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Title: Comparative study of the neurotoxicological effects of tramadol and tapentadol in SH-SY5Y cells

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**Full Title:** COMPARATIVE STUDY OF THE NEUROTOXICOLOGICAL EFFECTS OF TRAMADOL AND TAPENTADOL IN SH-SY5Y CELLS

**Running Head:** Tramadol and tapentadol neuronal toxicity

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## ABSTRACT

Opioid therapy and abuse is increasing, justifying the need to study their toxicity and underlying mechanisms. Given opioid pharmacodynamics at the central nervous system, the analysis of toxic effects in neuronal models gains particular relevance. The aim of this study was to compare the toxicological effects of acute exposure to tramadol and tapentadol in the undifferentiated human SH-SY5Y neuroblastoma cell line. Upon exposure to tramadol and tapentadol concentrations up to 600  $\mu$ M, cell toxicity was assessed through evaluation of oxidative stress, mitochondrial and metabolic alterations, as well as cell viability and death mechanisms through necrosis or apoptosis, and related

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