Toxic effects of the methyl ketone 2-dodecanone in *Drosophila melanogaster*

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Among the plant defence mechanisms against insects, glandular trichomes are specialised hairs responsible for an important part of their secondary metabolites. Some of these compounds are toxic substances that compromise insect survival and may delay their growth and pupation. Methyl ketones are a widely-produced group of chemicals synthesised by trichomes, and their insecticidal efficacy has been described against some arthropods, such as aphids or spider mites. However, information about their mode of action and molecular effects are still very scarce. Few models offer the opportunity to perform an integrated study with multiple approaches, from molecular variations to physiological consequences. In this sense, *Drosophila melanogaster* is a proven model organism for research in genetics and biology. The fruit fly has also been considered a suitable model in ecotoxicology in recent years due to its short developmental time and its extensive and well-described genome information.

This work analysed the effect of 2-dodecanone on different developmental stages of *D. melanogaster*. Specifically, transcriptional alterations induced by sub-lethal concentrations (5 µg/L and 500 µg/L) of this methyl ketone were evaluated in third instar larvae (acute 24-hour exposures), as well as in adult males and females (chronic full life-cycle exposures). Fertility (average number of eggs) in exposed adults was also analysed. Quantitative real-time PCR (qPCR) was used to measure the expression levels of selected genes related to the endocrine system (*EcR, ERR, HR3,* and *BR-C*), the cell-stress signalling pathway (*Tl*, *def*, *p38*, *hsf*, *hsp22*, *hsp40, hsp70,* and *hsc70*), and detoxification mechanisms (*cat*, *sod*, and *phgpx*). Our results showed that 2-dodecanone caused significant alterations in the transcriptional activity of most of the genes tested even after 24-hour exposures and that these toxic effects at the molecular level ultimately translated into a dose-dependent decrease in fertility.

This study provides for the first time in *D. melanogaster* novel and interesting results on the toxic effects of an isolated secondary metabolite naturally present in plants and highlights the potential suitability of this organism to delve into the molecular effects of plant defences in insects.

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