 8 | Leucine, Isoleucine and Valine Metabolism |
| Vanillate | 20 (20) | 6.8 | HC- (1.37) | 168.0424 | 0.9957 | 3.1 (0.9-6.5) | 1.6 (0.6-2.6) | 1.5 (0.4-7.0) | ≤ 19 | Food Component/Plant |
| Xylose | - (44) | 3.2 5.2 | - | 150.0525 | - | 10.4 (4.7-19.8) | 30.4 (1.6-126.8) | 18.8 (3.3-53.0) | 3 - 100 | Pentose Metabolism |
| β-Alanine | 30 (30) | 2.5 3.2 | RP+ (1.20) | 89.04749 | 0.9970 | 6.1 (3.5-11.0) | 6.2 (3.3-9.1) | 6.1 (2.2-15.0) | ≤ 15 | Pyrimidine Metabolism, Uracil containing |
| π-Methylhistidine | 29 (30) | 3.2 3.3 3.8 4.0 7.2\* 8.1\* | RP+ (3.60) | 169.0848 | 0.9944 | 22.8 (16.4-30.6) | 54.1 (1.1-267.1) | 13.9 (3.9-37.9) | 2 - 150 | Histidine Metabolism |
| τ-Methylhistidine | 19 (19) | 3.1 3.2 3.7 4.0 7.1\* 7.7\* | RP- (0.77)  HC+ (8.74) | 169.0847 | 0.9882 | 8.5 (0.7-14.7) | 7.5 (0.7-34.1) | 4.3 (0.6-17.1) | ≤ 60e | Histidine Metabolism |

aN: number of points used for correlation (NMR): number of assigned NMR spectra. bReference ranges taken from HMDB (Wishart et al., 2018). cConcentration in mM. d,eValues taken from (ref) and (ref), respectively.







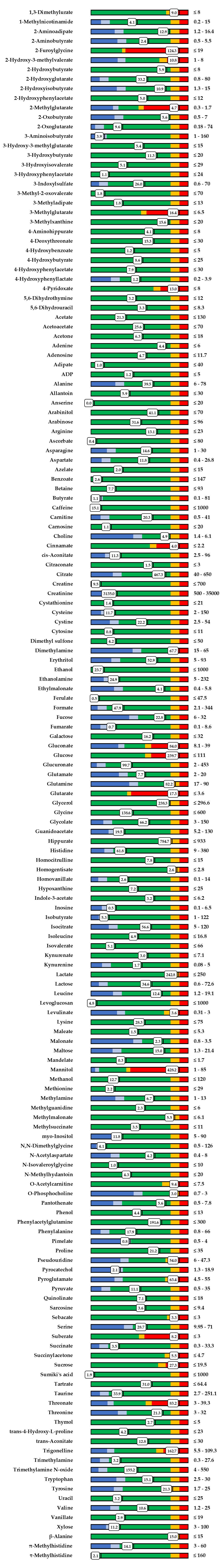


Figure S1. Personalized metabolic profile for subject 2852 showing the 164 metabolites identified and quantified by SYNHMET. Right values represent literature ranges for adults over 18 years old. Values within blue and red areas represent and lower and higher values, respectively.