marine drugs

MDPI

# Supplementary Materials: Bioactive Oxylipins Profile in Marine Microalgae

All quantification of non-enzymatic and enzymatic oxygenated metabolites of omega-6 and 3 in Mi124, Mi133, Mi134, Mi136 and Mi168 are available as Supplementary Materials, Table S1 for oxygenated metabolites of omega-6 and Table S2 for oxygenated metabolites of omega-3. Data are mean ± sd ($n$ = 3) expressed as ng/mg of dry weight biomass. ND for No Detected.

**Table S1.** Quantification of non-enzymatic and enzymatic oxygenated metabolites of omega-6 in Mi124, Mi133, Mi134, Mi136 and Mi168.

| | Component Name | Mi124 | | Mi133 | | Mi134 | | Mi136 | | Mi168 | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Concentration (ng/mg) | ± SD | Concentration (ng/mg) | ± SD | Concentration (ng/mg) | ± SD | Concentration (ng/mg) | ± SD | Concentration (ng/mg) | ± SD |
| LA | 9-HODE | 37.10 | ± 14.68 | 22.00 | ± 4.86 | 1.71 | ± 0,92 | 9.17 | ± 3.88 | 0.03 | ± 0.10 |
| | 13-HODE | 108.44 | ± 27.71 | 27.29 | ± 6.84 | 3.50 | ± 1.60 | 12.81 | ± 5.05 | 0.48 | ± 0.16 |
| ARA | 5-HETE | 0.53 | ± 0.06 | 66.92 | ± 24.92 | 1.55 | ± 0.67 | 5.11 | ± 5.38 | 5.30 | ± 0.65 |
| | 8-HETE | 0.14 | ± 0.03 | 41.50 | ± 11.29 | 1.28 | ± 0.37 | 3.36 | ± 3.28 | 2.95 | ± 0.68 |
| | 12-HETE | 0.58 | ± 0.07 | 50.96 | ± 17.22 | 2.13 | ± 0.75 | 4.45 | ± 4.30 | 3.44 | ± 0.88 |
| | 15-HETE | 0.75 | ± 0.09 | 53.72 | ± 13.91 | 0.22 | ± 0.09 | 1.00 | ± 0.87 | 0.99 | ± 0.05 |
| | 5,6-DiHETE | ND | ± ND | 0.07 | ± 0.03 | ND | ± ND | ND | ± ND | ND | ± ND |
| | 5oxoETE | 0.07 | ± 0,06 | 15.62 | ± 4.72 | 0.30 | ± 0.09 | 0.49 | ± 0.47 | 0.51 | ± 0.18 |
| | 5,6-EET | ND | ± ND | 6.67 | ± 2.96 | 0.11 | ± 0.02 | 0.19 | ± 0.16 | 0.32 | ± 0.04 |
| | 11,12-EET | ND | ± ND | 17.97 | ± 5.90 | 0.14 | ± 0.02 | 0.22 | ± 0.23 | 0.23 | ± 0.02 |
| | 14,15-EET | 0.06 | ± 0.01 | 14.35 | ± 4.36 | 0.14 | ± 0.03 | 0.23 | ± 0.20 | 0.27 | ± 0.02 |
| | LTB4 | ND | ± ND | 0.39 | ± 0.16 | ND | ± ND | ND | ± ND | ND | ± ND |
| | TXB2 | ND | ± ND | ND | ± ND | ND | ± ND | ND | ± ND | 0.07 | ± 0.01 |
| | PGE2 | ND | ± ND | 0.07 | ± 0.03 | ND | ± ND | ND | ± ND | ND | ± ND |
| | PGF2α | ND | ± ND | 0.34 | ± 0.19 | ND | ± ND | ND | ± ND | ND | ± ND |
| | 8-iso-PGA2 | ND | ± ND | 0.16 | ± 0.10 | ND | ± ND | ND | ± ND | ND | ± ND |
| | 15-d-PGJ2 | 0.70 | ± 0.68 | 0.31 | ± 0.40 | 0.56 | ± 0.16 | 1.09 | ± 0.69 | 2.03 | ± 1.00 |
| | PGD2 | ND | ± ND | 0.45 | ± 0.23 | ND | ± ND | ND | ± ND | ND | ± ND |
| | 15-$A_{2t}$-IsoP | 0.07 | ± 0.02 | 0.03 | ± 0.02 | ND | ± ND | 0.18 | ± 0.07 | 0.25 | ± 0.06 |
| | 5(RS)-5-$F_{2c}$-IsoP | 0.01 | ± < 0.01 | 0.04 | ± 0.02 | 0.10 | ± 0.04 | 0.42 | ± 0.30 | 0.17 | ± 0.05 |
| | 5(RS)-5-$F_{2t}$-IsoP | 0.01 | ± < 0.01 | 0.03 | ± 0.01 | 0.06 | ± 0.02 | 0.24 | ± 0.12 | 0.10 | ± 0.03 |
| | 15-epi-$F_{2t}$-IsoP | ND | ± ND | 0.01 | ± < 0.01 | 0.02 | ± 0.01 | 0.08 | ± 0.04 | 0.03 | ± 0.01 |
| | 15-$F_{2t}$-IsoP | ND | ± ND | < 0.01 | ± < 0.01 | 0.01 | ± 0.01 | 0.05 | ± 0.02 | 0.02 | ± < 0.01 |
| | 2,3-dinor-15-$F_{2t}$-IsoP | 0.01 | ± 0.01 | ND | ± ND | 0.01 | ± < 0.01 | 0.01 | ± < 0.01 | ND | ± ND |
| DPA | 4-$F_{3t}$-NeuroP | 0.04 | ± 0.02 | 0.01 | ± 0.01 | 0.01 | ± < 0.01 | 0.02 | ± < 0.01 | 0.22 | ± 0.09 |

