

Mechanism of action of two new synthetic drugs unravelled for the first time

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Substances such as 4-MEC and 4-MEPP belong to the category of new hybrid cathinone derivatives and have a highly stimulant and euphoria-inducing effect, similar to the synthetic drug mephedrone, which was banned in Austria five years ago. Until now, the mechanisms by which these two drugs worked have been unknown. Scientists at the MedUni Vienna have now been able, through an international cooperation agreement, to unravel this mechanism for the first time.

The two drugs 4-MEC and 4-MEPP, which are primarily taken via the nasal and oral route, belong to the group of amphetamines in the second

generation of chemically modified cathinone derivatives. The basic cathinone structure occurs naturally in the "khat" plant, which is mostly grown on plantations and consumed in the Horn of Africa, Somalia and the Yemen. Cathinone has central stimulating, euphoria-inducing and psychotropic properties. Khat itself, taken on its own, has only a slightly intoxicating effect, similar to that of a glass or two of beer.

Researchers led by primary author Kusumika Saha from the Institute of Pharmacology at the MedUni Vienna have now been able to demonstrate that 4-MEC (4-Methyl-N-Ethylcathinone) works in two ways, depending on which neurotransmitter transporter it binds to in the brain. "If the substance docks to the [serotonin transporter](#), it acts like amphetamine. If it docks to the [dopamine transporter](#), however, it acts like cocaine," explains Harald Sitte from the Institute of Pharmacology at the MedUni Vienna. It is therefore currently difficult to assess what effect it will have on the consumer, or which effect characteristic will prevail.

In the case of 4-MEPP (4-Methyl- α -pyrrolidinopropiophenone), it was discovered that it acts like a blocker similar to cocaine on dopamine as well as serotonin transporters, comparable with the "zombie drug" MDPV (3,4-Methylenedioxypropylamphetamine), which can cause tremendous loss of control and aggression if taken.

More information: "'Second-Generation' Mephedrone Analogs, 4-MEC and 4-MePPP, Differentially Affect Monoamine Transporter Function." *Neuropsychopharmacology*. 2015 May;40(6):1321-31. [DOI: 10.1038/npp.2014.325](https://doi.org/10.1038/npp.2014.325)

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