

5F-Cumyl-PINACA in ‘e-liquids’ for electronic cigarettes: comprehensive characterization of a new type of synthetic cannabinoid in a trendy product including investigations on the in vitro and in vivo phase I metabolism of 5F-Cumyl-PINACA and its non-fluorinated analog Cumyl-PINACA

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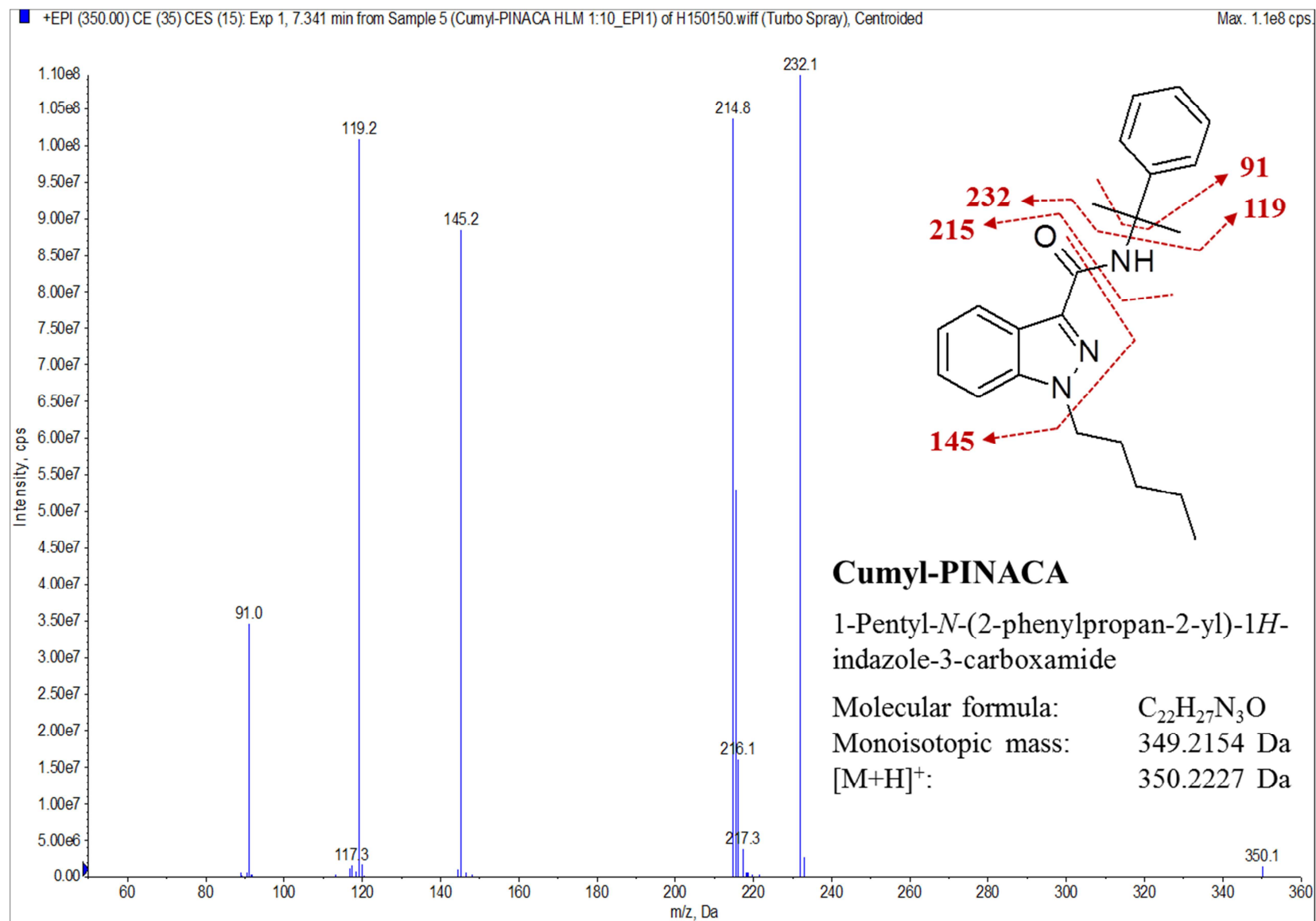
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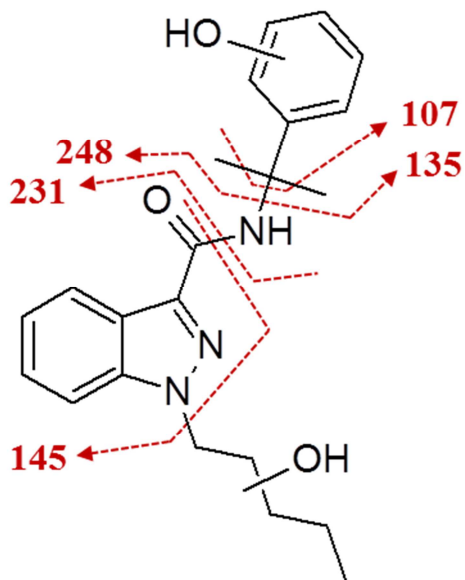
fax: +49 761 203 6826

e-mail: volker.auwaerter@uniklinik-freiburg.de

[†]V. Angerer and F. Franz contributed equally to this work.

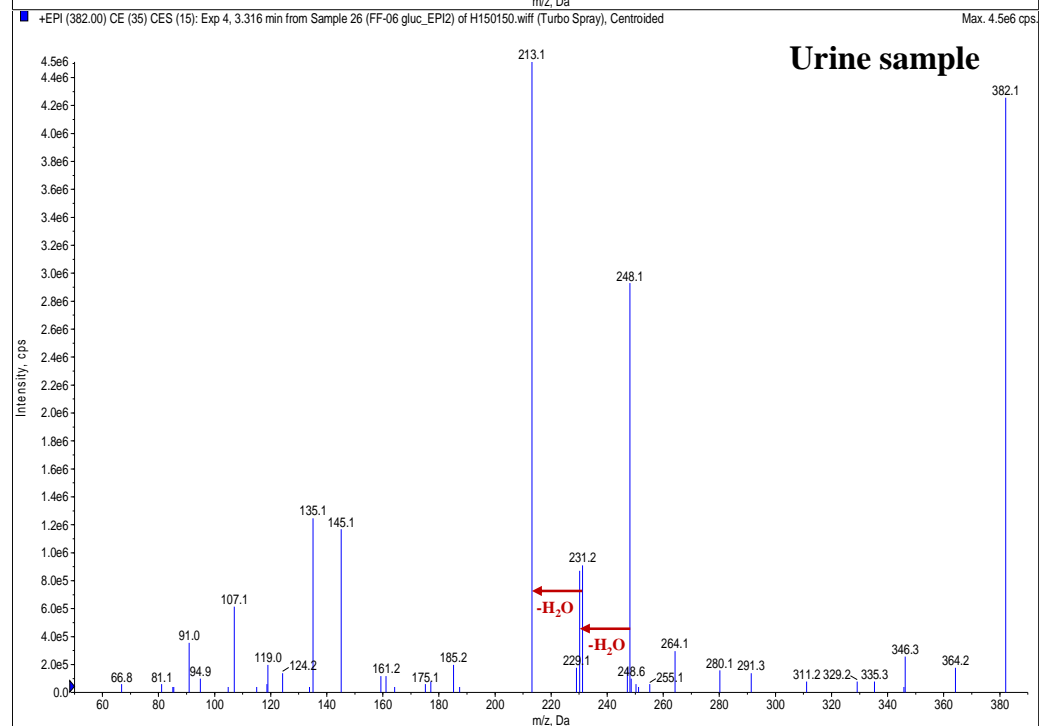
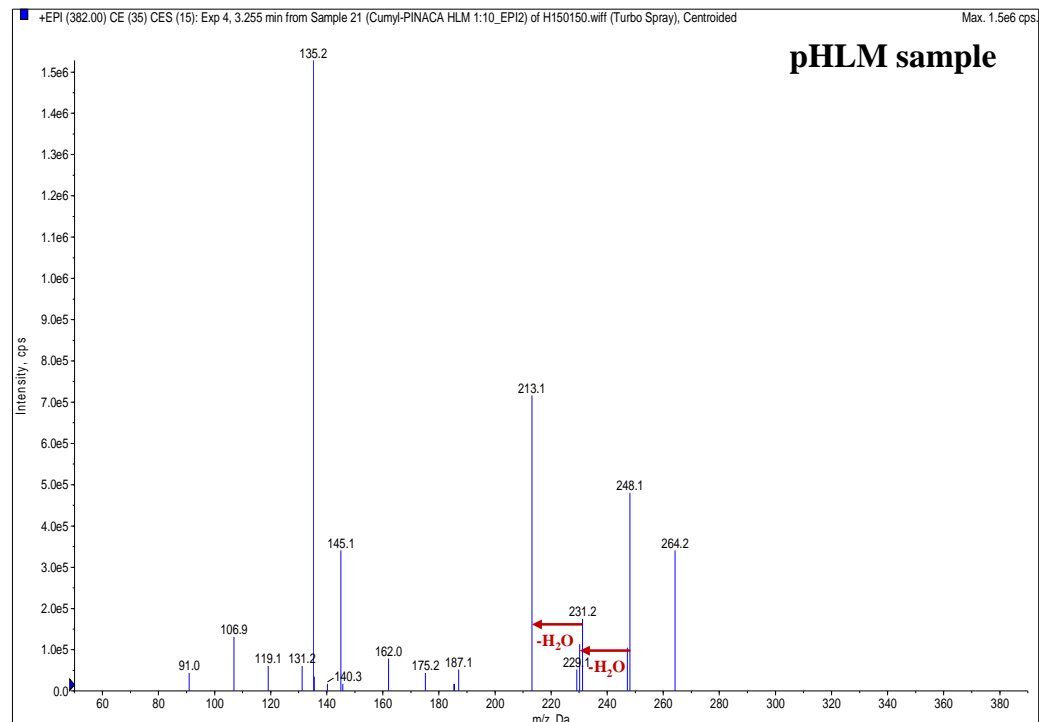
Fig. S1 Enhanced Product Ion (EPI) spectra of Cumyl-PINACA metabolites detected in pooled human liver microsome (pHLM) assay samples and authentic urine samples (recorded from urine sample 6 after treatment with glucuronidase) in comparison to the EPI spectrum of the parent compound 'Cumyl-PINACA'. Proposed structural formulae and fragmentation is shown for each compound along with their molecular formulae, monoisotopic and single-protonated masses. The EPI scans were recorded with a declustering potential (DP) of 40 V, an entrance potential (EP) of 8 V and a collision energy (CE) of 35 V with a collision energy spread (CES) of ± 15 V. The position of the dihydrodiol function at the indazole ring for A06 is exemplary and was not confirmed

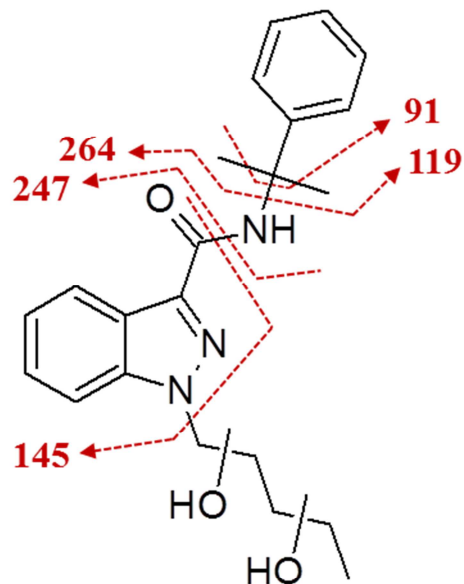




A01 (RT 3.3 min)

