Poster

[P25-11] P25-11: Clinical toxicology (1)

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[P25-11-6] In vitro human metabolism of the synthetic cannabinoid 5F-PY-PINACA

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Background

The illegal use of novel psychoactive substances including synthetic cannabinoids (SCs) is a serious problem worldwide. Although SCs possessing various chemical structures have still been designed, synthesized, and supplied, there are lack of information of SCs about PK. Thus, we tried to determine *in vitro* metabolism of 5F-PY-PINACA in human liver microsomes (HLMs).

Methods

Reaction mixtures containing HLMs (1 mg/mL), 5F-PY-PINACA (20 μM) and co-factors were incubated up to 3 hr. Samples for time-course analysis were collected every 1hr, followed by the termination of the reaction by adding acetonitrile. The supernatants obtained by centrifugation were evaporated under a nitrogen gas. After the reconstitution with 50% methanol, samples were subjected into LCMS-IT-TOF mass spectrometer (Shimadzu) with ZORBAX Eclipse Plus C8 column (150 x 2.1 mm, 3.5 μm, Agilent). 5F-PY-PINACA and its metabolites were monitored by ESI positive and negative mode. Data were analyzed with MetID Solution (Shimadzu) by measuring *m/z* of each precursor ion and corresponding product ions. Fourteen phase I metabolites, as well as six phase II metabolites, were detected and systematically annotated, among which three metabolites (M8, M10, and M14) were specified as majority due to LC/MS peak area ratio to internal standard of each pseudo-molecular ion ($[M-H]^-$).

Results

They were identified as simply oxygenated products (mono-hydroxylated; M8, di-hydroxylated; M14) and fluorine-hydroxyl exchanged product (M10) by the high quality MS2 spectra information. Unique metabolites characteristic for pyrrolidine ring cleavage (M6 and M12) were also detected as the second majority. Although 5F-PY-PINACA was relatively rapidly metabolized (half-life = 21.1 ±0.8 min), these phase I metabolites were found up to 3 hr.

Conclusions

These results suggest the combined detection of these metabolites in plasma or urine sample would become a surrogate maker of taking 5F-PY-PINACA.