Table S1 results of sensitivity tests (n=6)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Compound | Nominal Conc.(ng/ml) | Mean Conc.(ng/ml) | SD(ng/ml) | Mean Recov.(%) | RSD(%) |
| 1-Oleoyl-sn-glycero-3-phosphocholine | 1.0000 | 0.9335 | 0.1062 | 93.35 | 11.37 |
| 2-acetyl-1-alkyl-sn-glycero-3-phosphocholine | 1.0000 | 1.0340 | 0.1410 | 103.40 | 13.64 |
| 9-cis-Retinal | 1.0000 | 1.0125 | 0.1131 | 101.25 | 11.17 |
| Arachidonic acid | 1.0000 | 0.9705 | 0.0956 | 97.05 | 9.85 |
| Carnosine | 1.0000 | 0.9878 | 0.0787 | 98.78 | 7.96 |
| Choline phosphate | 1.0000 | 0.9828 | 0.1155 | 98.28 | 11.76 |
| CREATINE | 1.0000 | 1.0435 | 0.0789 | 104.35 | 7.57 |
| Cytidine | 1.0000 | 0.9735 | 0.0701 | 97.35 | 7.20 |
| Dl-Glutamic acid | 1.0000 | 0.9597 | 0.0991 | 95.97 | 10.32 |
| Glycocholic acid | 1.0000 | 0.8878 | 0.0620 | 88.78 | 6.99 |
| GUANIDINOACETATE | 1.0000 | 1.0225 | 0.1484 | 102.25 | 14.51 |
| Hypoxanthine | 1.0000 | 0.9949 | 0.0958 | 99.49 | 9.63 |
| L-Methionine | 1.0000 | 1.0111 | 0.1399 | 101.11 | 13.84 |
| L-Phenylalanine | 1.0000 | 0.9485 | 0.1153 | 94.85 | 12.16 |
| L-Tryptophan | 1.0000 | 0.9819 | 0.1360 | 98.19 | 13.85 |
| N-ACETYLNEURAMINATE | 1.0000 | 1.0502 | 0.1205 | 105.02 | 11.47 |
| Nicotinamide | 1.0000 | 0.9962 | 0.0866 | 99.62 | 8.69 |
| Palmitic acid | 1.0000 | 1.0120 | 0.1222 | 101.20 | 12.08 |
| Riboflavin | 1.0000 | 1.0415 | 0.1022 | 104.15 | 9.82 |
| Sphingonine 1-phosphate | 1.0000 | 0.9855 | 0.0651 | 98.55 | 6.61 |
| Taurocholate | 1.0000 | 0.9910 | 0.1082 | 99.10 | 10.91 |
| Tyrosine | 1.0000 | 1.0033 | 0.1008 | 100.33 | 10.05 |
| Uridine | 1.0000 | 1.0146 | 0.1016 | 101.46 | 10.01 |
| Xanthine | 1.0000 | 0.9990 | 0.1335 | 99.90 | 13.36 |

Table S2 Accuracy and precision(n=6)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Compound | Nominal Conc. (ng/ml) | Mean Conc.(ng/ml) | SD(ng/ml) | Mean Recov.(%) | RSD(%) |
|  | 5.0000 | 4.9536 | 0.3627 | 99.07 | 8.02 |
| 1-Oleoyl-sn-glycero-3-phosphocholine | 100.0000 | 102.0461 | 9.4559 | 102.05 | 10.15 |
|  | 800.0000 | 846.5166 | 34.0590 | 105.81 | 4.41 |
|  | 5.0000 | 4.7594 | 0.3985 | 95.19 | 9.17 |
| 2-acetyl-1-alkyl-sn-glycero-3-phosphocholine | 100.0000 | 103.9287 | 9.8137 | 103.93 | 10.34 |
|  | 800.0000 | 807.5651 | 74.9956 | 100.95 | 10.17 |
|  | 5.0000 | 4.8901 | 0.2868 | 97.80 | 6.43 |
| 9-cis-Retinal | 100.0000 | 102.5473 | 9.7887 | 102.55 | 10.46 |
|  | 800.0000 | 845.3693 | 51.0639 | 105.67 | 6.62 |
|  | 5.0000 | 4.7950 | 0.4873 | 95.90 | 11.13 |
| Arachidonic acid | 100.0000 | 101.6726 | 8.2858 | 101.67 | 8.93 |
|  | 800.0000 | 760.3505 | 71.6003 | 95.04 | 10.32 |
|  | 5.0000 | 4.9583 | 0.3423 | 99.17 | 7.56 |
| Carnosine | 100.0000 | 100.7825 | 7.8185 | 100.78 | 8.50 |
|  | 800.0000 | 785.9571 | 73.9165 | 98.24 | 10.30 |
|  | 5.0000 | 5.1214 | 0.3605 | 102.43 | 7.71 |
| Choline phosphate | 100.0000 | 105.7997 | 7.8011 | 105.80 | 8.08 |
|  | 800.0000 | 796.1743 | 56.2650 | 99.52 | 7.74 |
|  | 5.0000 | 4.7486 | 0.4598 | 94.97 | 10.61 |
| CREATINE | 100.0000 | 101.6430 | 6.9921 | 101.64 | 7.54 |
|  | 800.0000 | 798.9593 | 94.9004 | 99.87 | 13.01 |
|  | 5.0000 | 5.6175 | 0.2189 | 112.35 | 4.27 |
| Cytidine | 100.0000 | 110.4290 | 1.9371 | 110.43 | 1.92 |
|  | 800.0000 | 867.9298 | 43.2977 | 108.49 | 5.46 |
|  | 5.0000 | 4.7932 | 0.4197 | 95.86 | 9.59 |
| Dl-Glutamic acid | 100.0000 | 101.2731 | 8.9119 | 101.27 | 9.64 |
|  | 800.0000 | 820.2863 | 71.4023 | 102.54 | 9.54 |
|  | 5.0000 | 4.9622 | 0.4891 | 99.24 | 10.80 |
| Glycocholic acid | 100.0000 | 100.6173 | 7.2948 | 100.62 | 7.94 |
|  | 800.0000 | 796.1859 | 66.5185 | 99.52 | 9.15 |
|  | 5.0000 | 5.7309 | 0.3071 | 114.62 | 5.87 |
| GUANIDINOACETATE | 100.0000 | 114.4114 | 5.4926 | 114.41 | 5.26 |
|  | 800.0000 | 885.0517 | 62.4243 | 110.63 | 7.73 |
|  | 5.0000 | 5.1169 | 0.3491 | 102.34 | 7.47 |
| Hypoxanthine | 100.0000 | 99.4635 | 4.5830 | 99.46 | 5.05 |
|  | 800.0000 | 794.8170 | 70.2983 | 99.35 | 9.69 |
|  | 5.0000 | 5.1332 | 0.4458 | 102.66 | 9.51 |
| L-Methionine | 100.0000 | 105.8906 | 7.1478 | 105.89 | 7.39 |
|  | 800.0000 | 800.5588 | 52.7601 | 100.07 | 7.22 |
|  | 5.0000 | 5.0412 | 0.3967 | 100.82 | 8.62 |
| L-Phenylalanine | 100.0000 | 107.7392 | 6.4407 | 107.74 | 6.55 |
|  | 800.0000 | 737.0192 | 47.4106 | 92.13 | 7.05 |
|  | 5.0000 | 5.0036 | 0.2973 | 100.07 | 6.51 |
| L-Tryptophan | 100.0000 | 95.5523 | 10.5467 | 95.55 | 12.09 |
|  | 800.0000 | 811.9914 | 66.6315 | 101.50 | 8.99 |
|  | 5.0000 | 4.9767 | 0.3547 | 99.53 | 7.81 |
| N-ACETYLNEURAMINATE | 100.0000 | 98.2119 | 8.3512 | 98.21 | 9.31 |
|  | 800.0000 | 804.4274 | 53.0640 | 100.55 | 7.23 |
|  | 5.0000 | 4.9219 | 0.3306 | 98.44 | 7.36 |
| Nicotinamide | 100.0000 | 98.1494 | 7.9448 | 98.15 | 8.87 |
|  | 800.0000 | 792.2646 | 69.6056 | 99.03 | 9.62 |
|  | 5.0000 | 4.9035 | 0.3591 | 98.07 | 8.02 |
| Palmitic acid | 100.0000 | 102.8576 | 10.0902 | 102.86 | 10.75 |
|  | 800.0000 | 806.7084 | 46.1933 | 100.84 | 6.27 |
|  | 5.0000 | 5.3744 | 0.3418 | 107.49 | 6.97 |
| Riboflavin | 100.0000 | 102.6265 | 11.9533 | 102.63 | 12.76 |
|  | 800.0000 | 837.5619 | 35.0913 | 104.70 | 4.59 |
|  | 5.0000 | 4.7448 | 0.3390 | 94.90 | 7.83 |
| Sphingonine 1-phosphate | 100.0000 | 103.4710 | 7.5906 | 103.47 | 8.04 |
|  | 800.0000 | 789.3982 | 74.8307 | 98.67 | 10.38 |
|  | 5.0000 | 4.9782 | 0.3040 | 99.56 | 6.69 |
| Taurocholate | 100.0000 | 94.0295 | 7.1637 | 94.03 | 8.35 |
|  | 800.0000 | 795.7713 | 58.7066 | 99.47 | 8.08 |
|  | 5.0000 | 5.2326 | 0.3631 | 104.65 | 7.60 |
| Tyrosine | 100.0000 | 101.9245 | 8.7272 | 101.92 | 9.38 |
|  | 800.0000 | 822.9251 | 67.3985 | 102.87 | 8.97 |
|  | 5.0000 | 4.9948 | 0.4887 | 99.90 | 10.72 |
| Uridine | 100.0000 | 99.1976 | 8.0000 | 99.20 | 8.83 |
|  | 800.0000 | 788.2026 | 51.4441 | 98.53 | 7.15 |
|  | 5.0000 | 5.3542 | 0.3157 | 107.08 | 6.46 |
| Xanthine | 100.0000 | 97.3490 | 10.1438 | 97.35 | 11.41 |
|  | 800.0000 | 781.6017 | 69.5394 | 97.70 | 9.75 |

