Lysergic Acid Diethylamide. A Brief Review

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OBJECTIVE
- To make a general view of the main aspects related to LSD.
- To understand its pharmacokinetic and pharmacodynamic, making special attention in LSD’s effects in the central nervous system (CNS).
- To know its undesirable effects.

CONTEXTUALIZATION
- LSD: semisynthetic product of lysergic acid, a natural substance from the parasitic rye fungus Claviceps purpurea.
- Synthesized for the first time in 1938 by the Swiss chemist Albert Hofmann.
- 1950s: offered to the medical community like an experimental tool to study temporary psychotic-like states in normal people.
- 1950s: began to be use as a recreational drug. Forbidden in EUA in 1967.
- Nowadays, is one of the most consumed drugs of abuse due to its low cost and easy obtaining.

MATERIAL AND METHODS
- Systematic search with the medical database PubMed.
- Keywords: "LSD", "LSD effect", "LSD pharmacodynamics", "LSD pharmacokinetics", "Hallucinogen compounds", "Serotonin", "5-HT2A receptor".

PHARMACOKINETIC
- Dose: optimum dosage 100-200µg with high potency.
- Administration: no qualitative differences regarding psychological effects independently of the administration’s route.
- Absorption: after oral administration, completely absorbed in the digestive tract.
- Distribution: no data in human. LSD is able to penetrate the CNS.
- Metabolism and excretion:
  - Metabolized by liver enzymes into structurally similar metabolites.
  - Elimination half-life: 3.6h.
  - LSD metabolites detectable in urine until 4 days after administration.

PHARMACODYNAMIC
- The pharmacological basis of the stimulus produced by hallucinogenic compounds is serotoninergic.
  - Receptors:
    - 5-HT2A serotonin receptor:
      - Main receptor mediating hallucinations effects.
      - Widely expressed in CNS structures involved in psychosis.
      - G-protein coupled receptor: LSD acts as an agonist causing a dose-related inhibition of 5-HT neurons firing rate.
    - Operate via neuroanatomical circuits based on polysynaptic inputs to 5-HT neurons.
    - Located on non-S-HT neurons.
    - LSD acts as agonist. Its activation causes a dose-related inhibition of 5-HT neuron firing rate.
  - D2 dopamine receptor:
    - Responsible of the second phase of the clinical effects of LSD.
    - LSD acts as an agonist neuromodulating the decrease of extracellular glutamate in prefrontal cortex.

CONCLUSIONS
- Lysergic acid diethylamide (LSD) is a semisynthetic product of lysergic acid. It is an ergoline consisting of an indole system with a tetracycline ring.
- The pharmacological basis of LSD’s stimulus is serotoninergic. Its principal action takes place by the activation of 5-HT2A receptor of the serotoninergic neurons in the raphe nucleus, were lysergic acid acts as an agonist inhibiting the 5-HT neurons firing rate. It also activates 5-HT2A and 5-HT2C receptors, acting again like an agonist and working in the same direction.
- The undesirable effects mediated by LSD’s administration is the flashback, the reexperiencing of one or more of the perceptual symptoms experienced while the intoxication without the use of the hallucinogen.