## Supplementary Information

# In-depth comparison of the metabolic and pharmacokinetic behaviour of the structurally related synthetic cannabinoids AMB-FUBINACA and AMB-CHMICA in rats.

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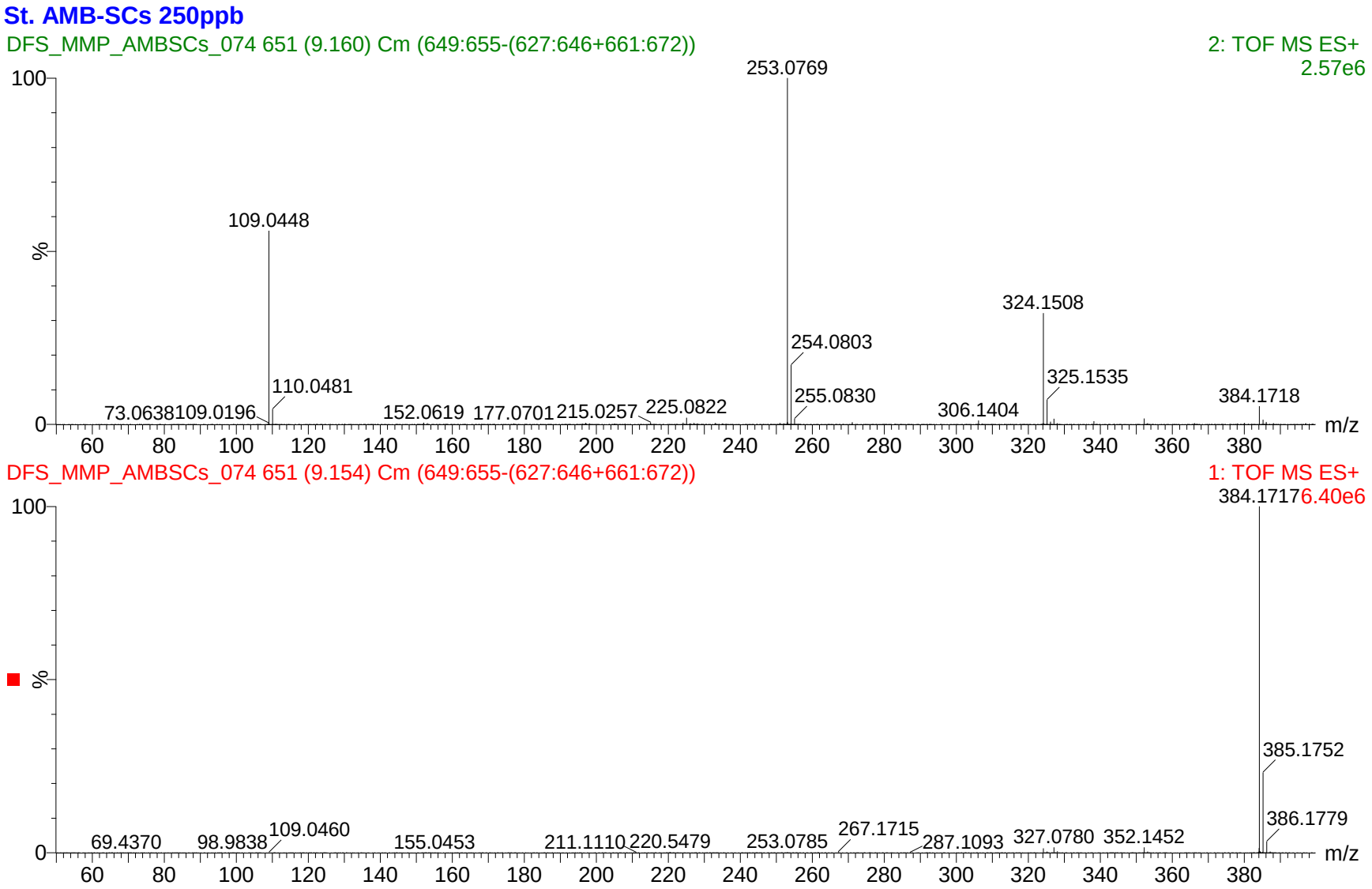