Table S3 Results of constant temperature stability tests (n=6)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Compound | Nominal Conc. (ng/ml) | Mean Conc.(ng/ml) | SD(ng/ml) | Mean Recov.(%) | RSD(%) |
|  | 5.0000 | 5.1627 | 0.3825 | 103.25 | 8.12 |
| 1-Oleoyl-sn-glycero-3-phosphocholine | 100.0000 | 100.2987 | 8.7062 | 100.30 | 9.51 |
|  | 800.0000 | 818.1225 | 61.9266 | 102.27 | 8.29 |
|  | 5.0000 | 4.9583 | 0.2090 | 99.17 | 4.62 |
| 2-acetyl-1-alkyl-sn-glycero-3-phosphocholine | 100.0000 | 106.2422 | 7.1643 | 106.24 | 7.39 |
|  | 800.0000 | 842.8723 | 74.3557 | 105.36 | 9.66 |
|  | 5.0000 | 4.6597 | 0.3766 | 93.19 | 8.85 |
| 9-cis-Retinal | 100.0000 | 101.3053 | 9.6420 | 101.31 | 10.43 |
|  | 800.0000 | 805.5112 | 77.5994 | 100.69 | 10.55 |
|  | 5.0000 | 4.9717 | 0.3900 | 99.43 | 8.59 |
| Arachidonic acid | 100.0000 | 100.9118 | 6.0989 | 100.91 | 6.62 |
|  | 800.0000 | 794.6246 | 64.7719 | 99.33 | 8.93 |
|  | 5.0000 | 4.5872 | 0.2031 | 91.74 | 4.85 |
| Carnosine | 100.0000 | 97.3840 | 10.4110 | 97.38 | 11.71 |
|  | 800.0000 | 815.9301 | 84.6765 | 101.99 | 11.37 |
|  | 5.0000 | 5.2319 | 0.3571 | 104.64 | 7.48 |
| Choline phosphate | 100.0000 | 95.6256 | 4.9512 | 95.63 | 5.67 |
|  | 800.0000 | 792.8678 | 57.7495 | 99.11 | 7.98 |
|  | 5.0000 | 4.7395 | 0.3149 | 94.79 | 7.28 |
| CREATINE | 100.0000 | 102.6188 | 6.3945 | 102.62 | 6.83 |
|  | 800.0000 | 760.4875 | 56.2816 | 95.06 | 8.11 |
|  | 5.0000 | 5.7466 | 0.2300 | 114.93 | 4.38 |
| Cytidine | 100.0000 | 108.1398 | 4.5627 | 108.14 | 4.62 |
|  | 800.0000 | 842.5817 | 31.3655 | 105.32 | 4.08 |
|  | 5.0000 | 4.9037 | 0.3131 | 98.07 | 6.99 |
| Dl-Glutamic acid | 100.0000 | 106.1717 | 7.9215 | 106.17 | 8.17 |
|  | 800.0000 | 788.8688 | 72.3853 | 98.61 | 10.05 |
|  | 5.0000 | 4.7251 | 0.4258 | 94.50 | 9.87 |
| Glycocholic acid | 100.0000 | 101.7750 | 5.2239 | 101.77 | 5.62 |
|  | 800.0000 | 769.2818 | 83.2410 | 96.16 | 11.85 |
|  | 5.0000 | 4.9545 | 0.3025 | 99.09 | 6.69 |
| GUANIDINOACETATE | 100.0000 | 85.0068 | 36.8141 | 85.01 | 47.44 |
|  | 800.0000 | 783.6370 | 63.6475 | 97.95 | 8.90 |
|  | 5.0000 | 5.2799 | 0.2774 | 105.60 | 5.76 |
| Hypoxanthine | 100.0000 | 99.8989 | 8.9063 | 99.90 | 9.77 |
|  | 800.0000 | 793.4020 | 41.4183 | 99.18 | 5.72 |
|  | 5.0000 | 5.0100 | 0.3143 | 100.20 | 6.87 |
| L-Methionine | 100.0000 | 100.0848 | 8.3949 | 100.08 | 9.19 |
|  | 800.0000 | 777.3027 | 63.0358 | 97.16 | 8.88 |
|  | 5.0000 | 5.0185 | 0.3096 | 100.37 | 6.76 |
| L-Phenylalanine | 100.0000 | 104.8219 | 2.4241 | 104.82 | 2.53 |
|  | 800.0000 | 719.9350 | 18.1953 | 89.99 | 2.77 |
|  | 5.0000 | 4.8594 | 0.2512 | 97.19 | 5.66 |
| L-Tryptophan | 100.0000 | 96.5215 | 5.7732 | 94.65 | 8.36 |
|  | 800.0000 | 798.6750 | 60.4536 | 99.83 | 8.29 |
|  | 5.0000 | 5.0800 | 0.3298 | 101.60 | 7.11 |
| N-ACETYLNEURAMINATE | 100.0000 | 106.8696 | 5.9870 | 106.87 | 6.14 |
|  | 800.0000 | 765.7356 | 49.0836 | 93.69 | 5.44 |
|  | 5.0000 | 4.2561 | 0.3387 | 85.12 | 8.72 |
| Nicotinamide | 100.0000 | 95.1831 | 2.9960 | 95.18 | 3.45 |
|  | 800.0000 | 749.5497 | 37.2349 | 95.72 | 7.02 |
|  | 5.0000 | 4.9266 | 0.2953 | 98.53 | 6.57 |
| Palmitic acid | 100.0000 | 91.8274 | 5.3157 | 91.83 | 6.34 |
|  | 800.0000 | 815.6808 | 37.3642 | 101.96 | 5.02 |
|  | 5.0000 | 4.9957 | 0.4900 | 99.91 | 10.74 |
| Riboflavin | 100.0000 | 94.3250 | 5.2851 | 94.33 | 6.14 |
|  | 800.0000 | 830.5895 | 74.5243 | 103.82 | 9.83 |
|  | 5.0000 | 5.1164 | 0.3828 | 102.33 | 8.20 |
| Sphingonine 1-phosphate | 100.0000 | 99.2235 | 7.2799 | 99.22 | 8.04 |
|  | 800.0000 | 801.4738 | 72.1070 | 100.18 | 9.86 |
|  | 5.0000 | 4.9120 | 0.4048 | 98.24 | 9.03 |
| Taurocholate | 100.0000 | 98.1368 | 9.8237 | 98.14 | 10.97 |
|  | 800.0000 | 769.0219 | 51.8680 | 96.13 | 7.39 |
|  | 5.0000 | 4.9300 | 0.4279 | 98.60 | 9.51 |
| Tyrosine | 100.0000 | 97.9824 | 10.3345 | 97.98 | 11.55 |
|  | 800.0000 | 875.4423 | 39.4711 | 109.43 | 4.94 |
|  | 5.0000 | 4.9144 | 0.5281 | 98.29 | 11.77 |
| Uridine | 100.0000 | 98.6299 | 8.6292 | 98.63 | 9.58 |
|  | 800.0000 | 775.8805 | 55.3721 | 96.99 | 7.82 |
|  | 5.0000 | 5.1736 | 0.5129 | 103.47 | 10.86 |
| Xanthine | 100.0000 | 100.3717 | 9.6217 | 100.37 | 10.50 |
|  | 800.0000 | 800.7672 | 65.3468 | 100.10 | 8.94 |