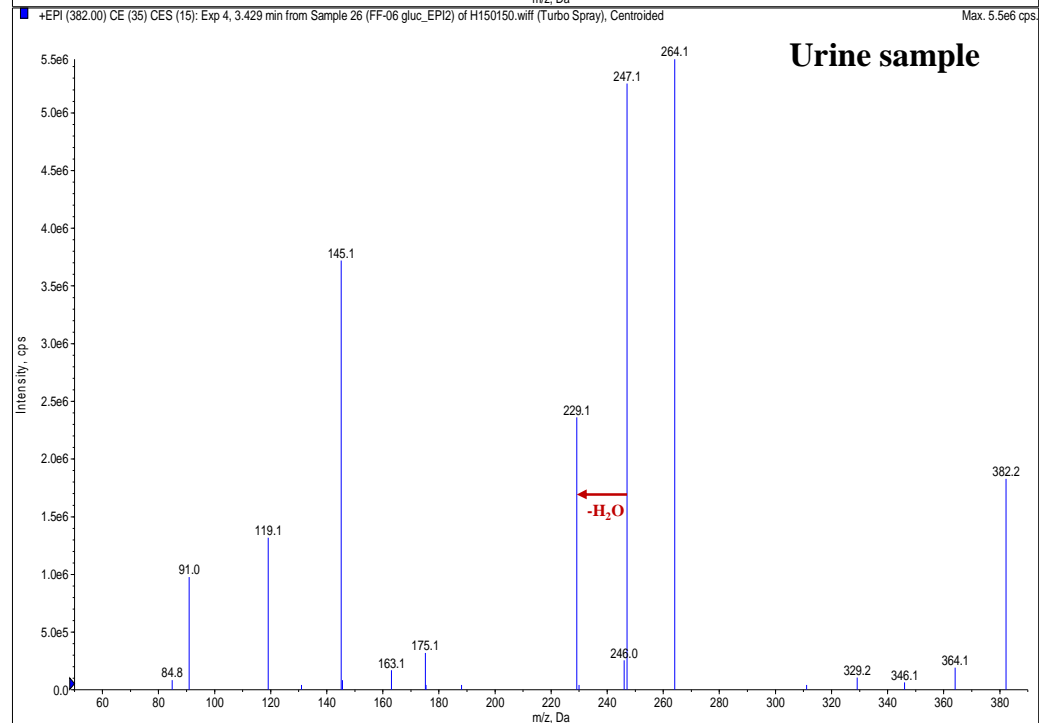
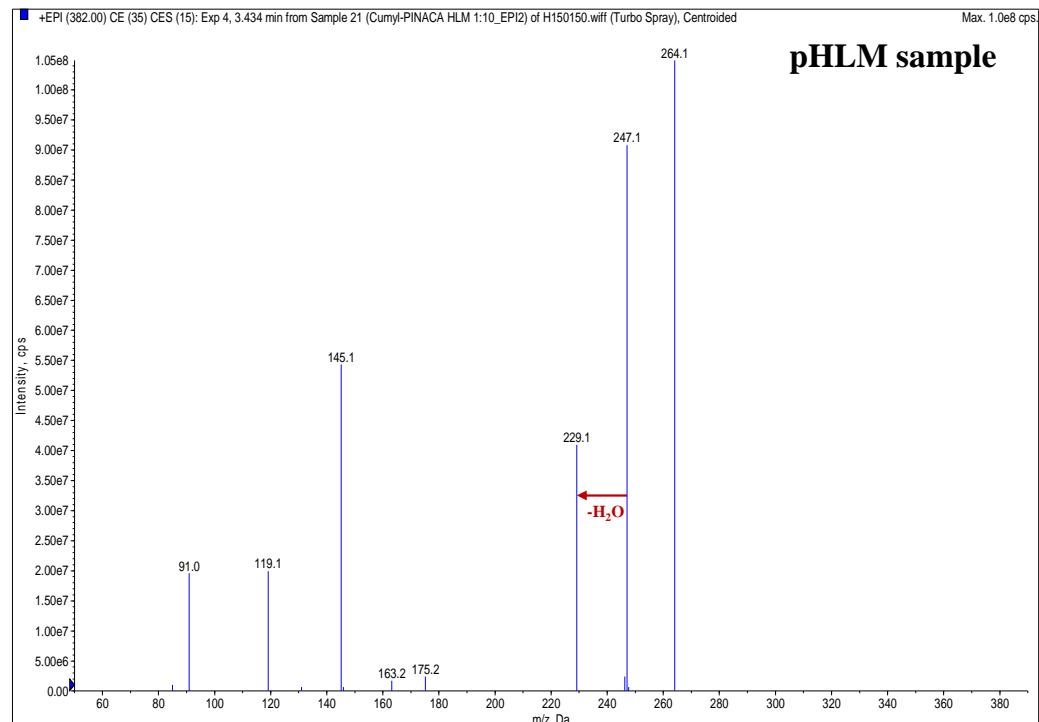
Molecular formula: $C_{22}H_{27}N_3O_3$
 Monoisotopic mass: 381.2052 Da
 $[M+H]^+$: 382.2125 Da

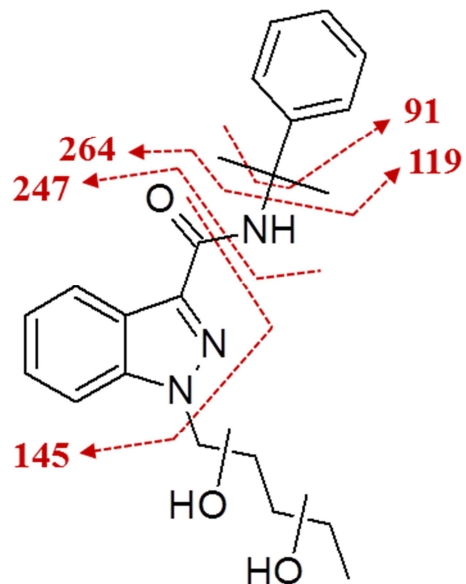




A02 (RT 3.4 min)

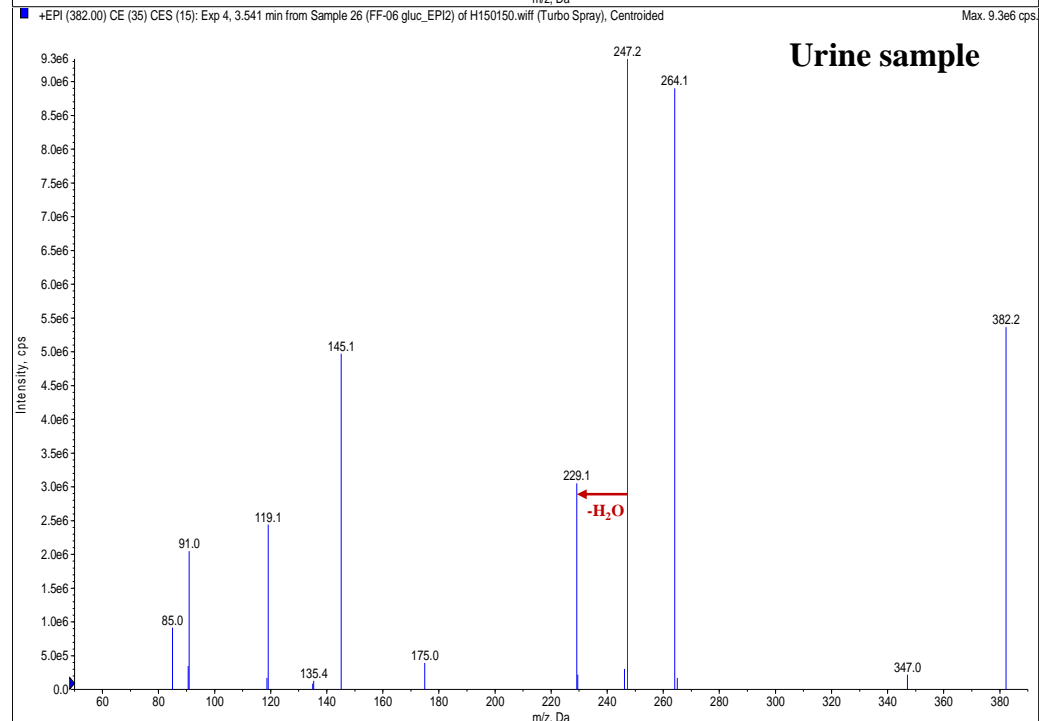
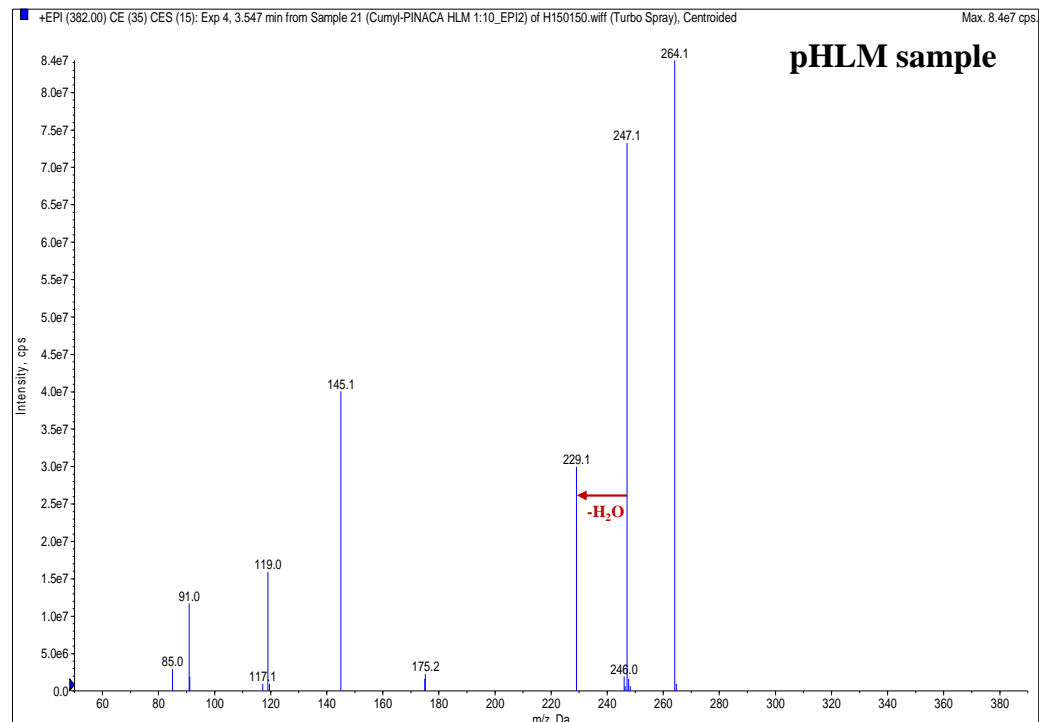
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 Monoisotopic mass: 381.2052 Da
 $[M+H]^+$: 382.2125 Da

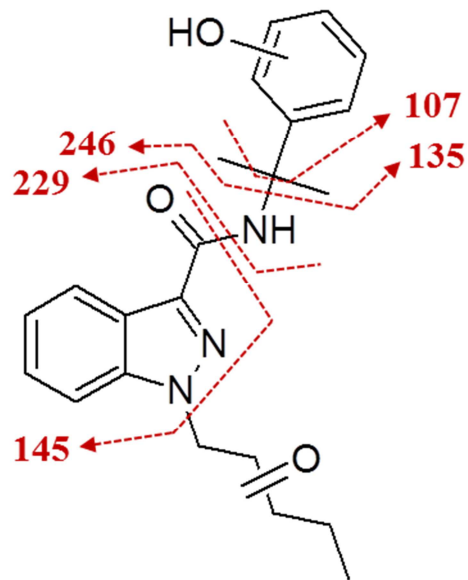




A03 (RT 3.5 min)

