Disposition of 4-Bromo-2,5-dimethoxyphenethylamine (2C-B) and its Metabolite (4-Bromo-2-hydroxy-5-methoxyphenethylamine) in Rats after Subcutaneous Administration

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AIMS: 2C-B (4-bromo-2,5-dimethoxyphenethylamine) is a psychedelic abused drug inducing considerable euphoria in humans with an increased receptiveness of sensations. The pharmacokinetics of the agent in controlled studies in humans or animals is unknown. Due to ethical restrictions, our study was focused on assessing the distribution time profiles of 2C-B and its prevailing metabolite 2H5M-BPEA (4-bromo-2-hydroxy-5-methoxyphenethylamine) in serum, brain, liver and lung organs after a single drug dose to experimental rats with a focus on the brain/serum ratio.

METHODS: Male Wistars rats were subcutaneously administered a 50 mg/Kg bolus dose of 2C-B HCl in aqueous solution. The animals were sacrificed at 30, 60, 120, and 360 minutes after dosing (ten animals per time point) and the serum, brain, liver and lung samples were collected and stored at -20°C until analysis. The analytes were assayed by GC-MS as acetylderivatives.

RESULTS: The absorption of parent drug into blood stream was rapid; peak serum concentration was attained at 30 min after dosing (2250 ± 266 ng/mL) with a fast decline (estimated elimination half-time 1.1 h, distribution volume 16 l/Kg, clearance 9.8 l/h). 2C-B concentrations in all tissues peaked in 60 min and were higher than in serum (lung>brain>liver>serum). The highest concentrations were found in lung after 1 h (Cmax 27028 ± 8156 ng/g) persisting high for up to 6 h, whereas the lowest concentrations were found in liver (Cmax 7485 ± 1534 ng/g). The peak concentrations of the metabolite 2H5M-BPEA in tissues occurred within 1 h (liver, lung) or 2 h (brain) after the 2C-B dose. The concentration of 2H5M-BPEA metabolite in brain and lung were much lower relative to the parent compound reaching maxima of 3761 ± 1744 ng/g (lung) and 2726 ± 938 ng/g (brain). In liver, the principal organ for metabolism, the concentrations of 2C-B and its metabolite were relatively close. 2C-B distribution from blood into the brain was fast with an average peak concentration of 17102 ± 5202 ng/g (tmax = 1 h). The peak brain/serum ratio was 13.9 ± 1.9 at 2 h. The distribution of the hydroxylated metabolite into lipophilic brain tissue was less efficient relative to the parent drug.

CONCLUSIONS: The pharmacokinetic disposition of psychedelic 2C-B and its metabolite described above would be problematic to verify in humans. To our knowledge, our findings provide the first approximate estimation of kinetic data of 2C-B and its metabolite based on controlled animal experiments. The 2C-B temporal concentration profile in brain seems to correspond to 2C-B psychedelic temporal dynamic response reported. The drug’s ability to accumulate in lung and persist in brain after a higher dose may explain the prolonged psychotropical effects. However, more experimental kinetic data are necessary, as there is a known steep dose response dependence.

Keywords: 4-Bromo-2,5-dimethoxyphenethylamine (2C-B), Pharmacokinetics, Rat model

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