Table S4 Results of bench-top stability tests (n=6)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Compound | Nominal Conc. (ng/ml) | Mean Conc.(ng/ml) | SD(ng/ml) | Mean Recov.(%) | RSD(%) |
|  | 5.0000 | 4.9175 | 0.2218 | 98.35 | 4.94 |
| 1-Oleoyl-sn-glycero-3-phosphocholine | 100.0000 | 105.1729 | 7.5451 | 105.17 | 7.86 |
|  | 800.0000 | 803.2401 | 75.0061 | 102.27 | 8.29 |
|  | 5.0000 | 5.0345 | 0.4437 | 100.69 | 9.66 |
| 2-acetyl-1-alkyl-sn-glycero-3-phosphocholine | 100.0000 | 107.4235 | 4.3665 | 107.42 | 4.45 |
|  | 800.0000 | 807.2112 | 64.8399 | 105.36 | 9.66 |
|  | 5.0000 | 4.9025 | 0.2421 | 98.05 | 5.41 |
| 9-cis-Retinal | 100.0000 | 103.1188 | 8.6173 | 103.12 | 9.15 |
|  | 800.0000 | 785.2669 | 50.3485 | 100.69 | 10.55 |
|  | 5.0000 | 4.9865 | 0.1450 | 99.73 | 3.19 |
| Arachidonic acid | 100.0000 | 101.8917 | 7.0151 | 101.89 | 7.54 |
|  | 800.0000 | 819.4795 | 25.7417 | 99.33 | 8.93 |
|  | 5.0000 | 4.6793 | 0.4384 | 93.59 | 10.26 |
| Carnosine | 100.0000 | 93.3111 | 6.3626 | 93.31 | 7.47 |
|  | 800.0000 | 823.5762 | 33.3346 | 101.99 | 11.37 |
|  | 5.0000 | 5.0334 | 0.5650 | 100.67 | 12.30 |
| Choline phosphate | 100.0000 | 97.0951 | 5.1888 | 97.10 | 5.85 |
|  | 800.0000 | 795.6282 | 82.2447 | 99.11 | 7.98 |
|  | 5.0000 | 5.1981 | 0.3828 | 103.96 | 8.07 |
| CREATINE | 100.0000 | 103.5292 | 8.8026 | 103.53 | 9.31 |
|  | 800.0000 | 782.2942 | 39.5640 | 95.06 | 8.11 |
|  | 5.0000 | 5.2724 | 0.3812 | 105.45 | 7.92 |
| Cytidine | 100.0000 | 108.9488 | 4.5375 | 108.95 | 4.56 |
|  | 800.0000 | 846.8404 | 34.9536 | 105.32 | 4.08 |
|  | 5.0000 | 4.8610 | 0.4206 | 97.22 | 9.48 |
| Dl-Glutamic acid | 100.0000 | 106.2825 | 6.2571 | 106.28 | 6.45 |
|  | 800.0000 | 745.7884 | 36.4817 | 98.61 | 10.05 |
|  | 5.0000 | 4.9156 | 0.4090 | 98.31 | 9.11 |
| Glycocholic acid | 100.0000 | 104.2289 | 8.3959 | 104.23 | 8.82 |
|  | 800.0000 | 807.4907 | 70.0525 | 96.16 | 11.85 |
|  | 5.0000 | 4.9742 | 0.2524 | 99.48 | 5.56 |
| GUANIDINOACETATE | 100.0000 | 103.7063 | 8.3461 | 103.71 | 8.82 |
|  | 800.0000 | 751.8692 | 37.8548 | 97.95 | 8.90 |
|  | 5.0000 | 5.2274 | 0.3866 | 104.55 | 8.10 |
| Hypoxanthine | 100.0000 | 97.5645 | 6.2330 | 97.56 | 7.00 |
|  | 800.0000 | 791.9312 | 72.5905 | 99.18 | 5.72 |
|  | 5.0000 | 5.0451 | 0.5131 | 100.90 | 11.14 |
| L-Methionine | 100.0000 | 104.5702 | 8.0144 | 104.57 | 8.40 |
|  | 800.0000 | 766.3402 | 72.6328 | 97.16 | 8.88 |
|  | 5.0000 | 4.7659 | 0.2779 | 95.32 | 6.39 |
| L-Phenylalanine | 100.0000 | 104.4529 | 4.7613 | 104.45 | 4.99 |
|  | 800.0000 | 720.5960 | 54.1245 | 89.99 | 2.77 |
|  | 5.0000 | 5.1157 | 0.4219 | 102.31 | 9.03 |
| L-Tryptophan | 100.0000 | 97.4228 | 5.3665 | 97.42 | 6.03 |
|  | 800.0000 | 784.3823 | 41.5190 | 99.83 | 8.29 |
|  | 5.0000 | 5.1735 | 0.4601 | 103.47 | 9.74 |
| N-ACETYLNEURAMINATE | 100.0000 | 100.7793 | 5.3682 | 100.78 | 5.84 |
|  | 800.0000 | 750.0851 | 51.4876 | 95.72 | 7.02 |
|  | 5.0000 | 4.9118 | 0.4831 | 98.24 | 10.77 |
| Nicotinamide | 100.0000 | 102.2989 | 6.7367 | 102.30 | 7.21 |
|  | 800.0000 | 731.7893 | 46.4317 | 93.69 | 5.44 |
|  | 5.0000 | 5.0031 | 0.4833 | 100.06 | 10.58 |
| Palmitic acid | 100.0000 | 96.0897 | 6.3806 | 96.09 | 7.27 |
|  | 800.0000 | 825.7309 | 59.0834 | 101.96 | 5.02 |
|  | 5.0000 | 4.8812 | 0.5320 | 97.62 | 11.94 |
| Riboflavin | 100.0000 | 98.1810 | 6.4117 | 98.18 | 7.15 |
|  | 800.0000 | 805.6864 | 96.6640 | 103.82 | 9.83 |
|  | 5.0000 | 5.2838 | 0.3719 | 105.68 | 7.71 |
| Sphingonine 1-phosphate | 100.0000 | 99.5914 | 8.7770 | 99.59 | 9.65 |
|  | 800.0000 | 748.3757 | 62.2715 | 100.18 | 9.86 |
|  | 5.0000 | 5.0578 | 0.4553 | 101.16 | 9.86 |
| Taurocholate | 100.0000 | 95.7172 | 8.1913 | 95.72 | 9.37 |
|  | 800.0000 | 786.4107 | 41.8093 | 96.13 | 7.39 |
|  | 5.0000 | 4.7233 | 0.3444 | 94.47 | 7.99 |
| Tyrosine | 100.0000 | 105.3988 | 8.9285 | 105.40 | 9.28 |
|  | 800.0000 | 842.8571 | 59.6020 | 109.43 | 4.94 |
|  | 5.0000 | 4.8924 | 0.4593 | 97.85 | 10.28 |
| Uridine | 100.0000 | 102.0079 | 10.1807 | 102.01 | 10.93 |
|  | 800.0000 | 777.6139 | 60.5505 | 96.99 | 7.82 |
|  | 5.0000 | 5.3200 | 0.5290 | 106.40 | 10.89 |
| Xanthine | 100.0000 | 101.6274 | 10.0640 | 101.63 | 10.85 |
|  | 800.0000 | 811.7114 | 45.6428 | 100.10 | 8.94 |