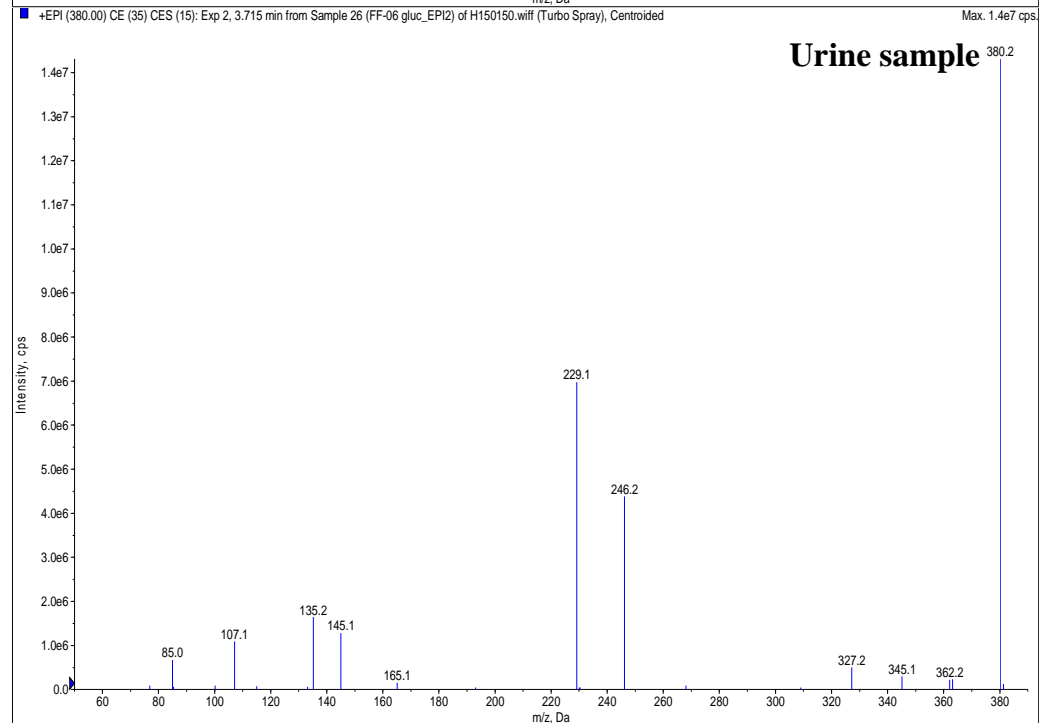
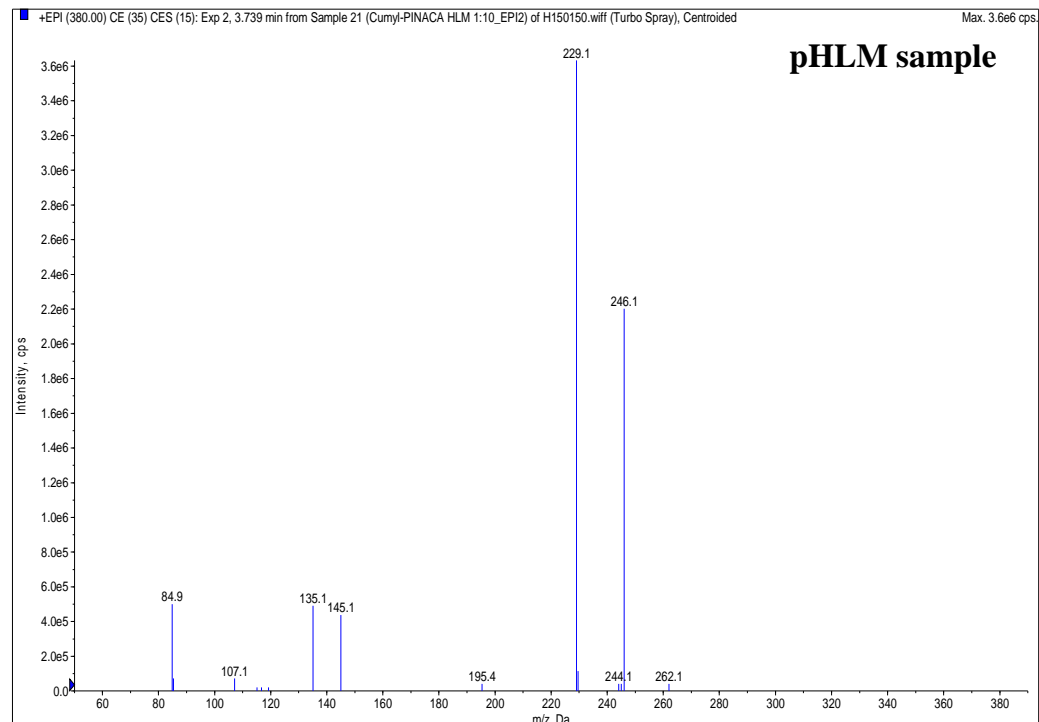
Molecular formula: $C_{22}H_{27}N_3O_3$
 Monoisotopic mass: 381.2052 Da
 $[M+H]^+$: 382.2125 Da

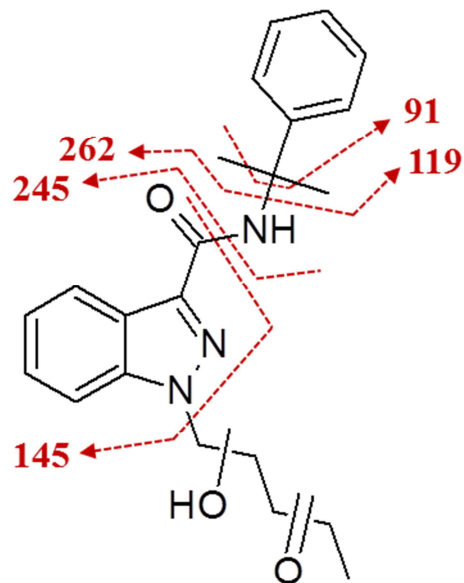




A04 (RT 3.7 min)

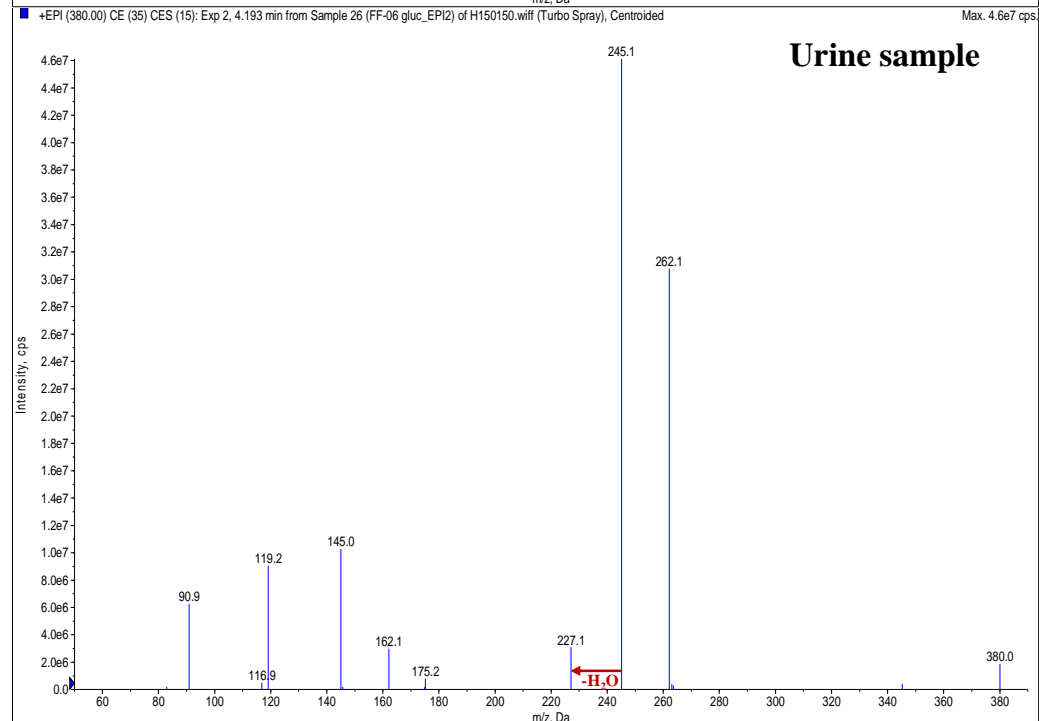
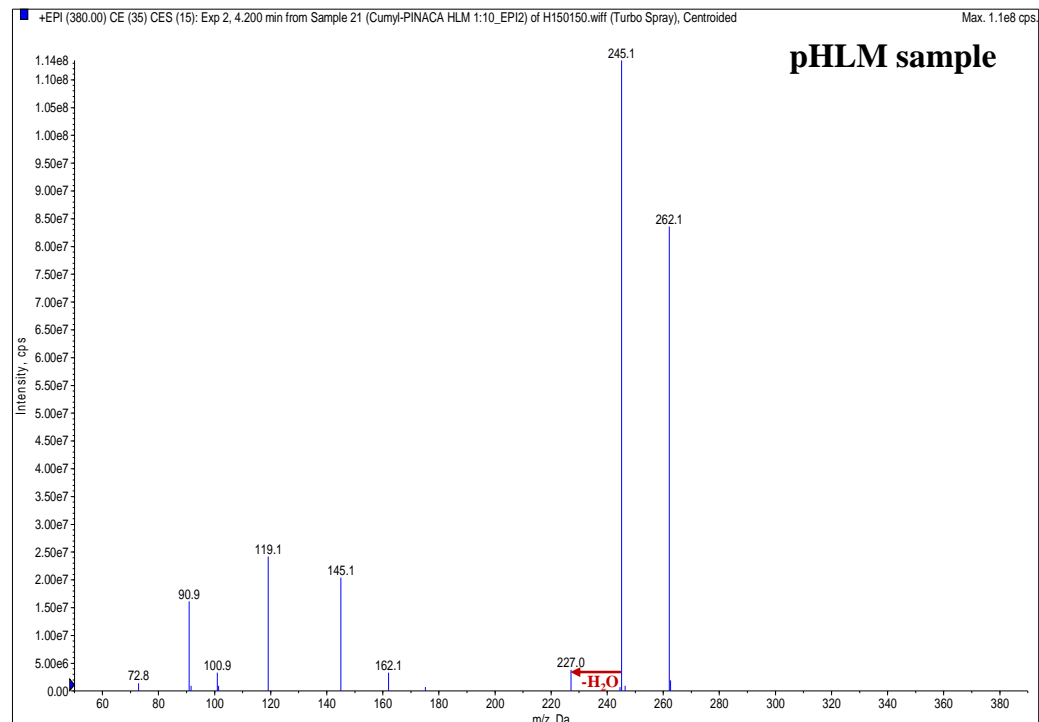
Molecular formula: $C_{22}H_{25}N_3O_3$
 Monoisotopic mass: 379.1896 Da
 $[M+H]^+$: 380.1969 Da

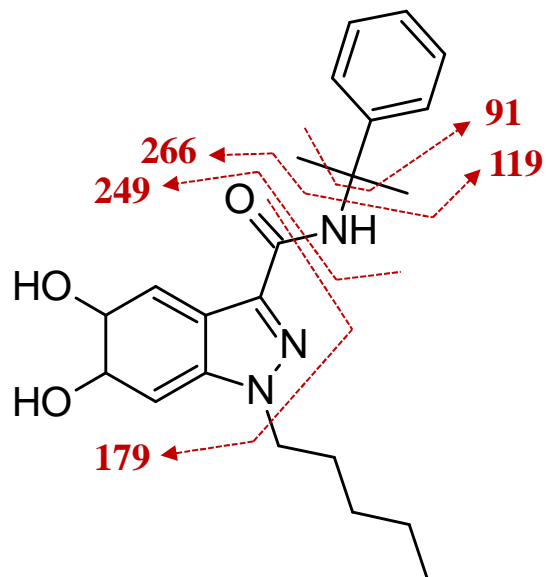




A05 (RT 4.2 min)

Molecular formula: $C_{22}H_{25}N_3O_3$
 Monoisotopic mass: 379.1896 Da
 $[M+H]^+$: 380.1969 Da





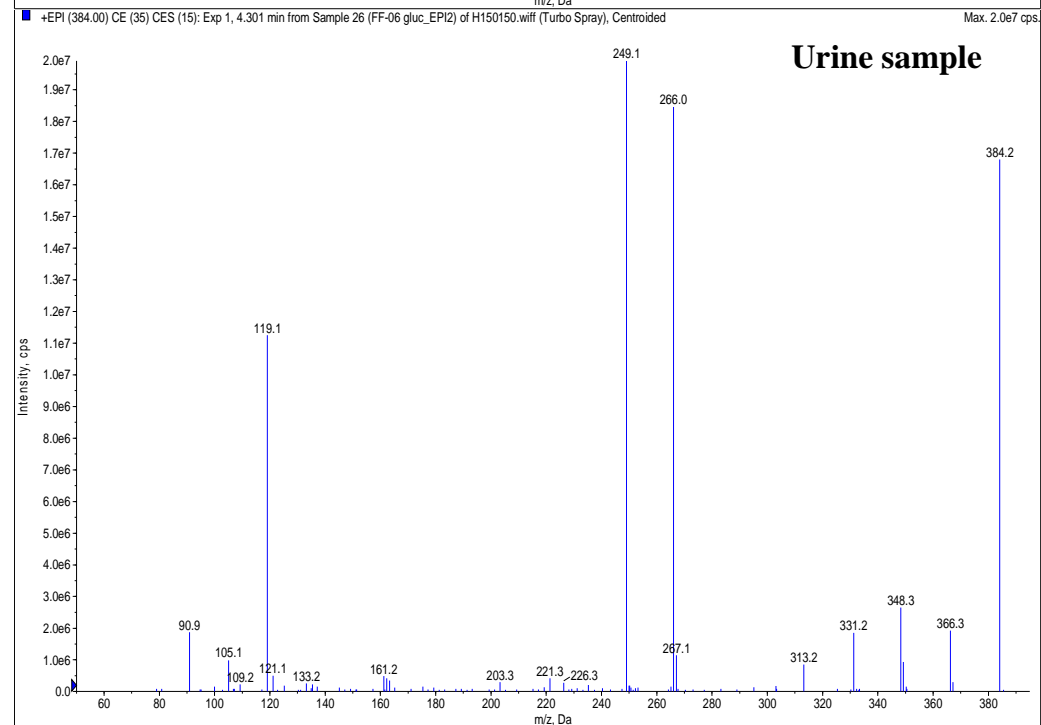
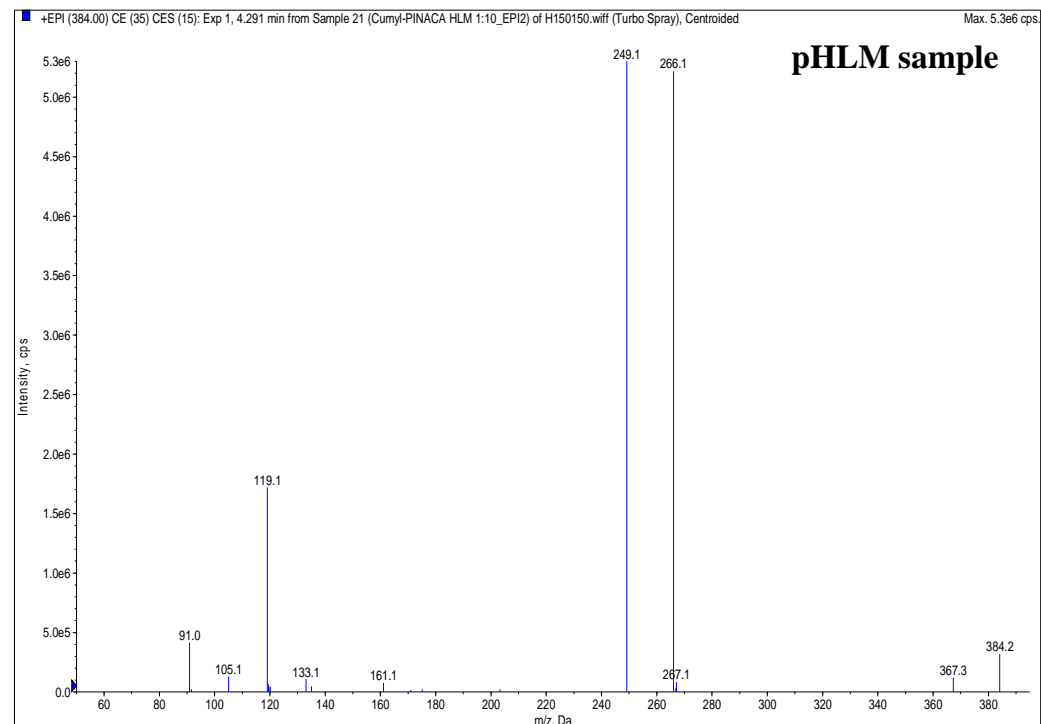
A06 (RT 4.3 min)

