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# REVIEW: THE NEWLY EMERGED DESIGNER PSYCHOSTIMULANT 3,4-DIMETHYLMETHCATHINONE (3,4-DMMC)

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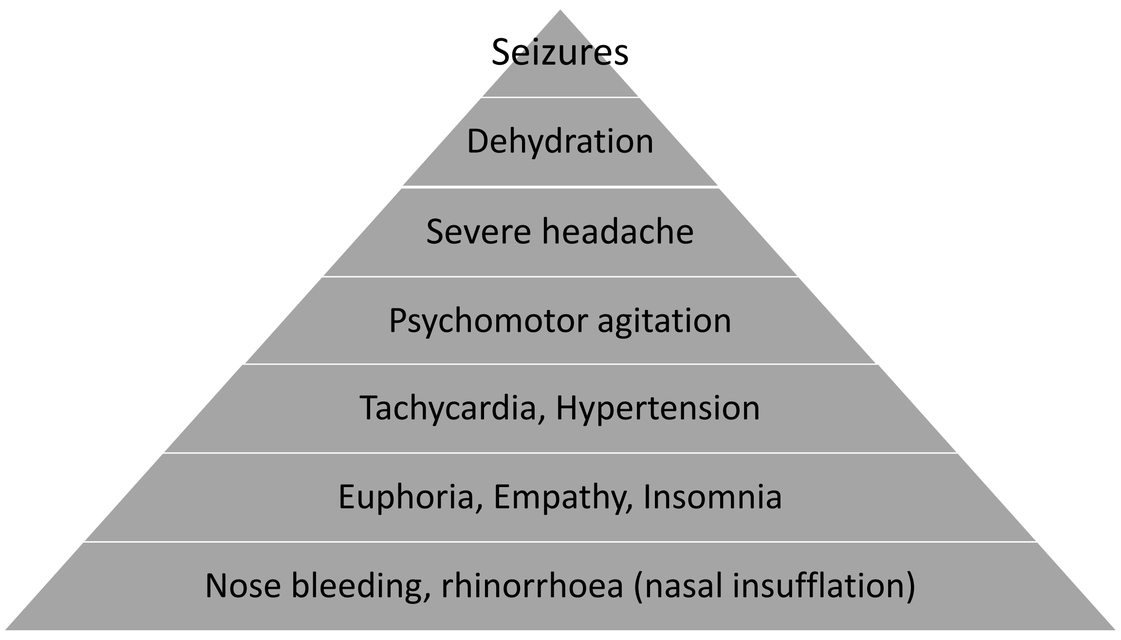
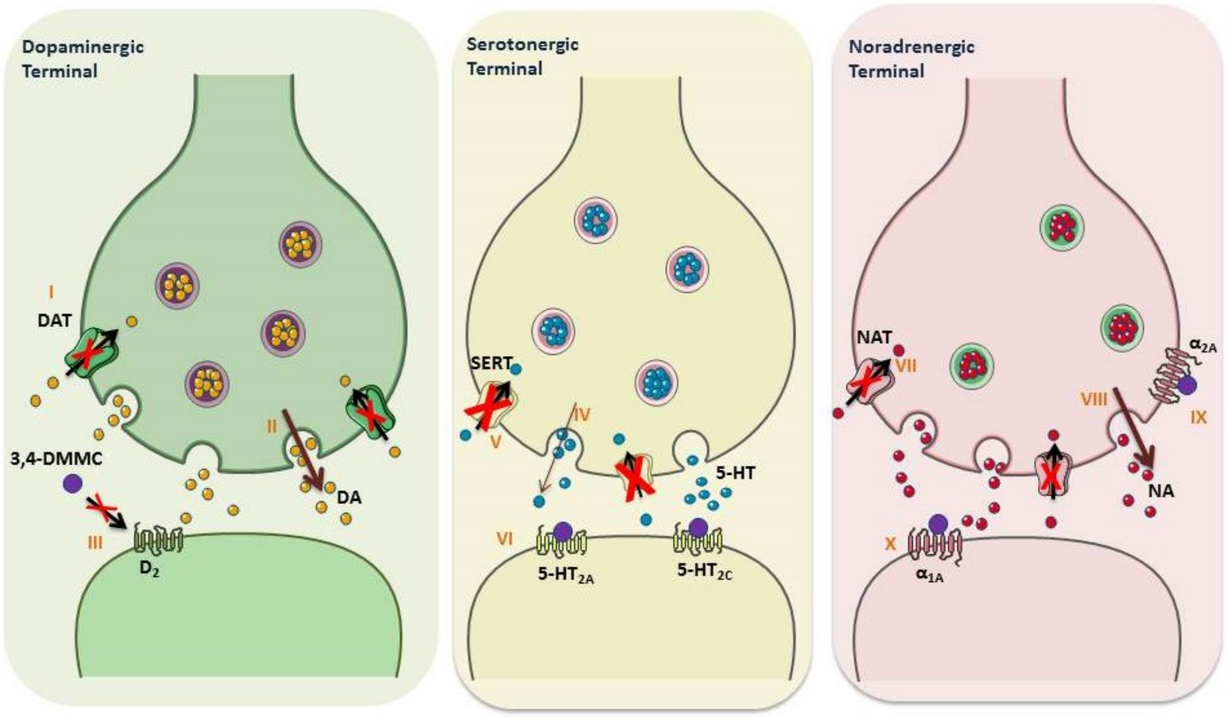
3,4-Dimethylmethcatinone (3,4-DMMC) is a synthetic cathinone that was detected via the EU Early Warning System in 2010, and sold under the aliases “Ocean” and “M2”. Its recreational use and trade in retail outlets have been prohibited in several countries, but this drug remains readily available for purchase through the internet. Along with the increasing number of anecdotal reports on its abuse published in drug forums and blogs, the number of poisonings described in scientific literature sharply increased, including one fatality, thus evidencing the health threats associated with 3,4-DMMC.

