

Supplementary data

Table S1: Complete table of modulated metabolites in digestive glands of male and female mussels after 1, 3 and 7 days of exposure to VLF sorted by their metabolic pathway (†: metabolites present in several pathways). Difference amplitudes are expressed in percentages. Bold values are for significant modulations ($p < 0.05$), other black values represent a trend of modulation ($p < 0.1$) and grey values are for modulations with a p -value > 0.1 . Slashes represent signals with a difference amplitude $< 20\%$ and are considered as not modulated. ND: Not Detected. Some metabolites from different pathways were not able to differentiate and a number in brackets was attributed to them.

| Metabolism Pathway | Metabolite | Rt (min) | Adduct | Calculated mass | Observed mass | $\Delta m/z$ (ppm) | RSD QC_M | M1 | | M3 | | M7 | | RSD QC_F | F1 | | F3 | | RSD QC | F7 | | Annotation level |
|---|---|----------|----------|-----------------|---------------|--------------------|----------|----------|--------|----------|--------|----------|--------|----------|----------|--------|----------|--------|--------|----------|--------|------------------|
| | | | | | | | | Diff Amp | pvalue | Diff Amp | pvalue | Diff Amp | pvalue | | Diff Amp | pvalue | Diff Amp | pvalue | | Diff Amp | pvalue | |
| Acetylcholine synthesis | Glycerophosphorylcholine | 1,53 | M+H+ | 258,11010 | 258,10972 | 1,5 | 13,42 | / | > 0.1 | / | < 0.05 | / | > 0.1 | 7,82 | ↗+29 | < 0.1 | ↗+25 | < 0.1 | 4,00 | / | > 0.1 | 1 |
| | Propionylcholine | 4,46 | M+ | 160,13375 | 160,13307 | 4,3 | 4,78 | ↗+90 | < 0.05 | ↘-25 | > 0.1 | / | > 0.1 | 8,36 | / | > 0.1 | / | > 0.1 | 5,17 | ↗+20 | > 0.1 | 2 |
| Alanine, aspartate and glutamate Metabolism | Acetic acid† (1) | 1,22 | M+FA-H- | 105,01933 | 105,01920 | 1,2 | 40,84 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 5,52 | / | < 0.05 | / | > 0.1 | 2,71 | / | > 0.1 | 1 |
| | Aspartylphenylalanine† | 11,03 | M+H+ | 281,11320 | 281,11302 | 0,6 | 5,87 | ↗+70 | < 0.05 | ↘-39 | < 0.05 | ↘-28 | < 0.05 | 13,03 | ↘-38 | < 0.05 | ↘-27 | < 0.05 | 11,46 | ↘-31 | > 0.1 | 2 |
| | Citric acid† | 1,43 | M-H- | 191,01973 | 191,01947 | 1,3 | 6,52 | ↘-43 | > 0.1 | ↗+26 | > 0.1 | / | > 0.1 | 4,63 | ↗+104 | > 0.1 | ↗+44 | > 0.1 | 37,04 | / | > 0.1 | 1 |
| | Fumaric acid† | 1,65 | M-H- | 115,00368 | 115,00356 | 1,1 | 62,36 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 3,66 | / | < 0.1 | / | > 0.1 | 89,01 | / | > 0.1 | 1 |
| | Gamma-l-glutamyl-l-leucine | 9,63 | M+H+ | 261,14450 | 261,14405 | 1,7 | 5,65 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 9,50 | ↘-33 | < 0.05 | ↘-23 | < 0.1 | 7,56 | ↗+26 | > 0.1 | 1 |
| | Glucosamine-6-phosphate† | 0,97 | M-H- | 258,03843 | 258,03795 | 1,9 | 4,57 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 2,46 | / | > 0.1 | / | > 0.1 | 3,27 | / | > 0.1 | 1 |
| | Glyoxylic acid† | 1,25 | M-H- | 72,99312 | 72,99286 | 3,5 | 43,46 | / | < 0.05 | / | > 0.1 | / | > 0.1 | 3,90 | / | < 0.1 | / | > 0.1 | 2,55 | / | > 0.1 | 1 |
| | Isovalerylalanine | 9,44 | M+H+ | 174,11247 | 174,11235 | 0,7 | 7,99 | / | > 0.1 | / | > 0.1 | / | < 0.1 | 8,53 | ↘-34 | < 0.05 | ↘-31 | < 0.05 | 6,34 | / | < 0.1 | 2 |
| | L-Alanine† (2) | 1,45 | M+H+ | 90,05495 | 90,05490 | 0,6 | 3,24 | / | > 0.1 | ↘-22 | > 0.1 | / | > 0.1 | 10,48 | / | > 0.1 | / | > 0.1 | 44,32 | / | < 0.05 | 1 |
| | L-aspartic acid† | 1,27 | M-H- | 132,03023 | 132,02999 | 1,8 | 18,20 | / | > 0.1 | / | > 0.1 | / | < 0.05 | 1,19 | / | > 0.1 | / | > 0.1 | 3,38 | / | > 0.1 | 1 |
| | L-citrulline† | 1,28 | M-H- | 174,08842 | 174,08694 | 8,5 | ND | ND | ND | ND | ND | ND | ND | 61,54 | / | > 0.1 | / | > 0.1 | ND | ND | ND | 1 |
| | L-Glutamic acid† | 1,36 | M-H- | 146,04588 | 146,04563 | 1,7 | 19,06 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 1,94 | / | > 0.1 | / | > 0.1 | 2,83 | / | > 0.1 | 1 |
| | Malonic acid† (3) | 1,52 | M-H- | 103,00368 | 103,00355 | 1,3 | 6,72 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 14,66 | ↗+98 | > 0.1 | ↗+35 | > 0.1 | 9,81 | ↘-24 | > 0.1 | 1 |
| | N-acetyl-L-aspartic acid | 1,48 | M-H- | 174,04080 | 174,04055 | 1,4 | 4,65 | ↘-33 | < 0.1 | / | > 0.1 | ↗+25 | > 0.1 | 4,79 | / | > 0.1 | ↗+40 | < 0.1 | 9,45 | ↘-40 | < 0.1 | 1 |
| | N-Acetyl-L-glutamic acid | 1,85 | M-H- | 188,05645 | 188,05609 | 1,9 | 24,42 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 13,39 | ↘-44 | < 0.05 | / | > 0.1 | 9,17 | / | > 0.1 | 1 |
| | Succinic acid† | 1,89 | M-H- | 117,01933 | 117,01914 | 1,6 | 4,98 | ↘-25 | > 0.1 | / | > 0.1 | ↗+85 | < 0.1 | 2,51 | ↘-28 | > 0.1 | / | > 0.1 | 4,26 | ↗+24 | > 0.1 | 1 |
| Amino Sugar Metabolism | Acetic acid† (1) | 1,22 | M+FA-H- | 105,01933 | 105,01920 | 1,2 | 40,84 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 5,52 | / | < 0.05 | / | > 0.1 | 2,71 | / | > 0.1 | 1 |
| | Glucosamine | 2,07 | M+H+ | 180,08665 | 180,08640 | 1,4 | 25,60 | / | > 0.1 | / | > 0.1 | ↘-37 | < 0.05 | 16,32 | / | > 0.1 | / | > 0.1 | 18,44 | ↘-28 | < 0.1 | 1 |
| | Glucosamine-6-phosphate† | 0,97 | M-H- | 258,03843 | 258,03795 | 1,9 | 4,57 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 2,46 | / | > 0.1 | / | > 0.1 | 3,27 | / | > 0.1 | 1 |
| | N-Acetyl-D-glucosamine or N-Acetylmannosamine | 1,21 | M+FA-H- | 266,08814 | 266,08776 | 1,4 | 8,38 | / | > 0.1 | / | > 0.1 | ↗+30 | < 0.05 | 10,46 | / | > 0.1 | / | > 0.1 | 1,59 | ↗+23 | > 0.1 | 1 |
| | 2-Oxoarginine | 1,92 | M-H2O-H- | 154,06165 | 154,06192 | -1,7 | 6,87 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 9,72 | / | > 0.1 | ↘-48 | < 0.05 | 27,51 | / | > 0.1 | 2 |
| Arginine and Proline Metabolism and derivatives | 4-(Glutamylamino) butanoate | 3,13 | M+H+ | 233,11320 | 233,11304 | 0,7 | 20,30 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 6,53 | / | < 0.1 | ↘-31 | < 0.05 | 24,74 | ↘-38 | < 0.05 | 2 |
| | 4-hydroxyproline† (4) | 1,22 | M+H+ | 132,06552 | 132,06536 | 1,2 | 39,47 | / | < 0.05 | / | > 0.1 | / | > 0.1 | 8,48 | / | > 0.1 | ↗+28 | > 0.1 | 9,59 | / | > 0.1 | 1 |
| | 5-aminovaleric acid† | 3,07 | M+H+ | 118,08625 | 118,08603 | 1,9 | 27,78 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 24,76 | / | > 0.1 | / | > 0.1 | 34,31 | / | > 0.1 | 1 |
| | Creatinine | 13,07 | 2M+H+ | 227,12510 | 227,12511 | -0,1 | 6,88 | ↘-32 | < 0.05 | / | > 0.1 | / | > 0.1 | 16,98 | / | > 0.1 | / | > 0.1 | 42,97 | / | > 0.1 | 1 |
| | Fumaric acid† | 1,65 | M-H- | 115,00368 | 115,00356 | 1,1 | 62,36 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 3,66 | / | < 0.1 | / | > 0.1 | 89,01 | / | > 0.1 | 1 |
| | Gamma-glutamyl-L-putrescine | 3,94 | M-H2O+H+ | 200,13880 | 200,13936 | -2,8 | 19,66 | ↗+23 | > 0.1 | ↘-44 | < 0.1 | / | > 0.1 | 21,84 | / | > 0.1 | ↘-37 | > 0.1 | ND | ND | ND | 2 |