**Table S2.** Quantification of non-enzymatic and enzymatic oxygenated metabolites of omega-3 in Mi124, Mi133, Mi134, Mi136 and Mi168.

| | Component Name | Mi124 | | Mi133 | | Mi134 | | Mi136 | | Mi168 | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Concentration (ng/mg) | ± SD | Concentration (ng/mg) | ± SD | Concentration (ng/mg) | ± SD | Concentration (ng/mg) | ± SD | Concentration (ng/mg) | ± SD |
| ALA | 9(R),16(R,S)-linotrins | 3.52 | ± 0.92 | 6.29 | ± 2.80 | 0.03 | ± 0.01 | ND | ± ND | ND | ± ND |
| | 9-$F_{1t}$-PhytoP | 0.30 | ± 0.16 | 0.04 | ± 0.01 | 0.16 | ± 0.05 | 0.01 | ± < 0.01 | 0.01 | ± < 0.01 |
| | ent-16-$F_{1t}$-PhytoP | 0.49 | ± 0.12 | 0.08 | ± 0.08 | 0.08 | ± 0.02 | 0.01 | ± < 0.01 | 0.43 | ± 0.02 |
| | ent-16-epi-16-$F_{1t}$-PhytoP | 0.40 | ± 0.11 | 0.07 | ± 0.05 | 0.09 | ± 0.02 | 0.13 | ± 0.10 | 0.32 | ± 0.02 |
| | 16$B_{1t}$-PhytoP | 0.68 | ± 0.41 | 0.02 | ± 0.03 | 0.25 | ± 0.09 | 0.01 | ± < 0.01 | 0.02 | ± < 0.01 |
| | 9$L_{1t}$-PhytoP | 0.58 | ± 0.34 | 0.02 | ± 0.02 | 0.22 | ± 0.09 | 0.01 | ± < 0.01 | 0.02 | ± < 0.01 |
| | ent-16(A)-13-epi-ST-$\Delta^{14}$-9-PhytoF | 0.06 | ± 0.04 | ND | ± ND | ND | ± ND | 0.02 | ± 0.01 | < 0.01 | ± < 0.01 |
| | ent-16(B)-13-epi-ST-$\Delta^{14}$-9-PhytoF | 0.15 | ± 0.10 | ND | ± ND | ND | ± ND | 0.03 | ± 0.02 | < 0.01 | ± < 0.01 |
| | ent-16(A)-9-epi-ST-$\Delta^{14}$-10-PhytoF | 0.26 | ± 0.08 | < 0.01 | ±< 0.01 | 0.10 | ± 0.02 | 0.11 | ± 0.07 | 0.01 | ± < 0.01 |
| | ent-16(B)-9-epi-ST-$\Delta^{14}$-10-PhytoF | 0.40 | ± 0.15 | 0.01 | ± 0.01 | 0.17 | ± 0.03 | 0.16 | ± 0.10 | 0.01 | ± < 0.01 |
| | ent-9(A)-12-epi-ST-$\Delta^{10}$-13-PhytoF | 0.14 | ± 0.06 | ND | ± ND | 0.05 | ± 0.01 | 0.07 | ± 0.04 | 0.01 | ± < 0.01 |
| | ent-9(B)-12-epi-ST-$\Delta^{10}$-13-PhytoF | 0.08 | ± 0.05 | ND | ± ND | 0.02 | ± < 0.01 | 0.03 | ± 0.02 | < 0.01 | ± < 0.01 |
| EPA | 18-HEPE | 2.28 | ± 0.45 | 39.47 | ± 14.65 | 0.30 | ± 0.14 | 78.61 | ± 3.10 | 39.96 | ± 3.07 |