**Fig. S1.** Low Energy (Function 1) and High Energy (Function 2) spectra for AMB-FUBINACA.

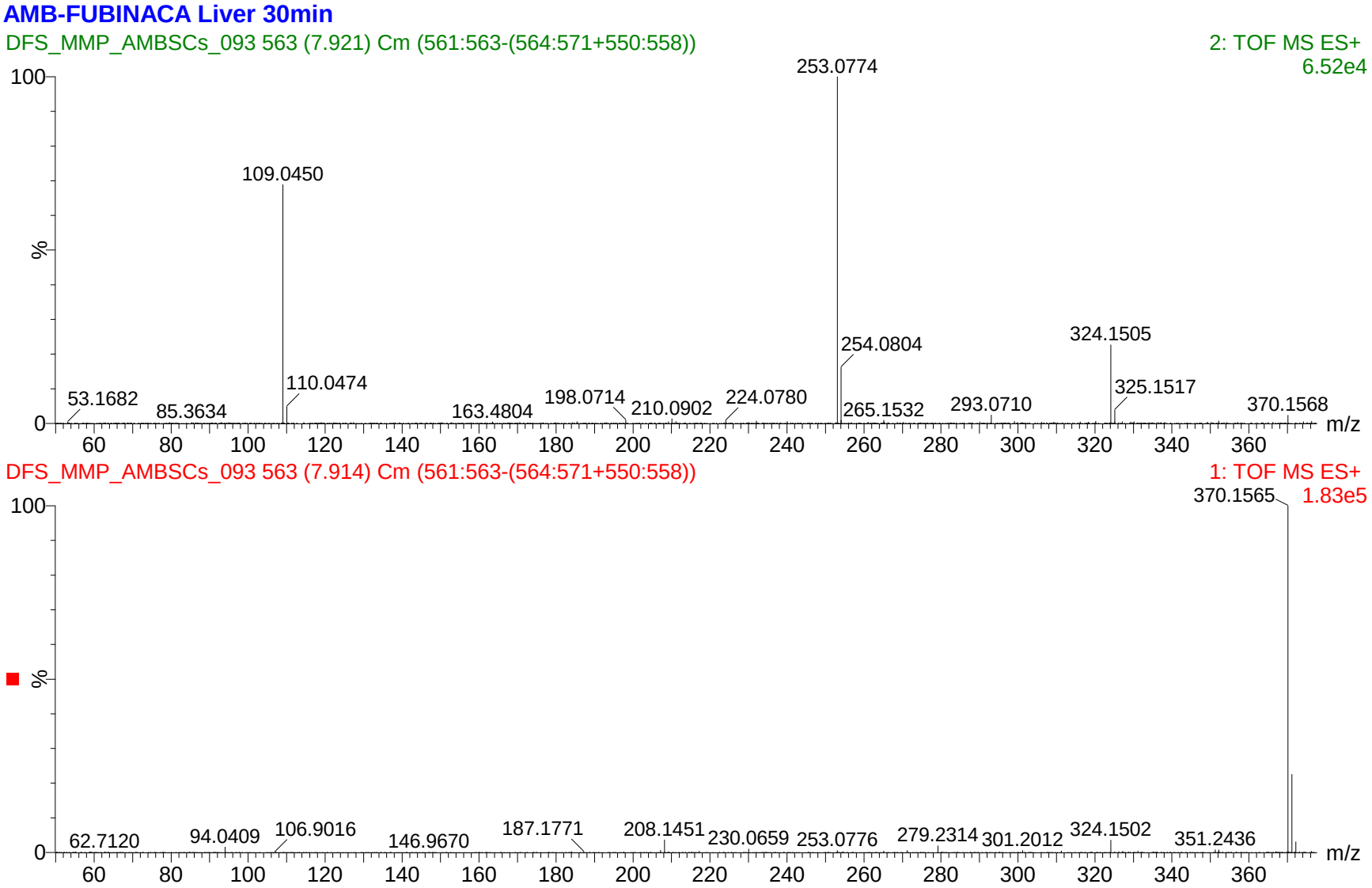


**Fig. S2.** Low Energy (Function 1) and High Energy (Function 2) spectra for AMB-FUBINACA M1.

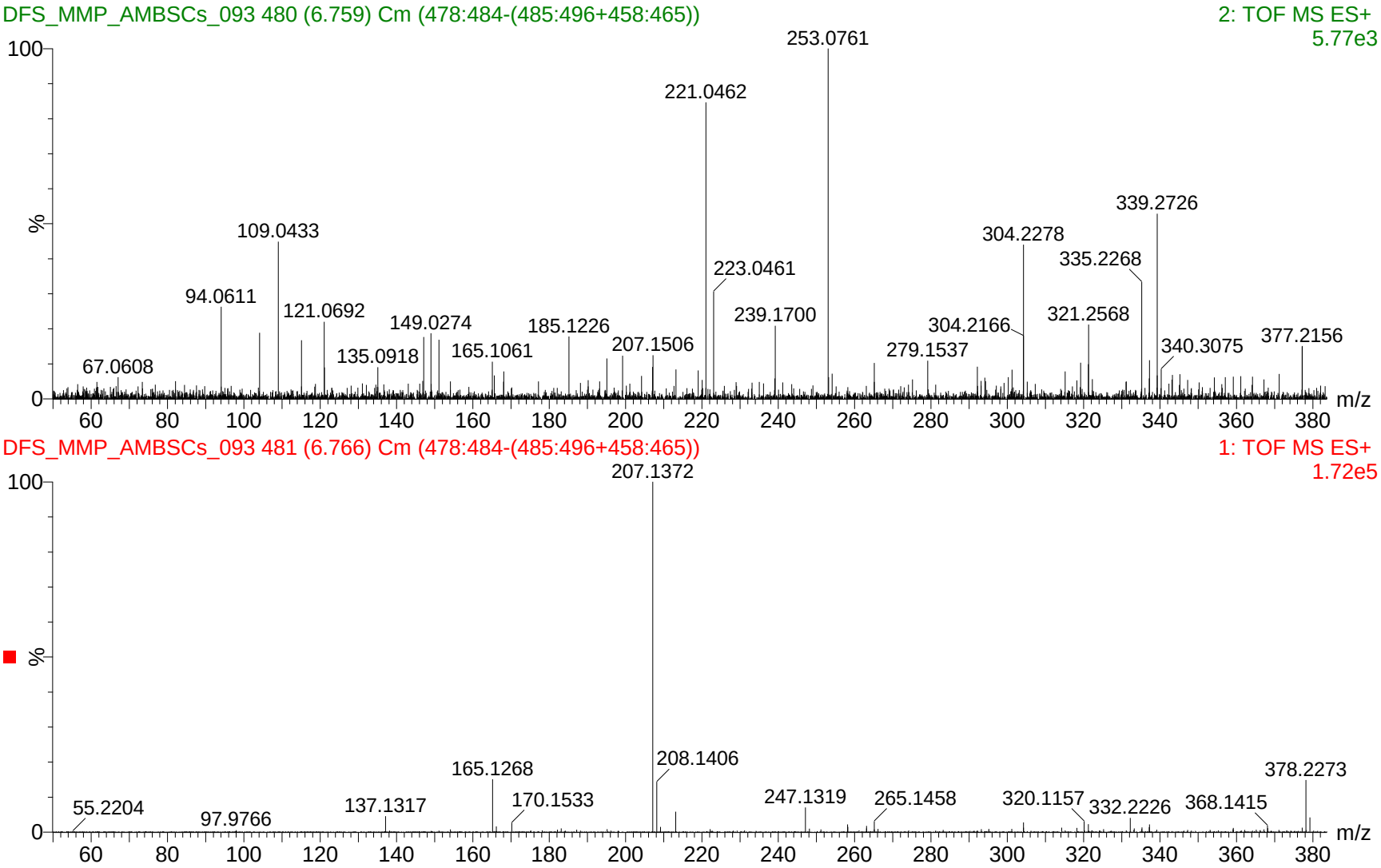


**Fig. S3.** Low Energy (Function 1) and High Energy (Function 2) spectra for AMB-FUBINACA M2.

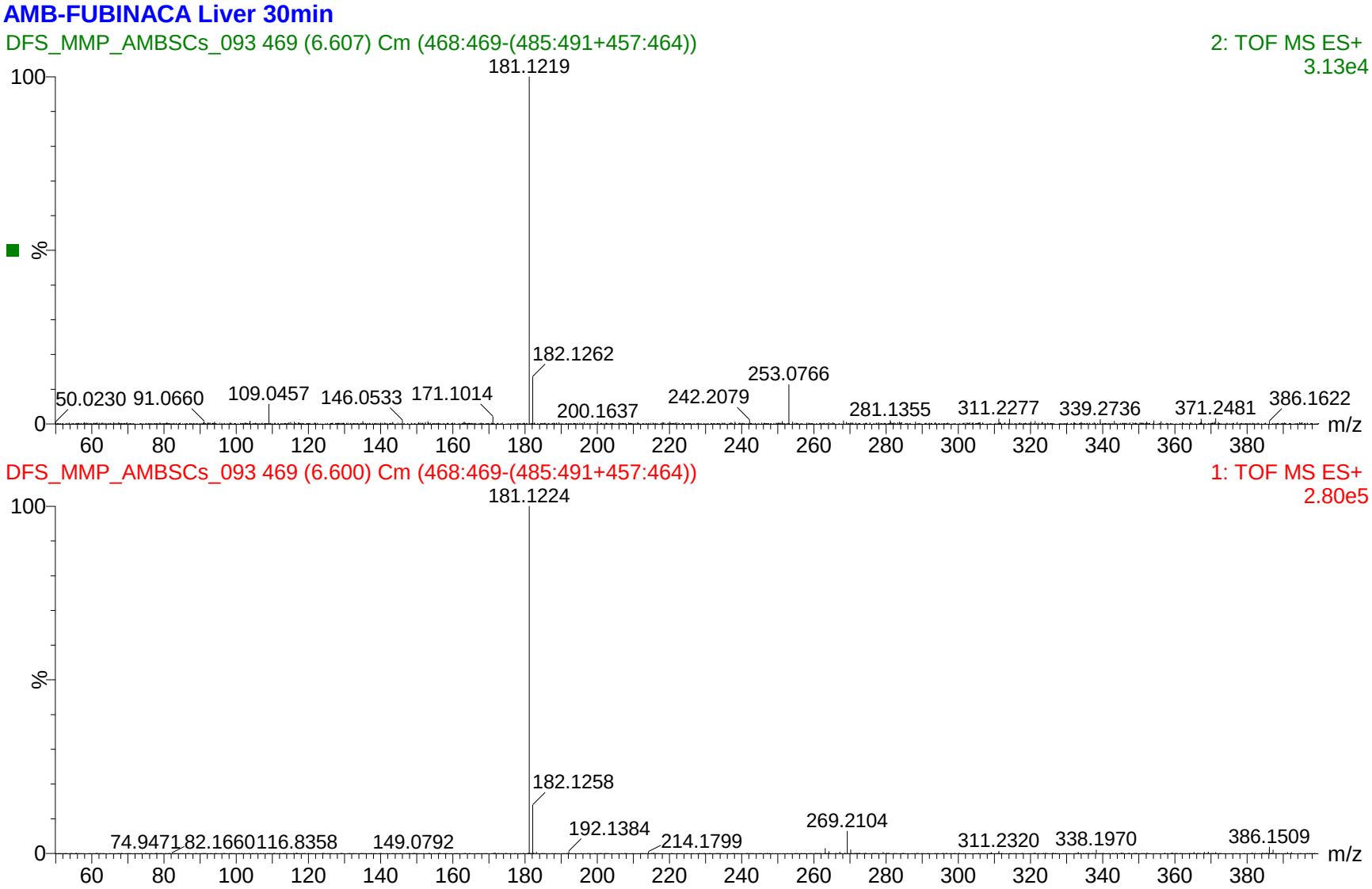


**Fig. S4.** Low Energy (Function 1) and High Energy (Function 2) spectra for AMB-FUBINACA M3.

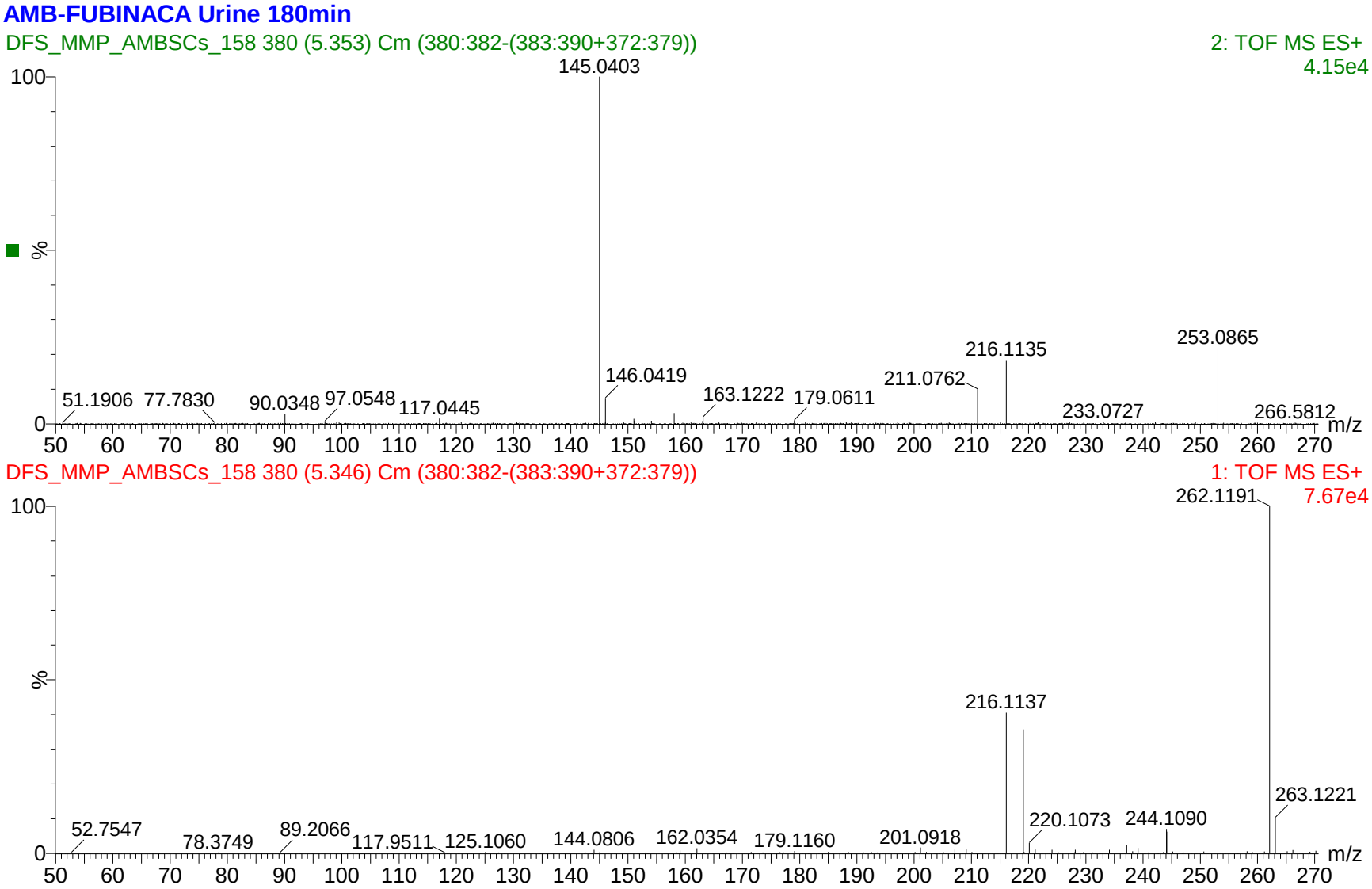


**Fig. S5.** Low Energy (Function 1) and High Energy (Function 2) spectra for AMB-FUBINACA M4.

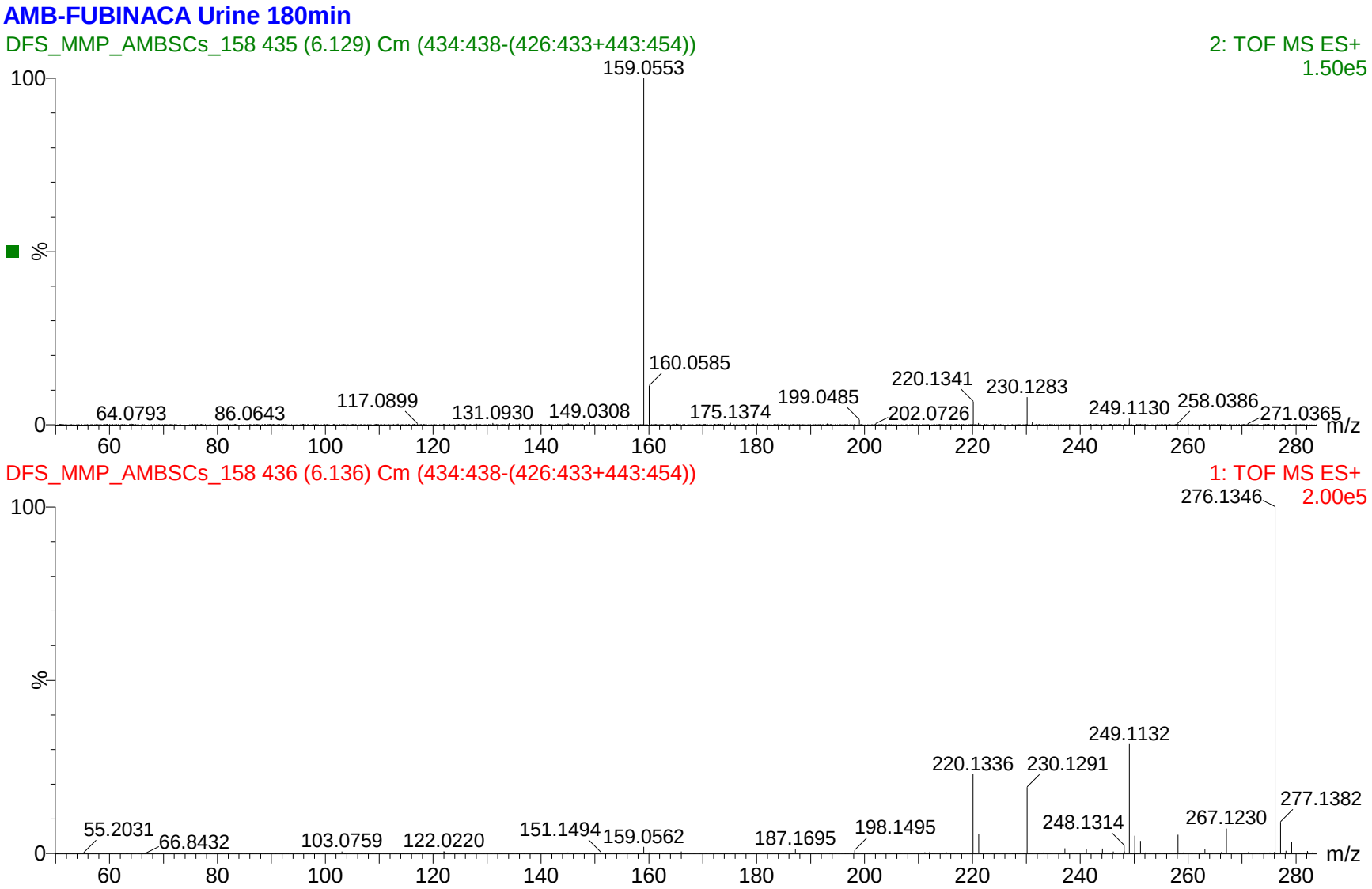


**Fig. S6.** Low Energy (Function 1) and High Energy (Function 2) spectra for AMB-FUBINACA M5.

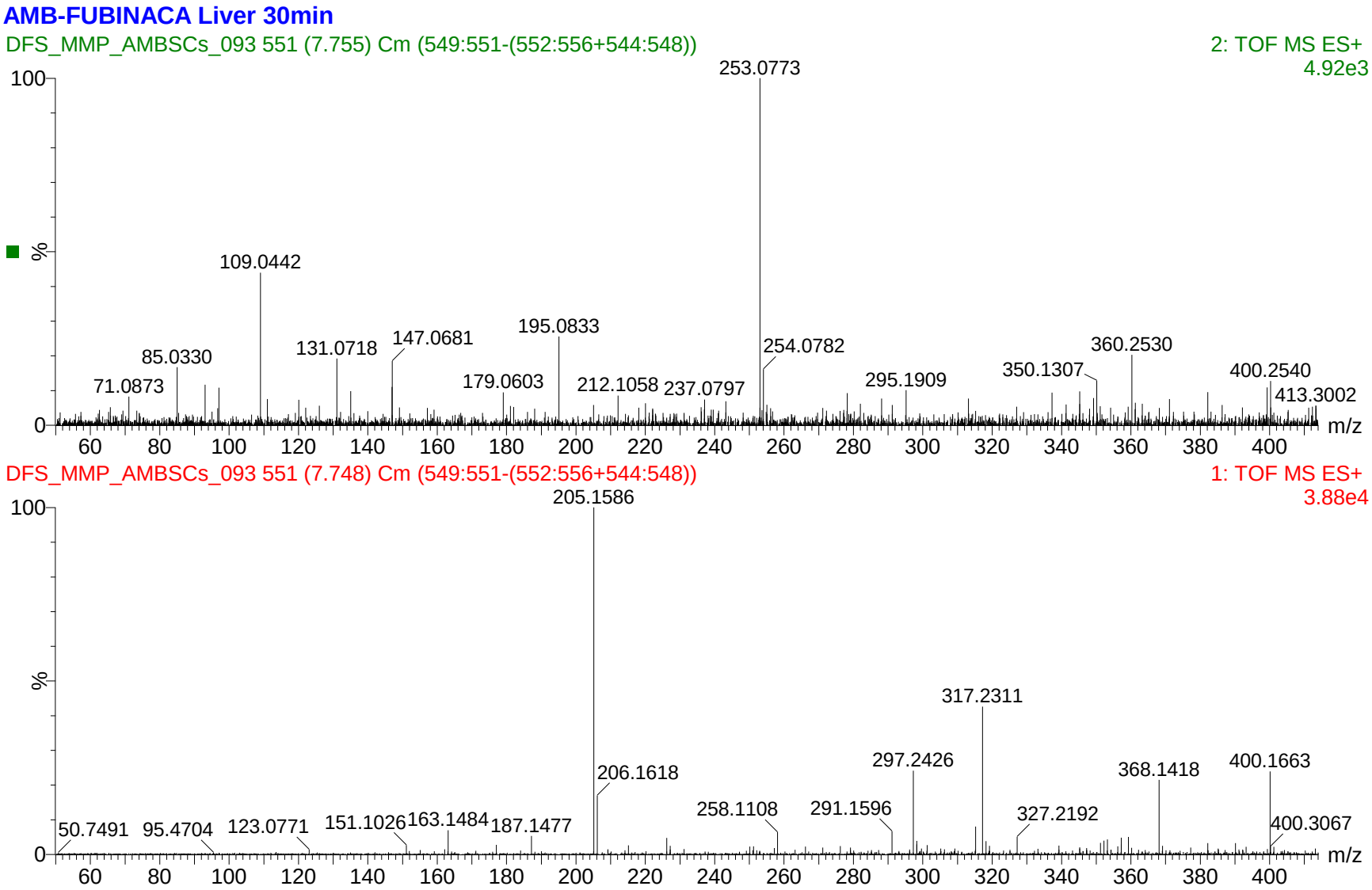