Table S5 Results of freeze-thaw stability tests (n=6)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Compound | Nominal Conc. (ng/ml) | Mean Conc.(ng/ml) | SD(ng/ml) | Mean Recov.(%) | RSD(%) |
|  | 5.0000 | 4.8467 | 0.3593 | 96.93 | 8.12 |
| 1-Oleoyl-sn-glycero-3-phosphocholine | 100.0000 | 101.7171 | 5.8946 | 101.72 | 6.35 |
|  | 800.0000 | 812.3086 | 68.8035 | 101.54 | 9.28 |
|  | 5.0000 | 5.3225 | 0.3142 | 106.45 | 6.47 |
| 2-acetyl-1-alkyl-sn-glycero-3-phosphocholine | 100.0000 | 103.6674 | 6.8408 | 103.67 | 7.23 |
|  | 800.0000 | 830.1557 | 60.1580 | 103.77 | 7.94 |
|  | 5.0000 | 4.6285 | 0.2760 | 92.57 | 6.53 |
| 9-cis-Retinal | 100.0000 | 98.6908 | 11.0127 | 98.69 | 12.22 |
|  | 800.0000 | 815.7360 | 48.1999 | 101.97 | 6.47 |
|  | 5.0000 | 4.5794 | 0.3283 | 91.59 | 7.85 |
| Arachidonic acid | 100.0000 | 96.7125 | 8.0646 | 96.71 | 9.13 |
|  | 800.0000 | 817.2518 | 71.3894 | 102.16 | 9.57 |
|  | 5.0000 | 4.6750 | 0.2419 | 93.50 | 5.67 |
| Carnosine | 100.0000 | 93.3093 | 5.8145 | 93.31 | 6.83 |
|  | 800.0000 | 833.1660 | 85.9582 | 104.15 | 11.30 |
|  | 5.0000 | 5.2649 | 0.3736 | 105.30 | 7.77 |
| Choline phosphate | 100.0000 | 95.9197 | 9.6524 | 95.92 | 11.02 |
|  | 800.0000 | 806.8368 | 33.4389 | 100.85 | 4.54 |
|  | 5.0000 | 5.1459 | 0.3542 | 102.92 | 7.54 |
| CREATINE | 100.0000 | 106.4678 | 8.8320 | 106.47 | 9.09 |
|  | 800.0000 | 774.7504 | 72.8703 | 96.84 | 10.30 |
|  | 5.0000 | 5.5245 | 0.1723 | 110.49 | 3.42 |
| Cytidine | 100.0000 | 103.3974 | 4.0546 | 103.40 | 4.30 |
|  | 800.0000 | 877.6079 | 28.5856 | 109.70 | 3.57 |
|  | 5.0000 | 4.8358 | 0.3848 | 96.72 | 8.72 |
| Dl-Glutamic acid | 100.0000 | 109.0846 | 5.5063 | 109.08 | 5.53 |
|  | 800.0000 | 770.0321 | 97.9486 | 96.25 | 13.93 |
|  | 5.0000 | 5.0045 | 0.4387 | 100.09 | 9.60 |
| Glycocholic acid | 100.0000 | 99.4769 | 8.7548 | 99.48 | 9.64 |
|  | 800.0000 | 803.9520 | 46.0523 | 100.49 | 6.27 |
|  | 5.0000 | 5.1056 | 0.5122 | 102.11 | 10.99 |
| GUANIDINOACETATE | 100.0000 | 98.0000 | 7.3199 | 98.00 | 8.18 |
|  | 800.0000 | 771.8937 | 54.2600 | 96.49 | 7.70 |
|  | 5.0000 | 5.1903 | 0.5127 | 103.81 | 10.82 |
| Hypoxanthine | 100.0000 | 97.9798 | 8.7150 | 97.98 | 9.74 |
|  | 800.0000 | 800.7005 | 52.0932 | 100.09 | 7.13 |
|  | 5.0000 | 4.9323 | 0.3365 | 98.65 | 7.47 |
| L-Methionine | 100.0000 | 101.6204 | 6.4326 | 101.62 | 6.93 |
|  | 800.0000 | 804.5176 | 48.0642 | 100.56 | 6.54 |
|  | 5.0000 | 5.0629 | 0.2122 | 101.26 | 4.59 |
| L-Phenylalanine | 100.0000 | 105.5102 | 5.4338 | 105.51 | 5.64 |
|  | 800.0000 | 738.8935 | 29.5881 | 92.36 | 4.39 |
|  | 5.0000 | 4.7852 | 0.3019 | 95.70 | 6.91 |
| L-Tryptophan | 100.0000 | 95.2877 | 7.0593 | 95.29 | 8.12 |
|  | 800.0000 | 813.4193 | 61.7771 | 101.68 | 8.32 |
|  | 5.0000 | 4.8900 | 0.4040 | 97.80 | 9.05 |
| N-ACETYLNEURAMINATE | 100.0000 | 103.4078 | 9.9559 | 103.41 | 10.55 |
|  | 800.0000 | 778.0824 | 57.3776 | 97.26 | 8.08 |
|  | 5.0000 | 4.7530 | 0.2793 | 95.06 | 6.44 |
| Nicotinamide | 100.0000 | 97.6744 | 5.6656 | 97.67 | 6.35 |
|  | 800.0000 | 777.7546 | 36.1664 | 97.22 | 5.09 |
|  | 5.0000 | 4.9394 | 0.2850 | 98.79 | 6.32 |
| Palmitic acid | 100.0000 | 93.4697 | 6.2744 | 93.47 | 7.35 |
|  | 800.0000 | 798.8125 | 62.9999 | 99.85 | 8.64 |
|  | 5.0000 | 4.8384 | 0.1842 | 96.77 | 4.17 |
| Riboflavin | 100.0000 | 98.5090 | 7.1374 | 98.51 | 7.94 |
|  | 800.0000 | 820.2495 | 50.3965 | 102.53 | 6.73 |
|  | 5.0000 | 5.1375 | 0.2924 | 102.75 | 6.24 |
| Sphingonine 1-phosphate | 100.0000 | 101.7642 | 5.7620 | 101.76 | 6.20 |
|  | 800.0000 | 815.0353 | 111.6079 | 101.88 | 15.00 |
|  | 5.0000 | 4.9233 | 0.3539 | 98.47 | 7.87 |
| Taurocholate | 100.0000 | 98.0791 | 7.1951 | 98.08 | 8.04 |
|  | 800.0000 | 799.4965 | 62.1842 | 99.94 | 8.52 |
|  | 5.0000 | 5.2983 | 0.3448 | 105.97 | 7.13 |
| Tyrosine | 100.0000 | 97.1779 | 9.5649 | 97.18 | 10.78 |
|  | 800.0000 | 877.3675 | 28.3153 | 109.67 | 3.54 |
|  | 5.0000 | 5.0969 | 0.4853 | 101.94 | 10.43 |
| Uridine | 100.0000 | 99.2930 | 6.9446 | 99.29 | 7.66 |
|  | 800.0000 | 786.9548 | 67.0271 | 98.37 | 9.33 |
|  | 5.0000 | 5.1122 | 0.4216 | 102.24 | 9.03 |
| Xanthine | 100.0000 | 98.1004 | 6.3397 | 98.10 | 7.08 |
|  | 800.0000 | 814.3396 | 95.1472 | 101.79 | 12.80 |

