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Supplementary materials

In Vitro Metabolic Fate of the Synthetic Cannabinoid Receptor Agonists QMPSB and QMPCB (SGT-11) Including Isozyme Mapping and Esterase Activity

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Table S1. List of QMPSB and all detected QMPSB metabolites with incubation type and the ESI mode they were detected in, precursor ion (PI) and characteristic fragment ions (FI) masses in MS\(^2\), relative intensities in MS\(^2\), calculated exact masses, elemental composition, and deviation from measured to calculated masses, and retention time (RT). pos, positive ionization mode; neg, negative ionization mode; gluc, glucuronic acid.

| Metabolite ID | Metabolite | Incubation | ESI Mode | Measured Masses of Characteristic Ions, m/z | Relative Intensity in MS\(^2\), % | Calculated Exact Masses, m/z | Elemental Composition | Error, ppm | RT, min |
|---------------|------------|------------|----------|---------------------------------|---------------------------------|----------------------------|----------------------|-----------|---------|
| QMPSB         | pHIL59/    | pos        | CYP      | PI at m/z 411.1375               | 28                              | 411.1373                  | C22H23O4N2S          | 0.48      | 9.4     |
|               | CYP        |            |          | FI at m/z 266.0846               | 100                             | 266.0845                  | C13H16O3NS           | 0.23      |         |
|               |            |            |          | FI at m/z 183.0111               | 32                              | 183.0110                  | C8H7O3S              | 0.33      |         |
|               |            |            |          | FI at m/z 135.0442               | 26                              | 135.0441                  | C8H7O2               | 1.07      |         |
|               |            |            |          | FI at m/z 119.0494               | 41                              | 119.0491                  | C8H7O               | 2.18      |         |
|               |            |            |          | FI at m/z 91.0548                | 17                              | 91.0542                   | C7H7O               |           |         |
| SM1           | N,N-bisdealkyl | pos        | CYP      | PI at m/z 343.0745               | 16                              | 343.0747                  | C17H15O4N2S          | -0.59     | 7.6     |
|               |            |            |          | FI at m/z 198.0220               | 100                             | 198.0219                  | C8H8O3NS             | 0.30      |         |
|               |            |            |          | FI at m/z 180.9954               | 29                              | 180.9954                  | C8H7O3S             | 0.06      |         |
|               |            |            |          | FI at m/z 153.0005               | 16                              | 153.0005                  | C7H5O2S             | 0.16      |         |
| SM2           | dehydro (isomer 1) | pos        | CYP      | PI at m/z 409.1218               | 22                              | 409.1217                  | C22H21O4N2S          | 0.36      | 8.8     |
|               |            |            |          | FI at m/z 264.0689               | 100                             | 264.0689                  | C13H14O3NS           | 0.04      |         |
|               |            |            |          | FI at m/z 183.0111               | 14                              | 183.0110                  | C8H7O3S             | 0.33      |         |
|               |            |            |          | FI at m/z 83.0736                | 45                              | 83.0730                   | C5H9N               | 7.81      |         |
| SM3           | dehydro (isomer 2) | pos        | CYP      | PI at m/z 409.1219               | 25                              | 409.1217                  | C22H21O4N2S          | 0.60      | 9.5     |
|               |            |            |          | FI at m/z 264.0690               | 100                             | 264.0689                  | C13H14O3NS           | 0.42      |         |
|               |            |            |          | FI at m/z 183.0112               | 14                              | 183.0110                  | C8H7O3S             | 0.87      |         |
|               |            |            |          | FI at m/z 83.0736                | 43                              | 83.0730                   | C5H9N               | 7.81      |         |
| SM4           | hydroxy + dehydro | pos        | CYP      | PI at m/z 425.1169               | 31                              | 425.1166                  | C22H21O5N2S          | 0.78      | 8.1     |
|               |            |            |          | FI at m/z 264.0693               | 100                             | 264.0689                  | C13H14O3NS           | 1.55      |         |
|               |            |            |          | FI at m/z 183.0112               | 15                              | 183.0110                  | C8H7O3S             | 0.87      |         |
|               |            |            |          | FI at m/z 119.0496               | 12                              | 119.0491                  | C8H7O               | 3.86      |         |
|               |            |            |          | FI at m/z 83.0737                | 47                              | 83.0730                   | C5H9ON              | 9.02      |         |
| SM5           | hydroxy (isomer 1) | pos        | CYP      | PI at m/z 427.1328               | 62                              | 427.1322                  | C22H23O5N2S          | 1.36      | 8.2     |
|               |            |            |          | FI at m/z 300.0901               | 100                             | 300.0900                  | C13H16O5NS           | 0.27      |         |
|               |            |            |          | FI at m/z 282.0796               | 38                              | 282.0795                  | C13H16O4NS           | 0.52      |         |
|               |            |            |          | FI at m/z 199.0061               | 39                              | 199.0060                  | C8H7O4S             | 0.73      |         |
|               |            |            |          | FI at m/z 163.0503               | 77                              | 163.0502                  | C8H7O2N2            | 0.59      |         |
|               |            |            |          | FI at m/z 135.0442               | 83                              | 135.0441                  | C8H7O2             | 1.07      |         |
|               |            |            |          | FI at m/z 107.0496               | 43                              | 107.0491                  | C7H7O              | 4.29      |         |
|               |            |            |          | FI at m/z 91.0548                | 26                              | 91.0542                   | C7H7               | 6.29      |         |
| Metabolite ID | Metabolite Description | Incubation | ESI Mode | Measured Masses of Characteristic Ions, m/z | Relative Intensity in MS², % | Calculated Exact Masses, m/z | Elemental Composition | Error, ppm | RT, min |
|---------------|------------------------|------------|----------|-------------------------------------------|-----------------------------|-----------------------------|------------------------|------------|--------|
| SM6           | hydroxy (isomer 2)     | CYP        | pos      | FI at m/z 427.1326                        | 41                          | 427.1322                    | C2H2O3SN25            | 0.89       | 8.8    |
|               |                        |            |          | FI at m/z 266.0850                        | 100                         | 266.0845                    | C13H16O3NS            | 1.73       |        |
|               |                        |            |          | FI at m/z 183.0113                        | 31                          | 183.0110                    | C8H7O2S               | 1.42       |        |
|               |                        |            |          | FI at m/z 135.0443                        | 23                          | 135.0441                    | C8H7O2               | 1.81       |        |
