

# Distribution characteristics of 2,5-dimethoxy-4-bromoamphetamine (DOB) in rats after oral and subcutaneous administration

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KATERINA BERANKOVA and MARIE BALIKOVA

Institute of Forensic Medicine and Toxicology, 1st Medical Faculty, Charles University in Prague

**AIM:** This study concerns the distribution profiles of 2,5-dimethoxy-4-bromoamphetamine (DOB) and its main metabolite 2-methoxy-5-hydroxy-4-bromoamphetamine (2M5H4BA) in blood, brain and other tissues in time course after oral and subcutaneous administrations to male rats. Little information has been published about pharmacokinetics and pharmacodynamics of this halogenated amphetamine with a strong potential of dangerous overdoses. DOB is a powerful hallucinogen with expected significant accumulation in brain tissue, therefore our attention was focused on the plasma/brain ratio in particular.

**METHOD:** Oral and subcutaneous bolus doses of DOB.HCl 20 mg/kg were administered to experimental rats. The animals were sacrificed at 0.5; 1; 2; 4; 8; 16 and 32 hours after the dose (three animals per time point) and plasma, brain, liver and lung tissues were kept under -20°C until analyses for DOB and its prevailing metabolite 2M5H4BA were performed. Tissues were subjected to homogenisation and analytes were reextracted with ethylacetate. DOB and its metabolite 2M5H4BA were assayed in acetylated forms by GC-MS in SIM mode using a HP GC-MS 6890/5973 instrument.

**RESULTS:** After the oral dose a rapid increase of DOB as well as 2M5H4BA plasma levels were observed with average peak concentrations of 320 ng/ml for DOB and 203 ng/ml for 2M5H4BA in 1 hour after administration. The rapid conversion of the parent compound to 2M5H4BA is a result of significant metabolism in the liver during the first pass effect. Both the parent compound and its main metabolite were detected in plasma even after 32 hours. In brain tissue, DOB top level was over 7000 ng/g ( $t_{max}$  1 hour) and the more polar metabolite 2M5H4BA was present in all samples at lower concentrations than DOB. The kinetic profile of DOB in plasma and brain was similar, however with much higher concentrations of more lipophilic DOB in the brain.

After subcutaneous administration, DOB peak plasma levels were more than three times higher than those after oral intake and the appearance of 2M5H4BA metabolite in the blood stream was delayed. The average DOB peak plasma level of 1143 ng/ml was achieved after 1 hour and the kinetic curve demonstrates a gradual slow decline of the parent compound in time with a slow parallel rise up of 2M5H4BA metabolite reaching the maximum of only 213 ng/ml 8 hours after administration when the plasma levels of both compounds became near and kept approximately equal until the end of our observation. DOB influx into the brain was fast with the peak concentration of 14157 ng/g ( $t_{max}$  2 hours) while its elimination was gradual as significant levels were still observed 16 hours after administration. 2M5H4BA appearance in the brain was less abundant reaching maximum value of 5725 ng/g in 8 hours after intake. Both plasma and brain time curves demonstrate massive DOB absorption from subcutaneous depot and its protracted elimination from brain tissue that indicates prolonged DOB effect.

**CONCLUSION:** Our experimental findings inform on disposition of strong hallucinogen DOB and its main phenolic metabolite 2M5H4BA in experimental rats. The kinetic profile of both compounds in plasma after peroral and subcutaneous administration revealed the existence of significant first pass effect after peroral dose. As expected, the plasma/brain transfer was more effective for the lipophilic parent substance than for the polar metabolite. The many times higher brain concentration of DOB related to plasma values can explain its strong hallucinogenic potential. The hallucinogenic effects of its metabolite 2M5H4BA, which was also found in significant amounts in brain tissue, remain unclear as its pharmacological activity has not yet been investigated.

**KEYWORDS:** *2,5-dimethoxy-4-bromoamphetamine, DOB, metabolites, Disposition in rats, Toxicological analysis*

**Corresponding author:** [kberanek@seznam.cz](mailto:kberanek@seznam.cz)