

**BEHAVIORAL CHANGES AND OXIDATIVE DAMAGE IN ZEBRAFISH
(*DANIO RERIO*) RELATED TO ACUTE MODAFINIL USE**

Luciane Dellazari da Silva do Prado^a; Nicole Berton^a; Nicoli da Rosa Amaral^a; Inara Carbonera Biazus^b; Laíse Mattiollo^b; Jessica Nardi^b; Karen Julia de Souza dos Santos^b; Natália Freddo^c; Leonardo José Gil Barcellos^{a,d,f}; Luciana Grazziotin Rossato Grando^{a,b,e}

^a Graduate Program in Bioexperimentation, University of Passo Fundo, BR 285, São José, Passo Fundo, Rio Grande do Sul, Brazil

^b Pharmacy Program, University of Passo Fundo, BR 285, São José, Passo Fundo, Rio Grande do Sul, Brazil

^c Pharmacy Program, Atitus Education, Rua Senador Pinheiro, 304, Rodrigues, Passo Fundo, Rio Grande do Sul, Brazil

^d Graduate Program in Pharmacology, Federal University of Santa Maria, Avenida Roraima, Camobi District, Santa Maria, Rio Grande do Sul, Brazil

^e Graduate Program in Human Aging, University of Passo Fundo, BR 285, São José, Passo Fundo, Rio Grande do Sul, Brazil

^f Veterinary Medicine Program, University of Passo Fundo, BR 285, São José, Passo Fundo, Rio Grande do Sul, Brazil

INTRODUCTION: Modafinil is a drug used for narcolepsy treatment due to its effect of increasing wakefulness. However, its use has been increasing in recent years due to improper use for healthy individuals and university students, as a cognitive enhancer. Considering the “off-label” use, with doses and administration regimens higher than pharmacological use, the drug harmful potential is even greater. **AIM:** to characterize the impact of behavioral changes and possible oxidative damage resulting from acute exposure to Modafinil in zebrafish. **METHODS:** adult zebrafish (*Danio rerio*) were used as animal model, purchased from the Fish Physiology Laboratory of the University of Passo Fundo (UPF). Four groups were tested: control, 200 mg/L, 300 mg/L, and 600 mg/L, exposed for 15 minutes. At the end of the exposures, the Novel Tank Test (NTT), Social Preference Test (SPT), Y-Maze Test, and Light-Dark Test (LDT) were performed.

After euthanasia, cortisol levels, non-protein thiols, protein levels, and lipid peroxidation were assessed. The study was approved by the Ethics in Animal Use Committee of UPF (protocol no. 008/2023). The results were compared depending on their normality and homoscedasticity, determined by the Kolmogorov-Smirnov and Bartlett tests. Data considered parametric were evaluated by one-way ANOVA followed by Dunnet's multicomparative test. Non-parametric data were evaluated by the Kruskal-Wallis test, followed by Dunn's multicomparative test, and $p < 0.05$ was considered statistically significant. **RESULTS:** Modafinil induced behavioral changes, including increased exploratory activity and reduced social preference at higher concentrations. Furthermore, exposure to 200 mg/L led to increased lipid peroxidation, suggesting an oxidative imbalance, while the 600 mg/L concentration resulted in elevated total protein levels, possibly associated with adaptive inflammatory responses. No significant changes in cortisol and non-protein thiol levels were observed. **CONCLUSION:** Acute use of Modafinil induces behavioral changes with possible involvement of inflammatory mechanisms and membrane dysfunction. Further investigations should explore the mechanisms involved, including analyses of inflammatory markers in order to elucidate the neurobiological and toxicological effects of Modafinil.

Keywords: Psychostimulants; Anxiety; Oxidative stress; Cognitive enhancement; Smart drugs