|               |                        |            |          | FI at m/z 119.0496                        | 38                          | 119.0491                    | C8H7O                | 3.86       |        |
|               |                        |            |          | FI at m/z 91.0549                         | 15                          | 91.0542                     | C7H7                 | 7.39       |        |
| SM7           | dihydroxy (isomer 1)   | CYP        | pos      | FI at m/z 443.1276                        | 50                          | 443.1271                    | C2H2O3O6N2S           | 1.05       | 8.1    |
|               |                        |            |          | FI at m/z 298.0745                        | 37                          | 298.0744                    | C13H16O5NS            | 0.44       |        |
|               |                        |            |          | FI at m/z 199.0060                        | 100                         | 199.0060                    | C8H7O4S               | 0.23       |        |
|               |                        |            |          | FI at m/z 163.0503                        | 54                          | 163.0502                    | C8H7O2N2              | 0.59       |        |
|               |                        |            |          | FI at m/z 135.0442                        | 73                          | 135.0441                    | C8H7O2               | 1.07       |        |
|               |                        |            |          | FI at m/z 107.0496                        | 57                          | 107.0491                    | C7H7O                | 4.29       |        |
|               |                        |            |          | FI at m/z 82.0658                         | 31                          | 82.0651                     | C5H8N                | 8.21       |        |
| SM8           | dihydroxy (isomer 2)   | CYP        | pos      | FI at m/z 443.1290                        | 28                          | 443.1271                    | C2H2O3O6N2S           | 4.21       | 8.1    |
|               |                        |            |          | FI at m/z 264.0695                        | 100                         | 264.0689                    | C13H14O3NS            | 2.31       |        |
|               |                        |            |          | FI at m/z 183.0113                        | 16                          | 183.0110                    | C8H7O2S               | 1.42       |        |
|               |                        |            |          | FI at m/z 162.0554                        | 50                          | 162.0550                    | C9H8O2N              | 2.75       |        |
|               |                        |            |          | FI at m/z 83.0738                         | 47                          | 83.0730                     | C5H9N                | 10.22      |        |
| SM9           | ester hydrolysis       | pHLS9/     | pos      | FI at m/z 284.0952                        | 47                          | 284.0951                    | C13H18O4NS            | 0.34       | 7.9    |
| (carboxylic   |                        | CYP        |          | FI at m/z 135.0442                        | 8                           | 135.0441                    | C8H7O2               | 1.07       |        |
| acid) + N,N-  |                        |            |          | FI at m/z 85.0892                         | 37                          | 85.0886                     | C5H11N               | 7.04       |        |
| bisdealkyl    | pHLS9/                 | neg        |          | FI at m/z 84.0814                         | 100                         | 84.0808                     | C5H10N               | 7.42       |        |
| SM10          | ester hydrolysis       | CYP        | neg      | FI at m/z 214.0173                        | 23                          | 214.0180                    | C8H8O4NS             | -3.04      | 5.0    |
| (carboxylic   |                        |            |          | FI at m/z 170.0271                        | 48                          | 170.0281                    | C7H8O2NS             | -6.01      |        |
| acid) +       |                        |            |          | FI at m/z 79.9797                         | 100                         | 79.981172                   | H2O2NS              | -18.40     |        |
| dehydro       |                        |            |          |                                                 |                             |                             |                       |            |        |
| SM11          | ester hydrolysis       | pHLS9/     | neg      | FI at m/z 280.0642                        | 34                          | 280.0649                    | C13H14O4NS            | -2.51      | 8.0    |
| (carboxylic   |                        | CYP        |          | FI at m/z 146.0269                        | 100                         | 146.0281                    | C5H8O2NS             | -8.37      |        |
| acid) +       | pHLS9/                 | neg        |          | FI at m/z 63.9610                         | 39                          | 63.9624                     | O2S                  | -22.64     |        |
| hydrosy (isom |                        |            |          |                                                 |                             |                             |                       |            |        |
| er 1)        |                        |            |          |                                                 |                             |                             |                       |            |        |

Table S1. (continued)
| Metabolite ID | Metabolite | Incubation | ESI Mode | Measured Masses of Characteristic Ions, m/z | Relative Intensity in MS\(^2\), % | Calculated Exact Masses, m/z | Elemental Composition | Error, ppm | RT, min |
|--------------|------------|------------|----------|---------------------------------------------|---------------------------------|-------------------------------|----------------------|-----------|---------|
| SM13         | ester hydrolysis (carboxylic acid) + hydroxy (isomer 2) | CYP | neg | PI at m/z 298.0758, FI at m/z 148.0425 | 44 | 298.0755 | C13H16O5NS | 1.12 | 6.6 |
| SM14         | ester hydrolysis (carboxylic acid) + hydroxy (isomer 3) | CYP | neg | PI at m/z 298.0753, FI at m/z 150.0271, FI at m/z 155.0159, FI at m/z 100.0753 | 82 | 298.0755 | C13H16O5NS | -0.56 | 7.0 |
| SM15         | ester hydrolysis (carboxylic acid) + dihydroxy | pHLS9/ CYP | neg | PI at m/z 314.0702, FI at m/z 270.0801, FI at m/z 170.0270 | 41 | 314.0704 | C13H16O6NS | -0.58 | 6.2 |
| SM16         | ester hydrolysis (carboxylic acid) + dihydroxy | pHLS9 | pos | PI at m/z 314.0704, FI at m/z 270.0801, FI at m/z 170.0270 | 100 | 314.0704 | C13H16O6NS | -1.67 | 6.6 |
| SM17         | ester hydrolysis (carboxylic acid) + dihydroxy + gluc | pHLS9/ CYP | neg | PI at m/z 314.0704, FI at m/z 270.0801, FI at m/z 170.0270 | 73 | 314.0704 | C13H16O6NS | -1.11 | 6.5 |
| SM18         | ester hydrolysis (8-hydroxyquinoline) | pHLS9/ CYP | pos | PI at m/z 146.0603, FI at m/z 118.0655 | 100 | 146.0600 | C9H8ON | 1.78 | 2.2 |
| SM19         | ester hydrolysis (8-hydroxyquinoline) + hydroxy | CYP | pos | PI at m/z 146.0603, FI at m/z 118.0655 | 100 | 146.0600 | C9H8O2N | 0.89 | 1.3 |
| SM20         | ester hydrolysis (8-hydroxyquinoline) + dihydroxy | pHLS9 | pos | PI at m/z 226.0169, FI at m/z 146.0601, FI at m/z 133.0286 | 12 | 226.0169 | C9H8O4NS | 0.20 | 2.2 |
| SM21         | ester hydrolysis (8-hydroxyquinoline) + gluc | pHLS9 | pos | PI at m/z 322.0919, FI at m/z 146.0601, FI at m/z 113.0236, FI at m/z 85.0290 | 11 | 322.0921 | C15H16O7N | -0.71 | 1.5 |

*Note: Calculated masses and compositions are based on putative structures and may need further validation.*
Table S2. List of QMPCB and all detected QMPCB metabolites with incubation type and the ESI mode they were detected in, precursor ion (PI) and characteristic fragment ions (FI) masses in MS², relative intensities in MS², calculated exact masses, elemental composition, and deviation from measured to calculated masses, and retention time (RT). pos, positive ionization mode; neg, negative ionization mode; gluc, glucuronic acid.

