SYNTHESIS AND BIOLOGICAL PROFILING OF MEPHEDRONE METABOLITES

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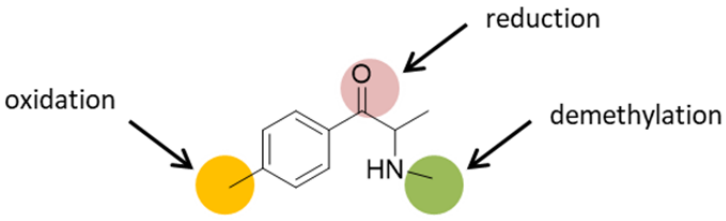
The endogenous monoamines dopamine, serotonin and norepinephrine are essential neurotransmitters in the mammalian system[1]. One diverse class of chemical compounds - the amphetamine type stimulants, acts as releasers at monoamine transporters and thus elicits strong psychostimulant effect which renders them liable for recreational abuse[2].

One frequently occurring recreational drug of this group is mephedrone - a derivative of naturally occurring alkaloids, the cathinones. Mephedrone has a short plasma half time, however, this compound has a long-lasting effect in humans[3]. We have previously shown that mephedrone undergoes extensive metabolism in the liver and that the Phase I metabolites are active.

Here, we present the enantioselective synthesis of Phase I mephedrone metabolites to (i) better understand mephedrone's mode of action and (ii) investigate the activity of single enantiomers of its metabolites. We performed pharmacological evaluation of synthesized metabolites which expressed chiral selectivity towards the monoamine transporters.

We also performed chiral detection of these metabolites in biological specimen (urine sample) which supported the findings of our *in vitro* experiments.



[1] Meltzer, P. C., Butler, D., Deschamps, J. R., Madras, B. K.: *J. Med. Chem.* **2006**, *49*, 1420-1432

[2] Sitte, H. H., Freissmuth, M.: *Trends in Pharmacological Sciences*, **2015**, *36*, 41-50

[3] Pedersen, A. J., Reotzel, L. A., Johansen, S. S., Linnet K.: *Drug Test. Analysis* **2012,** *5*, 313-319