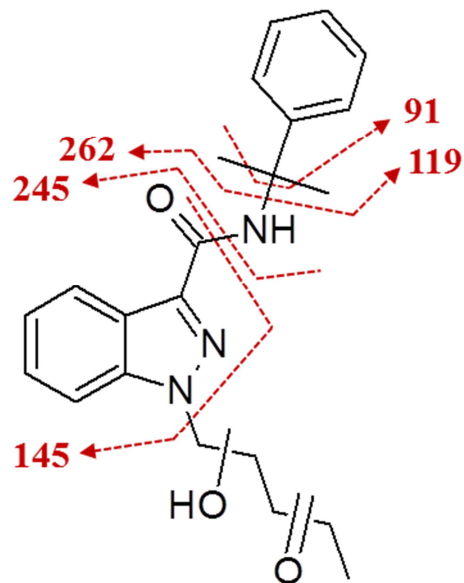
(dihydrodiol)

Molecular formula: $C_{22}H_{29}N_3O_3$

Monoisotopic mass: 383.2209 Da

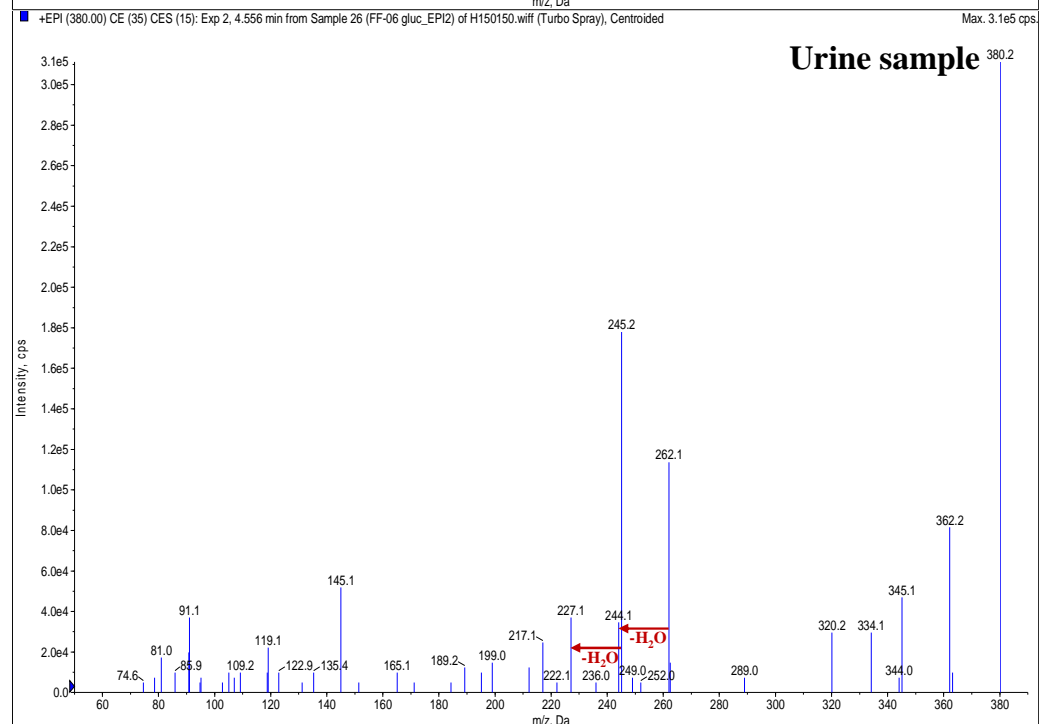
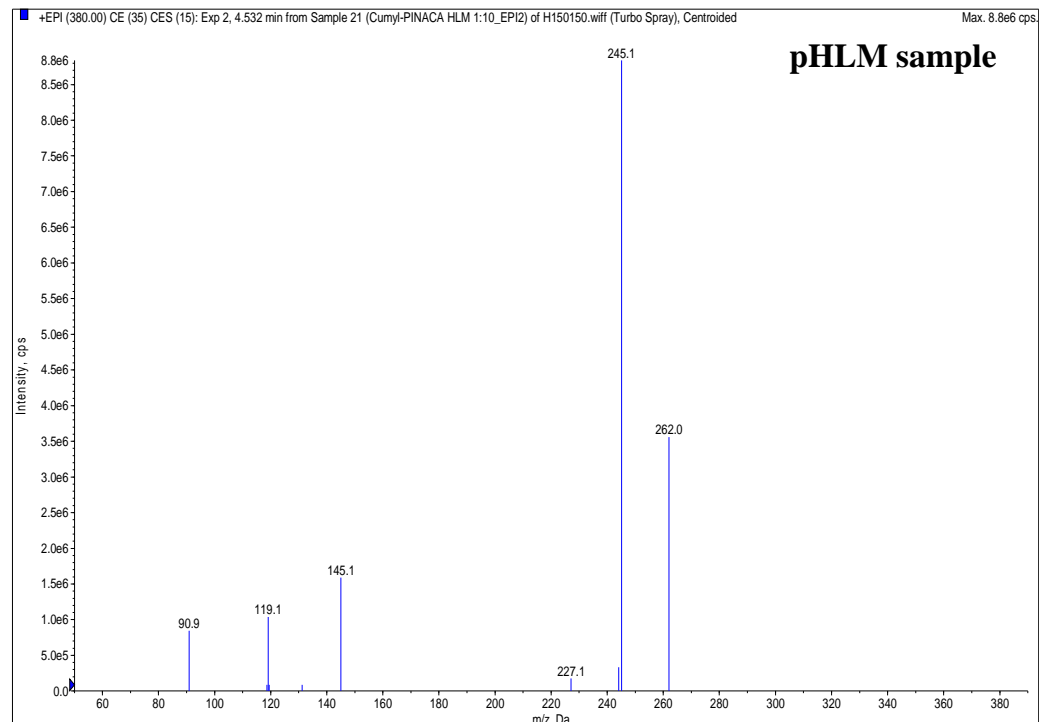
$[M+H]^+$: 384.2282 Da

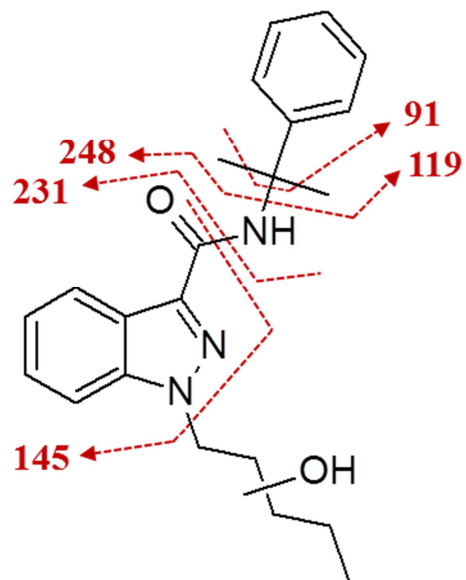




A07 (RT 4.5 min)

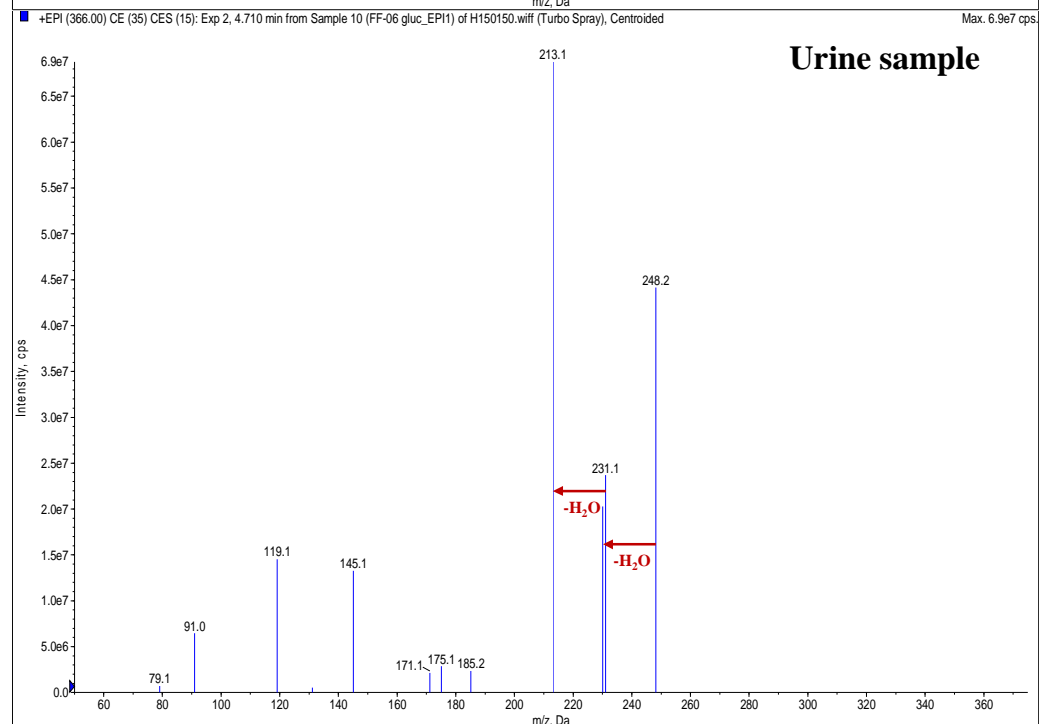
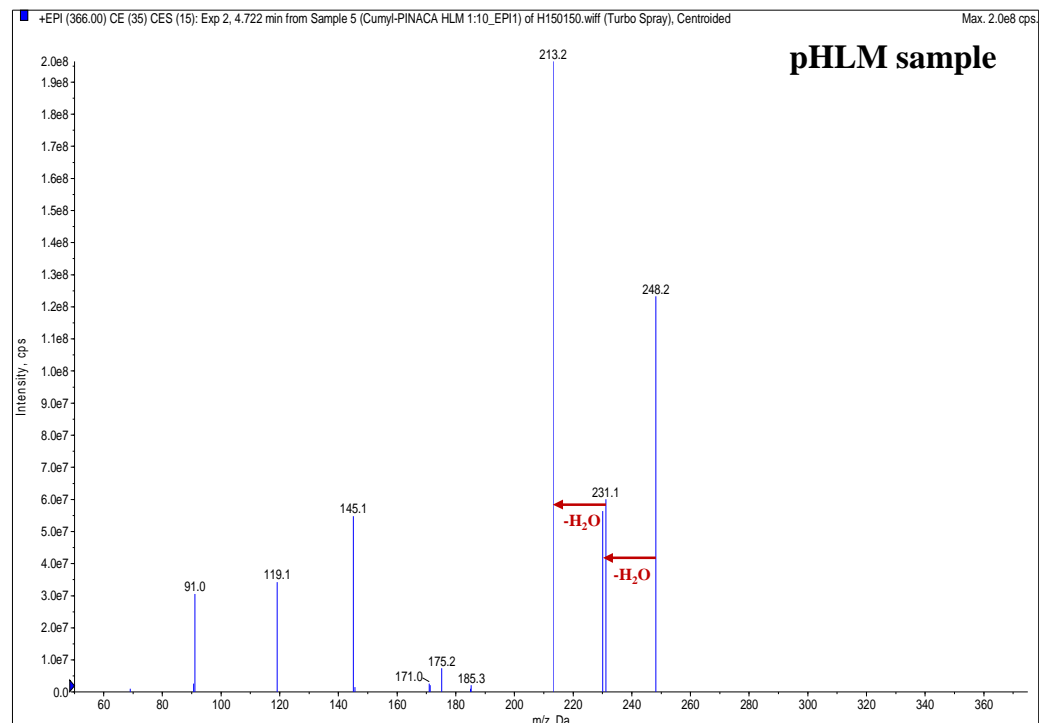
Molecular formula: $C_{22}H_{25}N_3O_3$
 Monoisotopic mass: 379.1896 Da
 $[M+H]^+$: 380.1969 Da