| Metabolite ID | Metabolite | Incubation | ESI Mode | Measured Masses of Characteristic Ions, m/z | Relative Intensity in MS², % | Calculated Exact Masses, m/z | Elemental Composition | Error, ppm | RT, min |
|---------------|------------|------------|-----------|---------------------------------------------|-----------------------------|-----------------------------|----------------------|------------|--------|
| QMPCB - pHLS9/ CYP | pos | PI at m/z | 375.1696 | 8 | 375.1703 | C23H23O3N2 | -1.92 | 8.7 |
| | FI at m/z | 230.1172 | 100 | 230.1176 | C14H16O2N | -1.54 |
| | FI at m/z | 147.0437 | 13 | 147.0441 | C9H7O2 | -2.42 |
| | FI at m/z | 145.0282 | 73 | 145.0284 | C9H5O2 | -1.42 |
| | FI at m/z | 117.0336 | 5 | 117.0335 | C8H5O | 0.93 |
| | FI at m/z | 89.0390 | 3 | 89.0386 | C7H5 | 4.75 |
| CM1 N,N-bisdealkyl CYP | pos | PI at m/z | 307.1073 | 6 | 307.1077 | C18H15O3N2 | -1.36 | 7.2 |
| | FI at m/z | 162.0547 | 100 | 162.0550 | C9H8O2N | -1.57 |
| | FI at m/z | 145.0282 | 50 | 145.0284 | C9H5O2 | -1.42 |
| | FI at m/z | 117.0335 | 4 | 117.0335 | C8H5O | 0.08 |
| CM2 carboxamide cleavage (carboxylic acid) CYP | pos | PI at m/z | 308.0916 | 6 | 308.0917 | C9H14O4N | -0.43 | 8.0 |
| | FI at m/z | 163.0387 | 100 | 163.0390 | C9H7O3 | -1.66 |
| | FI at m/z | 135.0439 | 11 | 135.0441 | C8H7O2 | -1.16 |
| CM3 N,N-bisdealkyl + hydroxy CYP | pos | PI at m/z | 323.1021 | 16 | 323.1026 | C18H15O4N2 | -1.65 | 6.5 |
| | FI at m/z | 178.0497 | 100 | 178.0499 | C9H8O3N | -0.95 |
| | FI at m/z | 161.0231 | 69 | 161.0233 | C9H5O3 | -1.37 |
| | FI at m/z | 133.0286 | 16 | 133.0284 | C8H5O2 | 1.46 |
| CM4 hydroxy + diehydro CYP | pos | PI at m/z | 387.1337 | 21 | 387.1339 | C9H14O4N2 | -0.60 | 8.1 |
| | FI at m/z | 242.0811 | 100 | 242.0812 | C14H12O3N | -0.29 |
| | FI at m/z | 145.0284 | 83 | 145.0284 | C9H5O2 | -0.04 |
| | FI at m/z | 117.0339 | 9 | 117.0335 | C8H5O | 3.49 |
| CM5 hydroxy + dehydro (isomer 1) CYP | pos | PI at m/z | 389.1493 | 5 | 389.1496 | C23H19O3N2 | -0.73 | 7.1 |
| | FI at m/z | 371.1382 | 18 | 371.1390 | C23H19O3N2 | -2.21 |
| | FI at m/z | 308.0909 | 26 | 308.0917 | C9H14O4N | -2.71 |
| | FI at m/z | 244.0965 | 62 | 244.0968 | C9H14O4N | -1.31 |
| | FI at m/z | 226.0860 | 21 | 226.0863 | C14H12O2N | -1.13 |
| | FI at m/z | 163.0387 | 61 | 163.0390 | C9H7O3 | -1.66 |
| | FI at m/z | 145.0282 | 100 | 145.0284 | C9H5O2 | -1.42 |
| CM6 hydroxy + dehydro (isomer 2) CYP | pos | PI at m/z | 389.1497 | 16 | 389.1496 | C23H21O3N2 | 0.30 | 7.4 |
| | FI at m/z | 228.1016 | 99 | 228.1019 | C14H14O2N | -1.34 |
| | FI at m/z | 145.0283 | 100 | 145.0284 | C9H5O2 | -0.73 |
| | FI at m/z | 117.0336 | 8 | 117.0335 | C8H5O | 0.93 |
Table S2. (continued)

| Metabolite ID | Metabolite                  | Incubation | ESI Mode | Measured Masses of Characteristic Ions, m/z | Relative Intensity in MS², % | Calculated Exact Masses, m/z | Elemental Composition | Error, ppm | RT, min |
|---------------|-----------------------------|------------|----------|---------------------------------------------|-----------------------------|-----------------------------|-----------------------|------------|---------|
| CM7           | hydroxy + dehydro (isomer 3)| CYP        | pos      | PI at m/z 389.1492                          | 22                          | 389.1496                    | C23H21O4N2            | -0.99      | 8.6     |
|               |                             |            |          | FI at m/z 244.0962                          | 100                         | 244.0968                    | C14H14O3N            | -2.54      |         |
|               |                             |            |          | FI at m/z 161.0231                          | 19                          | 161.0233                    | C9H5O3              | -1.37      |         |
|               |                             |            |          | FI at m/z 105.0336                          | 26                          | 105.0335                    | C7H5O               | 1.04       |         |
|               |                             |            |          | FI at m/z 84.0811                           | 18                          | 84.0808                     | C5H10N              | 3.85       |         |
| CM8           | hydroxy (isomer 1)          | CYP        | pos      | PI at m/z 391.1645                          | 10                          | 391.1652                    | C25H23O4N2           | -1.88      | 7.3     |
|               |                             |            |          | FI at m/z 246.1121                          | 100                         | 246.1125                    | C14H16O3N           | -1.50      |         |
|               |                             |            |          | FI at m/z 145.0282                          | 76                          | 145.0284                    | C9H5O2             | -1.42      |         |
|               |                             |            |          | FI at m/z 117.0336                          | 6                           | 117.0335                    | C8H5O              | 0.93       |         |
| CM9           | hydroxy (isomer 2)          | CYP        | pos      | PI at m/z 391.1671                          | 4                           | 391.1652                    | C25H23O4N2           | 4.77       | 7.3     |
|               |                             |            |          | FI at m/z 246.1123                          | 38                          | 246.1125                    | C14H16O3N           | -0.69      |         |
