Caenorhabditis elegans as an in vivo model for the systematic characterization of LSD metabolites by UHPLC-HRMS/MS

Christiane Martins de Vasconcellos Silveira[1], Vanessa Farelo dos Santos[1], Isis Moraes Ornelas[2,3], Beatriz de Sá Carrilho[3], Matheus Antônio Vieira de Castro Ventura[3], Henrique Marcelo Gualberto Pereira[1], Stevens Kastrup Rehen[3,4], Magno Junqueira[1]

[1.] IQ-UFRJ, Instituto de Química, Universidade Federal do Rio de Janeiro, Rio de Janeiro 21941-909, Brazil;
[2.] UFES, Departamento de Ciências Fisiológicas, Centro de Ciências da Saúde, Universidade Federal do Espírito Santo, Vitória, 29043-274, Brazil;
[3.] IDOR, Instituto D'Or de Pesquisa e Ensino, Rio de Janeiro 22281-100, Brazil;
[4.] IB-UFRJ, Departamento de Genética, Instituto de Biologia, Universidade Federal do Rio de Janeiro, Rio de Janeiro, 2141-902, Brazil;

Psychedelic compounds, such as Lysergic Acid Diethylamide (LSD), have been increasingly explored in studies of biological effects and characterization of metabolism, in order to explore potential therapeutic applications, mainly in the treatment of psychiatric disorders such as depression. The already known interactions with serotonin receptors and the mimicry of the effects of the neurotransmitter drive such research, being an alternative to monoamine oxidase inhibitors and selective serotonin reuptake inhibitors, the classic antidepressants. However, the complexity of analyzing the effects of LSD in biological models, mainly in humans, sometimes represents a barrier. Thus, an unprecedented study of the metabolic profile of LSD was carried out using the nematode *Caenorhabditis elegans* (*C. elegans*) as a biological model. *C. elegans* was the first multicellular organism to have its genome completely sequenced, presents easy genetic manipulation, in addition to having a high genetic homology with the human species. Therefore, it is a model widely used in neurological and biochemical studies, and now it is the first of the *Nematoda* phylum to have a study characterized on the effects of LSD. Therefore, a method was developed for the systematic characterization of LSD metabolites and their quantification by ultra-high performance liquid chromatography coupled to high-resolution tandem mass spectrometry (UHPLC-HRMS/MS), using the deuterated analyte LSD-D3 as an internal standard. It was observed that the worms absorb and metabolize the substance in a similar way to humans, with the production of four metabolites common in both species, in addition to similar enzymes possibly related in the metabolic degradation process. With the analysis of the metabolite spectra, a fragmentation profile can be obtained for each one, analyzing characteristic transitions of each, essential in the assembly of an identification profile. A study of the metabolic production rate was also carried out, which varies according to the time of exposure and absorption of the worm to LSD. This highlights the potential of *C. elegans* as an experimental model for research with psychedelics.

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