**Fig. S7.** Low Energy (Function 1) and High Energy (Function 2) spectra for AMB-FUBINACA M6.

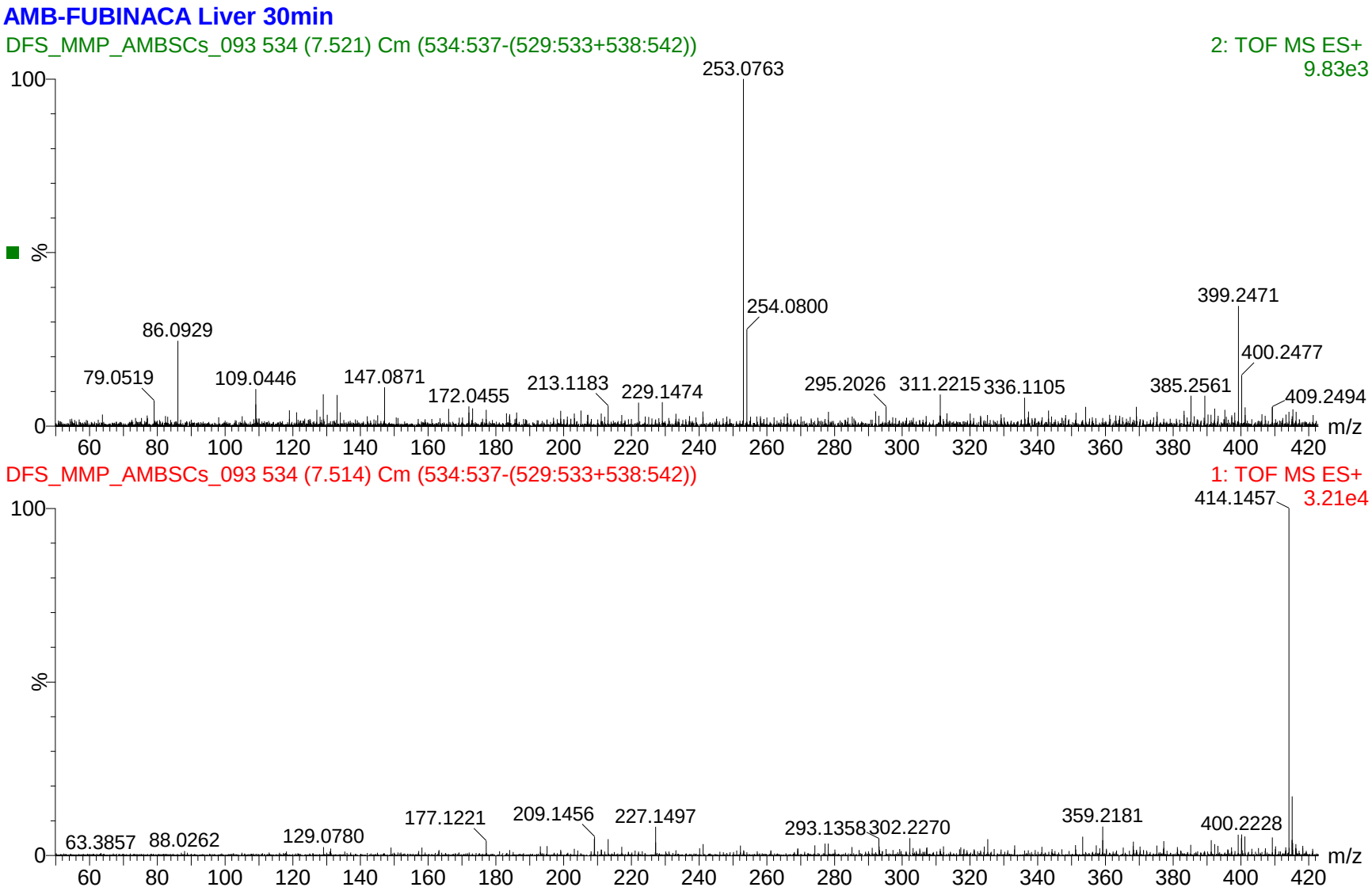


**Fig. S8.** Low Energy (Function 1) and High Energy (Function 2) spectra for AMB-FUBINACA M7.

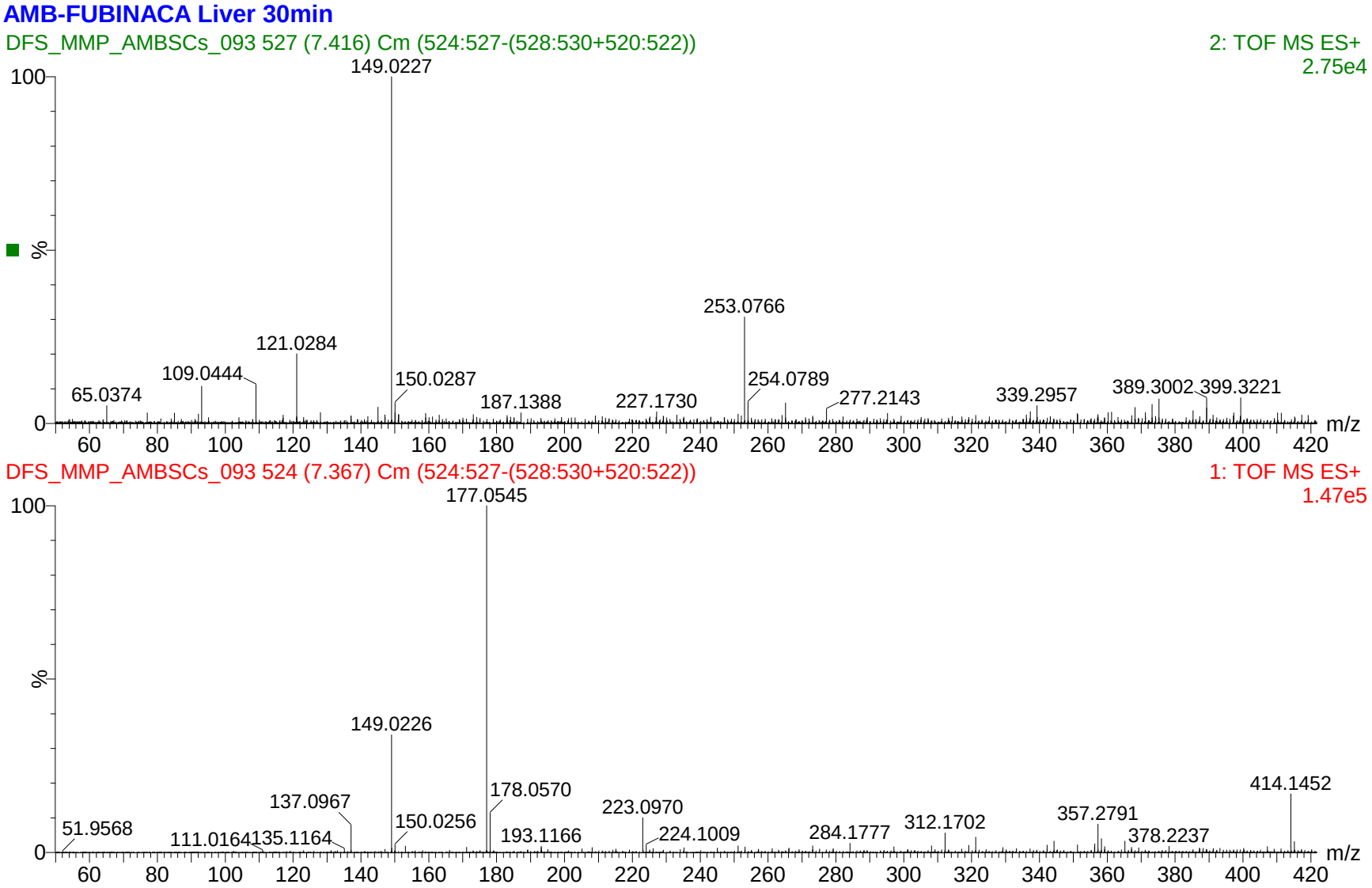


**Fig. S9.** Low Energy (Function 1) and High Energy (Function 2) spectra for AMB-FUBINACA M8.

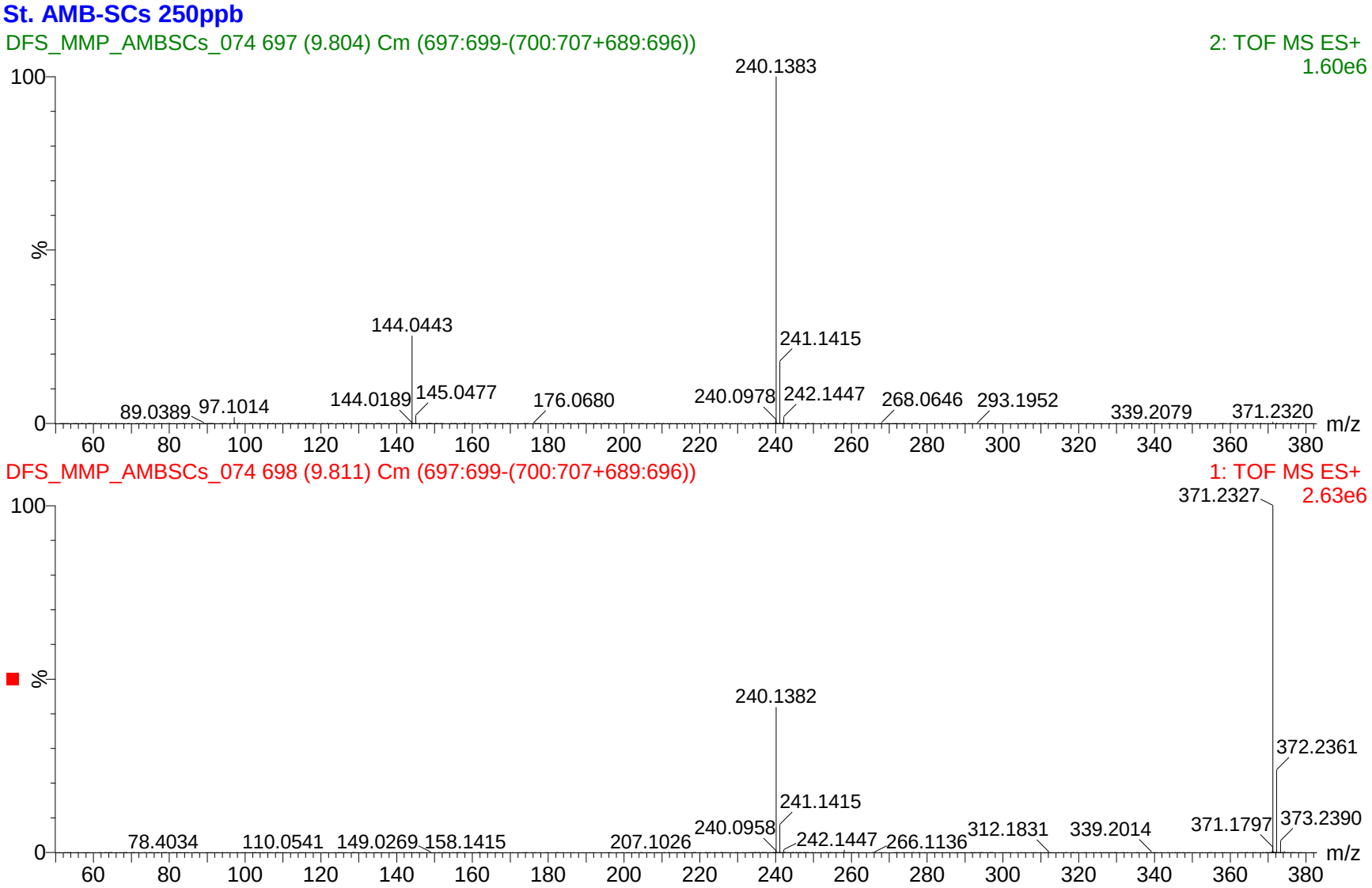


**Fig. S10.** Low Energy (Function 1) and High Energy (Function 2) spectra for AMB-CHMICA.

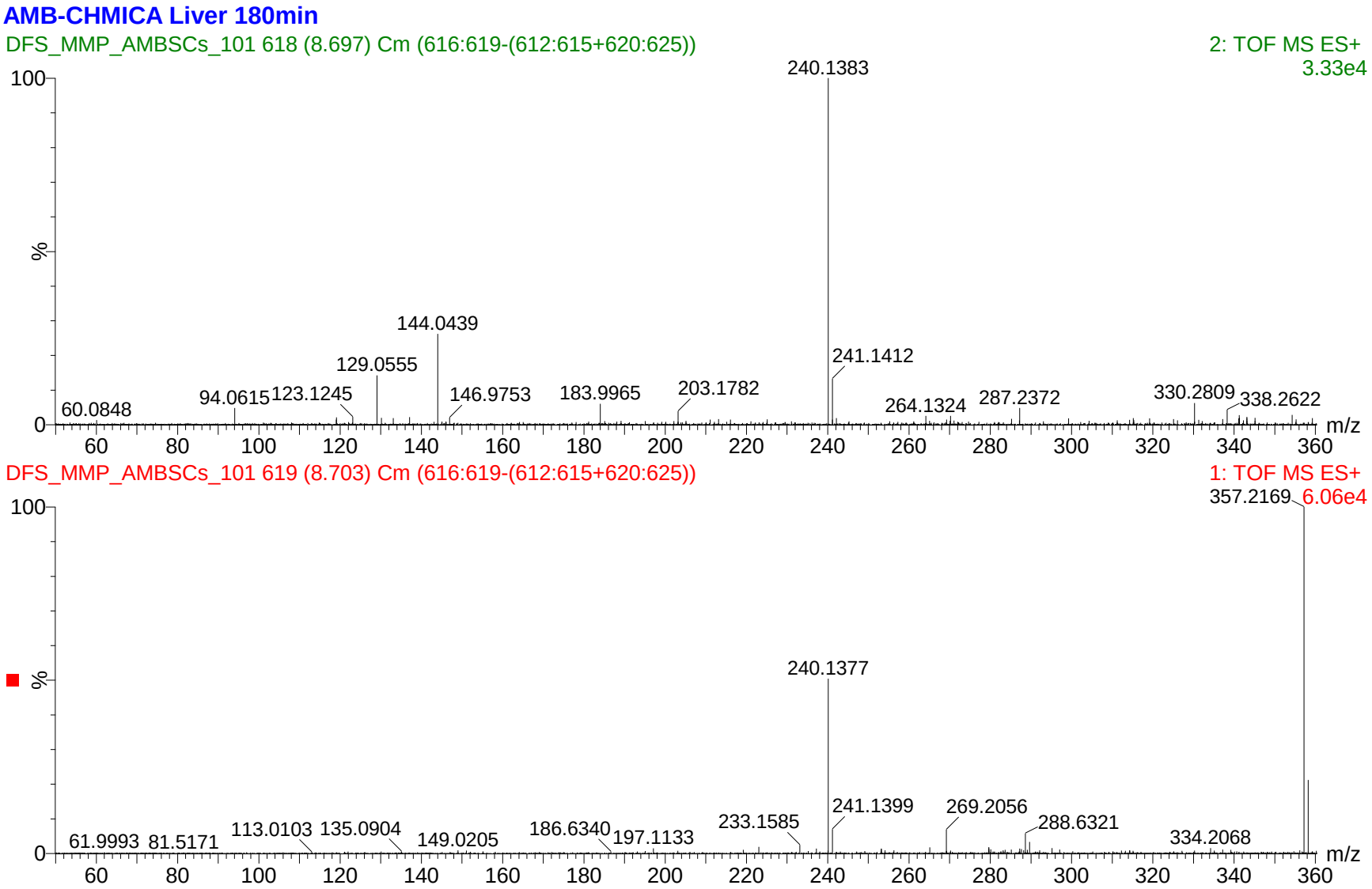


**Fig. S11.** Low Energy (Function 1) and High Energy (Function 2) spectra for AMB-CHMICA M1.

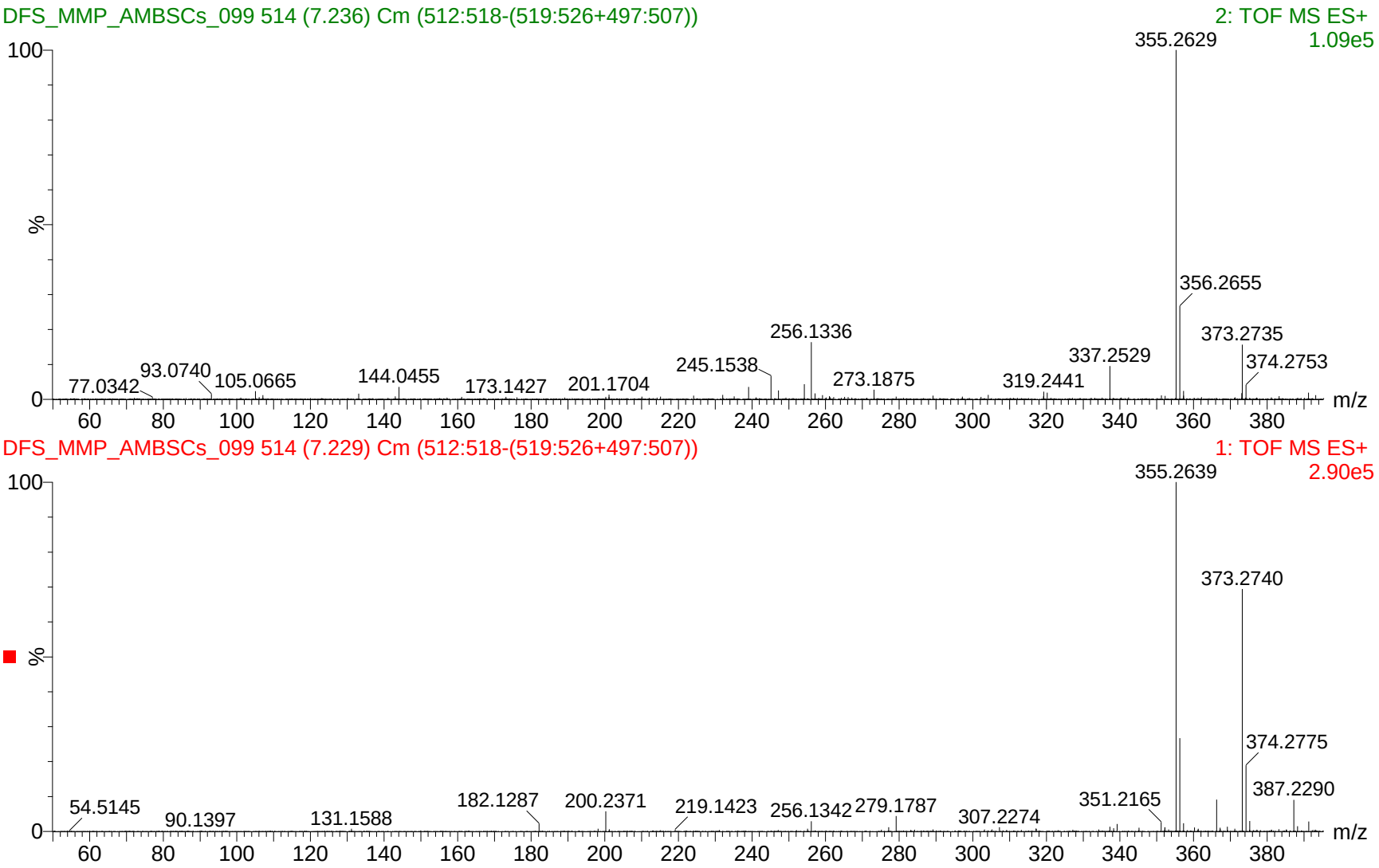