|               |                             |            |          | FI at m/z 149.0233                          | 100                         | 149.0233                    | C8H5O2             | -0.13      |         |
|               |                             |            |          | FI at m/z 71.0863                           | 12                          | 71.0855                     | C5H11              | 10.87      |         |
| CM10          | hydroxy (isomer 3)          | CYP        | pos      | PI at m/z 391.1648                          | 14                          | 391.1652                    | C23H23O4N2           | -1.11      | 7.6     |
|               |                             |            |          | FI at m/z 264.1227                          | 100                         | 264.1230                    | C14H18O4N           | -1.26      |         |
|               |                             |            |          | FI at m/z 246.1122                          | 30                          | 246.1125                    | C14H16O3N           | -1.10      |         |
|               |                             |            |          | FI at m/z 163.0386                          | 16                          | 163.0390                    | C9H7O3             | -2.27      |         |
|               |                             |            |          | FI at m/z 145.0282                          | 90                          | 145.0284                    | C9H5O2             | -1.42      |         |
|               |                             |            |          | FI at m/z 117.0337                          | 7                           | 117.0335                    | C8H5O              | 1.79       |         |
| CM11          | hydroxy (isomer 4)          | CYP        | pos      | PI at m/z 391.1645                          | 12                          | 391.1652                    | C23H23O4N2           | -1.88      | 8.0     |
|               |                             |            |          | FI at m/z 230.1172                          | 100                         | 230.1176                    | C14H16O2N           | -1.54      |         |
|               |                             |            |          | FI at m/z 145.0282                          | 76                          | 145.0284                    | C9H5O2             | -1.42      |         |
|               |                             |            |          | FI at m/z 117.0336                          | 5                           | 117.0335                    | C8H5O              | 0.93       |         |
| CM12          | dihydroxy + dehydro (isomer 1)| CYP        | pos      | PI at m/z 405.1437                          | 19                          | 405.1445                    | C23H21O5N2           | -1.97      | 7.2     |
|               |                             |            |          | FI at m/z 308.0910                          | 13                          | 308.0917                    | C18H14O4N           | -2.38      |         |
|               |                             |            |          | FI at m/z 163.0386                          | 100                         | 163.0390                    | C9H7O3             | -2.27      |         |
|               |                             |            |          | FI at m/z 145.0281                          | 52                          | 145.0284                    | C9H5O2             | -2.11      |         |
|               |                             |            |          | FI at m/z 117.0335                          | 6                           | 117.0335                    | C8H5O              | 0.08       |         |
| CM13          | dihydroxy + dehydro (isomer 2)| CYP        | pos      | PI at m/z 405.1437                          | 24                          | 405.1445                    | C23H21O5N2           | -1.97      | 7.6     |
|               |                             |            |          | FI at m/z 278.1022                          | 100                         | 278.1023                    | C14H16O5N           | -0.36      |         |
|               |                             |            |          | FI at m/z 260.0922                          | 3                            | 260.0917                    | C14H14O4N           | 1.79       |         |
|               |                             |            |          | FI at m/z 163.0387                          | 10                            | 163.0390                    | C9H7O3             | -1.66      |         |
|               |                             |            |          | FI at m/z 145.0284                          | 67                            | 145.0284                    | C9H5O2             | -0.04      |         |
|               |                             |            |          | FI at m/z 117.0334                          | 6                            | 117.0335                    | C8H5O              | -0.78      |         |
| Metabolite ID | Metabolite Description | Incubation | ESI Mode | Measured Masses of Characteristic Ions, m/z | Relative Intensity in MS%, | Calculated Exact Masses, m/z | Elemental Composition | Error, ppm | RT, min |
|---------------|------------------------|------------|----------|----------------------------------------|--------------------------|-----------------------------|----------------------|------------|--------|
| CM14 dihydroxy (isomer 1) | CYP | pos | PI at m/z | 407.1592 | 15 | 407.1601 | C23H23O5N2 | -2.33 | 6.6 |
| | | | FI at m/z | 246.1122 | 100 | 246.1125 | C14H16O3N | -1.10 |
| | | | FI at m/z | 145.0282 | 78 | 145.0284 | C9H5O2 | -1.42 |