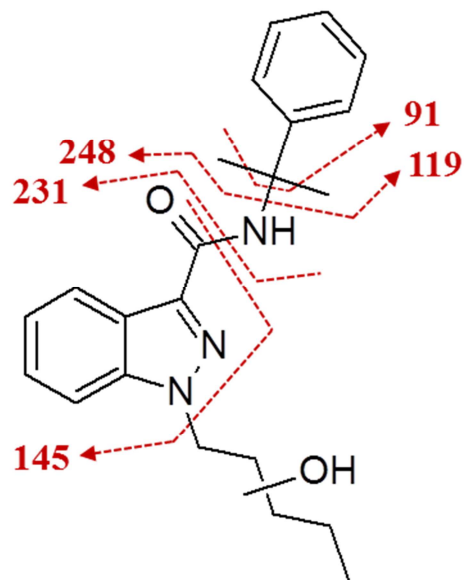




A08 (RT 4.8 min)

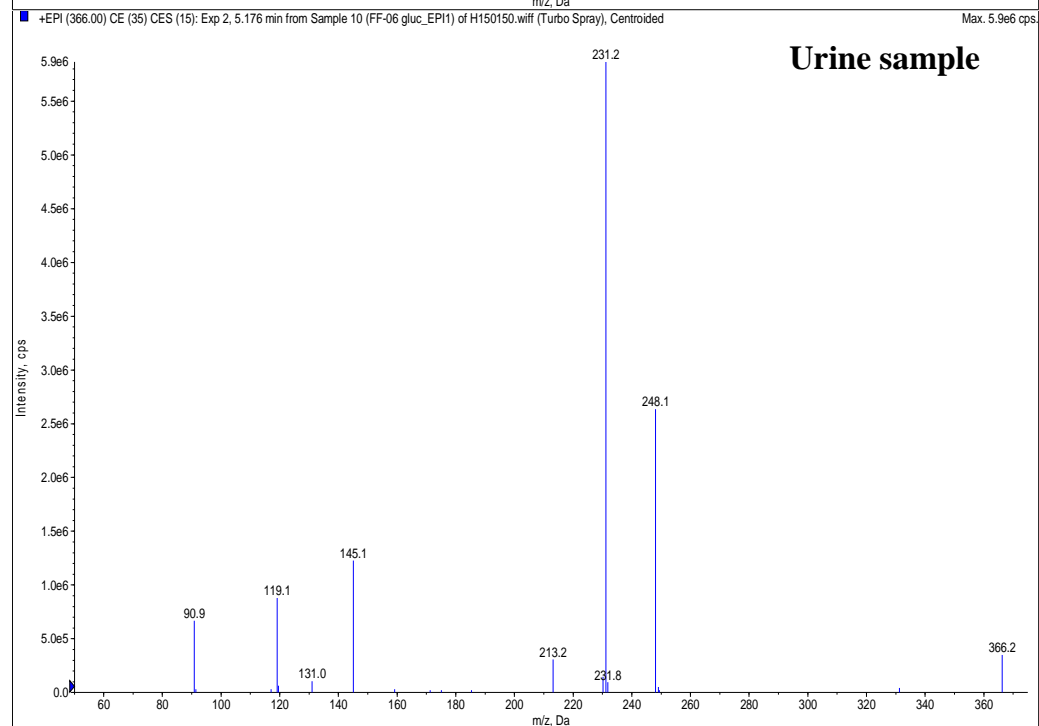
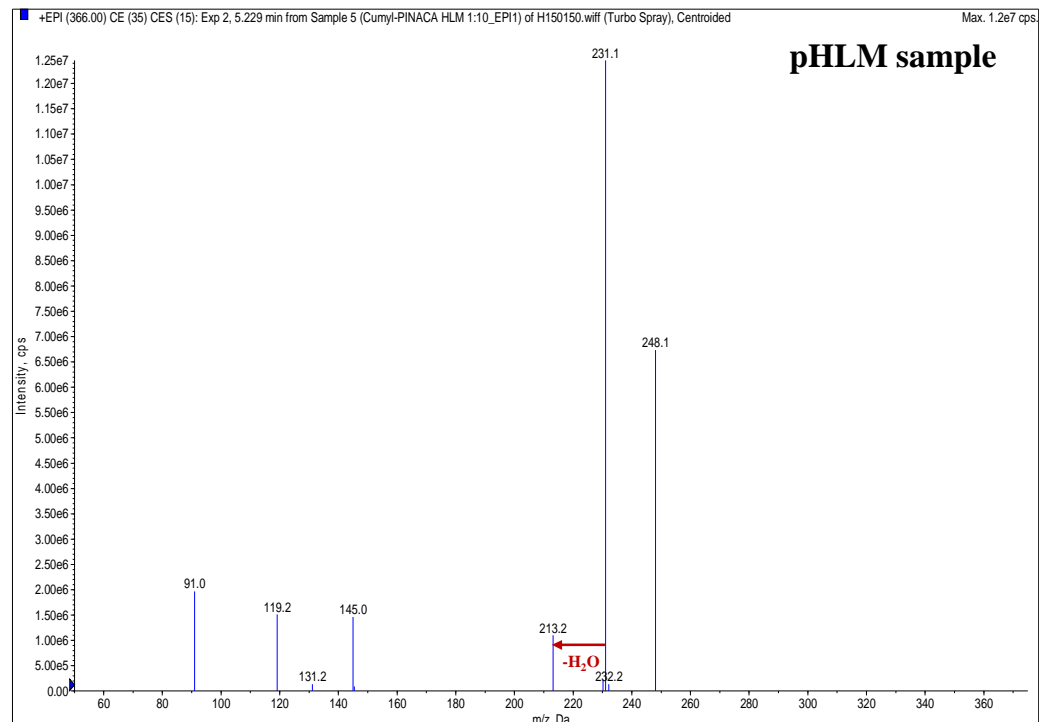
Molecular formula: $C_{22}H_{27}N_3O_2$
 Monoisotopic mass: 365.2103 Da
 $[M+H]^+$: 366.2176 Da

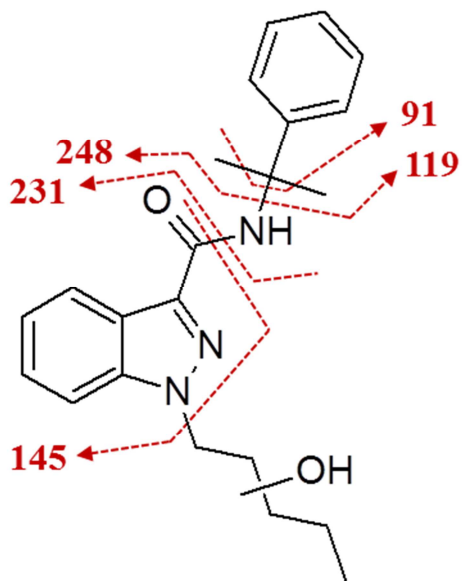




A09 (RT 5.2 min)

Molecular formula: $C_{22}H_{27}N_3O_2$
 Monoisotopic mass: 365.2103 Da
 $[M+H]^+$: 366.2176 Da





A10 (RT 5.6 min)

Molecular formula: $C_{22}H_{27}N_3O_2$
 Monoisotopic mass: 365.2103 Da
 $[M+H]^+$: 366.2176 Da

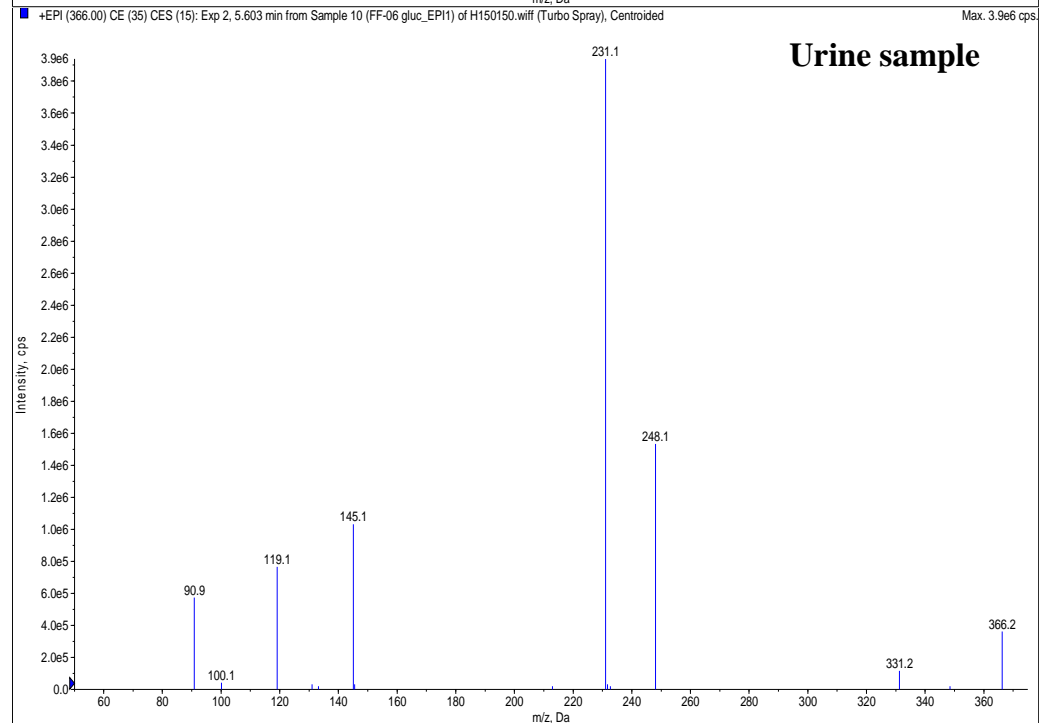
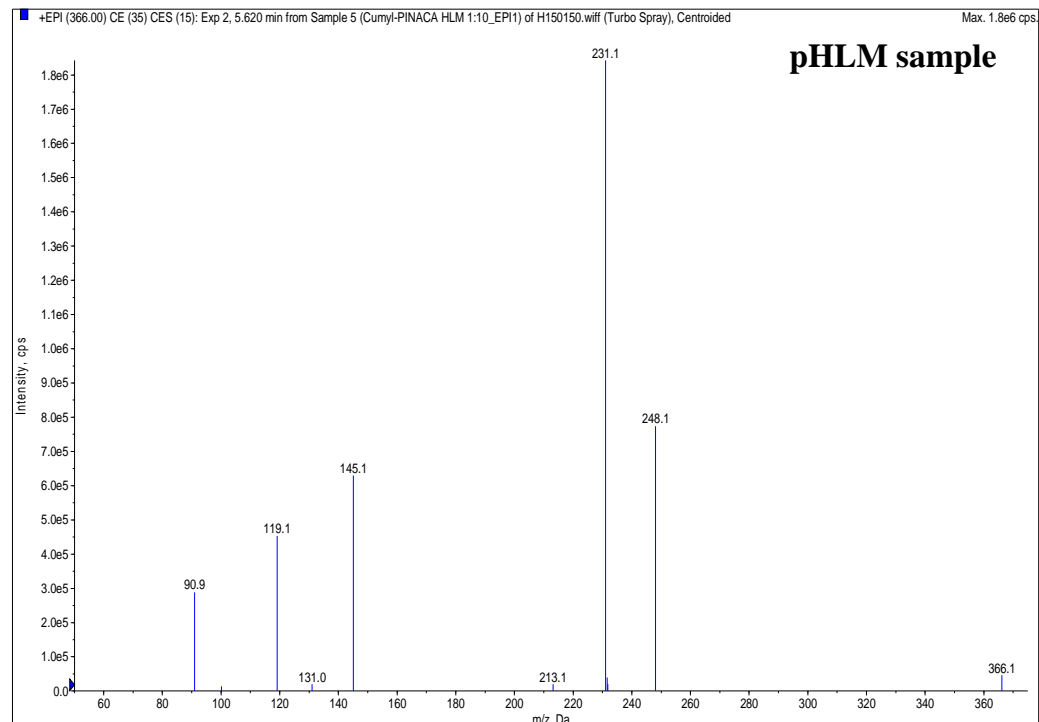


Fig. S2 GC–EI-MS and proposed fragmentation of the unknown compound, later identified as 5F-Cumyl-PINACA (retention time 11.7 min)