**Fig. S12.** Low Energy (Function 1) and High Energy (Function 2) spectra for AMB-CHMICA M2.

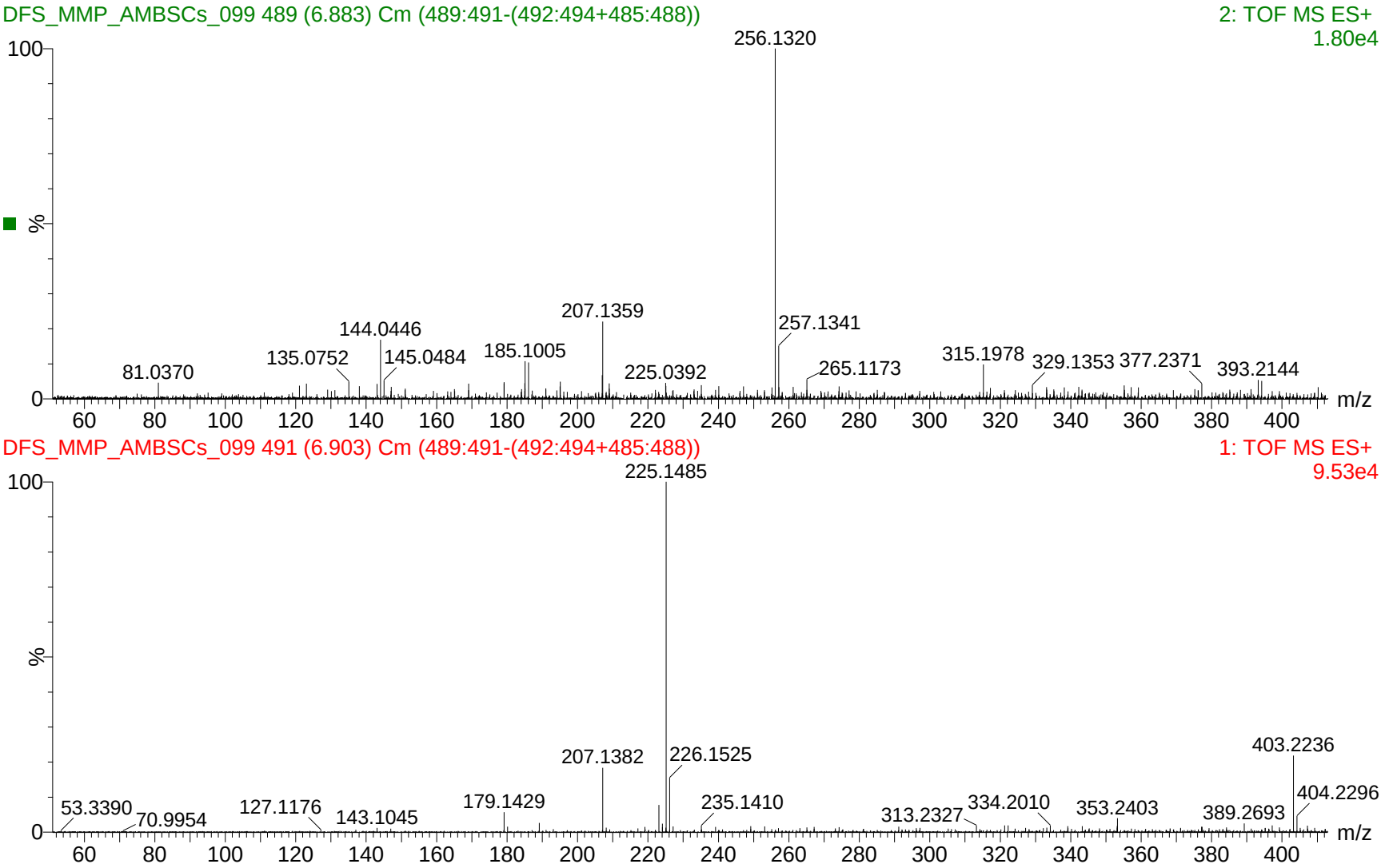


**Fig. S13.** Low Energy (Function 1) and High Energy (Function 2) spectra for AMB-CHMICA M3.

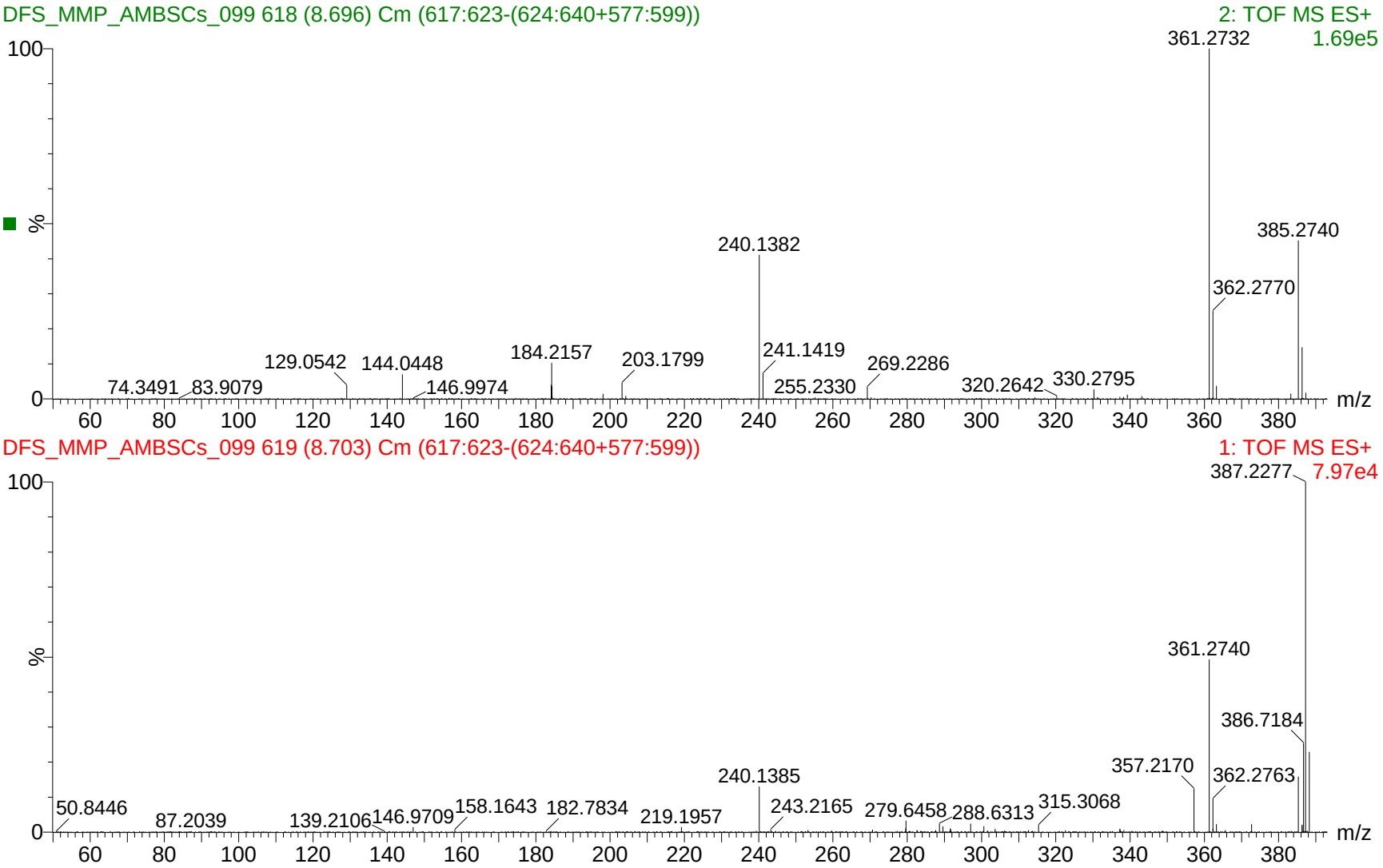


**Fig. S14.** Low Energy (Function 1) and High Energy (Function 2) spectra for AMB-CHMICA M4.

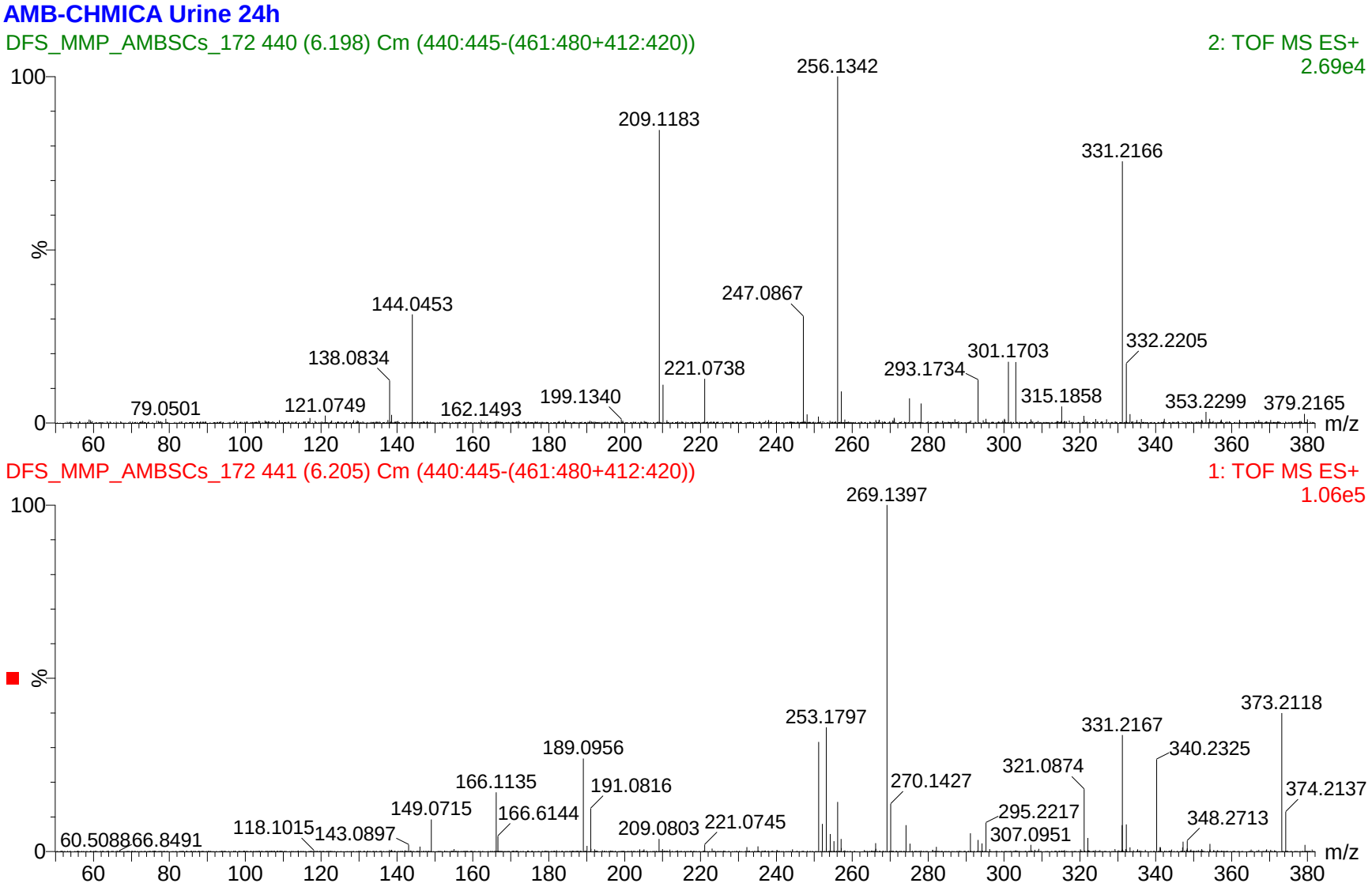


**Fig. S15.** Low Energy (Function 1) and High Energy (Function 2) spectra for AMB-CHMICA M5.

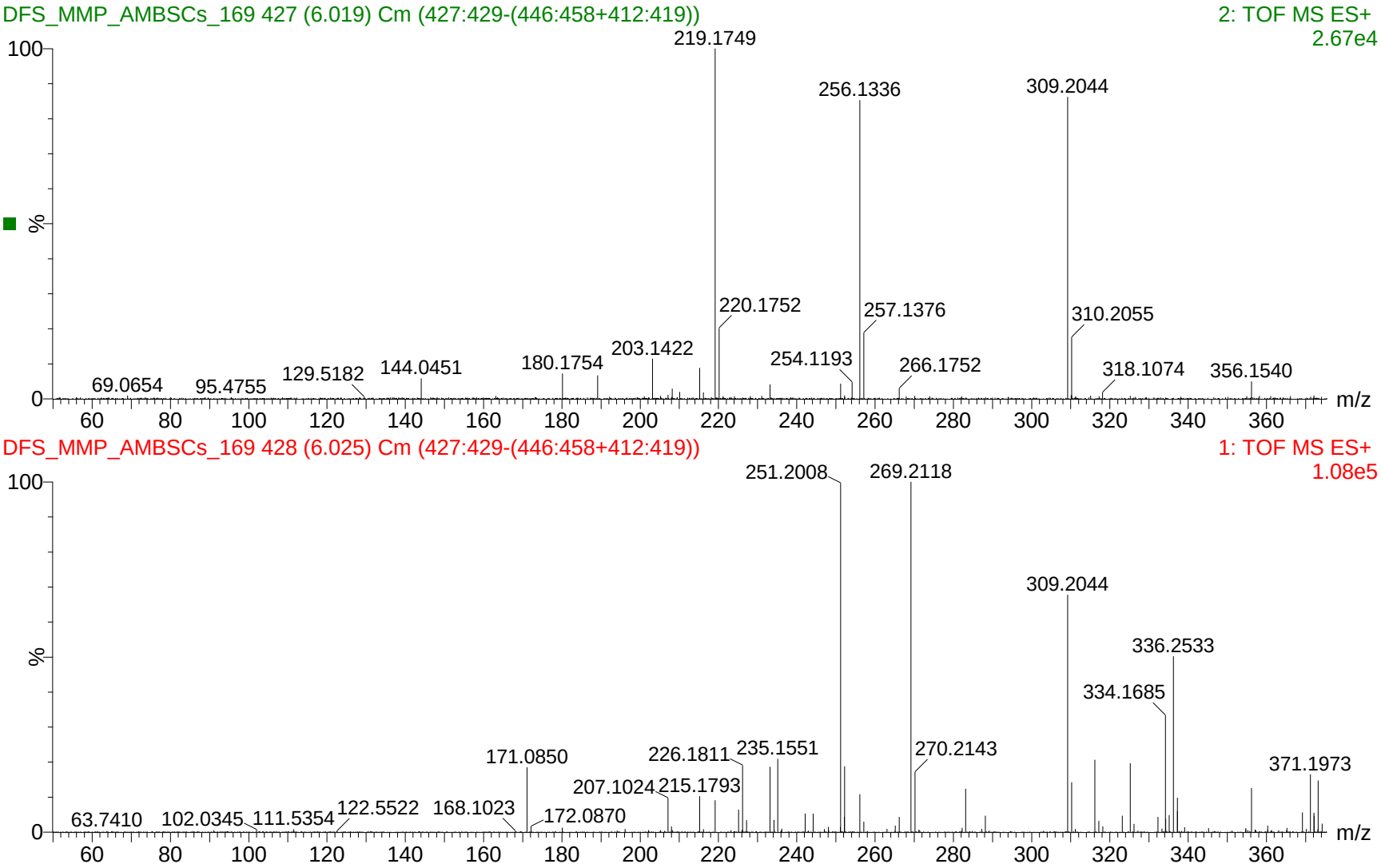


**Fig. S16.** Low Energy (Function 1) and High Energy (Function 2) spectra for AMB-CHMICA M6.

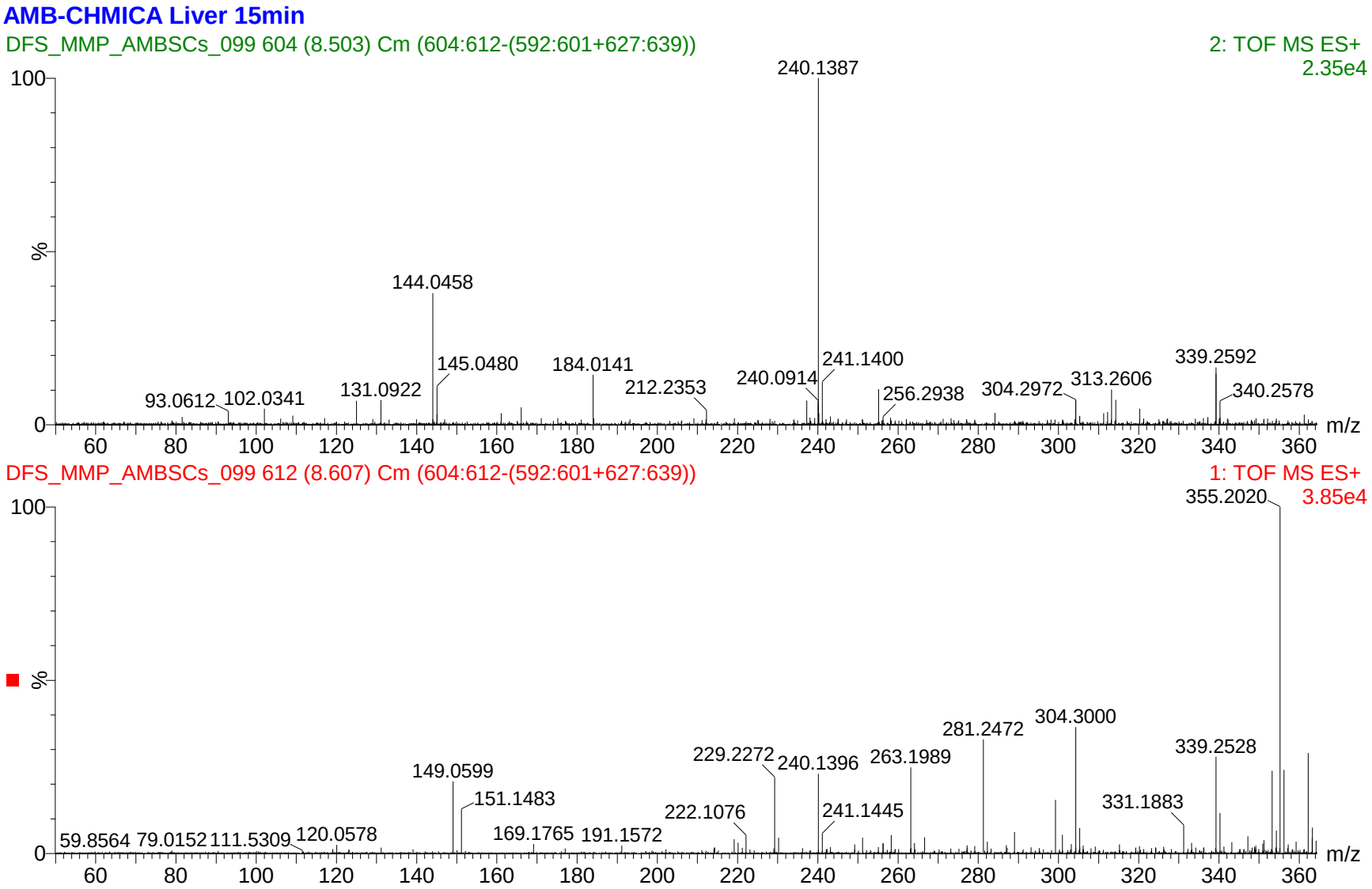


**Fig. S17.** Low Energy (Function 1) and High Energy (Function 2) spectra for AMB-CHMICA M7.

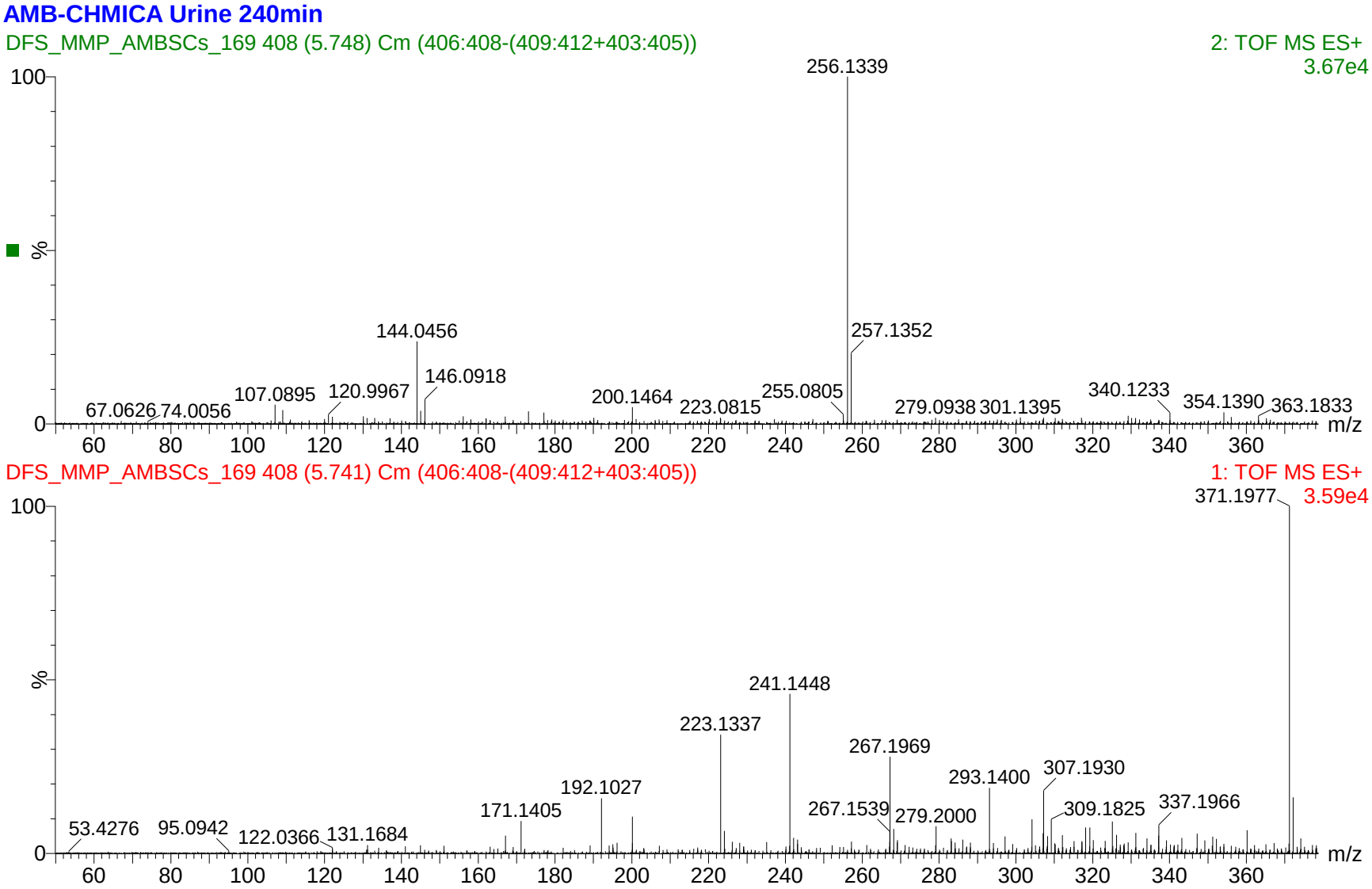