| | | | FI at m/z | 117.0336 | 6 | 117.0335 | C8H5O | 0.93 |
| CM15 dihydroxy (isomer 2) | CYP | pos | PI at m/z | 407.1594 | 19 | 407.1601 | C23H23O5N2 | -1.84 | 6.9 |
| | | | FI at m/z | 264.1229 | 100 | 264.1230 | C14H18O4N | -0.51 |
| | | | FI at m/z | 246.1119 | 16 | 246.1125 | C14H16O3N | -2.32 |
| | | | FI at m/z | 163.0390 | 15 | 163.0390 | C9H7O3 | 0.18 |
| | | | FI at m/z | 145.0283 | 94 | 145.0284 | C9H5O2 | -0.73 |
| | | | FI at m/z | 117.0337 | 8 | 117.0335 | C8H5O | 1.79 |
| CM16 dihydroxy (isomer 3) | CYP | pos | PI at m/z | 407.1596 | 9 | 407.1601 | C23H23O5N2 | -1.35 | 7.6 |
| | | | FI at m/z | 262.1062 | 1 | 262.1074 | C14H16O4N | -4.52 |
| | | | FI at m/z | 163.0387 | 100 | 163.0390 | C9H7O3 | -1.66 |
| | | | FI at m/z | 145.0283 | 9 | 145.0284 | C9H5O2 | -1.42 |
| CM17 trihydroxy | CYP | pos | PI at m/z | 423.1554 | 14 | 423.1551 | C23H23O6N2 | 0.80 | 7.1 |
| | | | FI at m/z | 278.1025 | 14 | 278.1023 | C14H16O5N | 0.72 |
| | | | FI at m/z | 163.0388 | 100 | 163.0390 | C9H7O3 | -1.04 |
| | | | FI at m/z | 100.0762 | 19 | 100.0757 | C5H10O2N | 5.10 |
| CM18 ester hydrolysis (carboxylic acid) pHLS9/CYP | pos | PI at m/z | 248.1261 | 100 | 248.1261 | C14H18O3N | -0.08 | 7.0 |
| | | | FI at m/z | 163.0389 | 67 | 163.0390 | C9H7O3 | -0.43 |
| | | | FI at m/z | 112.0760 | 7 | 112.0757 | C6H10O2N | 2.77 |
| | | | FI at m/z | 69.0706 | 10 | 69.0699 | C5H9 | 10.47 |
| | | pHLS9/CYP neg | PI at m/z | 246.1131 | 71 | 246.1136 | C14H16O3N | -1.90 |
| | | | FI at m/z | 202.1228 | 100 | 202.1237 | C13H16O2N | -4.64 |
| CM19 ester hydrolysis (carboxylic acid) + N,N-bisdealkyl | CYP | pos | PI at m/z | 180.0654 | 100 | 180.0655 | C9H10O3N | -0.67 | 0.6 |
| | | | FI at m/z | 162.0547 | 69 | 162.0550 | C9H8O2N | -1.57 |
| | | | FI at m/z | 134.0599 | 24 | 134.0600 | C8H8O2N | -1.04 |
| CM20 ester hydrolysis (carboxylic acid) + dehydro (isomer 1) | CYP | pos | PI at m/z | 246.1118 | 3 | 246.1125 | C14H16O3N | -2.72 | 6.3 |
| | | | FI at m/z | 163.0387 | 100 | 163.0390 | C9H7O3 | -1.66 |
| | | | FI at m/z | 135.0440 | 15 | 135.0441 | C8H7O2 | -0.41 |
| CM21 ester hydrolysis (carboxylic acid) + dehydro (isomer 2) | CYP | pos | PI at m/z | 246.1121 | 41 | 246.1125 | C14H16O3N | -1.50 | 7.3 |
| | | | FI at m/z | 145.0282 | 100 | 145.0284 | C9H5O2 | -1.42 |
| | | | FI at m/z | 117.0336 | 20 | 117.0335 | C8H5O | 0.93 |
| | | CYP neg | PI at m/z | 244.0971 | 55 | 244.0979 | C14H14O3N | -3.35 |
| | | | FI at m/z | 200.1070 | 100 | 200.1081 | C13H14O2N | -5.44 |
| Metabolite ID | Metabolite | Incubation | ESI Mode | Measured Masses of Characteristic Ions, m/z | Relative Intensity in MS², % | Calculated Exact Masses, m/z | Elemental Composition | Error, ppm | RT, min |
|--------------|------------|------------|----------|---------------------------------------------|-------------------------------|-----------------------------|----------------------|------------|--------|
| CM22         | ester hydrolysis (carboxylic acid) + hydroxy + dehydro | CYP | pos | PI at m/z 262.1070 | 18 | 262.1074 | C14H16O4N | -1.47 | 5.4    |
|              |            |            |          | FI at m/z 163.0387 | 100 | 163.0390 | C9H7O3 | -1.66 |        |
|              |            |            |          | FI at m/z 135.0439 | 10 | 135.0441 | C8H7O2 | -1.16 |        |
|              |            |            |          | FI at m/z 107.0493 | 6 | 107.0495 | C7H7O | 1.49 |        |
| CM23         | ester hydrolysis (carboxylic acid) + hydroxy (isomer 1) | pHLS9/ CYP | pos | PI at m/z 264.1231 | 29 | 264.1230 | C14H18O4N | 0.25 | 5.4    |
|              |            |            |          | FI at m/z 163.0390 | 100 | 163.0390 | C9H7O3 | 0.18 |        |
|              |            |            |          | FI at m/z 135.0442 | 7 | 135.0441 | C8H7O2 | 1.07 |        |
|              |            |            |          | FI at m/z 91.0549 | 11 | 91.0542 | C7H7 | 7.39 |        |
|              |            |            |          | FI at m/z 134.0596 | 100 | 134.0611 | C8H8ON | -11.46 |        |
|              |            |            |          | FI at m/z 98.0596 | 2 | 98.0611 | C5H8ON | -15.67 |        |
| CM24         | ester hydrolysis (carboxylic acid) + hydroxy (isomer 2) | CYP | pos | PI at m/z 264.1226 | 21 | 264.1230 | C14H18O4N | -1.64 | 5.7    |
|              |            |            |          | FI at m/z 246.1123 | 54 | 246.1125 | C14H16O3N | -0.69 |        |
|              |            |            |          | FI at m/z 163.0388 | 100 | 163.0390 | C9H7O3 | -1.04 |        |
|              |            |            |          | FI at m/z 135.0442 | 9 | 135.0441 | C8H7O2 | 1.07 |        |
|              |            |            |          | FI at m/z 84.0812 | 13 | 84.0808 | C5H10N | 5.04 |        |
|              |            |            |          | FI at m/z 262.1086 | 100 | 262.1085 | C14H16O4N | -1.84 |        |
|              |            |            |          | FI at m/z 218.1172 | 21 | 218.1187 | C13H16O2N | -6.66 |        |
|              |            |            |          | FI at m/z 148.0753 | 39 | 148.0768 | C9H10ON | -10.05 |        |
|              |            |            |          | FI at m/z 119.0487 | 50 | 119.0502 | C8H7O | -12.92 |        |
|              |            |            |          | FI at m/z 91.0538 | 11 | 91.0553 | C7H7 | -16.74 |        |
| CM25         | ester hydrolysis (carboxylic acid) + hydroxy (isomer 3) | pHLS9/ CYP | pos | PI at m/z 264.1229 | 2 | 264.1230 | C14H18O4N | -0.51 | 6.3    |
|              |            |            |          | FI at m/z 246.1122 | 10 | 246.1125 | C14H16O3N | -1.10 |        |
|              |            |            |          | FI at m/z 163.0387 | 100 | 163.0390 | C9H7O3 | -1.66 |        |