| | Glyoxylic acid† | 1,25 | M-H- | 72,99312 | 72,99286 | 3,5 | 43,46 | / | < 0.05 | / | > 0.1 | / | > 0.1 | 3,90 | / | < 0.1 | / | > 0.1 | 2,55 | / | > 0.1 | 1 |
| | L-4-Hydroxyglutamate semialdehyde | 1,56 | M-H2O-H- | 128,03477 | 128,03516 | -3,1 | 12,22 | / | > 0.1 | ↘-22 | > 0.1 | / | > 0.1 | 4,23 | / | > 0.1 | ↗+34 | > 0.1 | 5,77 | ↘-36 | < 0.05 | 2 |
| | L-Arginine† | 2,63 | M+H+ | 175,11895 | 175,11873 | 1,3 | 17,58 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 22,52 | ↗+39 | > 0.1 | / | < 0.1 | 6,56 | ↘-38 | < 0.1 | 1 |
| | L-Aspartate-semialdehyde† | 1,44 | M-H- | 116,03532 | 116,03517 | 1,3 | 5,04 | ↘-25 | > 0.1 | / | > 0.1 | ↗+22 | > 0.1 | 3,23 | / | > 0.1 | ↗+28 | < 0.05 | 4,14 | / | > 0.1 | 2 |
| | L-aspartic acid† | 1,27 | M-H- | 132,03023 | 132,02999 | 1,8 | 18,20 | / | > 0.1 | / | > 0.1 | / | < 0.05 | 1,19 | / | > 0.1 | / | > 0.1 | 3,38 | / | > 0.1 | 1 |
| | L-citrulline† | 1,28 | M-H- | 174,08842 | 174,08694 | 8,5 | ND | ND | ND | ND | ND | ND | ND | 61,54 | / | > 0.1 | / | > 0.1 | ND | ND | ND | 1 |
| | L-Glutamic acid† | 1,36 | M-H- | 146,04588 | 146,04563 | 1,7 | 19,06 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 1,94 | / | > 0.1 | / | > 0.1 | 2,83 | / | > 0.1 | 1 |
| | L-Glutamine† | 1,26 | M+H+ | 147,07642 | 147,07623 | 1,3 | 10,01 | / | > 0.1 | ↘-23 | > 0.1 | / | < 0.05 | 5,26 | / | > 0.1 | ↘-38 | < 0.05 | 9,98 | ↘-33 | < 0.05 | 1 |
| | L-Ornithine† | 2,35 | M+H+ | 133,09715 | 133,09695 | 1,5 | 5,46 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 54,70 | / | < 0.05 | / | < 0.05 | 6,51 | ↘-32 | > 0.1 | 1 |
| | L-Proline | 1,42 | M+H+ | 116,07060 | 116,07057 | 0,3 | 4,09 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 8,77 | / | < 0.05 | / | > 0.1 | 2,50 | / | > 0.1 | 1 |
| | N-acetylproline | 3,01 | M-H- | 156,06662 | 156,06628 | 2,2 | 9,59 | / | > 0.1 | ↘-20 | > 0.1 | ↗+58 | > 0.1 | 7,08 | / | > 0.1 | / | > 0.1 | 6,06 | / | > 0.1 | 1 |
| | N4-Acetylaminobutanal (5) | 2,04 | M+H+ | 130,08625 | 130,08620 | 0,4 | 8,24 | ↗+27 | > 0.1 | / | > 0.1 | ↗+26 | > 0.1 | 11,48 | ↘-37 | > 0.1 | ↘-22 | > 0.1 | 6,41 | ↗+28 | > 0.1 | 2 |

| Metabolism Pathway | Metabolite | Rt (min) | Adduct | Calculated mass | Observed mass | $\Delta m/z$ (ppm) | RSD QC_M | M1 Diff Amp | pvalue | M3 Diff Amp | pvalue | M7 Diff Amp | pvalue | RSD QC_F | F1 Diff Amp | pvalue | F3 Diff Amp | pvalue | RSD QC | F7 Diff Amp | pvalue | Annotation level |
|---|---------------------------------------|----------|-----------------------|-----------------|---------------|--------------------|----------|----------------|--------|----------------|--------|----------------|--------|----------|----------------|--------|----------------|--------|--------|----------------|--------|------------------|
| Arginine and Proline Metabolism and derivatives | Proline betaine | 1,49 | M+H+ | 144,10190 | 144,10174 | 1,1 | 3,72 | / | > 0.1 | / | < 0.05 | / | > 0.1 | 4,32 | / | > 0.1 | / | > 0.1 | 4,67 | ↘-26 | > 0.1 | 1 |
| | Putrescine [†] | 5,43 | M+H+ | 89,10732 | 89,10718 | 1,6 | 24,40 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 30,59 | / | > 0.1 | / | > 0.1 | 27,43 | / | > 0.1 | 1 |
| | Sarcosine [†] (2) | 1,45 | M+H+ | 90,05495 | 90,05490 | 0,6 | 3,24 | / | > 0.1 | ↘-22 | > 0.1 | / | > 0.1 | 10,48 | / | > 0.1 | / | > 0.1 | 44,32 | / | < 0.05 | 1 |
| | Succinic acid [†] | 1,89 | M-H- | 117,01933 | 117,01914 | 1,6 | 4,98 | ↘-25 | > 0.1 | / | > 0.1 | ↗+85 | < 0.1 | 2,51 | ↘-28 | > 0.1 | / | > 0.1 | 4,26 | ↗+24 | > 0.1 | 1 |
| | Symmetric dimethylarginine | 3,45 | M+H+ | 203,15025 | 203,15016 | 0,4 | 13,70 | / | > 0.1 | ↘-21 | < 0.1 | ↘-27 | > 0.1 | 6,80 | / | < 0.1 | ↘-46 | < 0.05 | 4,45 | ↘-47 | < 0.05 | 2 |
| beta-Alanine Metabolism | Hydroxypropionic acid [†] | 1,55 | M-H- | 89,02442 | 89,02440 | 0,2 | 7,75 | / | > 0.1 | / | > 0.1 | ↗+68 | < 0.05 | 3,98 | / | > 0.1 | / | < 0.05 | 6,90 | ↘-26 | > 0.1 | 1 |
| | L-aspartic acid [†] | 1,27 | M-H- | 132,03023 | 132,02999 | 1,8 | 18,20 | / | > 0.1 | / | > 0.1 | / | < 0.05 | 1,19 | / | > 0.1 | / | > 0.1 | 3,38 | / | > 0.1 | 1 |
| | L-Histidine [†] | 2,23 | M+H+ | 156,07675 | 156,07670 | 0,3 | 4,58 | / | > 0.1 | / | > 0.1 | / | < 0.1 | 40,78 | / | > 0.1 | / | > 0.1 | 5,61 | / | > 0.1 | 1 |
| | N-Acetyl-beta-alanine (4) | 1,77 | M-H- | 130,05097 | 130,05079 | 1,4 | 5,91 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 1,91 | / | < 0.05 | / | < 0.1 | 10,49 | / | > 0.1 | 1 |
| | Pantothenic acid | 2,64 | M-H- | 218,10340 | 218,10307 | 1,5 | 8,70 | / | > 0.1 | ↘-20 | > 0.1 | / | > 0.1 | 3,37 | / | > 0.1 | / | > 0.1 | 4,07 | ↗+24 | > 0.1 | 1 |
| Betaine Metabolism | Uracil [†] | 1,52 | M-H- | 111,02000 | 111,01988 | 1,1 | 6,25 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 16,21 | ↘-40 | < 0.05 | / | > 0.1 | 5,90 | / | > 0.1 | 1 |
| | Betaine [†] | 1,33 | M+H+ | 118,08625 | 118,08605 | 1,7 | 4,03 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 9,17 | / | > 0.1 | / | < 0.05 | 3,63 | / | > 0.1 | 1 |
| | Choline [†] | 2,51 | M+ | 104,10754 | 104,10685 | 6,6 | 4,35 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 11,16 | / | < 0.1 | / | > 0.1 | 2,55 | / | > 0.1 | 1 |
| | L-Lysine [†] | 2,50 | M+H+ | 147,11280 | 147,11261 | 1,3 | 5,22 | / | > 0.1 | ↘-33 | > 0.1 | / | > 0.1 | 12,04 | ↗+39 | > 0.1 | ↘-57 | < 0.05 | 4,00 | ↘-38 | > 0.1 | 1 |
| | Pimelic acid | 8,54 | M-H- | 159,06628 | 159,06601 | 1,7 | 1,98 | ↗+61 | > 0.1 | ↘-25 | > 0.1 | / | > 0.1 | 3,23 | ↗+47 | < 0.1 | ↗+21 | > 0.1 | 2,51 | / | > 0.1 | 1 |
| Citrate cycle | Citric acid [†] | 1,43 | M-H- | 191,01973 | 191,01947 | 1,3 | 6,52 | ↘-43 | > 0.1 | ↗+26 | > 0.1 | / | > 0.1 | 4,63 | ↗+104 | > 0.1 | ↗+44 | > 0.1 | 37,04 | / | > 0.1 | 1 |
| | Fumaric acid [†] | 1,65 | M-H- | 115,00368 | 115,00356 | 1,1 | 62,36 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 3,66 | / | < 0.1 | / | > 0.1 | 89,01 | / | > 0.1 | 1 |
| | L-malic acid [†] | 1,33 | M-H- | 133,01425 | 133,01402 | 1,7 | 3,82 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 3,09 | / | < 0.05 | / | > 0.1 | 4,74 | / | < 0.05 | 1 |
| Collagen Synthesis | 4-hydroxyproline [†] (4) | 1,22 | M+H+ | 132,06552 | 132,06536 | 1,2 | 39,47 | / | < 0.05 | / | > 0.1 | / | > 0.1 | 8,48 | / | > 0.1 | ↗+28 | > 0.1 | 9,59 | / | > 0.1 | 1 |
| | Glycylproline | 3,25 | M+H+ | 173,09207 | 173,09164 | 2,5 | 21,86 | / | > 0.1 | / | < 0.05 | / | > 0.1 | 31,78 | / | > 0.1 | / | > 0.1 | 8,34 | / | > 0.1 | 1 |
| Cysteine and methionine Metabolism | 2-Hydroxyphenethylamine | 7,81 | M-H ₂ O+H+ | 120,08023 | 120,08059 | -3,0 | 2,68 | ↗+30 | < 0.05 | ↘-30 | < 0.05 | / | < 0.1 | 3,27 | ↘-22 | < 0.05 | ↘-46 | < 0.05 | 4,81 | ↘-27 | < 0.1 | 2 |