Table S6 Results of long-trem stability tests (n=6)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Compound | Nominal Conc. (ng/ml) | Mean Conc.(ng/ml) | SD(ng/ml) | Mean Recov.(%) | RSD(%) |
|  | 5.0000 | 4.9590 | 0.4307 | 99.18 | 9.52 |
| 1-Oleoyl-sn-glycero-3-phosphocholine | 100.0000 | 98.6970 | 7.2082 | 98.70 | 8.00 |
|  | 800.0000 | 808.5454 | 70.8991 | 101.07 | 9.61 |
|  | 5.0000 | 4.9772 | 0.2253 | 99.54 | 4.96 |
| 2-acetyl-1-alkyl-sn-glycero-3-phosphocholine | 100.0000 | 103.5074 | 7.7529 | 103.51 | 8.21 |
|  | 800.0000 | 811.4128 | 51.5766 | 101.43 | 6.96 |
|  | 5.0000 | 4.6708 | 0.3833 | 93.42 | 8.99 |
| 9-cis-Retinal | 100.0000 | 98.5696 | 8.1922 | 98.57 | 9.10 |
|  | 800.0000 | 799.0786 | 46.6449 | 99.88 | 6.39 |
|  | 5.0000 | 4.7397 | 0.3839 | 94.79 | 8.87 |
| Arachidonic acid | 100.0000 | 98.6196 | 6.6605 | 98.62 | 7.40 |
|  | 800.0000 | 783.6845 | 52.0296 | 97.96 | 7.27 |
|  | 5.0000 | 4.5924 | 0.1782 | 91.85 | 4.25 |
| Carnosine | 100.0000 | 98.3555 | 10.3303 | 98.36 | 11.51 |
|  | 800.0000 | 785.5610 | 56.2411 | 98.20 | 7.84 |
|  | 5.0000 | 5.0801 | 0.3210 | 101.60 | 6.92 |
| Choline phosphate | 100.0000 | 94.3688 | 5.0475 | 94.37 | 5.86 |
|  | 800.0000 | 755.9731 | 52.1055 | 94.50 | 7.55 |
|  | 5.0000 | 5.1385 | 0.3992 | 102.77 | 8.51 |
| CREATINE | 100.0000 | 101.8574 | 8.6090 | 101.86 | 9.26 |
|  | 800.0000 | 778.3338 | 58.9934 | 97.29 | 8.30 |
|  | 5.0000 | 5.1034 | 0.3294 | 102.07 | 7.07 |
| Cytidine | 100.0000 | 108.3837 | 3.8280 | 108.38 | 3.87 |
|  | 800.0000 | 870.1824 | 32.2555 | 108.77 | 4.06 |
|  | 5.0000 | 4.9403 | 0.3547 | 98.81 | 7.87 |
| Dl-Glutamic acid | 100.0000 | 105.4750 | 4.6930 | 105.47 | 4.87 |
|  | 800.0000 | 803.1240 | 60.4148 | 100.39 | 8.24 |
|  | 5.0000 | 5.1215 | 0.4499 | 102.43 | 9.62 |
| Glycocholic acid | 100.0000 | 98.9020 | 7.4143 | 98.90 | 8.21 |
|  | 800.0000 | 861.2738 | 39.8950 | 107.66 | 5.07 |
|  | 5.0000 | 4.8794 | 0.2747 | 97.59 | 6.17 |
| GUANIDINOACETATE | 100.0000 | 99.7911 | 9.5589 | 99.79 | 10.49 |
|  | 800.0000 | 780.7197 | 52.2843 | 97.59 | 7.34 |
|  | 5.0000 | 4.9931 | 0.5455 | 99.86 | 11.97 |
| Hypoxanthine | 100.0000 | 102.2500 | 5.4586 | 102.25 | 5.85 |
|  | 800.0000 | 742.1369 | 51.6669 | 92.77 | 7.63 |
|  | 5.0000 | 4.8954 | 0.4784 | 97.91 | 10.71 |
| L-Methionine | 100.0000 | 101.2478 | 7.7987 | 101.25 | 8.44 |
|  | 800.0000 | 792.1782 | 68.4423 | 99.02 | 9.46 |
|  | 5.0000 | 4.8661 | 0.2941 | 97.32 | 6.62 |
| L-Phenylalanine | 100.0000 | 104.3950 | 6.2816 | 104.39 | 6.59 |
|  | 800.0000 | 735.7106 | 47.2372 | 91.96 | 7.03 |
|  | 5.0000 | 4.8148 | 0.2879 | 96.30 | 6.55 |
| L-Tryptophan | 100.0000 | 99.5418 | 8.9674 | 99.54 | 9.87 |
|  | 800.0000 | 780.1260 | 65.2344 | 97.52 | 9.16 |
|  | 5.0000 | 4.8983 | 0.4165 | 97.97 | 9.31 |
| N-ACETYLNEURAMINATE | 100.0000 | 101.6483 | 9.1452 | 101.65 | 9.86 |
|  | 800.0000 | 761.7421 | 60.7230 | 95.22 | 8.73 |
|  | 5.0000 | 4.5476 | 0.1757 | 90.95 | 4.23 |
| Nicotinamide | 100.0000 | 98.7001 | 6.6127 | 98.70 | 7.34 |
|  | 800.0000 | 738.6906 | 47.2554 | 92.34 | 7.01 |
|  | 5.0000 | 4.8355 | 0.3342 | 96.71 | 7.57 |
| Palmitic acid | 100.0000 | 91.7802 | 7.1161 | 91.78 | 8.49 |
|  | 800.0000 | 804.9923 | 52.2146 | 100.62 | 7.11 |
|  | 5.0000 | 4.8326 | 0.1957 | 97.85 | 6.37 |
| Riboflavin | 100.0000 | 92.8791 | 2.9722 | 96.65 | 4.44 |
|  | 800.0000 | 811.1967 | 78.7148 | 92.88 | 3.51 |
|  | 5.0000 | 4.8925 | 0.2846 | 101.40 | 10.63 |
| Sphingonine 1-phosphate | 100.0000 | 96.6345 | 7.1544 | 97.85 | 6.37 |
|  | 800.0000 | 779.4355 | 99.1934 | 96.63 | 8.11 |
|  | 5.0000 | 4.7467 | 0.3595 | 97.43 | 13.94 |
| Taurocholate | 100.0000 | 102.0113 | 5.5944 | 94.93 | 8.30 |
|  | 800.0000 | 782.0876 | 58.0942 | 102.01 | 6.01 |
|  | 5.0000 | 5.1763 | 0.4424 | 97.76 | 8.14 |
| Tyrosine | 100.0000 | 98.4561 | 7.3236 | 103.53 | 9.36 |
|  | 800.0000 | 861.0312 | 32.9029 | 98.46 | 8.15 |
|  | 5.0000 | 4.9078 | 0.4665 | 107.63 | 4.19 |
| Uridine | 100.0000 | 100.6506 | 8.3965 | 100.65 | 9.14 |
|  | 800.0000 | 760.5149 | 44.5609 | 95.06 | 6.42 |
|  | 5.0000 | 4.9414 | 0.2442 | 98.83 | 5.41 |
| Xanthine | 100.0000 | 101.8549 | 9.2301 | 101.85 | 9.93 |
|  | 800.0000 | 820.4421 | 58.6580 | 102.56 | 7.83 |