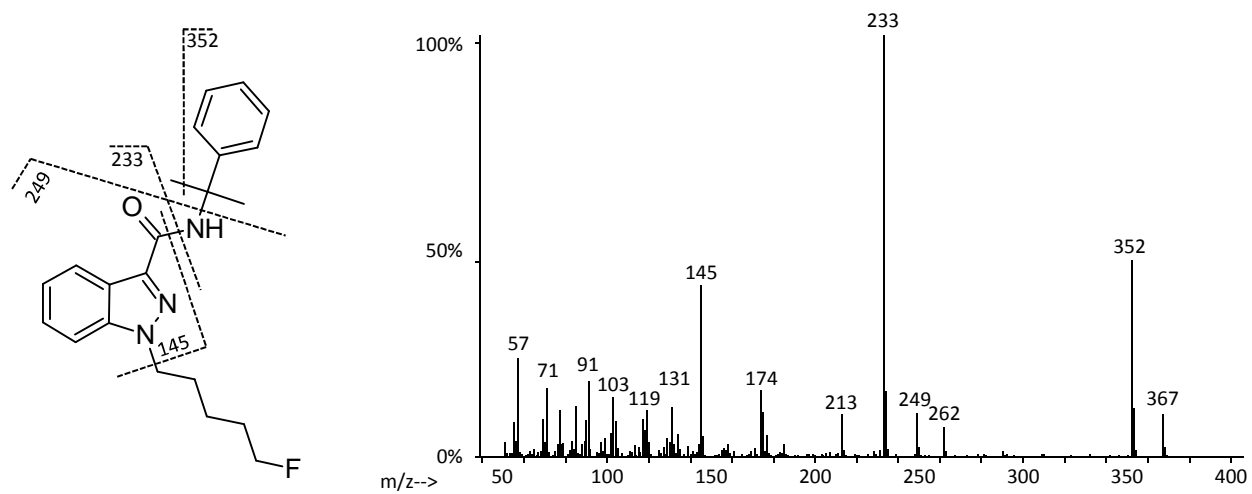


Fig. S3 Structural formula of the unknown compound identified as 5F-Cumyl-PINACA

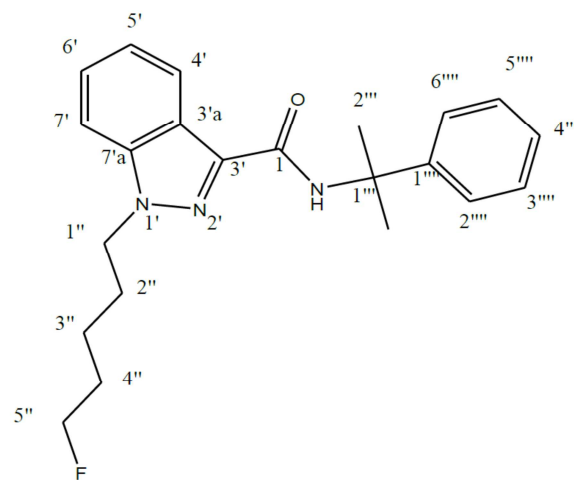
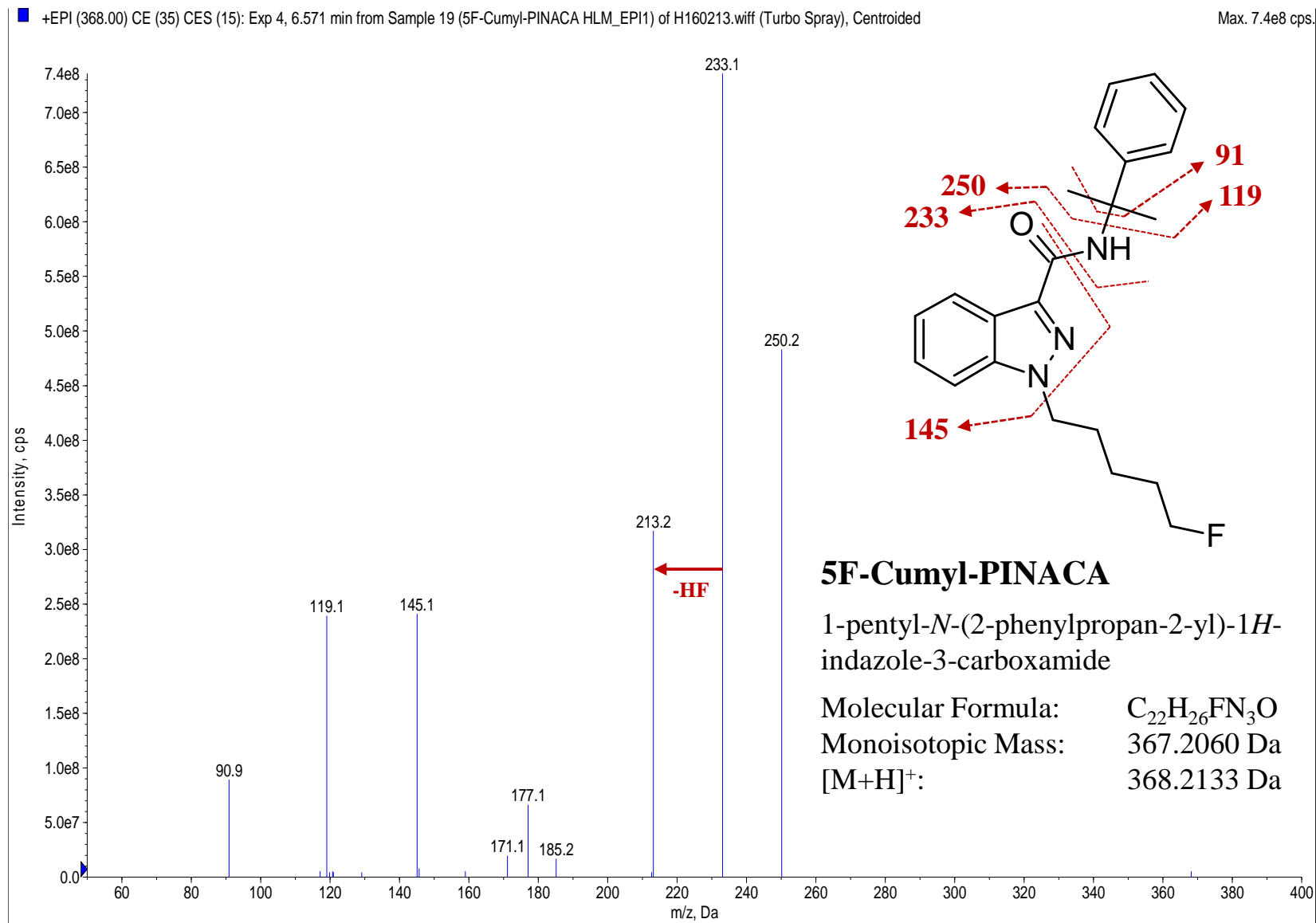
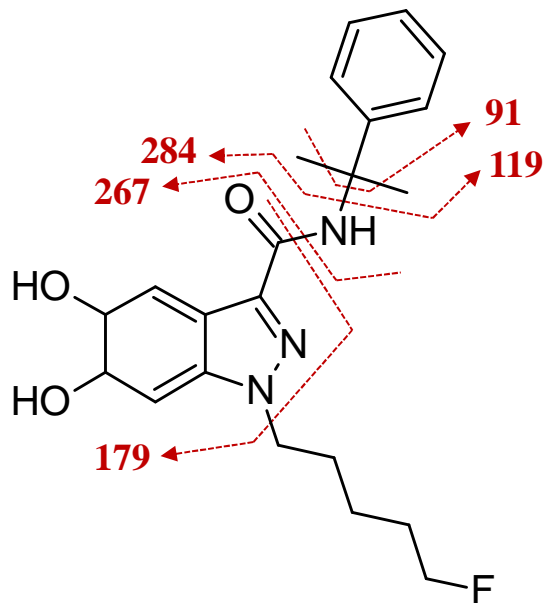


Fig. S4 Enhanced Product Ion (EPI) spectra of 5F-Cumyl-PINACA metabolites detected in pooled human liver microsome (pHLM) assay samples and authentic urine samples (recorded from urine sample 6 after treatment with glucuronidase) in comparison to the EPI spectrum of the parent compound '5F-Cumyl-PINACA'. Proposed structural formulae and fragmentation is shown for each compound along with their molecular formulae, monoisotopic and single-protonated masses. The EPI scans were recorded with a declustering potential (DP) of 65 V, an entrance potential (EP) of 12 V and a collision energy (CE) of 35 V with a collision energy spread (CES) of ± 15 V. The position of the dihydrodiol function at the indazole ring for B01 is exemplary and was not confirmed





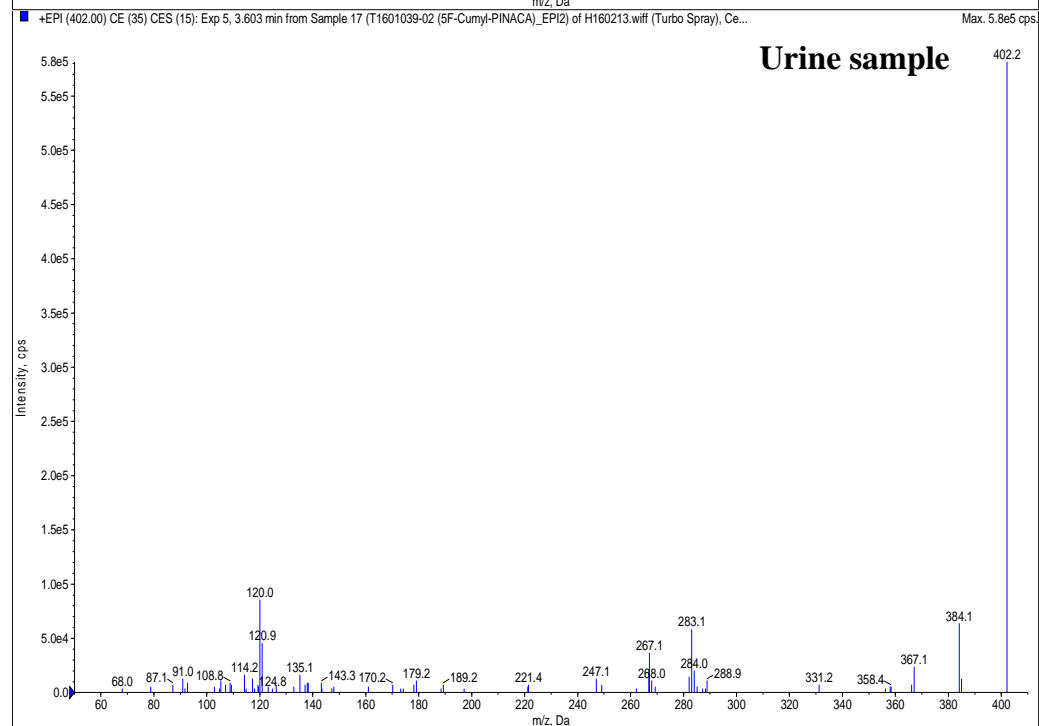
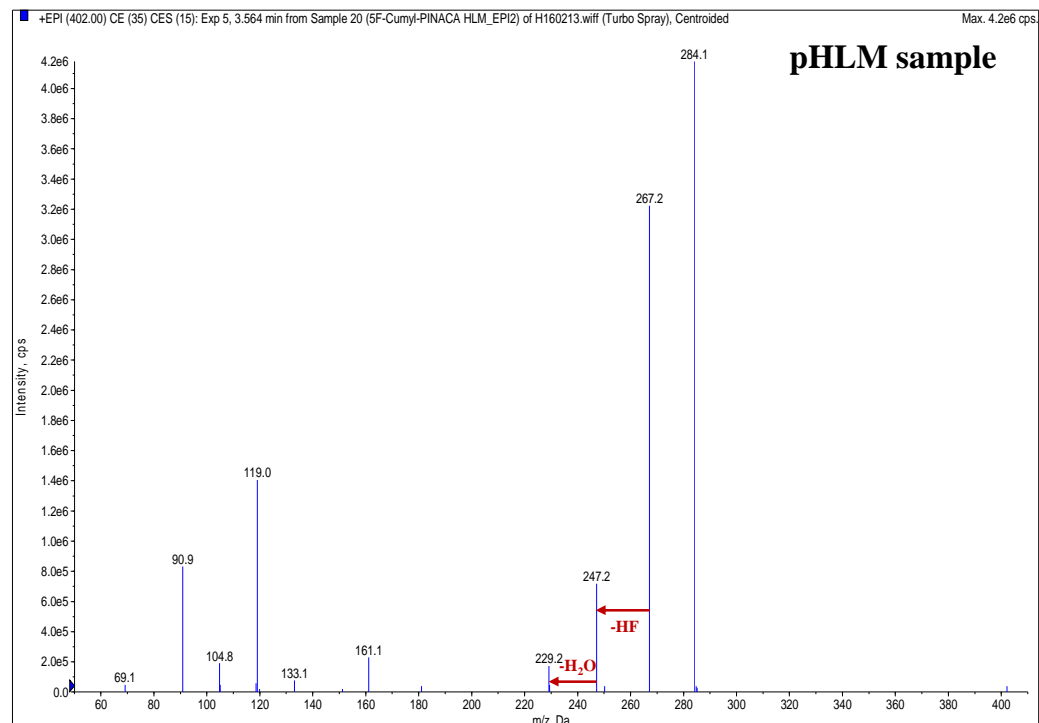
B01 (RT 3.6 min)