| | 5(R)-5-$F_{3t}$-IsoP | 0.08 | ± 0.03 | 0.20 | ± 0.21 | 0.01 | ± 0.01 | 2.59 | ± 3.52 | 2.24 | ± 0.70 |
| | 5(S)-5-$F_{3t}$-IsoP | 0.03 | ± 0.01 | 0.05 | ± 0.06 | 0.02 | ± < 0.01 | 0.37 | ± 0.45 | 0.69 | ± 0.20 |
| | 8(R)-8-$F_{3t}$-IsoP | ND | ± ND | 0.01 | ± 0.01 | 0.01 | ± < 0.01 | 0.13 | ± 0.16 | 0.14 | ± 0.04 |
| | 8(S)-8-$F_{3t}$-IsoP | ND | ± ND | 0.01 | ± 0.01 | ND | ± ND | 0.10 | ± 0.13 | 0.08 | ± 0.03 |
| | 18(R)-18-$F_{3t}$-IsoP | 0.05 | ± 0.02 | 0.03 | ± 0.04 | 0.05 | ± 0.02 | 0.56 | ± 0.67 | 0.38 | ± 0.01 |
| | 18(S)-18-$F_{3t}$-IsoP | ND | ± ND | 0.01 | ± 0,02 | ND | ± ND | 0.56 | ± 0.72 | 0.18 | ± 0.05 |
| DHA | 14-HDoHE | 7.44 | ± 1.34 | ND | ± ND | 1.90 | ± 0.12 | 0.95 | ± 0.42 | 7.22 | ± 0.74 |
| | 17-HDoHE | 45.86 | ± 6.62 | ND | ± ND | 1.58 | ± 0.22 | 1.12 | ± 0.30 | 11.41 | ± 2.33 |
| | $RvD_2$ | ND | ± ND | ND | ± ND | ND | ± ND | 0.15 | ± 0.04 | ND | ± ND |
| | PDx | 1.26 | ± 0.62 | ND | ± ND | ND | ± ND | ND | ± ND | 0.10 | ± 0.03 |
| | 4(RS)-4-$F_{4t}$-NeuroP | 0.12 | ± 0.06 | 0.01 | ± 0.01 | 0.08 | ± 0.01 | 0.12 | ± 0.05 | 0.17 | ± 0.07 |
| | 10(R)-$F_{4t}$-NeuroP | 0.12 | ± 0.07 | ND | ± ND | 0.06 | ± 0.01 | 0.10 | ± 0.04 | 0.16 | ± 0.06 |
| | 10(S)-$F_{4t}$-NeuroP | 0.07 | ± 0.04 | ND | ± ND | 0.03 | ± 0.01 | 0.05 | ± 0.02 | 0.09 | ± 0.04 |
| | 13(A)-13-$F_{4t}$-NeuroP | 0.13 | ± 0.08 | ND | ± ND | 0.10 | ± 0.01 | 0.11 | ± 0.04 | 0.16 | ± 0.06 |
| | 13(B)-13-$F_{4t}$-NeuroP | 0.16 | ± 0.09 | ND | ± ND | 0.07 | ± 0.02 | 0.11 | ± 0.03 | 0.16 | ± 0.06 |
| | 14(R)-14-$F_{4t}$-NeuroP | 0.04 | ± 0.02 | ND | ± ND | 0.03 | ± 0.01 | 0.04 | ± 0.01 | 0.06 | ± 0.02 |
| | 14(S)-14-$F_{4t}$-NeuroP | 0.06 | ± 0.03 | ND | ± ND | 0.03 | ± 0.02 | 0.04 | ± 0.01 | 0.05 | ± 0.02 |
| | 20(R)-20-$F_{4t}$-NeuroP | 0.08 | ± 0.03 | ND | ± ND | 0.04 | ± 0.01 | 0.06 | ± 0.01 | 0.09 | ± 0.01 |
| | 20(S)-20-$F_{4t}$-NeuroP | ND | ± ND | ND | ± ND | 0.30 | ± 0.02 | 0.21 | ± 0.07 | 0.13 | ± 0.02 |