## BIOLOGICAL EFFECTS

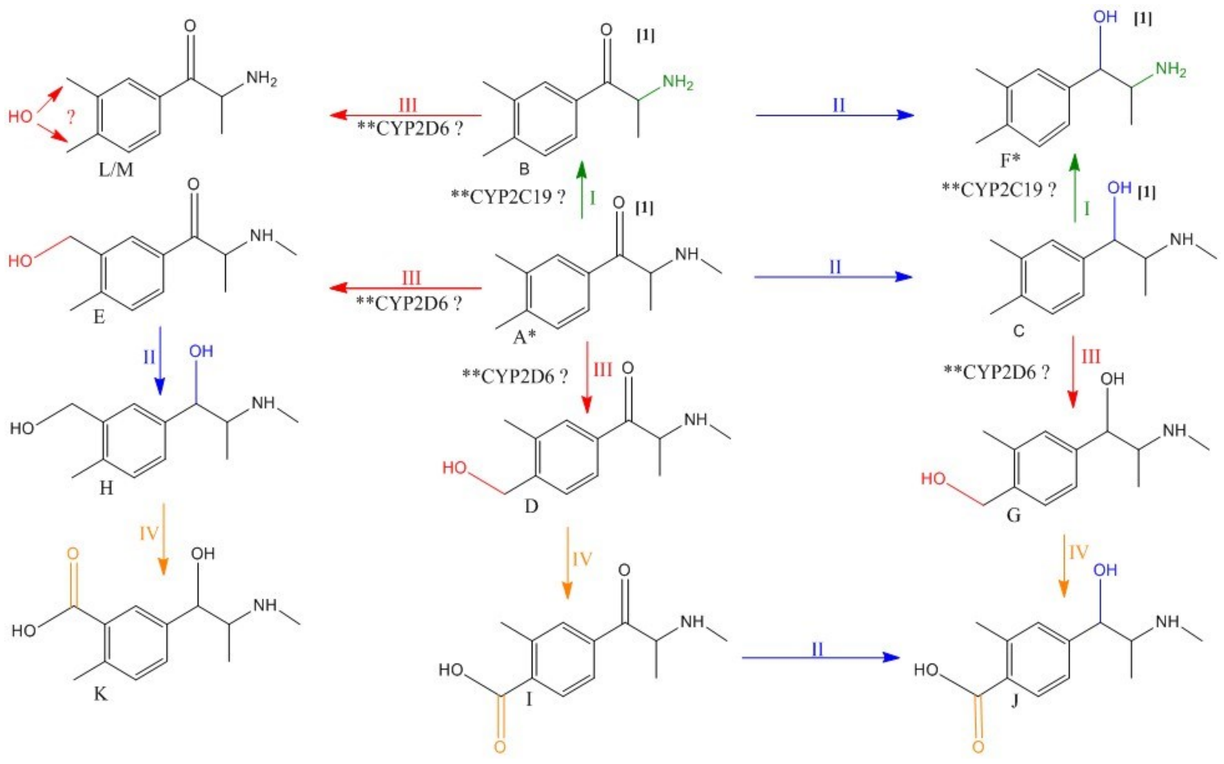



## PHARMACODYNAMICS




The drug promotes sustained increase of DA in the dopaminergic synapse by inhibiting uptake from DAT **(I)** and promoting strong DA release from the axon terminal **(II)**. Nevertheless, the drug seems to have no affinity for the D2 receptor **(III)**. In the serotonergic terminal, 3,4-DMMC induces a slighter release of 5-HT **(IV)** but more strongly inhibits the monoamine reuptake **(V)**, also activating postsynaptic 5-$HT_{2A}$ and 5-$HT_{2C}$ receptors **(VI)**. At the noradrenergic synapse, 3,4-DMMC also inhibits the reuptake from NAT **(VII)**, and is a potent releaser of NA **(VIII)**. 3,4-Dimethylmethcathinone has affinity to both $\alpha_{2A}$ presynaptic **(IX)** and $\alpha_{1A}$ postsynaptic **(X)** adrenergic receptors. **DA:** Dopamine; **DAT:** Dopamine transporter; **5-HT:** Serotonin; **SERT:** Serotonin transporter; **NA:** Noradrenaline; **NAT:** Noradrenaline transporter.

## METABOLISM




**I:** N-demethylation. **II:** β-Keto-reduction. **III:** Hydroxylation. **IV:** Oxidation. **A:** 3,4-Dimethylmethcathinone. **B:** Nor-dimethylmethcathinone. **C:** Dihydrodimethylmethcathinone. **D:** 3-Methyl-4-hydroxymethyl-methcathinone. **E:** 3-Hydroxymethyl-4-methylmethcathinone. **F:** Nor-dihydro-dimethylmethcathinone. **G:** 