| | Betaine [†] | 1,33 | M+H+ | 118,08625 | 118,08605 | 1,7 | 4,03 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 9,17 | / | > 0.1 | / | < 0.05 | 3,63 | / | > 0.1 | 1 |
| | Choline [†] | 2,51 | M+ | 104,10754 | 104,10685 | 6,6 | 4,35 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 11,16 | / | < 0.1 | / | > 0.1 | 2,55 | / | > 0.1 | 1 |
| | L-Alanine [†] (2) | 1,45 | M+H+ | 90,05495 | 90,05490 | 0,6 | 3,24 | / | > 0.1 | ↘-22 | > 0.1 | / | > 0.1 | 10,48 | / | > 0.1 | / | > 0.1 | 44,32 | / | < 0.05 | 1 |
| | L-alpha-Aminobutyric acid | 1,71 | M+H+ | 104,07060 | 104,07049 | 1,1 | 41,46 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 69,37 | / | > 0.1 | / | > 0.1 | 54,30 | ↘-65 | > 0.1 | 1 |
| Glutathione Metabolism | L-Aspartate-semialdehyde [†] | 1,44 | M-H- | 116,03532 | 116,03517 | 1,3 | 5,04 | ↘-25 | > 0.1 | / | > 0.1 | ↗+22 | > 0.1 | 3,23 | / | > 0.1 | ↗+28 | < 0.05 | 4,14 | / | > 0.1 | 2 |
| | L-aspartic acid [†] | 1,27 | M-H- | 132,03023 | 132,02999 | 1,8 | 18,20 | / | > 0.1 | / | > 0.1 | / | < 0.05 | 1,19 | / | > 0.1 | / | > 0.1 | 3,38 | / | > 0.1 | 1 |
| | L-Methionine [†] | 2,57 | M+H+ | 150,05833 | 150,05769 | 4,2 | 37,34 | / | < 0.05 | / | > 0.1 | / | > 0.1 | 9,79 | ↘-42 | < 0.05 | ↘-63 | < 0.05 | 12,00 | ↘-40 | > 0.1 | 1 |
| | L-serine [†] | 1,31 | M-H- | 104,03532 | 104,03522 | 1,0 | 6,18 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 5,64 | / | > 0.1 | ↘-22 | > 0.1 | 8,36 | / | > 0.1 | 1 |
| | Putrescine [†] | 5,43 | M+H+ | 89,10732 | 89,10718 | 1,6 | 24,40 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 30,59 | / | > 0.1 | / | > 0.1 | 27,43 | / | > 0.1 | 1 |
| | 5-l-glutamyl-l-alanine | 1,69 | M+H+ | 219,09755 | 219,09747 | 0,4 | 16,97 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 17,90 | ↘-33 | < 0.05 | / | > 0.1 | ND | ND | ND | 1 |
| | Cysteine glutathione disulfide | 1,30 | M-H- | 425,08063 | 425,07952 | 2,6 | ND | ND | ND | ND | ND | ND | ND | 27,02 | ↗+94 | < 0.05 | ↗+71 | < 0.05 | ND | ND | ND | 1 |
| | Glycine [†] | 1,34 | M+H+ | 76,03930 | 76,03914 | 2,2 | 16,67 | ↘-29 | > 0.1 | / | > 0.1 | ↘-21 | < 0.1 | 49,04 | / | > 0.1 | ↗+85 | < 0.05 | 43,21 | ↘-36 | > 0.1 | 1 |
| | L-Glutamic acid [†] | 1,36 | M-H- | 146,04588 | 146,04563 | 1,7 | 19,06 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 1,94 | / | > 0.1 | / | > 0.1 | 2,83 | / | > 0.1 | 1 |
| | L-Ornithine [†] | 2,35 | M+H+ | 133,09715 | 133,09695 | 1,5 | 5,46 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 54,70 | / | < 0.05 | / | < 0.05 | 6,51 | ↘-32 | > 0.1 | 1 |
| | Oxidized glutathione | 2,17 | M-H- | 611,14469 | 611,14429 | 0,6 | 18,02 | / | > 0.1 | ↘-31 | > 0.1 | / | > 0.1 | 3,81 | ↗+59 | > 0.1 | / | > 0.1 | 11,82 | / | > 0.1 | 1 |
| | Putrescine [†] | 5,43 | M+H+ | 89,10732 | 89,10718 | 1,6 | 24,40 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 30,59 | / | > 0.1 | / | > 0.1 | 27,43 | / | > 0.1 | 1 |
| | Pyroglutamic acid | 1,56 | M-H- | 128,03532 | 128,03517 | 1,1 | 12,22 | / | > 0.1 | ↘-22 | > 0.1 | / | > 0.1 | 4,23 | / | > 0.1 | ↗+34 | > 0.1 | 5,90 | ↘-33 | < 0.05 | 1 |
| | 5-aminolevulinic acid (4) | 1,22 | M+H+ | 132,06552 | 132,06536 | 1,2 | 39,47 | / | < 0.05 | / | > 0.1 | / | > 0.1 | 8,48 | / | > 0.1 | ↗+28 | > 0.1 | 9,59 | / | > 0.1 | 1 |
| | Aminoacetone | 1,33 | M+FA-H- | 118,05096 | 118,05084 | 1,1 | 3,18 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 4,40 | / | > 0.1 | ↘-25 | < 0.05 | 2,94 | / | > 0.1 | 2 |
| Glycine, serine and threonine Metabolism | Betaine [†] | 1,33 | M+H+ | 118,08625 | 118,08605 | 1,7 | 4,03 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 9,17 | / | > 0.1 | / | < 0.05 | 3,63 | / | > 0.1 | 1 |
| | Choline [†] | 2,51 | M+ | 104,10754 | 104,10685 | 6,6 | 4,35 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 11,16 | / | < 0.1 | / | > 0.1 | 2,55 | / | > 0.1 | 1 |
| | DL-2-hydroxybutyric acid | 2,09 | M-H- | 103,04007 | 103,03995 | 1,1 | 19,17 | ↗+23 | > 0.1 | / | > 0.1 | / | > 0.1 | 4,99 | ↗+43 | < 0.05 | / | > 0.1 | 19,70 | / | > 0.1 | 1 |
| | Glyceric acid [†] (1) | 1,24 | M-H- | 105,01933 | 105,01917 | 1,5 | 2,66 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 4,38 | / | < 0.05 | / | > 0.1 | 0,85 | / | > 0.1 | 1 |
| | Glycine [†] | 1,34 | M+H+ | 76,03930 | 76,03914 | 2,2 | 16,67 | ↘-29 | > 0.1 | / | > 0.1 | ↘-21 | < 0.1 | 49,04 | / | > 0.1 | ↗+85 | < 0.05 | 43,21 | ↘-36 | > 0.1 | 1 |
| | Glyoxylic acid [†] | 1,25 | M-H- | 72,99312 | 72,99286 | 3,5 | 43,46 | / | < 0.05 | / | > 0.1 | / | > 0.1 | 3,90 | / | < 0.1 | / | > 0.1 | 2,55 | / | > 0.1 | 1 |
| | Hydroxypyruvic acid (3) | 1,52 | M-H- | 103,00368 | 103,00355 | 1,3 | 6,28 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 18,51 | ↗+68 | > 0.1 | ↗+191 | < 0.05 | 10,22 | ↘-22 | > 0.1 | 1 |
| | L-allothreonine or L-threonine | 1,33 | M-H- | 118,05097 | 118,05084 | 1,1 | 3,18 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 4,40 | / | > 0.1 | ↘-25 | < 0.05 | 101,41 | ↗+47 | > 0.1 | 1 |
| | L-Arginine [†] | 2,63 | M+H+ | 175,11895 | 175,11873 | 1,3 | 17,58 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 22,52 | ↗+39 | > 0.1 | / | < 0.1 | 6,56 | ↘-38 | < 0.1 | 1 |
| | L-Aspartate-semialdehyde [†] | 1,44 | M-H- | 116,03532 | 116,03517 | 1,3 | 5,04 | ↘-25 | > 0.1 | / | > 0.1 | ↗+22 | > 0.1 | 3,23 | / | > 0.1 | ↗+28 | < 0.05 | 4,14 | / | > 0.1 | 2 |
| | L-aspartic acid [†] | 1,27 | M-H- | 132,03023 | 132,02999 | 1,8 | 18,20 | / | > 0.1 | / | > 0.1 | / | < 0.05 | 1,19 | / | > 0.1 | / | > 0.1 | 3,38 | / | > 0.1 | 1 |

| Metabolism Pathway | Metabolite | Rt (min) | Adduct | Calculated mass | Observed mass | $\Delta m/z$ (ppm) | RSD QC_M | M1 Diff Amp | pvalue | M3 Diff Amp | pvalue | M7 Diff Amp | pvalue | RSD QC_F | F1 Diff Amp | pvalue | F3 Diff Amp | pvalue | RSD QC | F7 Diff Amp | pvalue | Annotation level |
|--|-----------------------------------|----------|-----------------------|-----------------|---------------|--------------------|----------|----------------|--------|----------------|--------|----------------|--------|----------|----------------|--------|----------------|--------|--------|----------------|--------|------------------|
| Glycine, serine and threonine Metabolism | L-Homoserine | 1,38 | M+H+ | 120,06552 | 120,06537 | 1,2 | 16,80 | ↘-26 | < 0.1 | ↘-20 | > 0.1 | / | > 0.1 | 27,68 | / | > 0.1 | / | > 0.1 | 6,97 | / | > 0.1 | 1 |
| | L-Methionine† | 2,57 | M+H+ | 150,05833 | 150,05769 | 4,2 | 37,34 | / | < 0.05 | / | > 0.1 | / | > 0.1 | 9,79 | ↘-42 | < 0.05 | ↘-63 | < 0.05 | 12,00 | ↘-40 | > 0.1 | 1 |