**Fig. S18.** Low Energy (Function 1) and High Energy (Function 2) spectra for AMB-CHMICA M8.

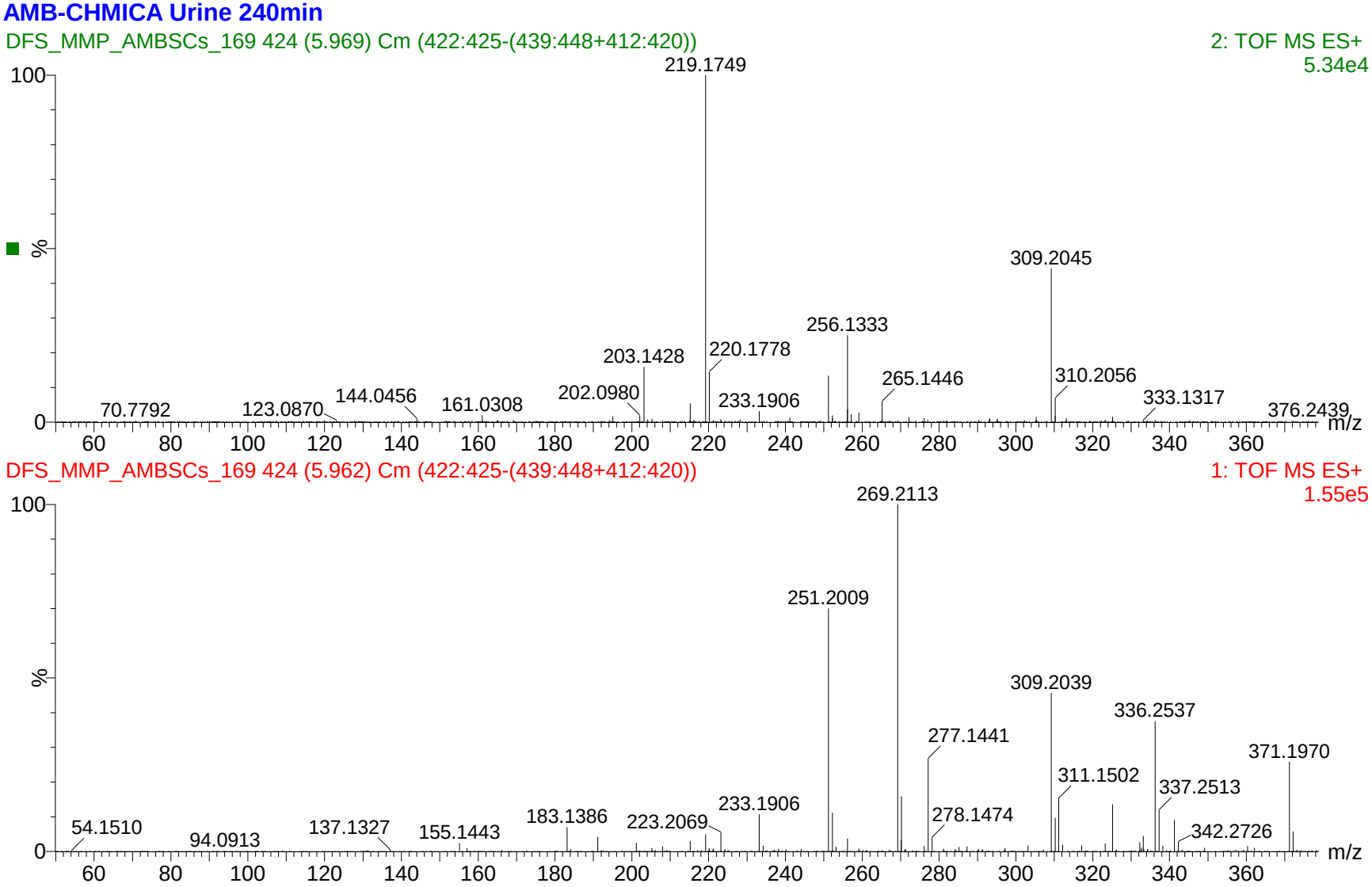


**Fig. S19.** Low Energy (Function 1) and High Energy (Function 2) spectra for AMB-CHMICA M9.

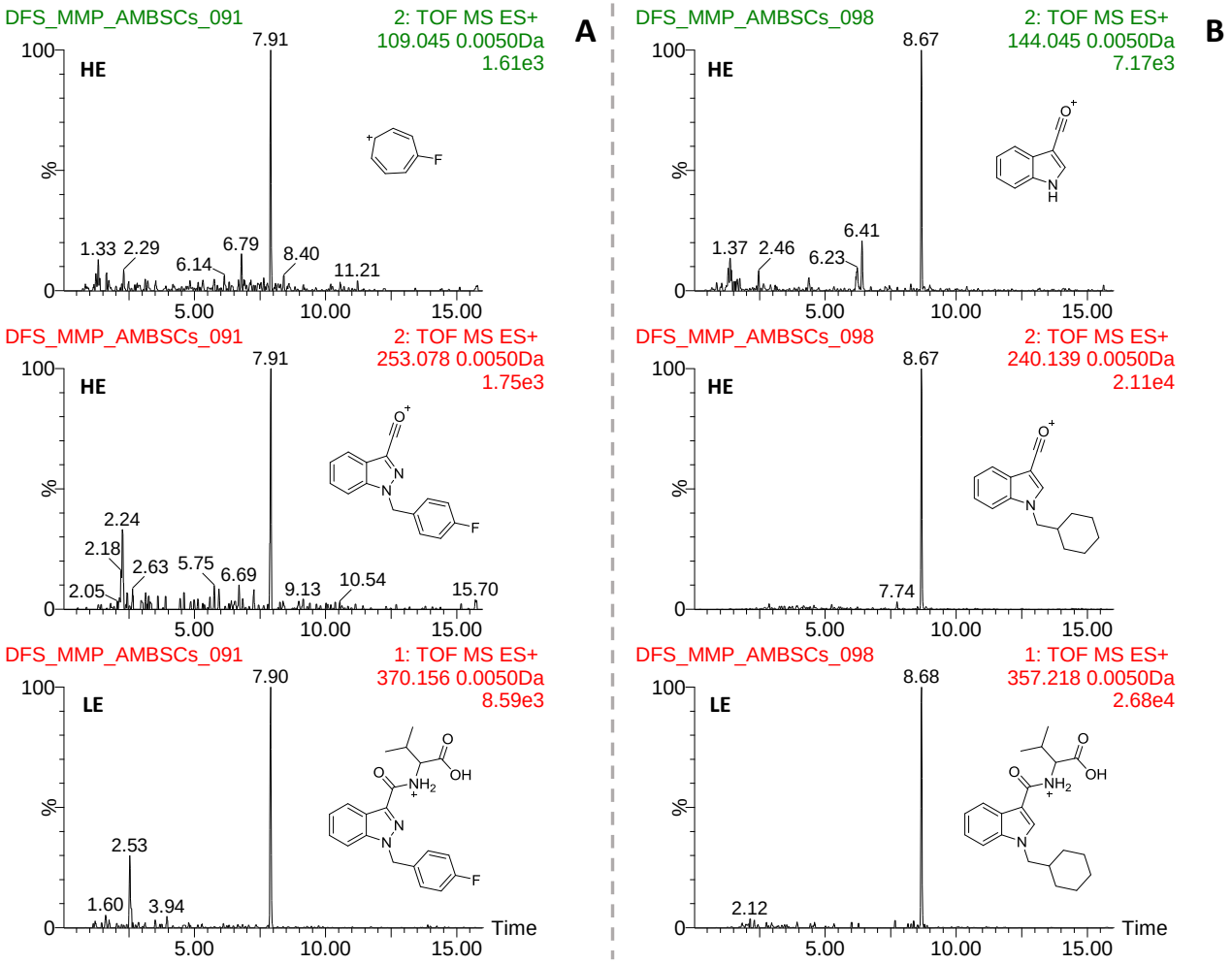


**Fig. S20.** Identification of the metabolites *O*-demethyl AMB-FUBINACA (**A**) and *O*-demethyl AMB-CHMICA (**B**) in liver samples collected 48 h after injection. Identification is based on chromatographic retention time and the presence of 2 accurate-mass fragment ions.

**Table S1.** Analytical response of AMB-FUBINACA and its detected metabolites in the different samples analysed.