The measured ER, ME and PE at high concentrations are available as Supplementary Materials, Table S3 for Mi124, Table S4 for Mi133, Table S5 for Mi134, Table S6 for Mi136 and Table S7 for Mi168.

**Table S3.** The efficiency of sample preparation of Mi124 with the extraction recovery (ER), the matrix effect (ME) and the global process efficiency (PE).

| Compound | Concentration (ng/mL) | Extraction recovery (ER) | ± | SD | Matrix Effect (ME) | ± | SD | Process Efficiency (PE) | ± | SD |
|---|---|---|---|---|---|---|---|---|---|---|
| D4-10(*R*)-10$F_{4t}$ NeuroP | 40 | 38.91% | ± | 17.37% | 59.81% | ± | 6.78% | 23.27% | ± | 17.02% |
| D4-15-$F_{2t}$-IsoP | 40 | 35.29% | ± | 15.60% | 70.07% | ± | 4.78% | 24.73% | ± | 16.71% |
| C21 15$F_{2t}$ IsoP | 40 | 41.01% | ± | 17.79% | 62.12% | ± | 6.22% | 25.47% | ± | 17.77% |
| C19 16-$F_{1t}$-PhytoP | 40 | 38.13% | ± | 17.93% | 62.67% | ± | 6.56% | 23.90% | ± | 15.96% |
| 15-$A_{2t}$-IsoP | 200 | 0.88% | ± | 28.40% | 50.28% | ± | 3.23% | 0.44% | ± | 26.20% |
| 5(*RS*)-5-$F_{2c}$-IsoP | 200 | 54.64% | ± | 9.01% | 73.44% | ± | 4.56% | 40.12% | ± | 5.06% |
| 5(*RS*)-5-$F_{2t}$-IsoP | 200 | 64.03% | ± | 8.87% | 71.78% | ± | 6.17% | 45.96% | ± | 3.70% |
| 2.3-*dinor*-15-$F_{2t}$-IsoP | 200 | 52.43% | ± | 13.53% | 80.73% | ± | 9.98% | 42.33% | ± | 5.29% |
| 4-$F_{3t}$-NeuroP | 200 | 58.05% | ± | 13.36% | 58.37% | ± | 4.68% | 33.89% | ± | 9.36% |
| 9-$F_{1t}$-PhytoP | 200 | 45.92% | ± | 9.78% | 80.86% | ± | 5.13% | 37.13% | ± | 6.25% |
| *ent*-16-*epi*-16-$F_{1t}$-PhytoP | 200 | 48.77% | ± | 8.90% | 76.89% | ± | 4.12% | 37.50% | ± | 6.56% |
| *ent*-16-$F_{1t}$-PhytoP | 200 | 46.65% | ± | 12.63% | 49.03% | ± | 5.71% | 22.87% | ± | 9.40% |
| 16$B_{1t}$-PhytoP | 200 | 51.80% | ± | 10.72% | 65.66% | ± | 4.42% | 34.01% | ± | 6.82% |
| 9$L_{1t}$-PhytoP | 200 | 79.74% | ± | 9.64% | 72.21% | ± | 4.42% | 57.58% | ± | 6.55% |
| *ent*-16(*A*)-13-*epi*-ST-$\Delta^{14}$-9-PhytoF | 200 | 45.81% | ± | 7.02% | 82.34% | ± | 3.94% | 37.72% | ± | 5.58% |
| *ent*-16(*B*)-13-*epi*-ST-$\Delta^{14}$-9-PhytoF | 200 | 43.82% | ± | 8.77% | 83.15% | ± | 4.34% | 36.43% | ± | 8.08% |
| *ent*-16(*A*)-9-*epi*-ST-$\Delta^{14}$-10-PhytoF | 200 | 47.71% | ± | 12.22% | 74.13% | ± | 4.88% | 35.37% | ± | 9.79% |
| *ent*-16(*B*)-9-*epi*-ST-$\Delta^{14}$-10-PhytoF | 200 | 49.56% | ± | 7.57% | 17.60% | ± | 4.75% | 8.72% | ± | 6.09% |
| *ent*-9(*A*)-12-*epi*-ST-$\Delta^{10}$-13-PhytoF | 200 | 44.02% | ± | 8.72% | 80.75% | ± | 3.19% | 35.55% | ± | 7.13% |
| *ent*-9(*B*)-12-*epi*-ST-$\Delta^{10}$-13-PhytoF | 200 | 44.30% | ± | 8.73% | 81.71% | ± | 5.88% | 36.20% | ± | 7.07% |
| 5(*R*)-5-$F_{3t}$-IsoP | 200 | 95.73% | ± | 10.87% | 42.29% | ± | 9.38% | 40.48% | ± | 8.55% |
| 5(*S*)-5-$F_{3t}$-IsoP | 200 | 64.96% | ± | 10.33% | 73.36% | ± | 6.11% | 47.65% | ± | 7.44% |
| 18(*R*)-18-$F_{3t}$-IsoP | 200 | 52.56% | ± | 8.17% | 87.09% | ± | 4.59% | 45.77% | ± | 6.43% |
| 4(*RS*)-4-$F_{4t}$-NeuroP | 200 | 52.65% | ± | 12.20% | 68.02% | ± | 4.61% | 35.81% | ± | 8.28% |
| 10(*R*)-$F_{4t}$-NeuroP | 200 | 53.23% | ± | 10.94% | 73.78% | ± | 5.44% | 39.28% | ± | 6.88% |
| 10(*S*)-$F_{4t}$-NeuroP | 200 | 51.27% | ± | 12.51% | 55.04% | ± | 7.90% | 28.22% | ± | 7.58% |
| 13(*A*)-13-$F_{4t}$-NeuroP | 200 | 53.43% | ± | 9.87% | 73.35% | ± | 5.35% | 39.19% | ± | 6.60% |
| 13(*B*)-13-$F_{4t}$-NeuroP | 200 | 50.37% | ± | 13.46% | 56.89% | ± | 5.81% | 28.65% | ± | 8.51% |
| 14(*S*)-14-$F_{4t}$-NeuroP | 200 | 50.56% | ± | 11.36% | 64.50% | ± | 7.07% | 32.61% | ± | 6.43% |
| 14(*S*)-14-$F_{4t}$-NeuroP | 200 | 50.15% | ± | 10.07% | 61.38% | ± | 5.65% | 30.78% | ± | 4.94% |
| 20(*R*)-20-$F_{4t}$-NeuroP | 200 | 49.07% | ± | 11.22% | 71.90% | ± | 7.18% | 35.28% | ± | 8.37% |

