EARLY-LIFE EXPOSURE TO CANNABIDIOL: SAFETY ASSESSMENT OF A CHRONIC EXPOSURE IN *Caenorhabditis elegans*

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INTRODUCTION: Cannabidiol (CBD), a major non-psychotropic compound from *Cannabis sativa*, has gained attention for its antioxidant, anti-inflammatory, and neuroprotective properties. However, the potential adverse effects of early-life exposure remain underexplored. The nematode *Caenorhabditis elegans (C. elegans)* serves as a valuable model to assess long-term toxicological effects due to its simplicity and translational relevance. **METHODS:** Synchronized L1 larvae (wild-type N2, BY200 vtIs1(*dat-1*p::GFP; rol-6) and LX929 (vsIs48 [*unc-17*::GFP]) were exposed to CBD (10, 150, or 600 µM) or 2% DMSO (control) for 60 minutes. After exposure, worms were transferred to nematode growth medium with E. coli OP50 for 48 or 72 hours. Endpoints included survival, development, locomotion, reproduction, neuronal integrity, and oxidative stress. Locomotion was assessed via body bends and swimming. Neurotoxicity was evaluated using GFP-labeled dopaminergic and cholinergic neuron strains. Oxidative stress was assessed by ROS quantification and expression of antioxidant reporters (SOD-3, GST-4). Reproductive performance was measured by egg count and brood size. **RESULTS AND DISCUSSION:** CBD at 10 and 150 µM did not induce significant toxicity across most parameters. A slight reduction in body length at 150 µM was observed without affecting developmental progression or survival. Locomotion and neuronal integrity remained intact, and no significant oxidative stress or activation of antioxidant pathways was detected. Egg production was reduced at 150 and 600 µM, but brood size was unaffected, suggesting compensatory mechanisms. In contrast, 600 µM CBD caused marked toxicity, including reduced survival, decreased body size, increased ROS levels, and no compensatory antioxidant response, indicating oxidative stress and cellular damage. **CONCLUSION:** Chronic early-life exposure to CBD is well tolerated in *C. elegans* up to 150 µM, with no major physiological or behavioral toxicity. However, higher concentrations (600 µM) induce oxidative stress and reduce survival, emphasizing the importance of concentration considerations, especially in pediatric contexts.

Cannabinoids, developmental, toxicity, oxidative stress.