| | L-serine† | 1,31 | M-H- | 104,03532 | 104,03522 | 1,0 | 6,18 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 5,64 | / | > 0.1 | ↘-22 | > 0.1 | 8,36 | / | > 0.1 | 1 |
| | L-Tryptophan† | 11,58 | M+H+ | 205,09715 | 205,09700 | 0,7 | 6,00 | / | > 0.1 | ↘-29 | < 0.05 | / | > 0.1 | 7,93 | / | < 0.05 | ↘-46 | < 0.05 | 26,28 | / | > 0.1 | 1 |
| | N-Acetyl-L-threonine | 1,50 | M-H- | 160,06153 | 160,06128 | 1,6 | 10,64 | ↘-24 | > 0.1 | / | > 0.1 | ↗+32 | < 0.1 | 13,62 | ↘-26 | < 0.05 | ↗+27 | < 0.05 | 21,75 | / | > 0.1 | 1 |
| Histidine Metabolism | Sarcosine† (2) | 1,45 | M+H+ | 90,05495 | 90,05490 | 0,6 | 3,24 | / | > 0.1 | ↘-22 | > 0.1 | / | > 0.1 | 10,48 | / | > 0.1 | / | > 0.1 | 44,32 | / | < 0.05 | 1 |
| | 3'-AMP† | 1,21 | M+H+ | 348,07036 | 348,06994 | 1,2 | 22,88 | / | > 0.1 | ↘-37 | > 0.1 | / | > 0.1 | 17,48 | ↗+472 | > 0.1 | / | > 0.1 | 16,86 | / | > 0.1 | 1 |
| | or Adenosine monophosphate† | | | | | | | | | | | | | | | | | | | | | |
| | Carnosine | 3,56 | M+H+ | 227,11387 | 227,11384 | 0,1 | ND | ND | ND | ND | ND | ND | ND | 35,44 | / | > 0.1 | ↘-51 | < 0.05 | ND | ND | ND | 1 |
| | Histamine | 5,84 | M+H+ | 112,08692 | 112,08671 | 1,9 | 60,63 | ↘-75 | < 0.05 | ↗+188 | < 0.05 | ↗+108 | > 0.1 | 13,54 | ↘-36 | < 0.1 | ↘-26 | > 0.1 | 39,81 | ↗+115 | > 0.1 | 1 |
| Lysine biosynthesis or degradation | L-aspartic acid† | 1,27 | M-H- | 132,03023 | 132,02999 | 1,8 | 18,20 | / | > 0.1 | / | > 0.1 | / | < 0.05 | 1,19 | / | > 0.1 | / | > 0.1 | 3,38 | / | > 0.1 | 1 |
| | L-Glutamic acid† | 1,36 | M-H- | 146,04588 | 146,04563 | 1,7 | 19,06 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 1,94 | / | > 0.1 | / | > 0.1 | 2,83 | / | > 0.1 | 1 |
| | L-Histidine† | 2,23 | M+H+ | 156,07675 | 156,07670 | 0,3 | 4,58 | / | > 0.1 | / | > 0.1 | / | < 0.1 | 40,78 | / | > 0.1 | / | > 0.1 | 5,61 | / | > 0.1 | 1 |
| | Methylimidazoleacetic acid | 3,10 | M+H+ | 141,06585 | 141,06572 | 0,9 | 24,65 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 2,79 | / | > 0.1 | ↘-21 | < 0.1 | ND | ND | ND | 1 |
| | 5-aminovaleric acid† | 3,07 | M+H+ | 118,08625 | 118,08603 | 1,9 | 27,78 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 24,76 | / | > 0.1 | / | > 0.1 | 34,31 | / | > 0.1 | 1 |
| | Aminoadipic acid | 1,59 | M+H+ | 162,07608 | 162,07598 | 0,7 | 37,41 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 107,20 | ↗+189 | < 0.1 | / | > 0.1 | 7,24 | / | > 0.1 | 1 |
| | Glutaric acid | 2,48 | M-H- | 131,03498 | 131,03474 | 1,9 | 5,23 | ↗+34 | > 0.1 | / | > 0.1 | / | > 0.1 | 3,12 | ↗+41 | < 0.05 | ↗+27 | > 0.1 | 4,06 | / | > 0.1 | 1 |
| | Glycine† | 1,34 | M+H+ | 76,03930 | 76,03914 | 2,2 | 16,67 | ↘-29 | > 0.1 | / | > 0.1 | ↘-21 | < 0.1 | 49,04 | / | > 0.1 | ↗+85 | < 0.05 | 43,21 | ↘-36 | > 0.1 | 1 |
| | L-Aspartate-semialdehyde† | 1,44 | M-H- | 116,03532 | 116,03517 | 1,3 | 5,04 | ↘-25 | > 0.1 | / | > 0.1 | ↗+22 | > 0.1 | 3,23 | / | > 0.1 | ↗+28 | < 0.05 | 4,14 | / | > 0.1 | 2 |
| | L-aspartic acid† | 1,27 | M-H- | 132,03023 | 132,02999 | 1,8 | 18,20 | / | > 0.1 | / | > 0.1 | / | < 0.05 | 1,19 | / | > 0.1 | / | > 0.1 | 3,38 | / | > 0.1 | 1 |
| | L-Lysine† | 2,50 | M+H+ | 147,11280 | 147,11261 | 1,3 | 5,22 | / | > 0.1 | ↘-33 | > 0.1 | / | > 0.1 | 12,04 | ↗+39 | > 0.1 | ↘-57 | < 0.05 | 4,00 | ↘-38 | > 0.1 | 1 |
| | N-Succinyl-2-amino-6-ketopimelate | 2,24 | M+H+ | 290,08704 | 290,08578 | 4,4 | 34,31 | / | > 0.1 | ↘-63 | > 0.1 | / | > 0.1 | 19,31 | ↘-37 | < 0.1 | ↘-50 | < 0.05 | 17,40 | / | > 0.1 | 2 |
| | N6-Acetyl-L-lysine | 1,89 | M+H+ | 189,12337 | 189,12302 | 1,8 | 32,68 | / | > 0.1 | / | > 0.1 | ↗+108 | > 0.1 | 29,58 | / | > 0.1 | / | < 0.05 | 7,80 | / | > 0.1 | 1 |
| | Oxadipic acid† | 1,63 | M-H- | 159,02990 | 159,02996 | -0,4 | 51,01 | / | < 0.05 | / | > 0.1 | ND | ND | ND | ND | ND | ND | ND | ND | ND | ND | 1 |
| | Pipecolic acid (5) | 2,04 | M+H+ | 130,08625 | 130,08620 | 0,4 | 8,24 | ↗+27 | > 0.1 | / | > 0.1 | ↗+26 | > 0.1 | 11,48 | ↘-37 | > 0.1 | ↘-22 | > 0.1 | 11,55 | ↗+38 | < 0.1 | 1 |
| | L-aspartic acid† | 1,27 | M-H- | 132,03023 | 132,02999 | 1,8 | 18,20 | / | > 0.1 | / | > 0.1 | / | < 0.05 | 1,19 | / | > 0.1 | / | > 0.1 | 3,38 | / | > 0.1 | 1 |
| Nicotinate and Nicotinamide Metabolism | Niacinamide | 2,46 | M+H+ | 123,05529 | 123,05511 | 1,5 | 10,36 | ↗+71 | > 0.1 | ↘-49 | < 0.1 | / | > 0.1 | 33,47 | ↗+72 | < 0.1 | / | > 0.1 | 4,38 | / | > 0.1 | 1 |
| | Nicotinamide N-oxide | 3,46 | M+H+ | 139,05020 | 139,05005 | 1,1 | 8,02 | ↗+32 | > 0.1 | / | > 0.1 | ↗+256 | < 0.05 | 8,94 | / | > 0.1 | / | > 0.1 | 8,68 | ↘-41 | < 0.05 | 2 |
| | Nicotinamide riboside | 14,29 | M+ | 255,09810 | 255,09892 | -3,2 | 12,38 | / | < 0.05 | / | < 0.05 | / | > 0.1 | 13,07 | / | > 0.1 | / | > 0.1 | 2,52 | ↘-35 | > 0.1 | 1 |
| | Nicotinic acid | 1,85 | M+H+ | 124,03930 | 124,03925 | 0,4 | 9,51 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 3,71 | / | > 0.1 | / | > 0.1 | 22,46 | ↘-46 | > 0.1 | 1 |
| | Nicotinuric acid | 2,61 | M-H- | 179,04622 | 179,04597 | 1,4 | ND | ND | ND | ND | ND | ND | ND | 20,47 | / | > 0.1 | / | > 0.1 | 24,90 | / | > 0.1 | 1 |
| Pentose phosphate pathway | Propionic acid | 2,02 | M-H- | 73,02950 | 73,02933 | 2,4 | 45,91 | ↗+69 | > 0.1 | / | > 0.1 | ↗+36 | > 0.1 | 3,67 | ↘-34 | > 0.1 | ↗+22 | > 0.1 | 3,84 | ↗+27 | > 0.1 | 1 |
| | Trigonelline | 1,45 | M+H+ | 138,05495 | 138,05480 | 1,1 | 7,20 | / | > 0.1 | ↘-45 | < 0.05 | / | > 0.1 | 12,60 | / | > 0.1 | / | > 0.1 | 23,87 | / | > 0.1 | 1 |
| | Deoxyribose | 1,21 | M+FA-H- | 179,05611 | 179,05589 | 1,2 | 4,25 | / | > 0.1 | ↗+25 | > 0.1 | ↗+43 | < 0.05 | 4,00 | ↘-25 | < 0.1 | / | > 0.1 | 7,30 | / | > 0.1 | 1 |
| | Gluconic acid | 1,15 | M-H- | 195,05103 | 195,05090 | 0,7 | 4,87 | / | < 0.1 | / | > 0.1 | ↗+31 | < 0.1 | 6,37 | / | > 0.1 | / | > 0.1 | 34,87 | ↘-65 | > 0.1 | 1 |
| | Glyceric acid† (1) | 1,24 | M-H- | 105,01933 | 105,01917 | 1,5 | 2,66 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 4,38 | / | < 0.05 | / | > 0.1 | 0,85 | / | > 0.1 | 1 |
| Phenylalanine Metabolism | Ribose 1-phosphate† | 2,93 | M-H ₂ O+H+ | 213,01532 | 213,01594 | -2,9 | 23,48 | ↗+37 | > 0.1 | / | > 0.1 | / | > 0.1 | 16,43 | ↗+86 | < 0.05 | ↗+26 | > 0.1 | 15,67 | / | > 0.1 | 2 |
| | 2-Phenylacetamide | 7,97 | M+H+ | 136,07569 | 136,07553 | 1,2 | 10,47 | ↗+21 | > 0.1 | ↘-22 | < 0.1 | / | > 0.1 | 60,23 | / | > 0.1 | / | < 0.05 | 52,78 | / | > 0.1 | 1 |
| | 3-(2-Hydroxyphenyl)propanoic acid | 11,30 | M-H- | 165,05572 | 165,05520 | 3,1 | 58,73 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 35,75 | / | > 0.1 | / | > 0.1 | 3,59 | / | > 0.1 | 1 |
| | 3-(3-Hydroxyphenyl)propanoic acid | 10,79 | M-H- | 165,05572 | 165,05529 | 2,6 | 30,39 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 19,96 | ↗+42 | < 0.05 | ↗+21 | > 0.1 | 25,98 | ↗+41 | < 0.1 | 1 |
