**Supplement Table 3: MRM transitions and MS parameters for determination of the drug metabolites and their internal standards with LC-MS-MS.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Compound | Polarity | Precursor ion [m/z] | Product ion [m/z] | Frag-mentor  [V] | Collision energy [V] | | Internal standard |
| caffeine | Positive | 195.1 | 138 | 100 | | 14 | 2H9-caffeine |
| 13C3-caffeine | Positive | 198.1 | 140 | 100 | | 14 | 2H9-caffeine |
| 2H9-caffeine | Positive | 204.1 | 144 | 100 | | 14 |  |
| paraxanthine | Positive | 181.1 | 124 | 80 | | 18 | 2H3-para-xanthine |
| 13C2-para-xanthine | Positive | 183.1 | 125 | 80 | | 18 | 2H6-para-xanthine |
| 2H3-paraxanthine | Positive | 184.1 | 124 | 80 | | 18 |  |
| 2H6-paraxanthine | Positive | 187.1 | 127 | 80 | | 18 |  |
| AFMU | Negative | 225.1 | 197.1 | 70 | | 4 | 2H3-AFMU |
| 13C-AFMU | Negative | 226.0 | 198 | 70 | | 4 | 2H3-AFMU |
| 2H3-AFMU | Negative | 228.1 | 200.1 | 85 | | 4 |  |
| AAMU | Negative | 197.1 | 127.1 | 110 | | 8 | 2H3-AAMU |
| 13C-AAMU | Negative | 198.0 | 128 | 110 | | 8 | 2H3-AAMU |
| 2H3-AAMU | Negative | 200.1 | 130.1 | 110 | | 8 |  |
| 1-methylxanthine | Negative | 165.0 | 108.1 | 135 | | 16 | [13C4,15N3]1-methylxanthine |
| 13C-1-methylxanthine | Negative | 166.0 | 108.1 | 135 | | 16 | [13C4,15N3]1-methylxanthine |
| [13C4,15N3]1-methylxanthin | Negative | 172.0 | 113.1 | 135 | | 16 |  |