|              |            |            |          | FI at m/z 135.0440 | 9 | 135.0441 | C8H7O2 | -0.41 |        |
|              |            |            |          | FI at m/z 84.0813 | 5 | 84.0808 | C5H10N | 6.23 |        |
|              |            |            |          | FI at m/z 262.1082 | 100 | 262.1085 | C14H16O4N | -1.08 |        |
|              |            |            |          | FI at m/z 218.1179 | 29 | 218.1187 | C13H16O2N | -3.45 |        |
|              |            |            |          | FI at m/z 134.0597 | 18 | 134.0611 | C8H8ON | -10.72 |        |
|              |            |            |          | FI at m/z 119.0488 | 96 | 119.0502 | C8H7O | -12.08 |        |
|              |            |            |          | FI at m/z 91.0538 | 11 | 91.0553 | C7H7 | -16.74 |        |
| CM26         | ester hydrolysis (carboxylic acid) + dihydroxy (isomer 1) | CYP | pos | PI at m/z Not detected | 0 | 280.1179 | C14H18O5N | - | 5.0    |
|              |            |            |          | FI at m/z 262.1075 | 18 | 262.1074 | C14H16O4N | 0.44 |        |
|              |            |            |          | FI at m/z 163.0385 | 100 | 163.0390 | C9H7O3 | -2.88 |        |
|              |            |            |          | FI at m/z 149.0232 | 61 | 149.0233 | C8H5O3 | -0.81 |        |
| Metabolite ID | Metabolite                                                                 | Incubation | ESI Mode | Measured Masses of Characteristic Ions, m/z | Relative Intensity in MS², % | Calculated Exact Masses, m/z | Elemental Composition | Error, ppm | RT, min |
|--------------|----------------------------------------------------------------------------|------------|----------|---------------------------------------------|------------------------------|-----------------------------|------------------------|------------|---------|
| CM27         | ester hydrolysis (carboxylic acid) + dihydroxy (isomer 2)                  | CYP        | neg      | PI at m/z 278.1021                          | 39                          | 278.1034                    | C14H16O5N             | -4.66      | 5.0     |
|              |                                                                           | FI at m/z  | 178.0499 | FI at m/z 134.0597                          | 75                          | 178.0510                    | C8H8O2N               | -5.99      |         |
| CM28         | ester hydrolysis (carboxylic acid) + dihydroxy (isomer 3)                  | pHLS9/     | neg      | PI at m/z 278.1031                          | 100                         | 278.1034                    | C14H16O5N             | -1.06      | 5.7     |
|              |                                                                           | CYP        |          | FI at m/z 260.0924                          | 26                          | 260.0928                    | C14H14O4N             | -1.66      |         |
|              |                                                                           | FI at m/z  | 216.1023 | FI at m/z 198.0912                          | 24                          | 198.0924                    | C13H12O2N             | -0.25      |         |
|              |                                                                           | FI at m/z  | 134.0596 | FI at m/z 91.0538                           | 28                          | 134.0611                    | C8H8O2N               | -11.46     |         |
| CM29         | ester hydrolysis (carboxylic acid) + gluc                                  | pHLS9      | pos      | PI at m/z 424.1601                          | 5                           | 424.1602                    | C20H26O9N             | -1.25      | 6.1     |
|              |                                                                           |            |          | FI at m/z 248.1281                          | 100                         | 248.1281                    | C14H18O3N             | -0.08      |         |
|              |                                                                           |            |          | FI at m/z 230.1176                          | 31                          | 230.1176                    | C14H16O2N             | -4.41      |         |
|              |                                                                           |            |          | FI at m/z 163.0389                          | 30                          | 163.0390                    | C9H7O3                | -0.43      |         |
|              |                                                                           |            |          | FI at m/z 145.0284                          | 15                          | 145.0284                    | C9H5O2                | -0.04      |         |
|              |                                                                           |            |          | FI at m/z 112.0760                          | 4                           | 112.0757                    | C6H10O2N              | -13.43     |         |
| CM30         | ester hydrolysis (8-hydroxyquinoline)                                     | pHLS9/     | pos      | PI at m/z 146.0603                          | 100                         | 146.0600                    | C9H8O2N               | 1.78       | 2.2     |
|              |                                                                           | CYP        |          | FI at m/z 118.0654                          | 6                           | 118.0651                    | C8H8N                 | 2.32       |         |