**Table S4.** The efficiency of sample preparation of Mi133 with the extraction recovery (ER), the matrix effect (ME) and the global process efficiency (PE).

| Compound | Concentration (ng/mL) | Extraction recovery (ER) | ± | SD | Matrix Effect (ME) | ± | SD | Process Efficiency (PE) | ± | SD |
|---|---|---|---|---|---|---|---|---|---|---|
| D4-10(*R*)-10$F_{4t}$ NeuroP | 40 | 80.67% | ± | 7.55% | 71.09% | ± | 7.04% | 57.35% | ± | 6.93% |
| D4-15-$F_{2t}$-IsoP | 40 | 74.52% | ± | 6.75% | 71.43% | ± | 6.22% | 53.23% | ± | 6.42% |
| C21 15$F_{2t}$ IsoP | 40 | 87.92% | ± | 6.74% | 66.22% | ± | 5.82% | 58.22% | ± | 7.12% |
| C19 16-$F_{1t}$-PhytoP | 40 | 76.38% | ± | 5.51% | 79.48% | ± | 4.56% | 60.71% | ± | 5.53% |
| 15-$A_{2t}$-IsoP | 200 | -23.79% | ± | 8.76% | 40.82% | ± | 14.24% | -9.71% | ± | 0.01% |
| 5(*RS*)-5-$F_{2c}$-IsoP | 200 | 88.89% | ± | 9.55% | 104.26% | ± | 6.24% | 92.68% | ± | 3.91% |
| 5(*RS*)-5-$F_{2t}$-IsoP | 200 | 89.63% | ± | 5.22% | 58.16% | ± | 4.95% | 52.13% | ± | 1.28% |
| 15-*epi*-$F_{2t}$-IsoP | 200 | 147.08% | ± | 4.54% | 41.06% | ± | 2.18% | 60.39% | ± | 3.86% |
| 2.3-*dinor*-15-$F_{2t}$-IsoP | 200 | 65.05% | ± | 1.87% | 86.64% | ± | 2.44% | 56.36% | ± | 1.17% |
| 4-$F_{3t}$-NeuroP | 200 | 81.56% | ± | 6.64% | 92.24% | ± | 7.54% | 50.52% | ± | 3.54% |
| 9-$F_{1t}$-PhytoP | 200 | 65.83% | ± | 2.33% | 87.22% | ± | 2.44% | 57.42% | ± | 1.50% |
| *ent*-16-$F_{1t}$-PhytoP | 200 | 70.85% | ± | 3.35% | 78.60% | ± | 3.20% | 55.69% | ± | 2.63% |
| *ent*-16-*epi*-16-$F_{1t}$-PhytoP | 200 | 66.80% | ± | 2.81% | 81.03% | ± | 2.45% | 54.13% | ± | 2.13% |
| 16$B_{1t}$-PhytoP | 200 | 75.58% | ± | 3.89% | 77.32% | ± | 2.56% | 58.44% | ± | 1.85% |
| 9$L_{1t}$-PhytoP | 200 | 103.72% | ± | 2.98% | 79.65% | ± | 2.42% | 82.62% | ± | 1.89% |
| *ent*-16(*A*)-9-*epi*-ST-$\Delta^{14}$-10-PhytoF | 200 | 67.98% | ± | 2.87% | 84.45% | ± | 3.40% | 57.41% | ± | 1.92% |
| *ent*-16(*B*)-9-*epi*-ST-$\Delta^{14}$-10-PhytoF | 200 | 67.18% | ± | 3.33% | 91.24% | ± | 4.05% | 61.29% | ± | 2.55% |
| 5(*R*)-5-$F_{3t}$-IsoP | 200 | 160.07% | ± | 9.97% | 54.38% | ± | 11.14% | 87.05% | ± | 5.89% |
| 5(*S*)-5-$F_{3t}$-IsoP | 200 | 87.57% | ± | 9.44% | 41.63% | ± | 8.66% | 36.45% | ± | 4.00% |
| 8(*R*)-8-$F_{3t}$-IsoP | 200 | 71.63% | ± | 4.23% | 79.59% | ± | 3.91% | 57.01% | ± | 1.47% |
| 8(*S*)-8-$F_{3t}$-IsoP | 200 | 68.77% | ± | 3.69% | 82.92% | ± | 2.98% | 57.03% | ± | 2.36% |
| 18(*R*)-18-$F_{3t}$-IsoP | 200 | 72.48% | ± | 5.71% | 72.27% | ± | 5.40% | 52.38% | ± | 3.17% |
| 4(*RS*)-4-$F_{4t}$-NeuroP | 200 | 78.15% | ± | 3.15% | 76.29% | ± | 2.69% | 59.62% | ± | 1.13% |

