

Poster Communication 37

Psilocybin and *Psilocybe cubensis* extract exhibit divergent behavioural and toxicological effects in rats

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Abstract

Background: Psilocybin, a key psychoactive compound found in *Psilocybe* mushrooms, has gained increasing attention due to its therapeutic potential in neuropsychiatric disorders [1]. However, comparative preclinical data between isolated psilocybin and whole mushroom extracts remain scarce, particularly regarding behavioural reinforcement and peripheral toxicity[2,3]. **Objective:** To compare the behavioural and toxicological effects of pure psilocybin and *Psilocybe cubensis* extract in Wistar Han rats. **Methods:** Male Wistar Han rats (n=18) were randomly assigned to control (0.9% NaCl), pure psilocybin (3 mg.kg⁻¹), or *P. cubensis* extract (equivalent to 3 mg.kg⁻¹ psilocybin/psilocin) groups. Treatments were administered orally. Behavioural effects were assessed using a conditioned place preference (CPP) paradigm, with evaluations at 1, 7, and 14 days post-treatment. Locomotor/exploratory activity was estimated by compartment entries. Peripheral effects were evaluated through relative organ weights and lipid peroxidation (TBARS assay) in heart, brain, liver, and kidney. Statistical analysis was performed using ANOVA (p<0.05). All procedures were approved by the institutional Animal Welfare Committee and DGAV, in accordance with European and national legislation. **Results:** Pure psilocybin significantly decreased CPP scores at days 1 and 7, suggesting aversive or non-reinforcing effects, while no significant preference changes were observed for the extract. The extract group showed a transient increase in exploratory behaviour at day 7, whereas psilocybin-treated animals consistently displayed reduced entries in the drug-paired compartment. At the peripheral level, psilocybin increased relative liver weight, indicating potential hepatic stress or metabolic adaptation. In contrast, the extract reduced renal lipid peroxidation, suggesting a protective or antioxidant effect likely associated with additional bioactive compounds. **Conclusions:** Pure psilocybin and *P. cubensis* extract exhibit distinct behavioural and toxicological profiles. These findings highlight the relevance of matrix effects in psychedelic research and reinforce the need to consider whole-extract formulations when assessing safety and pharmacological outcomes.

Keywords: Psilocybin; *Psilocybe cubensis*; behavioural toxicology

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