STUDY PACK

Key Facts

1. Tetracyclic ergoline core: four fused rings (A–D); rings A/B = indole portion (N1), ring D = amine nitrogen N6; diethylamide at C8.

   DOI 10.1073/pnas.2603412123

2. SAR: the positions that matter are N1 (acyl block → prodrugs), N6 (substitutions → active-per-se analogues) and the ergoline core itself.

3. The N1 paradox: acylation abolishes 5-HT2A affinity in vitro, but in vivo hydrolysis (chemical + hepatic) liberates LSD and restores activity.

   DOI 10.1016/j.neuropharm.2019.107856

4. N1-acyl series = prodrugs: ALD-52 (acetyl), 1P-LSD (propionyl), 1B-LSD (butyryl), 1V-LSD (valeroyl), 1cP-LSD (cyclopropanecarbonyl).

5. 1P-LSD: oral bioavailability of LSD ~100%; only LSD — never the parent compound — is detected in serum (human data, n = 2).

   PMID 32415750

6. 1B-LSD: murine HTR potency is 14% of LSD (ED50 976.7 vs 132.8 nmol/kg).

   PMID 31083768

7. 1V-LSD (in silico only): predicted pulmonary risk 92%; hERG IC50 1.4 µM — a potential proarrhythmic signal requiring experimental follow-up.

   DOI 10.1007/s00204-025-04255-1

8. N6 series = active per se: AL-LAD (~76% of LSD HTR potency) and ETH-LAD do not convert to LSD; ETH-LAD has no human data — maximum caution.

   DOI 10.1002/dta.1985

9. LSD human safety: 83 healthy subjects, 25–200 µg; common effects headache, anxiety, nausea, dizziness; at 200 µg heart rate >100 bpm in 25% and temperature >38 °C in 34%; no liver/kidney function changes. The analogues have no controlled human data.

   DOI 10.1007/s00213-021-05978-6

10. Analysis: rapid tests detect the indole class but cannot distinguish analogues; LC-MS/MS separates and identifies all of them; NMR provides complete structural characterization (e.g. 1B-LSD).

    PMID 31083768