| CM31         | ester hydrolysis (8-hydroxyquinoline) + hydroxy                           | CYP        | pos      | PI at m/z 162.0547                          | 100                         | 162.0550                    | C9H8O2N               | -1.57      | 1.2     |
|              |                                                                           | FI at m/z 134.0599 | 7 | 134.0600 | C8H8O2N | -1.04                          | | | |
| CM32         | ester hydrolysis (8-hydroxyquinoline) + sulfate                           | pHLS9      | pos      | PI at m/z 226.0169                          | 10                          | 226.0169                    | C9H8O4NS              | 0.20       | 2.2     |
|              |                                                                           | FI at m/z 146.0601 | 100 | 146.0600 | C9H8O2N | 0.41                          | | | |
| CM33         | ester hydrolysis (8-hydroxyquinoline) + gluc                              | pHLS9      | pos      | PI at m/z 322.0919                          | 10                          | 322.0921                    | C15H16O7N             | -0.71      | 1.5     |
|              |                                                                           | FI at m/z 146.0600 | 100 | 146.0600 | C9H8O2N | -0.27                          | | | |
|              |                                                                           | FI at m/z 113.0237 | 4 | 113.0233 | C5H5O2 | 3.36                          | | | |
| CM34         | ester hydrolysis (8-hydroxyquinoline) + hydroxy + gluc                     | pHLS9      | pos      | PI at m/z 338.0864                          | 12                          | 338.0870                    | C15H16O8N             | -1.90      | 0.9     |
|              |                                                                           | FI at m/z 162.0550 | 100 | 162.0550 | C9H8O2N | 0.28                          | | | |
Table S3. Detection of QMPSB metabolites in pHLS9 and monoxygenases activity screening incubations (chemical structures are given in Figure 2). SM, metabolites of QMPSB; CYP, cytochrome P450; FMO, flavin-containing monoxygenase; pHLM, pooled human liver microsomes; +, metabolite detected; -, metabolite not detected; gluc, glucuronic acid.

| Metabolite                              | pHLS9  | CYP     | FMO3 | pHLM |
|-----------------------------------------|--------|---------|------|------|
|                                         |        | 1A2     | 2A6  | 2B6  | 2C8  | 2C9  | 2C19 | 2D6  | 2E1  | 3A4  | 3A5  |
| SM1 N,N-bisdealkyl                      | -      | -       | -    | -    | +    | -    | -    | +    | +    | -    | -    |
| SM2 dehydro isomer 1                    | -      | -       | -    | -    | -    | +    | +    | +    | -    | -    | -    |
| SM3 dehydro isomer 2                    | -      | -       | -    | -    | +    | +    | +    | +    | -    | -    | -    |
| SM4 hydroxy + dehydro                   | -      | -       | -    | -    | -    | +    | +    | -    | -    | -    | -    |
| SM5 hydroxy isomer 1                    | -      | -       | -    | -    | +    | +    | +    | +    | -    | -    | -    |
| SM6 hydroxy isomer 2                    | -      | +       | -    | -    | +    | +    | +    | +    | -    | -    | -    |
| SM7 dihydroxy isomer 1                  | -      | -       | -    | -    | +    | -    | -    | +    | -    | -    | -    |
| SM8 dihydroxy isomer 2                  | -      | +       | -    | -    | -    | +    | +    | -    | -    | -    | -    |
| SM9 ester hydrolysis (carboxylic acid)  | +      | +       | +    | +    | +    | +    | +    | +    | -    | -    | -    |
| SM10 ester hydrolysis (carboxylic acid) + N,N-bisdealkyl | -      | -       | -    | -    | -    | -    | -    | -    | -    | -    | -    |
| SM11 ester hydrolysis (carboxylic acid) + dehydro | +      | -       | -    | -    | -    | +    | +    | +    | -    | -    | -    |
| SM12 ester hydrolysis (carboxylic acid) + hydroxy (isomer 1) | +      | +       | -    | +    | +    | -    | -    | -    | -    | -    | -    |
| SM13 ester hydrolysis (carboxylic acid) + hydroxy (isomer 2) | +      | +       | -    | +    | +    | +    | +    | -    | -    | -    | -    |
| SM14 ester hydrolysis (carboxylic acid) + hydroxy (isomer 3) | -      | -       | -    | +    | +    | -    | -    | +    | -    | -    | -    |
| SM15 ester hydrolysis (carboxylic acid) + dihydroxy | +      | -       | -    | -    | -    | -    | -    | -    | -    | -    | -    |
| SM16 ester hydrolysis (carboxylic acid) + gluc | +      | -       | -    | -    | -    | -    | -    | -    | -    | -    | -    |
| SM17 ester hydrolysis (carboxylic acid) + dihydroxy + gluc | +      | -       | -    | -    | -    | -    | -    | -    | -    | -    | -    |
| SM18 ester hydrolysis (8-hydroxyquinolin) | +      | +       | +    | +    | +    | +    | +    | +    | +    | +    | +    |
| SM19 ester hydrolysis (8-hydroxyquinolin) + hydroxy | -      | +       | +    | +    | +    | +    | +    | +    | +    | +    | +    |
| SM20 ester hydrolysis (8-hydroxyquinolin) + sulfate | +      | -       | -    | -    | -    | -    | -    | -    | -    | -    | -    |
| SM21 ester hydrolysis (8-hydroxyquinolin) + gluc | +      | -       | -    | -    | -    | -    | -    | -    | -    | -    | -    |
Table S4. Detection of QMPCB metabolites in pHLS9 and monooxygenases activity screening incubations (chemical structures are given in Figure 2). CM, metabolites of QMPCB; CYP, cytochrome P450; FMO, flavin-containing monooxygenase; pHLM, pooled human liver microsomes; +, metabolite detected; -, metabolite not detected; gluc, glucuronic acid.

