

Methcathinone (MCAT) and 2-methylamino-1-(3,4-methylenedioxy-phenyl)propan-1-one (MDMCAT) inhibit [³H]serotonin uptake into human platelets.

N.V. Cozzi,¹ A.T. Shulgin,² A.E. Ruoho¹

¹Department of Pharmacology, University of Wisconsin Medical School, Madison, WI 53706

²Alexander Shulgin Research Institute, 1483 Shulgin Road, Lafayette, CA 94549

The benzylic ketone analog of the psychoactive phenylisopropylamine methamphetamine (MA), MCAT, and of 3,4-methylenedioxymethamphetamine (MDMA), MDMCAT, were synthesized and compared to the nonketo compounds for their abilities to inhibit reuptake transporter-mediated [³H]serotonin accumulation into human platelets. MCAT inhibited [³H]serotonin uptake into platelets with an IC₅₀ of 33.7 ± 9.0 micromolar while MA exhibited an IC₅₀ of 11.7 ± 1.0 micromolar; this difference was not significant. The methylenedioxy-substituted compounds were about 6-fold more potent (p < 0.05) than the unsubstituted compounds in this assay; MDMCAT displayed an IC₅₀ of 5.8 ± 0.7 micromolar and MDMA had an IC₅₀ of 2.1 ± 0.3 micromolar. The difference in potencies between MDMCAT and MDMA was significant at p < 0.01. These results indicate that beta-keto derivatization of psychoactive phenylalkylamines does not have a major impact on the drugs' ability to inhibit serotonin uptake and that substitutions on the phenyl ring can enhance potency.