**Table S5.** The efficiency of sample preparation of Mi134 with the extraction recovery (ER), the matrix effect (ME) and the global process efficiency (PE).

| Compound | Concentration (ng/mL) | Extraction Recovery (ER) | ± | SD | Matrix Effect (ME) | ± | SD | Process Efficiency (PE) | ± | SD |
|---|---|---|---|---|---|---|---|---|---|---|
| D4-10(*R*)-10$F_{4t}$ NeuroP | 40 | 55.54% | ± | 8.38% | 54.81% | ± | 7.14% | 30.44% | ± | 7.66% |
| D4-15-$F_{2t}$-IsoP | 40 | 42.87% | ± | 6.53% | 65.08% | ± | 4.49% | 27.90% | ± | 7.93% |
| C21 15$F_{2t}$ IsoP | 40 | 52.93% | ± | 7.91% | 59.89% | ± | 6.77% | 31.70% | ± | 7.35% |
| C19 16-$F_{1t}$-PhytoP | 40 | 37.62% | ± | 6.82% | 62.49% | ± | 5.51% | 23.51% | ± | 5.89% |
| 5(*RS*)-5-$F_{2c}$-IsoP | 200 | 42.23% | ± | 21.23% | 66.73% | ± | 9.58% | 28.18% | ± | 12.26% |
| 5(*RS*)-5-$F_{2t}$-IsoP | 200 | 49.78% | ± | 22.63% | 60.39% | ± | 11.91% | 30.06% | ± | 11.72% |
| 15-*epi*-$F_{2t}$-IsoP | 200 | 37.06% | ± | 16.36% | 59.49% | ± | 7.82% | 22.05% | ± | 10.04% |
| 15(*RS*)-15-$F_{2t}$-IsoP | 200 | 41.84% | ± | 17.09% | 69.97% | ± | 5.98% | 29.27% | ± | 12.45% |
| 2.3-*dinor*-15-$F_{2t}$-IsoP | 200 | 36.26% | ± | 18.34% | 77.73% | ± | 6.00% | 28.19% | ± | 14.07% |
| 4-$F_{3t}$-NeuroP | 200 | 56.41% | ± | 19.57% | 48.37% | ± | 12.46% | 27.29% | ± | 7.80% |
| 9-$F_{1t}$-PhytoP | 200 | 29.75% | ± | 18.83% | 81.36% | ± | 3.39% | 24.20% | ± | 17.04% |
| *ent*-16-$F_{1t}$-PhytoP | 200 | 32.78% | ± | 21.35% | 77.42% | ± | 8.09% | 25.38% | ± | 15.74% |
| *ent*-16-*epi*-16-$F_{1t}$-PhytoP | 200 | 31.57% | ± | 18.34% | 80.52% | ± | 4.66% | 25.42% | ± | 15.45% |
| 16$B_{1t}$-PhytoP | 200 | 44.10% | ± | 17.67% | 70.42% | ± | 5.92% | 31.06% | ± | 12.27% |
| 9$L_{1t}$-PhytoP | 200 | 65.16% | ± | 13.99% | 99.10% | ± | 8.09% | 65.16% | ± | 13.99% |
| *ent*-16(*A*)-9-*epi*-ST-$\Delta^{14}$-10-PhytoF | 200 | 32.00% | ± | 25.01% | 72.15% | ± | 6.30% | 23.09% | ± | 21.15% |
| *ent*-16(*B*)-9-*epi*-ST-$\Delta^{14}$-10-PhytoF | 200 | 28.82% | ± | 24.28% | 79.68% | ± | 3.11% | 22.96% | ± | 24.44% |
| *ent*-9(*A*)-12-*epi*-ST-$\Delta^{10}$-13-PhytoF | 200 | 32.41% | ± | 19.87% | 75.76% | ± | 4.54% | 24.55% | ± | 16.93% |
| *ent*-9(*B*)-12-*epi*-ST-$\Delta^{10}$-13-PhytoF | 200 | 31.91% | ± | 19.57% | 70.56% | ± | 7.81% | 22.52% | ± | 15.97% |
| 5(*S*)-5-$F_{3t}$-IsoP | 200 | 46.04% | ± | 22.36% | 73.67% | ± | 9.70% | 33.92% | ± | 15.89% |
| 8(*R*)-8-$F_{3t}$-IsoP | 200 | 34.49% | ± | 19.06% | 53.79% | ± | 8.10% | 18.55% | ± | 12.11% |
| 18(*R*)-18-$F_{3t}$-IsoP | 200 | 39.56% | ± | 21.55% | 76.86% | ± | 8.09% | 30.41% | ± | 16.32% |
| 4(*RS*)-4-$F_{4t}$-NeuroP | 200 | 42.01% | ± | 19.03% | 66.63% | ± | 7.13% | 27.99% | ± | 12.59% |
| 10(*R*)-$F_{4t}$-NeuroP | 200 | 44.52% | ± | 18.14% | 68.41% | ± | 7.67% | 30.45% | ± | 11.86% |
| 10(*S*)-$F_{4t}$-NeuroP | 200 | 39.87% | ± | 16.43% | 64.27% | ± | 8.74% | 25.63% | ± | 10.67% |
| 13(*A*)-13-$F_{4t}$-NeuroP | 200 | 50.35% | ± | 22.67% | 64.16% | ± | 11.79% | 32.30% | ± | 12.96% |
| 13(*B*)-13-$F_{4t}$-NeuroP | 200 | 38.74% | ± | 24.05% | 67.53% | ± | 10.88% | 26.16% | ± | 14.03% |
| 14(*R*)-14-$F_{4t}$-NeuroP | 200 | 44.64% | ± | 19.04% | 61.02% | ± | 11.20% | 27.24% | ± | 9.98% |
| 14(*S*)-14-$F_{4t}$-NeuroP | 200 | 50.15% | ± | 10.07% | 61.38% | ± | 5.65% | 30.78% | ± | 4.94% |
| 20(*R*)-20-$F_{4t}$-NeuroP | 200 | 50.00% | ± | 25.04% | 61.55% | ± | 16.56% | 30.78% | ± | 12.80% |
| 20(*S*)-20-$F_{4t}$-NeuroP | 200 | 45.89% | ± | 19.81% | 64.93% | ± | 10.39% | 29.80% | ± | 10.13% |