| Metabolite                                      | pHLS9 | CYP | FMO3 | pHLM |
|------------------------------------------------|-------|-----|------|------|
|                                                |       | 1A2 | 2A6  | 2B6  | 2C8  | 2C9  | 2C19 | 2D6  | 2E1  | 3A4  | 3A5  |
| CM1 N,N-bisdealkyl                             | -     | -   | -    | -    | -    | -    | -    | -    | -    | +    | +    |
| CM2 carboxamide cleavage (carboxylic acid)     | -     | -   | -    | -    | -    | -    | -    | -    | +    | +    | -    |
| CM3 N,N-bisdealkyl + hydroxy                   | -     | -   | -    | -    | -    | -    | -    | +    | +    | -    | -    |
| CM4 hydroxy + dihydro                          | -     | -   | -    | -    | -    | -    | -    | +    | +    | -    | -    |
| CM5 hydroxy + dehydro (isomer 1)               | -     | -   | -    | -    | +    | +    | -    | -    | +    | -    | -    |
| CM6 hydroxy + dehydro (isomer 2)               | -     | -   | -    | +    | +    | -    | -    | -    | -    | -    | -    |
| CM7 hydroxy + dehydro (isomer 3)               | -     | -   | +    | -    | -    | -    | -    | -    | +    | -    | -    |
| CM8 hydroxy (isomer 1)                         | -     | -   | -    | +    | +    | -    | -    | -    | -    | +    | -    |
| CM9 hydroxy (isomer 2)                         | -     | +   | -    | -    | -    | +    | -    | -    | +    | -    | -    |
| CM10 hydroxy (isomer 3)                        | -     | -   | -    | +    | +    | +    | -    | -    | -    | +    | -    |
| CM11 hydroxy (isomer 4)                        | -     | +   | -    | +    | +    | -    | -    | -    | -    | -    | -    |
| CM12 dihydroxy + dehydro (isomer 1)            | -     | -   | -    | -    | -    | -    | -    | -    | +    | -    | +    |
| CM13 dihydroxy + dehydro (isomer 2)            | -     | -   | -    | -    | -    | -    | -    | -    | +    | -    | -    |
| CM14 dihydroxy (isomer 1)                      | -     | -   | -    | +    | -    | -    | -    | -    | -    | -    | -    |
| CM15 dihydroxy (isomer 2)                      | -     | -   | -    | -    | -    | -    | -    | -    | -    | -    | -    |
| CM16 dihydroxy (isomer 3)                      | -     | -   | -    | -    | -    | -    | -    | -    | -    | +    | +    |
| CM17 trihydroxy                                | -     | -   | -    | -    | -    | -    | -    | -    | -    | +    | -    |
| CM18 ester hydrolysis (carboxylic acid)        | +     | +   | +    | +    | +    | +    | +    | +    | +    | +    |
| CM19 ester hydrolysis (carboxylic acid) + N,N-bisdealkyl | -     | +   | -    | +    | -    | -    | -    | -    | -    | -    |
| CM20 ester hydrolysis (carboxylic acid) + hydroxy | -     | -   | -    | -    | -    | -    | -    | +    | +    | -    |
| CM21 ester hydrolysis (carboxylic acid) + dehydro (isomer 1) | -     | -   | -    | -    | -    | -    | -    | +    | +    | -    |
| CM22 ester hydrolysis (carboxylic acid) + hydroxy + dehydro | -     | -   | -    | -    | -    | -    | -    | +    | +    | -    |
| CM23 ester hydrolysis (carboxylic acid) + hydroxy (isomer 1) | +     | -   | +    | +    | +    | +    | -    | +    | -    | -    |
| Metabolite | pHLS9 | CYP | FMO3 | pHLM |
|------------|-------|-----|------|------|
| CM24       |       |     |      |      |
| CM25       |       |     |      |      |
| CM26       |       |     |      |      |
| CM27       |       |     |      |      |
| CM28       |       |     |      |      |
| CM29       |       |     |      |      |
| CM30       |       |     |      |      |
| CM31       |       |     |      |      |
| CM32       |       |     |      |      |
| CM33       |       |     |      |      |
| CM34       |       |     |      |      |
Figure S1. Chromatograms of QMPSB and its five most abundant metabolites in pHLS9 incubation (6h sample) in positive or negative ionization mode: QMPSB [m/z 411.1373], SM9 [ester hydrolysis (carboxylic acid), m/z 282.0806], SM12 [ester hydrolysis (carboxylic acid) + hydroxy (isomer 1), m/z 298.0755], SM16 [ester hydrolysis (carboxylic acid) + glucuronic acid, m/z 458.1126], SM18 [ester hydrolysis (8-hydroxyquinoline), m/z 146.0600], SM21 [ester hydrolysis (8-hydroxyquinoline) + glucuronic acid, m/z 322.0921]; SM21 artifact [degluconuridated in ESI source, m/z 146.0600].

Figure S2. Chromatograms of QMPCB and its five most abundant metabolites in pHLS9 incubation (6h sample) in positive ionization mode: QMPCB [m/z 375.1703], CM18 [ester hydrolysis (carboxylic acid), m/z 248.1281], CM23 [ester hydrolysis (carboxylic acid) + hydroxy (isomer 1), m/z 264.1230], CM29 [ester hydrolysis (carboxylic acid) + glucuronic acid, m/z 424.1602], CM30 [ester hydrolysis (8-hydroxyquinoline), m/z 146.0600], CM33 [ester hydrolysis (8-hydroxyquinoline) + glucuronic acid, m/z 322.0921]; CM33 artifact [degluconuridated in ESI source, m/z 146.0600].
Figure S3. High-resolution MS² spectra of QMPSB metabolites detected in pHLS9 and monoxygenases activity screening. RT, retention time; pos, positive ionization mode; neg, negative ionization mode; gluc, glucuronic acid.
Figure S3. (continued)
Figure S3. (continued)
Figure S4. High-resolution MS² spectra of QMPCB metabolites detected in pHLS9 and monooxygenases activity screening. RT, retention time; pos, positive ionization mode; neg, negative ionization mode; gluc, glucuronic acid.
Figure S4. (continued)
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