| Compound | Brain | | | | Liver | | | | Serum | | | | Kidney | | | | Urine | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 15 min | 30 min | 180 min | 48 h | 15 min | 30 min | 180 min | 48 h | 15 min | 30 min | 180 min | 48 h | 15 min | 30 min | 180 min | 48 h | 30 min | 60 min | 90 min | 180 min | 300 min | 24 h |
| AMB-FUBINACA | 791 | 219 | 42 | | 77 | 49 | | | 162 | 38 | | | 548 | 200 | 37 | | | | | | | |
| M1 | | 22 | | | 1109 | 3519 | 2647 | 420 | 137 | 424 | 752 | 28 | 118 | 246 | 354 | | | | | 46 | 9 | 58 |
| M2 | | | | | | 188 | 98 | | | | | | | | | | | | | 15 | 46 | |
| M3 | | | | | | 135 | 108 | | | | | | | | | | | | | 87 | 48 | 106 |
| M4 | | | | | | | | | 33 | 83 | | | 62 | 86 | | | 1204 | 540 | 243 | 1646 | 886 | 352 |
| M5 | | | | | 55 | 76 | | | | | | | 139 | 128 | | | 2083 | 1204 | 530 | 3031 | 1483 | 227 |
| M6 | | | | | 114 | 190 | | | | | | | 20 | 66 | | | | | | | | |
| M7 | | | | | 100 | 523 | 286 | | | 23 | 17 | | | 38 | 41 | | | 13 | 12 | 160 | 136 | 194 |
| M8 | | | | | 49 | 405 | 229 | | | 23 | 22 | | | 42 | 12 | | | | | 39 | 67 | 42 |

**Table S2.** Analytical response of AMB-CHMICA and its detected metabolites in the different samples analysed.

| Compound | Brain | | | | Liver | | | | Serum | | | | Kidney | | | | Urine | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 15 min | 30 min | 180 min | 48 h | 15 min | 30 min | 180 min | 48 h | 15 min | 30 min | 180 min | 48 h | 15 min | 30 min | 180 min | 48 h | 30 min | 60 min | 90 min | 120 min | 240 min | 300 min | 360 min | 24 h |
| AMB-CHMICA | 214 | 205 | | | 7928 | 6735 | 43 | | 394 | 576 | 34 | | 313 | 478 | | | | | | | | | | |
| M1 | | | | | 325 | 441 | 1000 | 1252 | | | 45 | | 275 | 191 | | | | | | | | | | 254 |
| M2 | | | | | 591 | 268 | | | 46 | 70 | | | | | | | | | | | | | | |
| M3 | | | | | 490 | 387 | | | | | | | | | | | | | | | | | | |
| M4 | 13 | 31 | | | 1433 | 1083 | | | | 36 | | | | 154 | | | | | | | | | | |
| M5 | | | | | | | | | | | | | | | | | | | | 79 | 127 | 261 | 187 | 806 |
| M6 | | | | | | | | | | | | | | | | | | | 164 | 348 | 495 | 430 | 362 | 134 |
| M7 | | 79 | | | 588 | 880 | 65 | | 79 | 244 | 53 | | 129 | 258 | 50 | | | | | | | | | |
| M8 | | | | | | 132 | | | | | | | | 117 | | | | 58 | 318 | 594 | 712 | 724 | 600 | 192 |
| M9 | | | | | | | | | | | | | | | | | | | 169 | 439 | 665 | 647 | 515 | 231 |