**Table S6.** The efficiency of sample preparation of Mi136 with the extraction recovery (ER), the matrix effect (ME) and the global process efficiency (PE).

| Compound | Concentration (ng/mL) | Extraction Recovery (ER) | ± | SD | Matrix Effect (ME) | ± | SD | Process Efficiency (PE) | ± | SD |
|---|---|---|---|---|---|---|---|---|---|---|
| D4-10(*R*)-10$F_{4t}$ NeuroP | 40 | 82.07% | ± | 4.21% | 51.93% | ± | 4.91% | 42.62% | ± | 5.72% |
| D4-15-$F_{2t}$-IsoP | 40 | 78.51% | ± | 5.83% | 50.73% | ± | 5.49% | 39.83% | ± | 6.22% |
| C21 15$F_{2t}$ IsoP | 40 | 90.87% | ± | 4.54% | 55.11% | ± | 4.91% | 50.08% | ± | 5.83% |
| C19 16-$F_{1t}$-PhytoP | 40 | 76.65% | ± | 4.27% | 60.82% | ± | 3.75% | 46.62% | ± | 5.11% |
| 15-$A_{2t}$-IsoP | 200 | 68.81% | ± | 17.28% | 89.51% | ± | 12.58% | 61.59% | ± | 5.72% |
| 5(*RS*)-5-$F_{2c}$-IsoP | 200 | 81.15% | ± | 12.65% | 37.35% | ± | 10.39% | 30.31% | ± | 2.87% |
| 5(*RS*)-5-$F_{2t}$-IsoP | 200 | 98.67% | ± | 12.21% | 43.11% | ± | 9.65% | 42.54% | ± | 3.57% |
| 15-*epi*-$F_{2t}$-IsoP | 200 | 82.79% | ± | 9.39% | 33.69% | ± | 7.53% | 27.89% | ± | 3.36% |
| 15(*RS*)-15-$F_{2t}$-IsoP | 200 | 79.10% | ± | 10.33% | 39.76% | ± | 8.37% | 31.45% | ± | 3.30% |
| 2.3-*dinor*-15-$F_{2t}$-IsoP | 200 | 69.04% | ± | 11.82% | 81.33% | ± | 11.71% | 56.15% | ± | 7.21% |
| 4-$F_{3t}$-NeuroP | 200 | 113.11% | ± | -58.42% | -0.14% | ± | -13.89% | -0.14% | ± | 13.89% |
| 9-$F_{1t}$-PhytoP | 200 | 62.59% | ± | 15.14% | 50.80% | ± | 9.21% | 31.79% | ± | 7.53% |
| *ent*-16-*epi*-16-$F_{1t}$-PhytoP | 200 | 62.09% | ± | 16.16% | 52.12% | ± | 9.34% | 32.36% | ± | 8.58% |
| *ent*-16-$F_{1t}$-PhytoP | 200 | 60.97% | ± | 13.78% | 37.76% | ± | 9.00% | 23.02% | ± | 7.26% |
| 16$B_{1t}$-PhytoP | 200 | 79.07% | ± | 13.18% | 45.73% | ± | 9.45% | 36.16% | ± | 4.24% |
| 9$L_{1t}$-PhytoP | 200 | 107.07% | ± | 11.38% | 48.20% | ± | 8.78% | 51.61% | ± | 3.93% |
| *ent*-16(*A*)-13-*epi*-ST-$\Delta^{14}$-9-PhytoF | 200 | 52.89% | ± | 16.44% | 33.31% | ± | 10.72% | 17.62% | ± | 13.14% |
| *ent*-16(*B*)-13-*epi*-ST-$\Delta^{14}$-9-PhytoF | 200 | 55.01% | ± | 16.85% | 43.47% | ± | 11.73% | 23.92% | ± | 12.55% |
| *ent*-16(*A*)-9-*epi*-ST-$\Delta^{14}$-10-PhytoF | 200 | 58.07% | ± | 17.30% | 49.31% | ± | 9.03% | 28.63% | ± | 10.73% |
| *ent*-16(*B*)-9-*epi*-ST-$\Delta^{14}$-10-PhytoF | 200 | 59.93% | ± | 17.94% | 51.42% | ± | 9.48% | 30.81% | ± | 11.74% |
| *ent*-9(*A*)-12-*epi*-ST-$\Delta^{10}$-13-PhytoF | 200 | 52.88% | ± | 19.14% | 48.01% | ± | 8.80% | 25.39% | ± | 11.93% |
| *ent*-9(*B*)-12-*epi*-ST-$\Delta^{10}$-13-PhytoF | 200 | 53.34% | ± | 19.24% | 45.23% | ± | 11.07% | 24.12% | ± | 12.39% |
| 5(*R*)-5-$F_{3t}$-IsoP | 200 | 172.34% | ± | 190.74% | 4.75% | ± | 77.42% | 8.19% | ± | 120.38% |
| 5(*S*)-5-$F_{3t}$-IsoP | 200 | 58.68% | ± | 36.37% | 58.57% | ± | 18.26% | 34.37% | ± | 21.34% |
| 8(*R*)-8-$F_{3t}$-IsoP | 200 | 78.97% | ± | 12.33% | 42.01% | ± | 9.01% | 33.17% | ± | 4.47% |
| 8(*S*)-8-$F_{3t}$-IsoP | 200 | 75.60% | ± | 12.59% | 44.72% | ± | 9.41% | 33.81% | ± | 4.84% |
| 18(*R*)-18-$F_{3t}$-IsoP | 200 | 74.84% | ± | 21.46% | 47.51% | ± | 11.23% | 35.56% | ± | 13.08% |
| 18(*S*)-18-$F_{3t}$-IsoP | 200 | 74.34% | ± | 14.29% | 41.40% | ± | 10.53% | 30.77% | ± | 5.33% |
| 4(*RS*)-4-$F_{4t}$-NeuroP | 200 | 85.45% | ± | 9.81% | 37.52% | ± | 8.25% | 32.06% | ± | 2.24% |
| 10(*R*)-$F_{4t}$-NeuroP | 200 | 85.66% | ± | 11.47% | 48.81% | ± | 9.42% | 41.81% | ± | 3.44% |
| 10(*S*)-$F_{4t}$-NeuroP | 200 | 78.84% | ± | 12.45% | 44.68% | ± | 10.54% | 35.22% | ± | 4.89% |
| 13(*A*)-13-$F_{4t}$-NeuroP | 200 | 91.37% | ± | 11.19% | 42.67% | ± | 9.56% | 38.98% | ± | 3.71% |
| 13(*B*)-13-$F_{4t}$-NeuroP | 200 | 84.34% | ± | 13.67% | 41.66% | ± | 10.81% | 35.14% | ± | 3.72% |
| 14(*R*)-14-$F_{4t}$-NeuroP | 200 | 82.12% | ± | 10.59% | 40.70% | ± | 9.45% | 33.42% | ± | 3.28% |
| 14(*S*)-14-$F_{4t}$-NeuroP | 200 | 82.11% | ± | 9.39% | 39.83% | ± | 8.53% | 32.70% | ± | 1.38% |
| 20(*R*)-20-$F_{4t}$-NeuroP | 200 | 78.31% | ± | 11.99% | 45.13% | ± | 10.90% | 35.34% | ± | 5.41% |
| 20(*S*)-20-$F_{4t}$-NeuroP | 200 | 83.12% | ± | 11.69% | 44.84% | ± | 9.65% | 37.28% | ± | 2.75% |

**Table S7.** The efficiency of sample preparation of Mi168 with the extraction recovery (ER), the matrix effect (ME) and the global process efficiency (PE).

