Objective: Lysergic acid diethylamide (LSD) is used recreationally and in clinical research. The aim of the present study was to characterize the pharmacokinetics and exposure-response relationship of representative oral doses of LSD.

Methods: We conducted two placebo-controlled, double-blind, cross-over studies using oral administration of 100 and 200 µg LSD in 24 and 16 subjects, respectively. Plasma concentrations of LSD, subjective effects and vital signs were repeatedly assessed. Pharmacokinetic parameters were determined using compartmental modeling. Concentration-effect relationships were described using pharmacokinetic-pharmacodynamic modeling.

Results: Geometric mean (95% confidence interval) Cmax values of 1.3 (1.2–1.9) and 3.1 (2.6–4.0) ng/mL were reached 1.4 and 1.5 hours after administration of 100 and 200 µg LSD, respectively. The plasma half-life was 2.6 hours (2.2–3.4). The subjective effects lasted (mean ± SD) 8.2 ± 2.1 and 11.6 ± 1.7 hours for the 100 and 200 µg LSD doses, respectively. Subjective peak effects were reached 2.8 and 2.5 hours after administration of 100 and 200 µg LSD, respectively. A close relationship was observed between the LSD concentration and subjective response within-subjects, with moderate counter clockwise hysteresis. The half maximal effective concentration EC50 values were in the range of 1 ng/mL. No correlations were found between plasma LSD concentrations and its effects across subjects.

Conclusion: The present pharmacokinetic data are important for the interpretation of LSD intoxication. Oral LSD presented dose-proportional pharmacokinetics and first-order elimination up to 12 hours. The effects of LSD were related to changes in plasma concentrations over time, with no evidence of acute tolerance.

References