| | 3-Hydroxyphenylacetic acid† | 9,69 | M-H- | 151,04007 | 151,03971 | 2,4 | 5,47 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 15,54 | / | > 0.1 | / | > 0.1 | 5,06 | / | > 0.1 | 1 |
| | Aspartylphenylalanine† | 11,03 | M+H+ | 281,11320 | 281,11302 | 0,6 | 5,87 | ↗+70 | < 0.05 | ↘-39 | < 0.05 | ↘-28 | < 0.05 | 13,03 | ↘-38 | < 0.05 | ↘-27 | < 0.05 | 11,46 | ↘-31 | > 0.1 | 2 |
| | Fumaric acid† | 1,65 | M-H- | 115,00368 | 115,00356 | 1,1 | 62,36 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 3,66 | / | < 0.1 | / | > 0.1 | 89,01 | / | > 0.1 | 1 |
| | L-3-phenyllactic acid | 10,48 | M-H- | 165,05572 | 165,05522 | 3,0 | 3,24 | / | > 0.1 | ↗+130 | < 0.05 | / | > 0.1 | 4,32 | ↘-55 | < 0.05 | / | > 0.1 | 4,38 | ↗+32 | > 0.1 | 1 |
| | L-Phenylalanine | 7,81 | M+H+ | 166,08625 | 166,08613 | 0,8 | 3,39 | ↗+31 | < 0.05 | ↘-31 | < 0.05 | / | < 0.05 | 2,89 | ↘-24 | < 0.05 | ↘-45 | < 0.05 | 14,10 | ↘-51 | > 0.1 | 1 |
| | L-Tyrosine† | 3,54 | M+H+ | 182,08117 | 182,08109 | 0,4 | 3,48 | / | > 0.1 | ↘-21 | < 0.1 | / | > 0.1 | 7,07 | / | < 0.05 | ↘-37 | < 0.05 | 7,35 | / | > 0.1 | 1 |
| | N-Acetyl-L-phenylalanine | 10,66 | M-H- | 206,08227 | 206,08182 | 2,2 | 3,46 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 15,02 | ↘-33 | < 0.05 | ↘-26 | < 0.05 | 4,79 | / | > 0.1 | 1 |
| | Phenylacetylglutamine | 8,55 | M-H- | 263,10373 | 263,10342 | 1,2 | 21,98 | ↘-43 | > 0.1 | ↘-38 | > 0.1 | / | > 0.1 | 4,32 | / | > 0.1 | / | > 0.1 | 4,76 | / | > 0.1 | 1 |
| | Phenylacetylglycine | 9,53 | M-H- | 192,06662 | 192,06639 | 1,2 | 4,68 | ↘-37 | < 0.05 | / | > 0.1 | / | > 0.1 | 4,99 | ↘-29 | > 0.1 | / | > 0.1 | 2,33 | / | > 0.1 | 1 |
| | Phenylethylamine | 13,93 | M+H+ | 122,09643 | 122,09624 | 1,5 | 17,46 | / | > 0.1 | / | < 0.05 | / | > 0.1 | 6,51 | / | > 0.1 | ↘-41 | < 0.05 | 8,09 | / | > 0.1 | 1 |

| Metabolism Pathway | Metabolite | Rt (min) | Adduct | Calculated mass | Observed mass | Δm/z (ppm) | RSD QC_M | M1 | | M3 | | M7 | | RSD QC_F | F1 | | F3 | | RSD QC | F7 | | Annotation level |
|-----------------------|-----------------------------|-------------|----------|--------------------|------------------|---------------|-------------|-------------|--------|-------------|--------|-------------|--------|-------------|-------------|--------|-------------|--------|-----------|-------------|--------|---------------------|
| | | | | | | | | Diff Amp | pvalue | Diff Amp | pvalue | Diff Amp | pvalue | | Diff Amp | pvalue | Diff Amp | pvalue | | Diff Amp | pvalue | |
| Purine Metabolism | 2-Hydroxyadenine | 2,34 | M+Na+ | 174,03863 | 174,03854 | 0,5 | 8,40 | ↗+22 | > 0.1 | ↗+71 | < 0.1 | / | > 0.1 | 15,43 | / | < 0.1 | / | > 0.1 | 10,67 | ↗+24 | > 0.1 | 2 |
| | 2'-Deoxyguanosine | 2,27 | M+H+ | 268,10403 | 268,10376 | 1,0 | 6,15 | ↗+45 | < 0.05 | ↘-36 | > 0.1 | / | > 0.1 | 16,70 | ↘-27 | > 0.1 | ↘-47 | < 0.05 | ND | ND | ND | 1 |
| | 3-Methylxanthine | 0,97 | M+FA-H- | 211,04728 | 211,04756 | -1,3 | 2,58 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 12,40 | / | > 0.1 | ↗+24 | > 0.1 | 3,28 | / | > 0.1 | 2 |
| | 3'-AMP† | 1,21 | M+H+ | 348,07036 | 348,06994 | 1,2 | 22,88 | / | > 0.1 | ↘-37 | > 0.1 | / | > 0.1 | 17,48 | ↗+472 | > 0.1 | / | > 0.1 | 16,86 | / | > 0.1 | 1 |
| | or Adenosine monophosphate† | | | | | | | | | | | | | | | | | | | | | |
| | 8-Hydroxy-deoxyguanosine | 1,92 | M-H- | 282,08439 | 282,08414 | 0,9 | 3,83 | / | < 0.05 | / | > 0.1 | / | < 0.1 | 10,03 | / | > 0.1 | / | < 0.1 | 7,49 | / | > 0.1 | 1 |
| | or Guanosine | | | | | | | | | | | | | | | | | | | | | |
| | Adenine | 2,89 | M-H- | 134,04722 | 134,04703 | 1,4 | 1,97 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 10,28 | / | > 0.1 | / | > 0.1 | 5,67 | / | > 0.1 | 1 |
| | Adenosine | 3,14 | M+H+ | 268,10403 | 268,10386 | 0,6 | 7,97 | ↘-52 | > 0.1 | ↘-28 | > 0.1 | / | > 0.1 | 10,89 | ↗+117 | > 0.1 | ↘-25 | > 0.1 | 5,77 | ↘-36 | > 0.1 | 1 |
| | ADP | 1,06 | M-H- | 426,02214 | 426,02168 | 1,1 | 23,97 | / | > 0.1 | / | > 0.1 | / | > 0.1 | ND | ND | ND | ND | ND | ND | ND | ND | 1 |
| | Cyclic amp | 1,51 | M-H- | 328,04524 | 328,04500 | 0,7 | 7,21 | ↗+85 | < 0.05 | / | > 0.1 | / | > 0.1 | 15,32 | ↘-40 | < 0.1 | ↘-27 | > 0.1 | 2,55 | ↘-30 | > 0.1 | 1 |
| | Deoxyinosine | 1,87 | M-H- | 251,07858 | 251,07830 | 1,1 | 14,42 | ↗+52 | < 0.1 | ↘-45 | > 0.1 | ↘-27 | > 0.1 | 9,40 | ↘-32 | < 0.1 | ↘-53 | < 0.05 | 9,75 | ↘-29 | > 0.1 | 1 |
| | dGDP | 1,20 | M-H- | 426,02214 | 426,01991 | 5,2 | 24,18 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 28,46 | ↗+676 | > 0.1 | / | > 0.1 | ND | ND | ND | 1 |
| | FAPy-adenine | 2,29 | M+H+ | 154,07234 | 154,07281 | -3,1 | 33,99 | / | > 0.1 | / | > 0.1 | / | > 0.1 | ND | ND | ND | ND | ND | 19,03 | ↘-25 | > 0.1 | 1 |
| | Glycine† | 1,34 | M+H+ | 76,03930 | 76,03914 | 2,2 | 16,67 | ↘-29 | > 0.1 | / | > 0.1 | ↘-21 | < 0.1 | 49,04 | / | > 0.1 | ↗+85 | < 0.05 | 43,21 | ↘-36 | > 0.1 | 1 |
| | Glyoxylic acid† | 1,25 | M-H- | 72,99312 | 72,99286 | 3,5 | 43,46 | / | < 0.05 | / | > 0.1 | / | > 0.1 | 3,90 | / | < 0.1 | / | > 0.1 | 2,55 | / | > 0.1 | 1 |
| | Guanine | 2,33 | M+H+ | 152,05669 | 152,05655 | 0,9 | 5,22 | ↗+25 | < 0.1 | / | > 0.1 | / | > 0.1 | 16,63 | / | > 0.1 | / | > 0.1 | 12,53 | / | > 0.1 | 1 |
| | Guanosine | 1,92 | M+H+ | 284,09894 | 284,09883 | 0,4 | 13,44 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 7,86 | / | > 0.1 | / | < 0.05 | 2,18 | ↗+34 | > 0.1 | 1 |
| | Guanosine monophosphate | 1,10 | M-H- | 362,05072 | 362,05005 | 1,9 | ND | ND | ND | ND | ND | ND | ND | 23,25 | / | < 0.1 | ↘-34 | > 0.1 | ND | ND | ND | 1 |
| | Hypoxanthine | 1,74 | M+H+ | 137,04579 | 137,04570 | 0,6 | 11,71 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 11,14 | / | > 0.1 | / | > 0.1 | 9,88 | / | > 0.1 | 1 |
| | Inosine | 1,77 | M-H- | 267,07349 | 267,07331 | 0,7 | 4,60 | / | > 0.1 | / | > 0.1 | / | < 0.05 | 5,92 | / | > 0.1 | / | > 0.1 | 1,75 | / | > 0.1 | 1 |
| | Inosine-5'-monophosphate | 1,18 | M-H- | 347,03982 | 347,03989 | -0,2 | 27,40 | / | > 0.1 | / | > 0.1 | ↗+42 | > 0.1 | 6,09 | / | > 0.1 | ↘-46 | < 0.05 | ND | ND | ND | 1 |
| | Ribose 1-phosphate† | 2,93 | M-H2O+H+ | 213,01532 | 213,01594 | -2,9 | 23,48 | ↗+37 | > 0.1 | / | > 0.1 | / | > 0.1 | 16,43 | ↗+86 | < 0.05 | ↗+26 | > 0.1 | 15,67 | / | > 0.1 | 2 |
| | Succinyladenosine | 3,60 | M+H+ | 384,11499 | 384,11485 | 0,4 | 23,18 | / | > 0.1 | ↗+56 | > 0.1 | / | > 0.1 | 20,49 | ↘-39 | < 0.05 | / | > 0.1 | 4,11 | ↘-33 | > 0.1 | 2 |
| | Xanthine | 1,64 | M-H- | 151,02615 | 151,02592 | 1,5 | 10,66 | / | > 0.1 | ↗+79 | < 0.05 | / | > 0.1 | 7,59 | ↘-31 | < 0.1 | / | > 0.1 | 3,98 | / | > 0.1 | 1 |