Table S6 results of the matrix effect (plasma, n=6)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Compound | Nominal Conc. (ng/ml) | Mean Conc.(ng/ml) | SD(ng/ml) | Mean Recov.(%) | RSD(%) |
|  | 5.0000 | 4.7226 | 0.3527 | 94.45 | 8.18 |
| 1-Oleoyl-sn-glycero-3-phosphocholine | 100.0000 | 103.6410 | 7.5774 | 103.64 | 8.01 |
|  | 800.0000 | 795.0882 | 73.1633 | 99.39 | 10.08 |
|  | 5.0000 | 5.0092 | 0.3805 | 100.18 | 8.32 |
| 2-acetyl-1-alkyl-sn-glycero-3-phosphocholine | 100.0000 | 108.9400 | 2.8856 | 108.94 | 2.90 |
|  | 800.0000 | 839.0804 | 63.2108 | 104.89 | 8.25 |
|  | 5.0000 | 4.7283 | 0.3760 | 94.57 | 8.71 |
| 9-cis-Retinal | 100.0000 | 100.3688 | 8.7473 | 100.37 | 9.55 |
|  | 800.0000 | 795.3982 | 45.9853 | 99.42 | 6.33 |
|  | 5.0000 | 4.7843 | 0.4159 | 95.69 | 9.52 |
| Arachidonic acid | 100.0000 | 103.5776 | 2.8937 | 103.58 | 3.06 |
|  | 800.0000 | 831.0592 | 29.5537 | 103.88 | 3.90 |
|  | 5.0000 | 4.5641 | 0.3119 | 91.28 | 7.49 |
| Carnosine | 100.0000 | 98.4096 | 5.4923 | 98.41 | 6.11 |
|  | 800.0000 | 804.1250 | 62.9869 | 100.52 | 8.58 |
|  | 5.0000 | 5.0369 | 0.5035 | 100.74 | 10.95 |
| Choline phosphate | 100.0000 | 101.1904 | 6.7578 | 101.19 | 7.32 |
|  | 800.0000 | 806.0611 | 35.6584 | 100.76 | 4.85 |
|  | 5.0000 | 4.7900 | 0.3902 | 95.80 | 8.92 |
| CREATINE | 100.0000 | 103.0049 | 7.9994 | 103.00 | 8.51 |
|  | 800.0000 | 768.5393 | 36.7953 | 96.07 | 5.24 |
|  | 5.0000 | 4.6553 | 0.4361 | 93.11 | 10.26 |
| Cytidine | 100.0000 | 111.6099 | 1.6273 | 111.61 | 1.60 |
|  | 800.0000 | 852.0588 | 40.8944 | 106.51 | 5.26 |
|  | 5.0000 | 4.8394 | 0.4240 | 96.79 | 9.60 |
| Dl-Glutamic acid | 100.0000 | 108.3319 | 4.5103 | 108.33 | 4.56 |
|  | 800.0000 | 785.3669 | 68.9310 | 98.17 | 9.61 |
|  | 5.0000 | 4.7059 | 0.4106 | 94.12 | 9.56 |
| Glycocholic acid | 100.0000 | 108.9101 | 4.2186 | 108.91 | 4.24 |
|  | 800.0000 | 768.5872 | 54.4622 | 96.07 | 7.76 |
|  | 5.0000 | 4.8549 | 0.2503 | 97.10 | 5.65 |
| GUANIDINOACETATE | 100.0000 | 101.9646 | 8.3795 | 101.96 | 9.00 |
|  | 800.0000 | 781.4942 | 75.0854 | 97.69 | 10.52 |
|  | 5.0000 | 5.0981 | 0.3796 | 101.96 | 8.16 |
| Hypoxanthine | 100.0000 | 101.3103 | 6.9795 | 101.31 | 7.55 |
|  | 800.0000 | 786.6783 | 55.6891 | 98.33 | 7.75 |
|  | 5.0000 | 4.9393 | 0.3118 | 98.79 | 6.92 |
| L-Methionine | 100.0000 | 104.6467 | 5.6356 | 104.65 | 5.90 |
|  | 800.0000 | 777.7999 | 73.5835 | 97.22 | 10.36 |
|  | 5.0000 | 5.1472 | 0.4889 | 102.94 | 10.40 |
| L-Phenylalanine | 100.0000 | 110.2644 | 3.6811 | 110.26 | 3.66 |
|  | 800.0000 | 714.7411 | 46.6810 | 89.34 | 7.15 |
|  | 5.0000 | 4.8238 | 0.4206 | 96.48 | 9.55 |
| L-Tryptophan | 100.0000 | 98.7538 | 4.4438 | 98.75 | 4.93 |
|  | 800.0000 | 784.4378 | 59.8376 | 98.05 | 8.36 |
|  | 5.0000 | 4.8098 | 0.3555 | 96.20 | 8.10 |
| N-ACETYLNEURAMINATE | 100.0000 | 110.7862 | 4.1599 | 110.79 | 4.11 |
|  | 800.0000 | 768.4429 | 84.3609 | 96.06 | 12.03 |
|  | 5.0000 | 4.3092 | 0.0661 | 86.18 | 1.68 |
| Nicotinamide | 100.0000 | 102.6622 | 3.9579 | 102.66 | 4.22 |
|  | 800.0000 | 769.4637 | 36.2212 | 96.18 | 5.16 |
|  | 5.0000 | 4.8464 | 0.3066 | 96.93 | 6.93 |
| Palmitic acid | 100.0000 | 99.1004 | 7.5978 | 99.10 | 8.40 |
|  | 800.0000 | 804.7804 | 60.7073 | 100.60 | 8.26 |
|  | 5.0000 | 4.9189 | 0.3896 | 98.38 | 8.68 |
| Riboflavin | 100.0000 | 97.3498 | 4.3364 | 97.35 | 4.88 |
|  | 800.0000 | 792.3081 | 72.5636 | 99.04 | 10.03 |
|  | 5.0000 | 4.8017 | 0.2342 | 96.03 | 5.34 |
| Sphingonine 1-phosphate | 100.0000 | 104.0832 | 9.0596 | 104.08 | 9.53 |
|  | 800.0000 | 791.9539 | 70.9785 | 98.99 | 9.82 |
|  | 5.0000 | 4.7779 | 0.2706 | 95.56 | 6.21 |
| Taurocholate | 100.0000 | 99.4533 | 8.8917 | 99.45 | 9.79 |
|  | 800.0000 | 762.6744 | 79.4117 | 95.33 | 11.41 |
|  | 5.0000 | 4.7764 | 0.3474 | 95.53 | 7.97 |
| Tyrosine | 100.0000 | 94.4861 | 6.0496 | 94.49 | 7.01 |
|  | 800.0000 | 853.2629 | 49.7671 | 106.66 | 6.39 |
|  | 5.0000 | 4.8614 | 0.4134 | 97.23 | 9.31 |
| Uridine | 100.0000 | 100.8927 | 7.7020 | 100.89 | 8.36 |
|  | 800.0000 | 765.3946 | 61.7749 | 95.67 | 8.84 |
|  | 5.0000 | 5.0260 | 0.4530 | 100.52 | 9.87 |
| Xanthine | 100.0000 | 100.1333 | 6.2776 | 100.13 | 6.87 |
|  | 800.0000 | 800.6955 | 43.8016 | 100.09 | 5.99 |

