Scientific Letters

Poster Communication 55

Decoding the underexplored biological impact of synthetic cathinones using *C. elegans* as a translational toxicity model

Cristina Mendes [1,2,*], Renata Silva [3,4] and Daniel José Barbosa [1,2]

[1] Associate Laboratory i4HB-Institute for Health and Bioeconomy, University Institute of Health Sciences - IUCS-CESPU, 4585-116 Gandra, Portugal
[2] UCIBIO - Research Unit on Applied Molecular Biosciences, Translational Toxicology Research Laboratory, University Institute of Health Sciences (1H-TOXRUN, IUCS-CESPU), 4585-116 Gandra, Portugal
[3] Associate Laboratory i4HB-Institute for Health and Bioeconomy, Faculty of Pharmacy, University of Porto, 4050-313 Porto, Portugal
[4] UCIBIO - Research Unit on Applied Molecular Biosciences, Laboratory of Toxicology, Faculty of Pharmacy, University of Porto, 4050-313 Porto, Portugal

* Correspondence: a33272@alunos.cespu.pt

Abstract

Background: The recreational use of New Psychoactive Substances (NPSs) represents a significant and growing public health concern. Among these, synthetic cathinones are increasingly consumed, yet their biotoxicological effects remain poorly characterized [1, 2]. In this context, *in vivo* models such as *Caenorhabditis elegans*, a suitable model for high-throughput toxicity screening that exhibits a high degree of conservation of molecular pathways with humans [3], are essential to elucidate the systemic and long-term effects of these substances on critical biological processes, which remain poorly understood. **Objective:** Using *C. elegans* as a discovery platform, this study aimed to evaluate the toxic effects of methylone and pentedrone on animal development, reproduction, and lifespan. **Methods:** Synchronized L1-stage animals of the DC19 strain [*bus-5(br19)*] (~200 animals/condition) were exposed, in liquid medium, to increasing concentrations of synthetic cathinones (0–10 mM) for 24–72 h. Survival rates were assessed by counting the number of live and dead worms. Using sublethal to low-lethal concentrations (0–2.5 mM), we further explored the impact of synthetic cathinones on (1) animal development, by measuring the body length using Fiji software; (2) reproductive behavior, by counting the total number of embryos laid by individual F0-exposed animals within a 24-h time window; and (3) lifespan, by monitoring exposed animals every two days throughout their lifespan. **Results:** Short-term exposure (24 h) of *C. elegans* to methylone or pentedrone did not affect animal survival rates at concentrations ≤1.0 mM, whereas higher concentrations (≥5.0 mM) significantly reduced viability. In contrast, prolonged exposure (72 h) significantly reduced animal survival rates at concentrations ≥1.0 mM, indicating enhanced toxicity over time. Sublethal concentrations of both compounds impaired animal development in a reversible manner and significantly reduced reproductive output, while progeny viability remained unaffected. Additionally, no significant effects on animal lifespan were observed, suggesting selective disruption of developmental and reproductive processes. **Conclusions:** These findings indicate that synthetic cathinones exhibit pronounced time-dependent toxicity in *C. elegans*. This highlights previously underexplored systemic risks and reinforces the value of *C. elegans* as a powerful *in vivo* platform to uncover the biological impact of psychoactive substances.

Keywords: Synthetic cathinones; systemic toxicity; C. *elegans*

Acknowledgments/Funding

This work was supported by FCT - Fundação para a Ciência e Tecnologia, I.P., in the scope of the project UID/04378/2025 (DOI identifier 10.54499/UID/04378/2025), and UID/PRR/04378/2025 (DOI identifier 10.54499/UID/PRR/04378/2025), of the Research Unit on Applied Molecular Biosciences – UCIBIO, the project LA/P/0140/2020 (DOI identifier 10.54499/LA/P/0140/2020) of the Associate Laboratory Institute for Health and Bioeconomy - i4HB, and by CESPU – Cooperativa de Ensino Superior Politécnico e Universitário under the grant "DeTTeCaK-GI2-CESPU-2025".

References

1. Mendes, C. et al. Synthetic Cathinones Induce Developmental Arrest, Reduce Reproductive Capacity, and Shorten Lifespan in the *C. elegans* Model. *J Xenobiot* **2025**, *15*, 33, doi:10.3390/jox15010033.
2. Kuropka, P. et al. A Review of S cathinones Emerging in Recent Years (2019-2022). *Forensic Toxicol* **2023**, *41*, 25-46, doi: 10.1007/s11419-022-00639-5.
3. Barbosa, D.J. et al. *C. elegans* as a Powerful Model for Neurotoxicity Assessment. *Neurotoxicology* **2025**, *110*, 85-110, doi: 10.1016/j.neuro.2025.07.009.