| Pyrimidine Metabolism | 3-methyluridine | 2,27 | M+FA-H- | 303,08339 | 303,08270 | 2,3 | ND | ND | ND | ND | ND | ND | ND | 35,89 | / | > 0.1 | / | > 0.1 | ND | ND | ND | 1 |
| | 5-Hydroxymethyluracil | 1,51 | M-H- | 141,03057 | 141,03029 | 2,0 | 45,93 | / | > 0.1 | / | > 0.1 | / | < 0.1 | 31,43 | / | > 0.1 | ↗+29 | > 0.1 | 12,22 | / | > 0.1 | 1 |
| | 5-Methylcytosine | 2,31 | M-H- | 124,05164 | 124,05143 | 1,7 | 23,02 | ↘-48 | < 0.05 | ↗+59 | < 0.1 | ↗+62 | > 0.1 | 16,40 | ↗+21 | > 0.1 | / | > 0.1 | 2,32 | / | > 0.1 | 2 |
| | Cytidine | 2,66 | M+H+ | 244,09280 | 244,09251 | 1,2 | 5,92 | / | > 0.1 | / | > 0.1 | / | < 0.05 | 12,66 | / | < 0.1 | / | > 0.1 | 10,18 | / | > 0.1 | 1 |
| | Cytosine | 2,41 | M+H+ | 112,05054 | 112,05035 | 1,7 | 7,47 | / | > 0.1 | ↗+32 | > 0.1 | / | > 0.1 | 18,06 | ↘-21 | < 0.1 | / | > 0.1 | 8,08 | / | > 0.1 | 1 |
| | Deoxycytidine | 3,10 | M+H+ | 228,09788 | 228,09765 | 1,0 | 7,90 | / | > 0.1 | / | > 0.1 | ↘-24 | > 0.1 | 15,20 | ↘-36 | < 0.05 | ↘-42 | < 0.05 | 11,61 | / | > 0.1 | 1 |
| | Deoxyuridine | 1,85 | M+FA-H- | 273,07282 | 273,07239 | 1,6 | 18,56 | / | > 0.1 | / | > 0.1 | ↘-42 | > 0.1 | ND | ND | ND | ND | ND | 3,89 | ↘-23 | > 0.1 | 1 |
| | Dihydrothymine | 1,97 | M+H+ | 129,06585 | 129,06568 | 1,3 | 15,34 | ↘-41 | > 0.1 | ↘-24 | > 0.1 | ↗+58 | < 0.05 | 3,23 | / | > 0.1 | ↘-27 | < 0.05 | 14,75 | / | > 0.1 | 1 |
| | DL-Lactic Acid† | 6,38 | M-H- | 89,02442 | 89,02438 | 0,4 | 8,10 | / | > 0.1 | / | > 0.1 | ↗+60 | < 0.05 | 10,87 | / | > 0.1 | ↗+23 | < 0.05 | 5,37 | ↘-27 | > 0.1 | 1 |
| | Hydroxypropionic acid† | 1,55 | M-H- | 89,02442 | 89,02440 | 0,2 | 7,75 | / | > 0.1 | / | > 0.1 | ↗+68 | < 0.05 | 3,98 | / | > 0.1 | / | < 0.05 | 6,90 | ↘-26 | > 0.1 | 1 |
| | L-Glutamine† | 1,26 | M+H+ | 147,07642 | 147,07623 | 1,3 | 10,01 | / | > 0.1 | ↘-23 | > 0.1 | / | < 0.05 | 5,26 | / | > 0.1 | ↘-38 | < 0.05 | 9,98 | ↘-33 | < 0.05 | 1 |
| | Malonic acid† (3) | 1,52 | M-H- | 103,00368 | 103,00355 | 1,3 | 6,72 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 14,66 | ↗+98 | > 0.1 | ↗+35 | > 0.1 | 9,81 | ↘-24 | > 0.1 | 1 |
| | Methylmalonic acid† | 2,10 | M-H- | 117,01933 | 117,01917 | 1,4 | 29,45 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 6,07 | / | > 0.1 | / | < 0.05 | 25,94 | / | > 0.1 | 1 |
| | Pseudouridine | 1,31 | M-H- | 243,06226 | 243,06153 | 3,0 | ND | ND | ND | ND | ND | ND | ND | 16,76 | / | > 0.1 | ↗+40 | < 0.05 | 19,25 | ↘-37 | < 0.05 | 1 |
| | Thymidine | 2,39 | M+FA-H- | 287,08847 | 287,08832 | 0,5 | 14,77 | ↗+50 | < 0.05 | ↘-42 | < 0.05 | / | > 0.1 | 7,66 | ↘-42 | < 0.05 | ↘-48 | < 0.05 | 3,55 | / | > 0.1 | 1 |
| | Thymine | 1,92 | M-H- | 125,03565 | 125,03553 | 1,0 | 24,21 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 15,04 | / | > 0.1 | / | > 0.1 | 9,69 | / | > 0.1 | 1 |
| | Uracil† | 1,52 | M-H- | 111,02000 | 111,01988 | 1,1 | 6,25 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 16,21 | ↘-40 | < 0.05 | / | > 0.1 | 5,90 | / | > 0.1 | 1 |
| | Ureidoisobutyric acid | 1,65 | M-H- | 145,06187 | 145,06047 | 9,6 | ND | ND | ND | ND | ND | ND | ND | 40,16 | ↘-32 | > 0.1 | / | < 0.05 | 38,93 | / | > 0.1 | 1 |
| | Uridine | 1,74 | M+FA-H- | 289,06774 | 289,06764 | 0,3 | 12,15 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 4,97 | / | > 0.1 | / | > 0.1 | 3,65 | / | > 0.1 | 1 |
| Pyruvate Metabolism | Acetic acid† (1) | 1,22 | M+FA-H- | 105,01933 | 105,01920 | 1,2 | 40,84 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 5,52 | / | < 0.05 | / | > 0.1 | 2,71 | / | > 0.1 | 1 |
| | DL-Lactic Acid† | 6,38 | M-H- | 89,02442 | 89,02438 | 0,4 | 8,10 | / | > 0.1 | / | > 0.1 | ↗+60 | < 0.05 | 10,87 | / | > 0.1 | ↗+23 | < 0.05 | 5,37 | ↘-27 | > 0.1 | 1 |
| | Fumaric acid† | 1,65 | M-H- | 115,00368 | 115,00356 | 1,1 | 62,36 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 3,66 | / | < 0.1 | / | > 0.1 | 89,01 | / | > 0.1 | 1 |
| | L-malic acid† | 1,33 | M-H- | 133,01425 | 133,01402 | 1,7 | 3,82 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 3,09 | / | < 0.05 | / | > 0.1 | 4,74 | / | < 0.05 | 1 |

| Metabolism Pathway | Metabolite | Rt (min) | Adduct | Calculated mass | Observed mass | Δm/z (ppm) | RSD QC_M | M1 | | M3 | | M7 | | RSD QC_F | F1 | | F3 | | RSD QC | F7 | | Annotation level |
|---|---|-------------|----------|--------------------|------------------|---------------|-------------|-------------|--------|-------------|--------|-------------|--------|-------------|-------------|--------|-------------|--------|-----------|-------------|--------|---------------------|
| | | | | | | | | Diff Amp | pvalue | Diff Amp | pvalue | Diff Amp | pvalue | | Diff Amp | pvalue | Diff Amp | pvalue | | Diff Amp | pvalue | |
| Steroid hormone biosynthesis | 4-Methylpentanal | 10,07 | M+ACN+H+ | 142,12264 | 142,12243 | 1,5 | 64,73 | / | > 0.1 | ↗+124 | < 0.05 | / | > 0.1 | 9,93 | / | > 0.1 | / | > 0.1 | 9,32 | / | > 0.1 | 1 |
| | Cortolone | 11,95 | M+FA-H- | 411,23883 | 411,23826 | 1,4 | 24,20 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 10,37 | / | < 0.1 | / | > 0.1 | 24,76 | / | < 0.1 | 1 |
| | Mevalonic acid | 1,90 | M-H- | 147,06628 | 147,06607 | 1,4 | 38,13 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 6,37 | ↗+25 | > 0.1 | / | > 0.1 | 8,10 | / | > 0.1 | 1 |
| Tryptophan Metabolism | Tetrahydrocortisol | 12,24 | M+FA-H- | 411,23883 | 411,23790 | 2,2 | 36,67 | ↗+49 | < 0.05 | / | > 0.1 | / | > 0.1 | 21,29 | / | > 0.1 | / | > 0.1 | 12,15 | / | > 0.1 | 1 |
| | 3-hydroxyanthranilic acid | 5,53 | M+H+ | 154,04987 | 154,04939 | 3,1 | 49,32 | / | > 0.1 | / | > 0.1 | / | > 0.1 | ND | ND | ND | ND | ND | ND | ND | ND | 1 |
| | 5-Hydroxykynurenine | 8,49 | M+H+ | 225,08698 | 225,08675 | 1,0 | 8,00 | ↘-25 | < 0.05 | / | > 0.1 | / | < 0.05 | 8,75 | / | < 0.1 | / | < 0.1 | 5,93 | / | > 0.1 | 2 |
| | Anthranilate | 5,77 | M+H+ | 138,05495 | 138,05461 | 2,5 | 20,46 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 4,71 | / | > 0.1 | / | > 0.1 | 8,54 | ↘-20 | > 0.1 | 1 |
| | DL-kynurenine | 8,73 | M+H+ | 209,09207 | 209,09197 | 0,5 | 7,68 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 9,18 | / | < 0.05 | ↘-24 | < 0.05 | 6,53 | / | > 0.1 | 1 |
| | Formylanthranilic acid | 11,46 | M-H- | 164,03532 | 164,03499 | 2,0 | 8,63 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 3,67 | ↗+23 | < 0.05 | / | > 0.1 | 4,12 | / | > 0.1 | 1 |
| | Indolelactic acid | 1,40 | M+H+ | 206,08117 | 206,08296 | -8,7 | 42,84 | / | > 0.1 | / | > 0.1 | / | > 0.1 | ND | ND | ND | ND | ND | ND | ND | ND | 1 |
| | Kynurenic acid | 10,27 | M+H+ | 190,04987 | 190,04922 | 3,4 | 36,51 | ↗+882 | < 0.05 | ↗+126 | > 0.1 | / | < 0.05 | 30,65 | ↘-50 | > 0.1 | / | > 0.1 | ND | ND | ND | 1 |