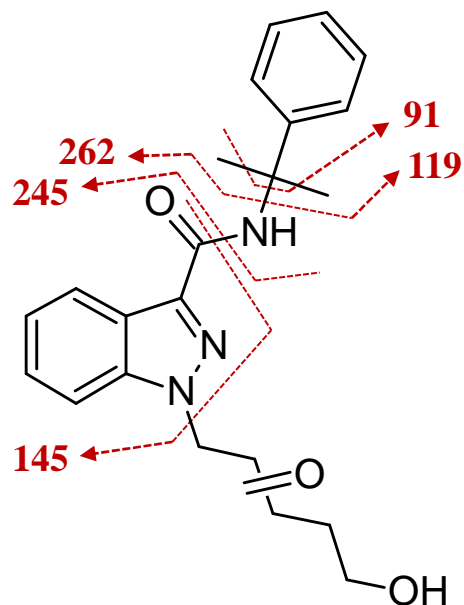
(dihydrodiol)

Molecular formula: $C_{22}H_{28}FN_3O_3$

Monoisotopic mass: 401.2115 Da

$[M+H]^+$: 402.2187 Da



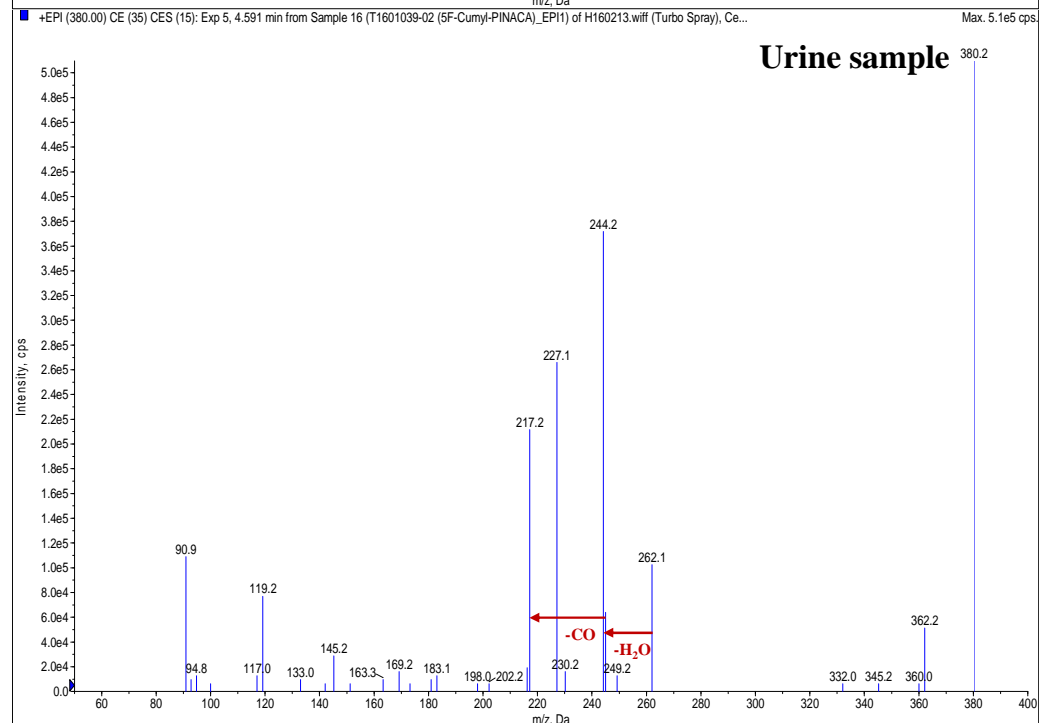
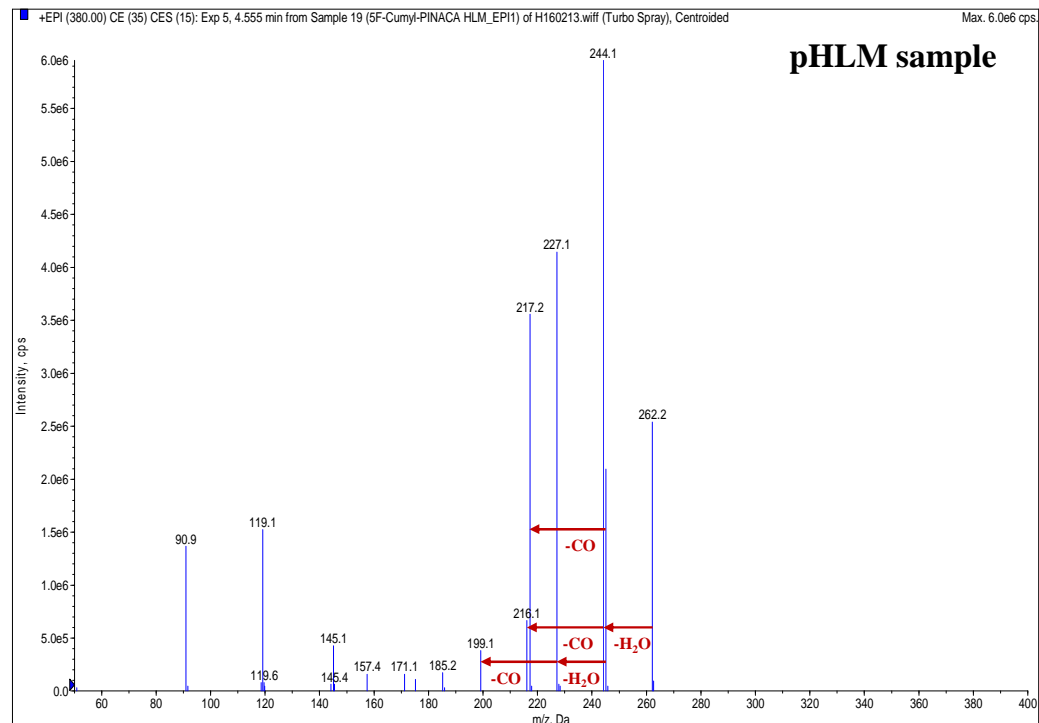


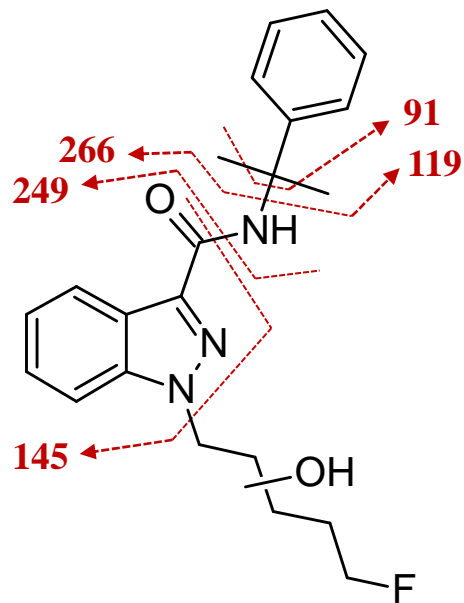
B02 (RT 4.5 min)

Molecular Formula: $C_{22}H_{25}N_3O_3$

Monoisotopic Mass: 379.1896 Da

$[M+H]^+$: 380.1969 Da



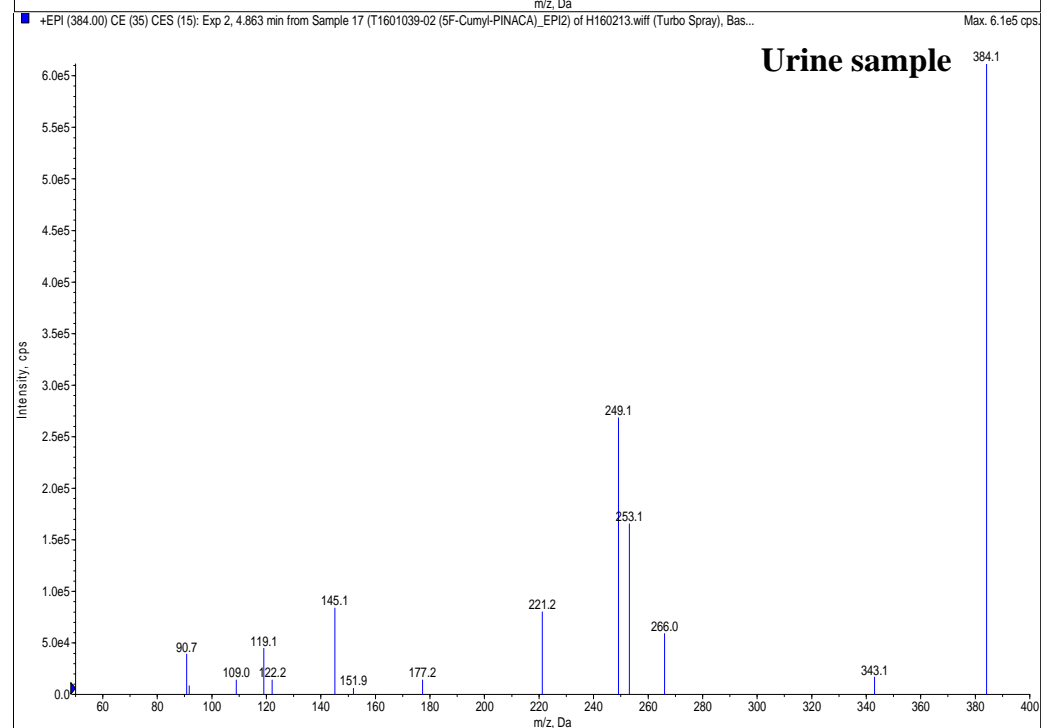
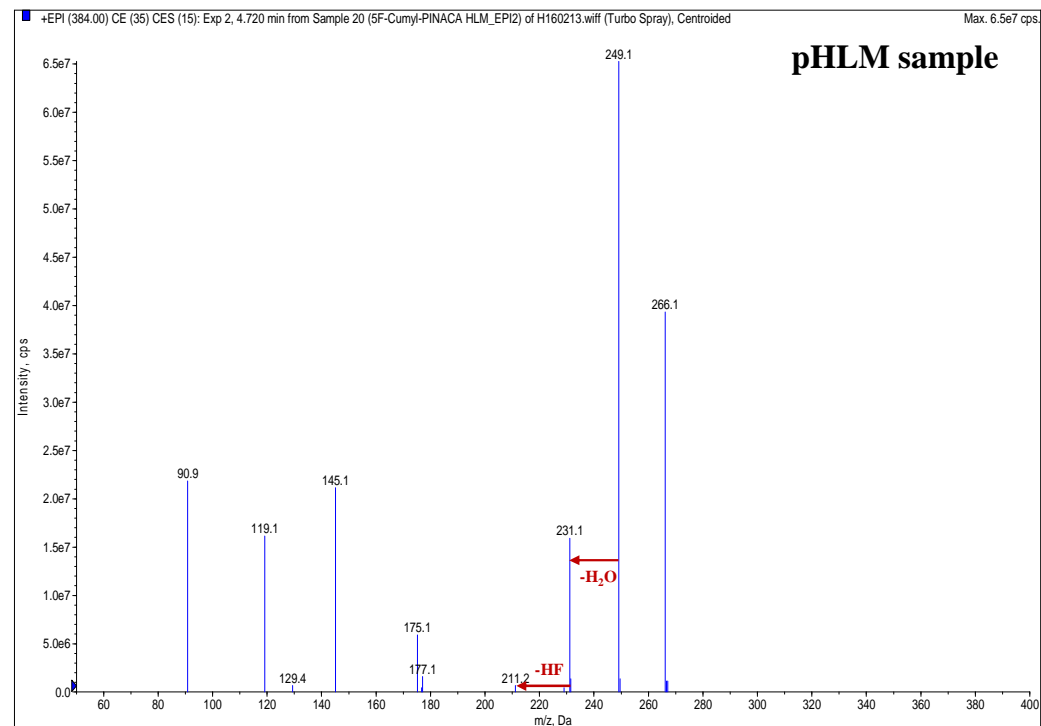