Table S7 results of the matrix effect (solvent, n=6)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Compound | Nominal Conc. (ng/ml) | Mean Conc.(ng/ml) | SD(ng/ml) | Mean Recov.(%) | RSD(%) |
|  | 5.0000 | 5.2407 | 0.2359 | 104.81 | 4.93 |
| 1-Oleoyl-sn-glycero-3-phosphocholine | 100.0000 | 99.3769 | 8.7669 | 99.38 | 9.66 |
|  | 800.0000 | 784.3880 | 65.9390 | 98.05 | 9.21 |
|  | 5.0000 | 4.7014 | 0.2956 | 94.03 | 6.89 |
| 2-acetyl-1-alkyl-sn-glycero-3-phosphocholine | 100.0000 | 105.1918 | 4.6726 | 105.19 | 4.87 |
|  | 800.0000 | 812.1185 | 57.8922 | 101.51 | 7.81 |
|  | 5.0000 | 4.7744 | 0.2274 | 95.49 | 5.22 |
| 9-cis-Retinal | 100.0000 | 98.7525 | 8.4181 | 98.75 | 9.34 |
|  | 800.0000 | 801.6938 | 74.7553 | 100.21 | 10.21 |
|  | 5.0000 | 4.7730 | 0.2839 | 95.46 | 6.52 |
| Arachidonic acid | 100.0000 | 102.0728 | 9.2883 | 102.07 | 9.97 |
|  | 800.0000 | 805.0588 | 59.1526 | 100.63 | 8.05 |
|  | 5.0000 | 4.4291 | 0.1681 | 88.58 | 4.16 |
| Carnosine | 100.0000 | 98.7944 | 6.8610 | 98.79 | 7.61 |
|  | 800.0000 | 788.9179 | 52.1620 | 98.61 | 7.24 |
|  | 5.0000 | 5.1464 | 0.3045 | 102.93 | 6.48 |
| Choline phosphate | 100.0000 | 98.4136 | 8.7355 | 98.41 | 9.72 |
|  | 800.0000 | 758.2921 | 57.7879 | 94.79 | 8.35 |
|  | 5.0000 | 5.0946 | 0.3009 | 101.89 | 6.47 |
| CREATINE | 100.0000 | 101.5644 | 9.4656 | 101.56 | 10.21 |
|  | 800.0000 | 744.5939 | 39.8821 | 93.07 | 5.87 |
|  | 5.0000 | 5.4476 | 0.1997 | 108.95 | 4.02 |
| Cytidine | 100.0000 | 113.1528 | 8.1580 | 113.15 | 7.90 |
|  | 800.0000 | 897.3199 | 11.1698 | 112.16 | 1.36 |
|  | 5.0000 | 4.8625 | 0.2636 | 97.25 | 5.94 |
| Dl-Glutamic acid | 100.0000 | 99.7745 | 4.3093 | 99.77 | 4.73 |
|  | 800.0000 | 809.6763 | 49.0250 | 101.21 | 6.63 |
|  | 5.0000 | 4.9753 | 0.3985 | 99.51 | 8.77 |
| Glycocholic acid | 100.0000 | 102.8360 | 6.1317 | 102.84 | 6.53 |
|  | 800.0000 | 799.8524 | 60.0502 | 99.98 | 8.22 |
|  | 5.0000 | 5.0751 | 0.2840 | 101.50 | 6.13 |
| GUANIDINOACETATE | 100.0000 | 99.1428 | 8.3131 | 99.14 | 9.19 |
|  | 800.0000 | 786.6327 | 80.1018 | 98.33 | 11.15 |
|  | 5.0000 | 4.8731 | 0.2435 | 97.46 | 5.47 |
| Hypoxanthine | 100.0000 | 100.2433 | 9.0019 | 100.24 | 9.84 |
|  | 800.0000 | 812.2350 | 68.0438 | 101.53 | 9.18 |
|  | 5.0000 | 5.1258 | 0.2993 | 102.52 | 6.40 |
| L-Methionine | 100.0000 | 100.6228 | 9.0681 | 100.62 | 9.87 |
|  | 800.0000 | 774.0565 | 69.2086 | 96.76 | 9.79 |
|  | 5.0000 | 5.0181 | 0.2190 | 100.36 | 4.78 |
| L-Phenylalanine | 100.0000 | 100.1492 | 6.4070 | 100.15 | 7.01 |
|  | 800.0000 | 740.0702 | 39.7215 | 92.51 | 5.88 |
|  | 5.0000 | 4.7617 | 0.2760 | 95.23 | 6.35 |
| L-Tryptophan | 100.0000 | 99.0505 | 5.8100 | 99.05 | 6.43 |
|  | 800.0000 | 804.5497 | 50.2738 | 100.57 | 6.85 |
|  | 5.0000 | 4.9669 | 0.3596 | 99.34 | 7.93 |
| N-ACETYLNEURAMINATE | 100.0000 | 104.6919 | 5.7906 | 104.69 | 6.06 |
|  | 800.0000 | 810.9373 | 59.2553 | 101.37 | 8.00 |
|  | 5.0000 | 4.5336 | 0.1972 | 90.67 | 4.77 |
| Nicotinamide | 100.0000 | 95.9766 | 7.6584 | 95.98 | 8.74 |
|  | 800.0000 | 729.1707 | 22.2377 | 91.15 | 3.34 |
|  | 5.0000 | 4.8840 | 0.2976 | 97.68 | 6.68 |
| Palmitic acid | 100.0000 | 99.5286 | 5.4027 | 99.53 | 5.95 |
|  | 800.0000 | 816.9222 | 75.1103 | 102.12 | 10.07 |
|  | 5.0000 | 4.8960 | 0.4870 | 97.92 | 10.90 |
| Riboflavin | 100.0000 | 97.4048 | 6.6799 | 97.40 | 7.51 |
|  | 800.0000 | 839.7746 | 61.8402 | 104.97 | 8.07 |
|  | 5.0000 | 5.1444 | 0.2967 | 102.89 | 6.32 |
| Sphingonine 1-phosphate | 100.0000 | 98.7942 | 7.6912 | 98.79 | 8.53 |
|  | 800.0000 | 811.1039 | 75.0804 | 101.39 | 10.14 |
|  | 5.0000 | 4.9338 | 0.4884 | 98.68 | 10.84 |
| Taurocholate | 100.0000 | 102.8637 | 8.9352 | 102.86 | 9.52 |
|  | 800.0000 | 757.5916 | 28.8281 | 94.70 | 4.17 |
|  | 5.0000 | 4.9680 | 0.4047 | 99.36 | 8.92 |
| Tyrosine | 100.0000 | 95.9089 | 9.1291 | 95.91 | 10.43 |
|  | 800.0000 | 869.1789 | 81.2151 | 108.65 | 10.24 |
|  | 5.0000 | 4.7596 | 0.4710 | 95.19 | 10.84 |
| Uridine | 100.0000 | 106.7242 | 3.7830 | 106.72 | 3.88 |
|  | 800.0000 | 769.3508 | 74.7882 | 96.17 | 10.65 |
|  | 5.0000 | 5.0407 | 0.5166 | 100.81 | 11.23 |
| Xanthine | 100.0000 | 101.1086 | 12.8274 | 101.11 | 13.90 |
|  | 800.0000 | 794.2138 | 84.6997 | 99.28 | 11.68 |