| | L-Tryptophan† | 11,58 | M+H+ | 205,09715 | 205,09700 | 0,7 | 6,00 | / | > 0.1 | ↘-29 | < 0.05 | / | > 0.1 | 7,93 | / | < 0.05 | ↘-46 | < 0.05 | 26,28 | / | > 0.1 | 1 |
| | N'-Formylkynurenine | 7,23 | M-H- | 235,07243 | 235,07182 | 2,6 | ND | ND | ND | ND | ND | ND | ND | 9,02 | ↘-36 | > 0.1 | ↘-52 | < 0.05 | 42,11 | / | > 0.1 | 1 |
| Tyrosine Metabolism | Oxadipic acid† | 1,63 | M-H- | 159,02990 | 159,02996 | -0,4 | 51,01 | / | < 0.05 | / | > 0.1 | ND | ND | ND | ND | ND | ND | ND | ND | ND | ND | 1 |
| | Serotonin | 10,46 | M+H+ | 177,10224 | 177,10175 | 2,8 | 27,30 | ↘-36 | > 0.1 | / | > 0.1 | ↗+334 | < 0.05 | 13,68 | ↘-63 | < 0.05 | ↘-26 | > 0.1 | 7,78 | ↗+95 | < 0.1 | 1 |
| | 1,2-Dehydrosalsolinol | 9,84 | M+H+ | 178,08625 | 178,08608 | 1,0 | 12,16 | ↗+31 | > 0.1 | ↗+55 | > 0.1 | / | > 0.1 | 18,86 | ↗+84 | > 0.1 | ↘-31 | < 0.1 | 16,79 | ↗+87 | > 0.1 | 2 |
| | 3-Hydroxyphenylacetic acid† | 9,69 | M-H- | 151,04007 | 151,03971 | 2,4 | 5,47 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 15,54 | / | > 0.1 | / | > 0.1 | 5,06 | / | > 0.1 | 1 |
| | 3,4-Dihydroxybenzeneacetic acid | 5,67 | M-H- | 167,03498 | 167,03480 | 1,1 | ND | ND | ND | ND | ND | ND | ND | 23,22 | / | > 0.1 | / | > 0.1 | 103,85 | / | > 0.1 | 1 |
| | 3,4-dihydroxymandelaldehyde | 4,49 | M-H- | 167,03498 | 167,03462 | 2,2 | 45,02 | / | > 0.1 | ↗+71 | < 0.1 | / | > 0.1 | 32,64 | / | > 0.1 | / | < 0.1 | 32,50 | / | > 0.1 | 1 |
| | 4-Hydroxyphenylacetaldehyde | 11,61 | M-H- | 135,04515 | 135,04517 | -0,1 | 30,26 | / | < 0.1 | / | > 0.1 | / | > 0.1 | 21,58 | / | > 0.1 | / | > 0.1 | 12,66 | / | > 0.1 | 1 |
| | 4-Hydroxyphenylacetylglutamic acid | 8,24 | M+H+ | 282,09721 | 282,09697 | 0,9 | 6,51 | ↘-36 | > 0.1 | ↘-20 | > 0.1 | ↗+57 | < 0.1 | 25,61 | ↘-49 | < 0.1 | / | > 0.1 | 4,88 | / | > 0.1 | 2 |
| | 4-methoxytyramine | 10,70 | M+H+ | 168,10190 | 168,10149 | 2,5 | ND | ND | ND | ND | ND | ND | ND | 56,11 | / | > 0.1 | / | > 0.1 | 10,06 | ↗+56 | > 0.1 | 1 |
| | 6-Hydroxydopamine | 3,40 | M+H+ | 170,08117 | 170,08075 | 2,5 | 16,57 | ↘-42 | > 0.1 | ↗+50 | > 0.1 | / | > 0.1 | 43,64 | / | > 0.1 | / | > 0.1 | ND | ND | ND | 1 |
| | Dopamine 4-sulfate | 2,09 | M-H- | 232,02852 | 232,02826 | 1,1 | 64,71 | / | > 0.1 | ↗+95 | > 0.1 | / | < 0.05 | 23,96 | / | > 0.1 | ↘-27 | > 0.1 | 40,91 | / | > 0.1 | 1 |
| | Epinephrine | 3,67 | M+H+ | 184,09682 | 184,09673 | 0,5 | 21,22 | ↗+88 | < 0.05 | / | > 0.1 | ↗+43 | > 0.1 | 35,09 | / | > 0.1 | / | > 0.1 | ND | ND | ND | 1 |
| | Fumaric acid† | 1,65 | M-H- | 115,00368 | 115,00356 | 1,1 | 62,36 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 3,66 | / | < 0.1 | / | > 0.1 | 89,01 | / | > 0.1 | 1 |
| | Gamma-glutamyltyrosine | 6,98 | M-H- | 309,10921 | 309,10871 | 1,6 | 7,04 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 6,64 | ↘-31 | < 0.05 | ↘-20 | < 0.05 | 4,29 | ↘-23 | < 0.05 | 1 |
| | Homovanillic acid | 9,86 | M-H- | 181,05063 | 181,04992 | 3,9 | ND | ND | ND | ND | ND | ND | ND | 19,06 | ↗+22 | > 0.1 | / | > 0.1 | 69,36 | / | > 0.1 | 1 |
| | Hydroxyphenylacetylglycine | 5,02 | M-H- | 208,06153 | 208,06126 | 1,3 | 36,39 | ↘-50 | < 0.1 | ↗+73 | < 0.1 | / | > 0.1 | ND | ND | ND | ND | ND | ND | ND | ND | 1 |
| | L-Tyrosine† | 3,54 | M+H+ | 182,08117 | 182,08109 | 0,4 | 3,48 | / | > 0.1 | ↘-21 | < 0.1 | / | > 0.1 | 7,07 | / | < 0.05 | ↘-37 | < 0.05 | 7,35 | / | > 0.1 | 1 |
| | N-Acetyl-L-tyrosine | 7,29 | M-H- | 222,07718 | 222,07692 | 1,2 | 5,10 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 18,46 | ↘-33 | < 0.05 | ↘-27 | < 0.05 | 4,00 | / | > 0.1 | 1 |
| | Norepinephrine | 2,73 | M-H- | 168,06662 | 168,06636 | 1,6 | 24,58 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 17,27 | / | < 0.05 | / | > 0.1 | 8,69 | / | > 0.1 | 1 |
| | Normetanephine | 4,84 | M-H2O+H+ | 166,08571 | 166,08594 | -1,4 | 68,15 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 11,66 | / | > 0.1 | / | > 0.1 | 27,92 | / | > 0.1 | 1 |
| | O-tyrosine | 7,40 | M+H+ | 182,08117 | 182,08061 | 3,1 | 19,76 | ↗+37 | < 0.1 | ↘-24 | > 0.1 | / | > 0.1 | 27,38 | / | > 0.1 | / | > 0.1 | 4,31 | / | > 0.1 | 1 |
| Valine, leucine and isoleucine Metabolism and derivatives | P-octopamine | 3,54 | M-H2O+H+ | 136,07514 | 136,07558 | -3,3 | 5,28 | / | > 0.1 | ↘-21 | < 0.1 | / | > 0.1 | 5,31 | / | < 0.05 | ↘-37 | < 0.05 | 6,78 | ↘-33 | < 0.05 | 1 |
| | Phenol | 7,81 | M-H2O+H+ | 77,03803 | 77,03796 | 0,9 | 34,25 | / | < 0.1 | ↘-46 | < 0.05 | / | > 0.1 | 17,62 | / | < 0.1 | ↘-49 | < 0.05 | 1,47 | ↘-31 | > 0.1 | 2 |
| | Tyramine | 8,11 | M+H+ | 138,09134 | 138,09120 | 1,0 | 15,36 | / | > 0.1 | ↘-21 | < 0.1 | ↗+30 | > 0.1 | 21,72 | / | > 0.1 | / | > 0.1 | 25,93 | / | > 0.1 | 1 |
| | 3-Methyl-2-oxovaleric acid | 7,05 | M-H- | 129,05572 | 129,05557 | 1,1 | 42,03 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 26,41 | ND | ND | / | > 0.1 | 15,67 | / | > 0.1 | 1 |
| | DL-isoleucine or L-Alloisoleucine or L-Isoleucine or L-Leucine | 3,92 | M+H+ | 132,10190 | 132,10175 | 1,2 | 68,62 | / | > 0.1 | / | > 0.1 | / | < 0.05 | 18,82 | ↘-26 | < 0.05 | / | > 0.1 | 3,19 | ↘-22 | > 0.1 | 1 |
| | Erythronilic acid | 2,71 | M-H2O-H- | 99,04460 | 99,04504 | -4,4 | 9,16 | ↗+60 | > 0.1 | ↘-28 | > 0.1 | / | > 0.1 | 5,61 | ↗+48 | < 0.1 | / | > 0.1 | 4,90 | / | > 0.1 | 2 |
| | Hydroxyisocaproic acid | 8,74 | M-H- | 131,07137 | 131,07114 | 1,8 | 2,29 | / | > 0.1 | ↗+125 | < 0.05 | / | > 0.1 | 2,36 | ↘-40 | < 0.05 | ↘-22 | > 0.1 | 78,98 | / | > 0.1 | 1 |
| | L-Valine | 2,69 | M+H+ | 118,08625 | 118,08606 | 1,6 | 6,42 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 67,03 | / | < 0.05 | / | < 0.05 | 50,61 | ↗+89 | > 0.1 | 1 |
| | Methylmalonic acid† | 2,10 | M-H- | 117,01933 | 117,01917 | 1,4 | 29,45 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 6,07 | / | > 0.1 | / | < 0.05 | 25,94 | / | > 0.1 | 1 |
| | N-acetylisoleucine | 9,44 | M-H- | 172,09792 | 172,09771 | 1,2 | 4,41 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 2,30 | ↘-34 | < 0.05 | ↘-30 | < 0.05 | 4,96 | / | > 0.1 | 1 |
| | N-Acetylvaline | 4,80 | M-H- | 158,08227 | 158,08198 | 1,8 | 11,99 | ↘-29 | < 0.05 | / | > 0.1 | / | > 0.1 | 19,66 | ↘-35 | < 0.05 | / | > 0.1 | 11,07 | / | > 0.1 | 1 |
| | Pyridoxal† | 3,29 | M+H+ | 168,06552 | 168,06556 | -0,2 | ND | ND | ND | ND | ND | ND | ND | 40,24 | / | > 0.1 | / | > 0.1 | 30,99 | / | > 0.1 | 1 |

| Metabolism Pathway | Metabolite | Rt (min) | Adduct | Calculated mass | Observed mass | Δm/z (ppm) | RSD QC_M | M1 | | M3 | | M7 | | RSD QC_F | F1 | | F3 | | RSD QC | F7 | | Annotation level |