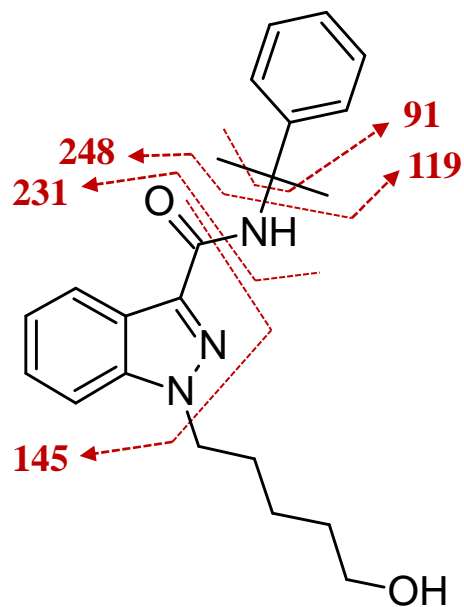
B03 (RT 4.7 min)

Molecular Formula: $C_{22}H_{26}FN_3O_2$

Monoisotopic Mass: 383.2009 Da

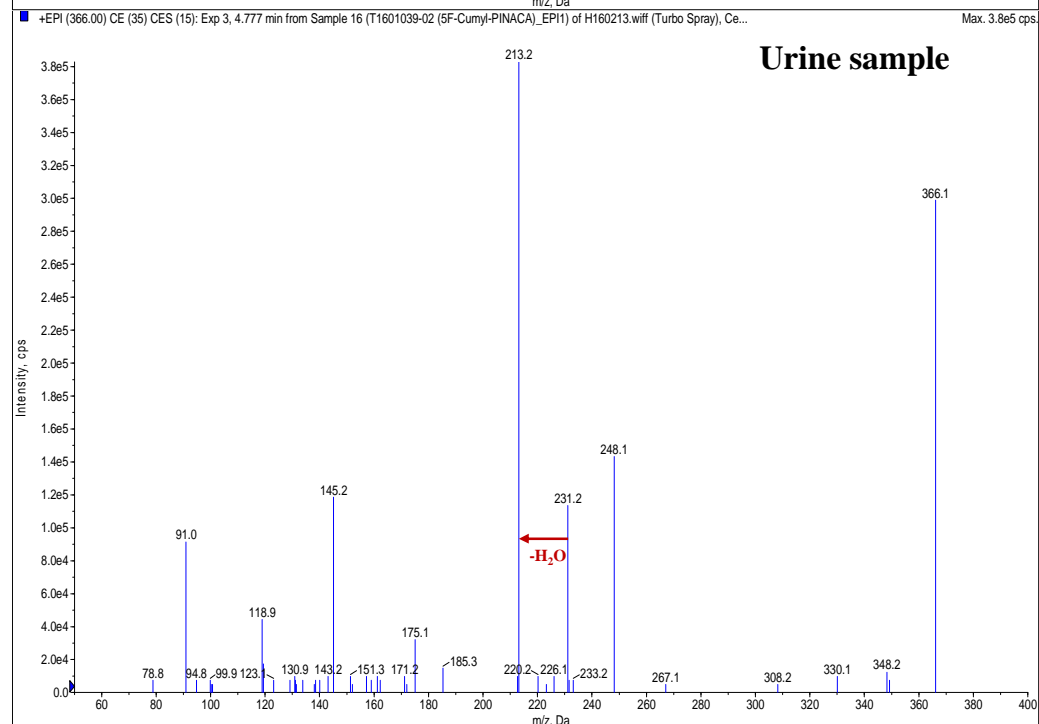
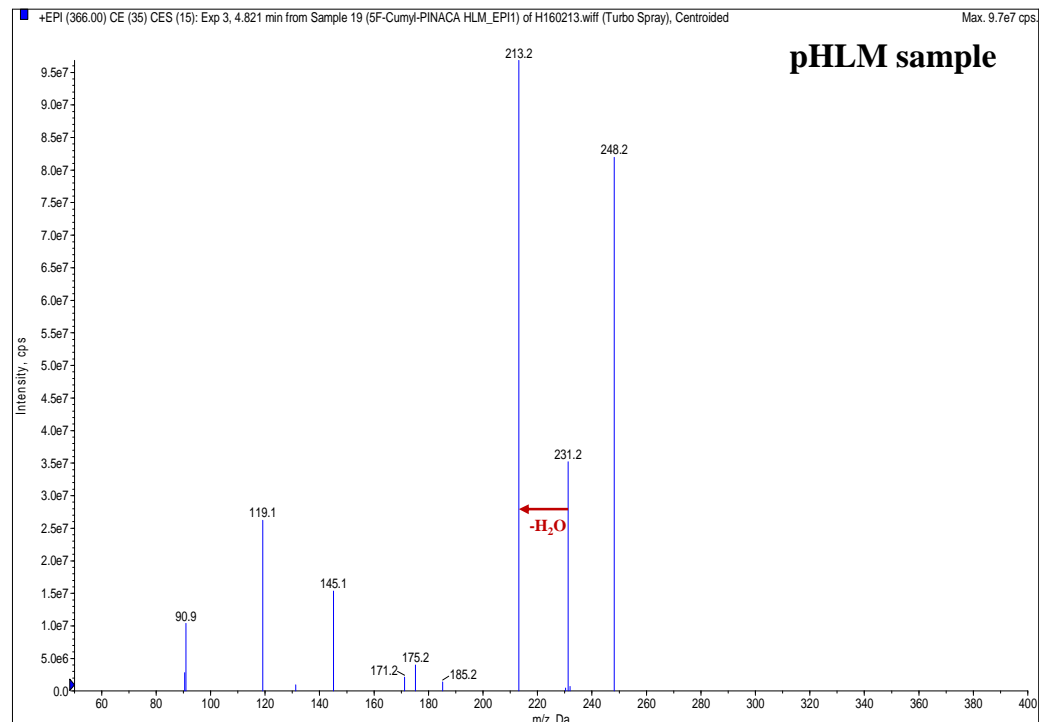
$[M+H]^+$: 384.2082 Da

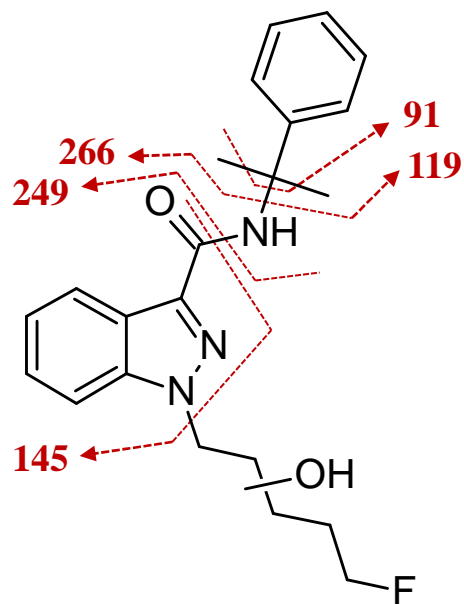




B04 (RT 4.8 min)

Molecular Formula: $C_{22}H_{27}N_3O_2$
 Monoisotopic Mass: 365.2103 Da
 $[M+H]^+$: 366.2176 Da



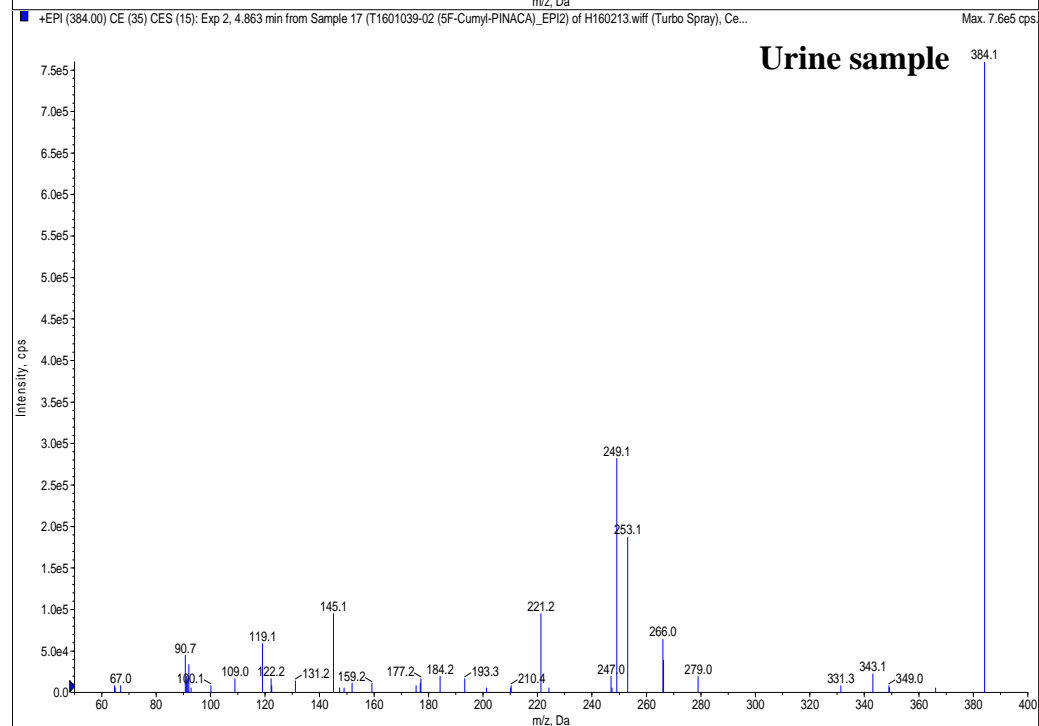
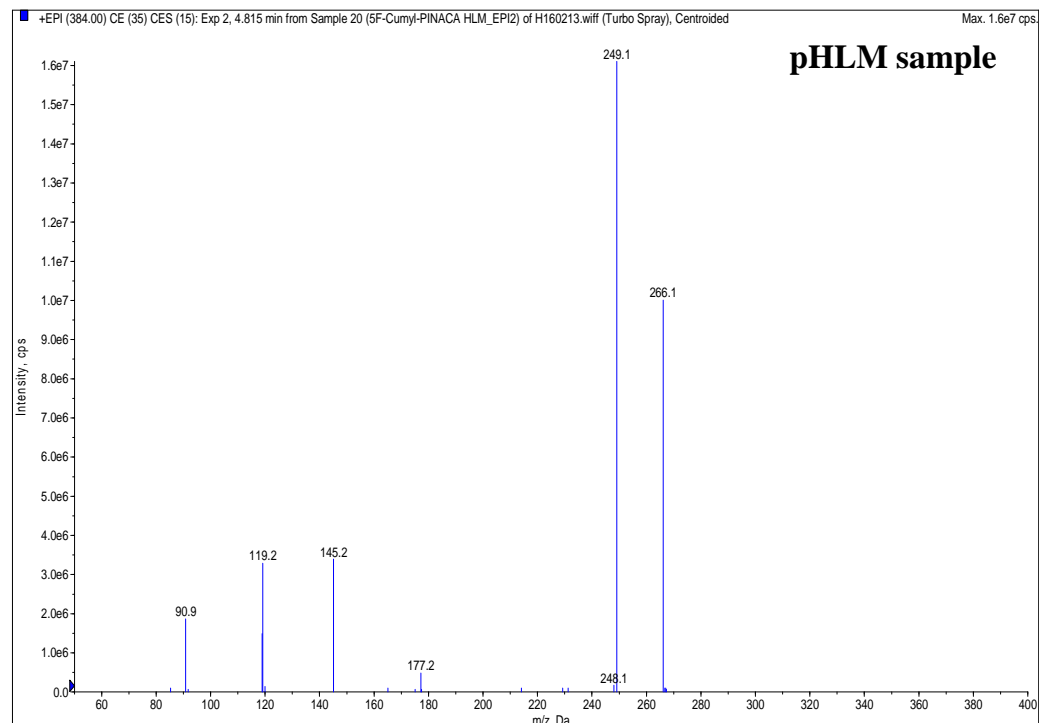


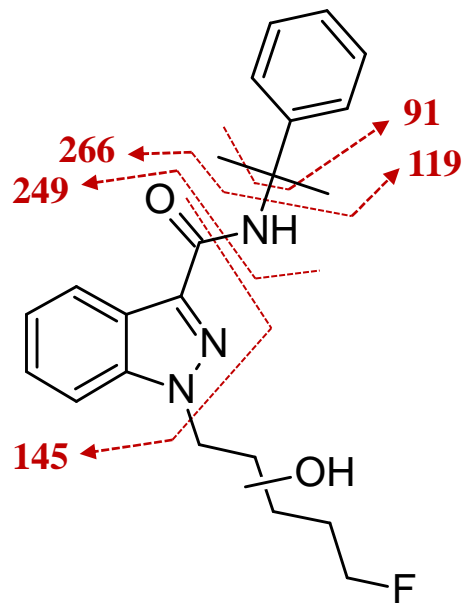
B05 (RT 4.8 min)

Molecular Formula: $C_{22}H_{26}FN_3O_2$

Monoisotopic Mass: 383.2009 Da

$[M+H]^+$: 384.2082 Da





B06 (RT 5.0 min)

Molecular Formula: $C_{22}H_{26}FN_3O_2$

Monoisotopic Mass: 383.2009 Da

$[M+H]^+$: 384.2082 Da