| Compound | Concentration (ng/mL) | Extraction Recovery (ER) | ± | SD | Matrix Effect (ME) | ± | SD | Process Efficiency (PE) | ± | SD |
|---|---|---|---|---|---|---|---|---|---|---|
| D4-10(*R*)-10$F_{4t}$ NeuroP | 40 | 51.10% | ± | 6.87% | 88.90% | ± | 5.80% | 45.43% | ± | 7.50% |
| D4-15-$F_{2t}$-IsoP | 40 | 43.52% | ± | 5.21% | 78.45% | ± | 5.04% | 34.14% | ± | 6.06% |
| C21 15$F_{2t}$ IsoP | 40 | 46.43% | ± | 5.91% | 89.91% | ± | 5.30% | 41.74% | ± | 6.81% |
| C19 16-$F_{1t}$-PhytoP | 40 | 42.30% | ± | 6.32% | 84.63% | ± | 4.53% | 35.80% | ± | 6.38% |
| 15-$A_{2t}$-IsoP | 200 | 0.18% | ± | 46.31% | 45.88% | ± | 6.21% | 0.08% | ± | 41.12% |
| 5(*RS*)-5-$F_{2c}$-IsoP | 200 | 45.40% | ± | 6.22% | 87.24% | ± | 2.29% | 39.61% | ± | 4.54% |
| 5(*RS*)-5-$F_{2t}$-IsoP | 200 | 68.78% | ± | 6.54% | 88.22% | ± | 3.06% | 60.68% | ± | 4.49% |
| 15-*epi*-$F_{2t}$-IsoP | 200 | 46.12% | ± | 4.61% | 76.88% | ± | 1.63% | 35.46% | ± | 4.48% |
| 15(*RS*)-15-$F_{2t}$-IsoP | 200 | 48.31% | ± | 4.63% | 82.66% | ± | 2.09% | 39.94% | ± | 3.89% |
| 4-$F_{3t}$-NeuroP | 200 | 66.12% | ± | 7.80% | 79.63% | ± | 2.48% | 52.65% | ± | 6.00% |
| 9-$F_{1t}$-PhytoP | 200 | 36.03% | ± | 5.34% | 85.09% | ± | 2.98% | 30.66% | ± | 3.97% |
| *ent*-16-*epi*-16-$F_{1t}$-PhytoP | 200 | 35.51% | ± | 6.38% | 89.44% | ± | 2.84% | 31.76% | ± | 5.31% |
| *ent*-16-$F_{1t}$-PhytoP | 200 | 40.69% | ± | 5.97% | 93.42% | ± | 3.43% | 38.01% | ± | 5.03% |
| 16$B_{1t}$-PhytoP | 200 | 65.97% | ± | 7.17% | 86.07% | ± | 1.59% | 56.78% | ± | 6.10% |
| 9$L_{1t}$-PhytoP | 200 | 92.23% | ± | 5.08% | 88.92% | ± | 1.67% | 82.02% | ± | 4.73% |
| *ent*-16(*A*)-13-*epi*-ST-$\Delta^{14}$-9-PhytoF | 200 | 61.33% | ± | 7.74% | 84.47% | ± | 3.23% | 51.80% | ± | 7.00% |
| *ent*-16(*B*)-13-*epi*-ST-$\Delta^{14}$-9-PhytoF | 200 | 60.39% | ± | 7.17% | 87.43% | ± | 2.56% | 52.80% | ± | 8.27% |
| *ent*-16(*A*)-9-*epi*-ST-$\Delta^{14}$-10-PhytoF | 200 | 57.74% | ± | 6.36% | 81.58% | ± | 2.34% | 47.10% | ± | 6.47% |
| *ent*-9(*A*)-12-*epi*-ST-$\Delta^{10}$-13-PhytoF | 200 | 59.67% | ± | 7.66% | 82.83% | ± | 2.32% | 49.43% | ± | 6.94% |
| *ent*-9(*B*)-12-*epi*-ST-$\Delta^{10}$-13-PhytoF | 200 | 59.56% | ± | 7.21% | 81.96% | ± | 2.92% | 48.82% | ± | 8.51% |
| 5(*R*)-5-$F_{3t}$-IsoP | 200 | 114.06% | ± | 10.48% | 53.15% | ± | 7.48% | 60.63% | ± | 10.06% |
| 5(*S*)-5-$F_{3t}$-IsoP | 200 | 55.58% | ± | 13.08% | 79.99% | ± | 10.81% | 44.46% | ± | 5.50% |
| 8(*R*)-8-$F_{3t}$-IsoP | 200 | 54.22% | ± | 6.97% | 84.56% | ± | 2.32% | 45.85% | ± | 5.79% |
| 8(*S*)-8-$F_{3t}$-IsoP | 200 | 50.15% | ± | 4.87% | 83.39% | ± | 1.45% | 41.82% | ± | 5.07% |
| 18(*R*)-18-$F_{3t}$-IsoP | 200 | 49.47% | ± | 5.76% | 88.98% | ± | 3.53% | 44.02% | ± | 5.08% |
| 18(*S*)-18-$F_{3t}$-IsoP | 200 | 44.20% | ± | 6.84% | 88.08% | ± | 2.72% | 38.93% | ± | 5.68% |
| 4(*RS*)-4-$F_{4t}$-NeuroP | 200 | 63.96% | ± | 7.57% | 85.18% | ± | 2.05% | 54.48% | ± | 6.20% |
| 10(*R*)-$F_{4t}$-NeuroP | 200 | 59.77% | ± | 6.36% | 93.16% | ± | 2.25% | 55.68% | ± | 5.49% |
| 10(*S*)-$F_{4t}$-NeuroP | 200 | 51.96% | ± | 5.34% | 88.68% | ± | 3.08% | 46.08% | ± | 5.23% |
| 13(*A*)-13-$F_{4t}$-NeuroP | 200 | 55.79% | ± | 5.19% | 87.28% | ± | 2.32% | 48.69% | ± | 4.95% |
| 13(*B*)-13-$F_{4t}$-NeuroP | 200 | 55.92% | ± | 7.34% | 81.47% | ± | 1.74% | 45.56% | ± | 6.46% |
| 14(*R*)-14-$F_{4t}$-NeuroP | 200 | 56.11% | ± | 6.73% | 87.36% | ± | 3.01% | 49.02% | ± | 5.85% |
| 14(*S*)-14-$F_{4t}$-NeuroP | 200 | 59.17% | ± | 6.51% | 79.60% | ± | 2.16% | 47.10% | ± | 4.87% |
| 20(*R*)-20-$F_{4t}$-NeuroP | 200 | 46.61% | ± | 4.18% | 82.86% | ± | 2.96% | 38.62% | ± | 5.55% |
| 20(*S*)-20-$F_{4t}$-NeuroP | 200 | 44.93% | ± | 4.02% | 81.30% | ± | 1.30% | 36.53% | ± | 3.27% |