|-----------------------|--------------------------|-------------|----------|--------------------|------------------|---------------|-------------|-------------|--------|-------------|--------|-------------|--------|-------------|-------------|--------|-------------|--------|-----------|-------------|--------|---------------------|
| | | | | | | | | Diff Amp | pvalue | Diff Amp | pvalue | Diff Amp | pvalue | | Diff Amp | pvalue | Diff Amp | pvalue | | Diff Amp | pvalue | |
| Vitamin B6 metabolism | 4-Pyridoxic acid | 1,44 | M-H- | 182,04588 | 182,04566 | 1,2 | 7,38 | / | > 0.1 | ↘-46 | < 0.1 | / | > 0.1 | 2,04 | / | > 0.1 | / | > 0.1 | 3,63 | / | > 0.1 | 1 |
| | 5-Pyridoxolactone | 3,25 | M-H- | 164,03532 | 164,03500 | 1,9 | 8,12 | / | > 0.1 | ↗+24 | > 0.1 | / | > 0.1 | 5,94 | ↗+26 | < 0.1 | / | > 0.1 | 1,47 | / | > 0.1 | 2 |
| | L-Glutamine† | 1,26 | M+H+ | 147,07642 | 147,07623 | 1,3 | 10,01 | / | > 0.1 | ↘-23 | > 0.1 | / | < 0.05 | 5,26 | / | > 0.1 | ↘-38 | < 0.05 | 9,98 | ↘-33 | < 0.05 | 1 |
| | Pyridoxal† | 3,29 | M+H+ | 168,06552 | 168,06556 | -0,2 | ND | ND | ND | ND | ND | ND | ND | 40,24 | / | > 0.1 | / | > 0.1 | 30,99 | / | > 0.1 | 1 |
| | Pyridoxine | 10,81 | M-H2O-H- | 150,05550 | 150,05581 | -2,1 | 31,43 | / | > 0.1 | / | > 0.1 | / | < 0.1 | 16,81 | ↗+66 | < 0.05 | / | > 0.1 | 10,92 | ↗+24 | > 0.1 | 2 |
| Other metabolites | 2-Aminoisobutyric acid | 1,55 | M-H- | 102,05605 | 102,05577 | 2,7 | 4,86 | / | > 0.1 | / | < 0.1 | / | > 0.1 | 65,88 | / | > 0.1 | / | < 0.05 | ND | ND | ND | 1 |
| | 2-Ketohexanoic acid | 3,56 | M+H+ | 131,07027 | 131,07023 | 0,3 | 39,56 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 12,72 | ↗+49 | < 0.1 | / | > 0.1 | 9,85 | / | > 0.1 | 2 |
| | 2-Methylglutaric acid | 4,46 | M-H- | 145,05063 | 145,05034 | 2,0 | 5,21 | ↗+66 | > 0.1 | ↘-31 | > 0.1 | / | > 0.1 | 16,01 | / | < 0.1 | / | > 0.1 | 19,42 | / | > 0.1 | 1 |
| | 4-Aminobutyraldehyde | 1,37 | M+FA-H- | 132,06661 | 132,06641 | 1,6 | 19,38 | ↘-21 | > 0.1 | / | > 0.1 | / | > 0.1 | 28,55 | / | > 0.1 | / | < 0.05 | 32,51 | / | > 0.1 | 2 |
| | 8-Methylnonenoate | 12,93 | M+FA-H- | 215,12888 | 215,12845 | 2,0 | 64,21 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 45,42 | / | > 0.1 | / | > 0.1 | 8,18 | / | > 0.1 | 1 |
| | Acetolactate | 1,21 | M-H- | 131,03498 | 131,03466 | 2,5 | 57,49 | / | < 0.05 | / | < 0.1 | / | > 0.1 | 34,69 | / | > 0.1 | / | < 0.05 | 28,73 | / | > 0.1 | 1 |
| | Ascorbic acid | 1,31 | M-H- | 175,02481 | 175,02594 | -6,4 | ND | ND | ND | ND | ND | ND | ND | 12,10 | / | > 0.1 | / | > 0.1 | 4,80 | / | > 0.1 | 1 |
| | Ethyladipic acid | 10,35 | M-H- | 173,08193 | 173,08160 | 1,9 | 5,94 | ↗+81 | < 0.1 | ↘-28 | > 0.1 | / | > 0.1 | 3,18 | ↗+40 | < 0.1 | ↗+26 | > 0.1 | 2,68 | / | > 0.1 | 2 |
| | Gamma glutamyl ornithine | 3,19 | M-H2O+H+ | 244,12863 | 244,12905 | -1,7 | ND | ND | ND | ND | ND | ND | ND | 34,59 | / | > 0.1 | / | < 0.05 | 31,46 | ↘-53 | < 0.05 | 2 |
| | Indoleacrylic acid | 11,58 | M+H+ | 188,07060 | 188,07043 | 1,0 | 21,35 | / | > 0.1 | / | < 0.05 | / | > 0.1 | 6,94 | / | < 0.05 | ↘-47 | < 0.05 | 8,12 | / | > 0.1 | 2 |
| | L-Acetylcarnitine | 5,78 | M+H+ | 204,12303 | 204,12283 | 1,0 | 4,28 | / | > 0.1 | / | > 0.1 | ↗+63 | < 0.1 | 7,76 | ↘-33 | > 0.1 | / | > 0.1 | 37,57 | / | > 0.1 | 1 |
| | L-Carnitine | 2,68 | M+H+ | 162,11247 | 162,11228 | 1,1 | 3,90 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 22,58 | / | > 0.1 | / | < 0.1 | 10,78 | / | > 0.1 | 1 |
| | L-homocysteic acid | 1,02 | M-H- | 182,01287 | 182,01254 | 1,8 | 2,44 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 3,03 | / | > 0.1 | / | > 0.1 | 0,98 | / | > 0.1 | 1 |
| | N-acetyl-L-alanineØ | 1,81 | M-H- | 130,05097 | 130,05079 | 1,4 | 13,27 | / | > 0.1 | / | > 0.1 | / | < 0.05 | 1,91 | / | < 0.05 | / | < 0.05 | 3,37 | / | > 0.1 | 1 |
| | N-alpha-Acetyl-L-lysine | 2,60 | M+H+ | 189,12337 | 189,12311 | 1,4 | 33,09 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 43,17 | / | > 0.1 | / | < 0.05 | 15,58 | / | > 0.1 | 1 |
| | N-alpha-acetylcitrulline | 1,47 | M-H- | 216,09898 | 216,09843 | 2,5 | ND | ND | ND | ND | ND | ND | ND | ND | ND | ND | ND | ND | 15,13 | ↘-22 | < 0.05 | 1 |
| | O-Propanoyl-D-carnitine | 10,38 | M+H+ | 218,13868 | 218,13854 | 0,7 | 9,90 | ↗+172 | > 0.1 | ↗+478 | > 0.1 | ↗+779 | < 0.1 | 14,08 | ↗+25 | > 0.1 | / | > 0.1 | 15,46 | ↘-40 | > 0.1 | 2 |
| | Phosphate | 0,98 | M+FA-H- | 142,97510 | 142,97481 | 2,0 | 8,69 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 3,28 | / | > 0.1 | / | > 0.1 | 1,96 | / | > 0.1 | 2 |
| | Phosphoglycolic acid | 0,93 | M-H- | 154,97510 | 154,97536 | -1,7 | 50,55 | ↗+78 | > 0.1 | / | > 0.1 | / | > 0.1 | ND | ND | ND | ND | ND | 24,35 | / | > 0.1 | 1 |
| | Phtalic acid | 9,31 | M-H- | 165,01933 | 165,01904 | 1,8 | 6,44 | / | > 0.1 | / | > 0.1 | ↗+84 | < 0.05 | 20,39 | / | > 0.1 | / | > 0.1 | 3,54 | / | > 0.1 | 1 |
| | Pyrrolidin-2-one | 1,85 | M+Na+ | 108,04198 | 108,04183 | 1,4 | 7,98 | ↗+147 | < 0.05 | / | > 0.1 | ↘-22 | > 0.1 | 9,66 | / | > 0.1 | / | > 0.1 | 14,47 | / | > 0.1 | 1 |
| | Salsoline-1-carboxylate | 9,94 | M+H+ | 238,10738 | 238,10709 | 1,2 | 14,57 | ↘-28 | < 0.1 | / | > 0.1 | / | > 0.1 | 13,13 | ↘-24 | < 0.05 | / | > 0.1 | 8,50 | / | > 0.1 | 2 |
| | Salsolinol 1-carboxylate | 3,15 | M+FA-H- | 268,08266 | 268,07997 | 10,0 | 36,24 | / | < 0.05 | / | > 0.1 | / | < 0.05 | ND | ND | ND | ND | ND | ND | ND | ND | 1 |
| | Tetradecandioic acid | 14,19 | M-H- | 257,17583 | 257,17552 | 1,2 | 3,49 | / | > 0.1 | / | > 0.1 | / | > 0.1 | 3,61 | / | < 0.1 | / | < 0.1 | 9,72 | / | > 0.1 | 1 |
| | Vanillactic acid | 8,64 | M-H- | 211,06120 | 211,06092 | 1,3 | 14,52 | ↗+39 | > 0.1 | ↘-28 | > 0.1 | / | > 0.1 | 8,97 | / | > 0.1 | / | > 0.1 | 16,73 | / | > 0.1 | 1 |
| | Vanillic acid 4-sulfate | 10,65 | M+FA-H- | 293,11430 | 293,11410 | 0,7 | 7,21 | / | > 0.1 | / | > 0.1 | ↘-25 | < 0.1 | 6,54 | ↘-38 | < 0.05 | ↘-26 | < 0.05 | 4,96 | ↘-37 | < 0.05 | 2 |
| | Vanillylamine | 11,75 | M+H+ | 154,08625 | 154,08603 | 1,4 | 20,71 | ↗+43 | > 0.1 | ↘-34 | > 0.1 | / | > 0.1 | 11,40 | ↗+24 | > 0.1 | / | > 0.1 | 8,52 | / | > 0.1 | 2 |

Figure S1: Quantitative enrichment analysis for male mussels exposed to 10 µg/L of venlafaxine after 1 day (A), 3 days (B) and 7 days (C). Red lines and rectangles represent pathways with a p -value < 0.1, blue lines and rectangles represent pathways with p -value < 0.05.

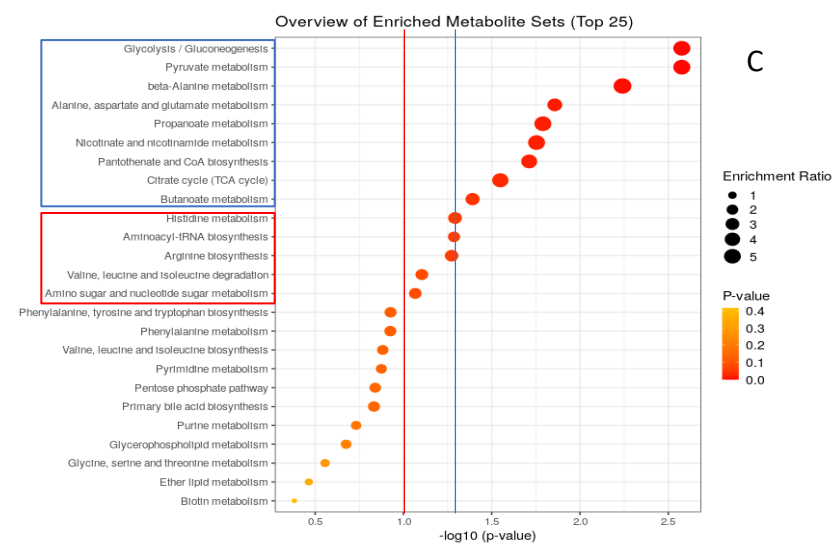
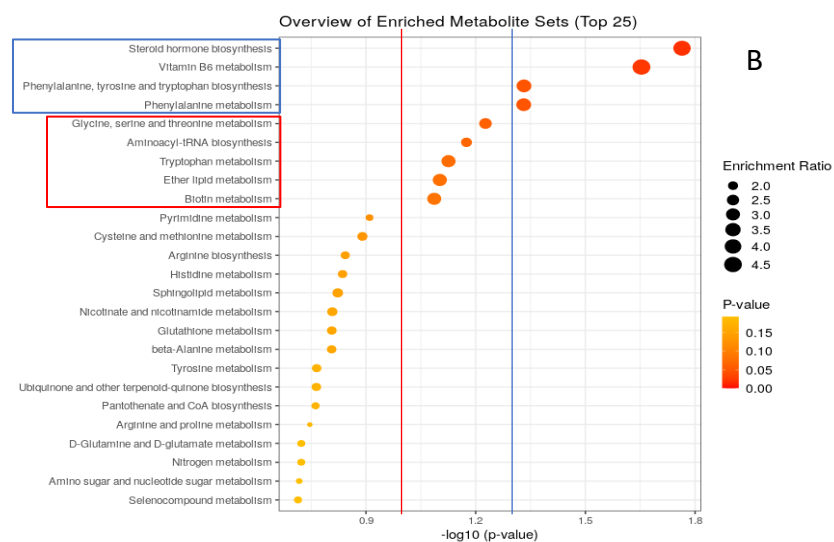
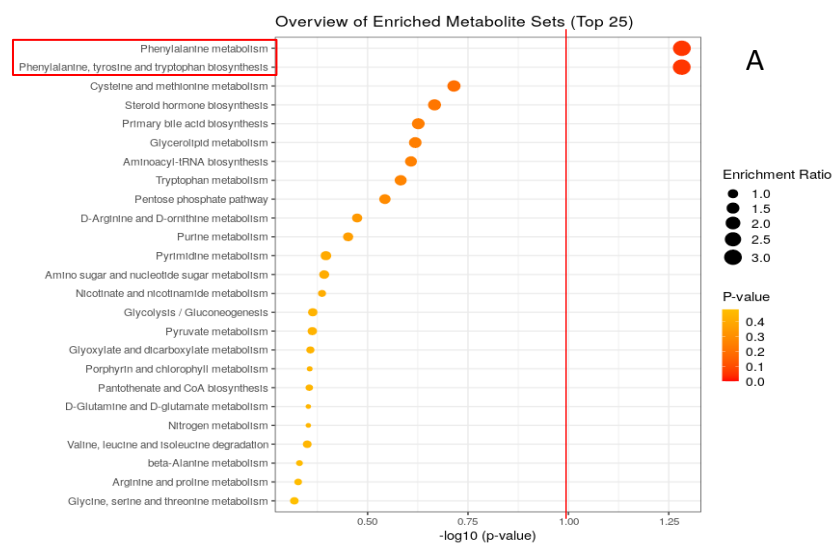


Figure S2: Quantitative enrichment analysis for female mussels exposed to 10 µg/L of venlafaxine after 1 day (A), 3 days (B) and 7 days (C). Red lines and rectangles represent pathways with a p-value < 0.1, blue lines and rectangles represent pathways with p-value < 0.05.