3-Methyl-4-hydroxymethyl-dihydro-methcathinone. **H:** 3-Hydroxymethyl-4-methyl-dihydro-methcathinone. **I:** 3-Methyl-4-carboxy-methcathinone. **J:** 3-Methyl-4-carboxydihydro-methcathinone. **K:** 3-Carboxy-4-methyl-dihydro-methcathinone. **L:** Nor-3-methyl-4-hydroxymethylmethcathinone. **M:** Nor-3-hydroxymethyl-4-methyl-methcathinone. **[1]** Conjugation with glucuronic acid. ***Abundant in human urine. ****Enzyme that catalyses this metabolic reaction for mephedrone. Adapted from *Tyrkko et al.* (2013) and *Shima et al.* (2013).

## CONCLUSION

- 3,4-DMMC is a potent releaser of dopamine and noradrenaline, and preferentially inhibits noradrenaline and serotonin uptake transporters, leading to sympathomimetic stimulation.
- N-Demethylation, β-keto-reduction, hydroxylation, and oxidation are the major reactions involved in the production of 3,4-DMMC metabolites with higher relevance for toxicological analysis in urine, along with the parent compound.
- Further clarification on the pharmacodynamics, pharmacokinetics and clinical effects of 3,4-DMMC is essential to help find possible therapeutic solutions for this drug poisoning, as well as to assist in future clinical and forensic investigations.

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