Information of components in Gyp

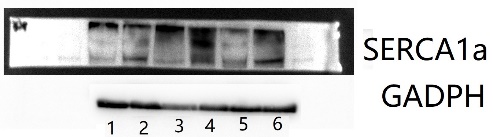
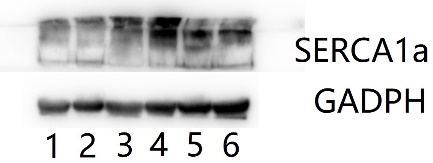
**Components identified by UPLC-TOF-MS**

The UPLC-TOF-MS detection of Gyp extract found 64 compounds accompanied with database that giving higher possibility of compound in each peak (figure 3). For more accurate identification, apart from literature examination that exempt the component impossible to appear in Gyp extract, peak area was used as another criteria for selection, which means peak with less than 0.05% of the total area in corresponding polarity (positive or negative, respectively) was excluded. Through the above-mentioned detection, selection and analysis, compounds namely Rutin, Narcissoside, Quercetin, Isoquercitrin, isorhamnetin, Linoleic acid, Kaempferol, Gypenoside A, Gypenoside XVII and Gypenoside LXXIV, their ion pairs and mass detection parameters were listed in table 1. And the selected components were set as candidates for further evaluation.

**PXR-IL-6 regulatory activity of each candidate compounds**

The PCR results indicated that all the candidate components have significant regulatory effect on PXR expressions (p<0.05), in which, such regulatory were all stimulation; furthermore, the regulatory activity of those compounds were dose-dependent of different extent (figure 4, table S2), indicating that the candidates are all with real regulatory effect other than affecting the target with merely toxicity. For ELISA tests evaluating the candidates’ IL-6 regulation, except rutin, all other 9 components showed obvious regulation (p<0.05) to IL-6 concentration (also dose-dependent); and among those 9 compounds, only Kaempferol was down-regulation, the other 8 was up-regulation. According to the results of PXR-IL-6 regulation, the 9 compounds with both stimulation and regulation effects should all be chosen to experience the next step of investigation, for the reason of their obvious influence on the pathway.

Figure S1 western blot images of three independent experiments



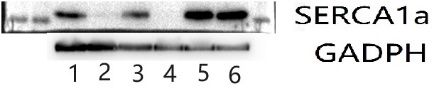


Figure S2, results of metabolite determination in different groups from various matrix, BLK, blank; Sham, sham operation; POS, positive control; GYPL, GYP low dose; GYPM, GYP medium dose; GYPH, GYP high dose.



Figure S3, heat maps for metabolomic analysis, A. Serum, B. Skeletal muscle, C. Liver, D. Kidney, E. Spleen; annotation of the x-axis: C. control, M. Sham, P. Positive control, GL, GYP low dose; GM, GYP medium dose; GH, GYP high dose.



Figure S4, PCA analysis of each group (including both negative and positive ions), A. Serum, B. Skeletal muscle, C. Liver, D. Kidney, E. Spleen; Groups: BLK, blank; Sham, sham operation; POS, positive control; GYPL, GYP low dose; GYPM, GYP medium dose; GYPH, GYP high dose.



Figure S5, PLS-DA analysis of each group (including both negative and positive ions), A. Serum, B. Skeletal muscle, C. Liver, D. Kidney, E. Spleen; Groups: BLK, blank; Sham, sham operation; POS, positive control; GYPL, GYP low dose; GYPM, GYP medium dose; GYPH, GYP high dose.

