aquatic ecosystems. Zebrafish *(Danio rerio)* is a vertebrate animal model widely used in different areas of laboratory investigation, namely in ecotoxicology [1, 2]. Psychoactive substances (PAS) like MDMA, a synthetic drug (with high potential of abuse in young people) is difficult to remove in wastewater treatments plants (WWTP) and thus is an increasing environmental concern [3]. Consequently, the use of *D. rerio* as a model in laboratory studies presents a growing importance, including in behavioral studies, such as those associated with visual stimuli [4]. **Objectives:** The main goal of this study was to evaluate the effects of MDMA in spontaneous and visual behavior of zebrafish larvae at 120 hours post-fertilization (hpf). **Materials and Methods:** Zebrafish embryos with 2-3 hpf were previously exposed to different concentrations of MDMA (0.02, 0.2, 2.0, 20, 200 µg/L) during 96 hpf. At 120 hpf, the behaviour of the larvae was recorded, and the following parameters were analyzed: velocity, total distance traveled, distance to the well center, percentage of activity/inactivity, curvature angles, and reaction to an aversive visual stimulus (red bouncing ball in a PowerPoint slide) [5]. **Results:** Data show no significant statistical differences in all the parameters evaluated, except for the percentage of time in the upper zone, with and without aversive visual stimulus. In the latter, it is worth noting considerable variations for higher concentrations (2 and 20 µg/L) that suggest no behaviour change when exposed to the aversive visual stimulus. **Conclusions:** The higher concentrations of MDMA in water medium affects the behavior of *D. rerio* and theoretically affects their ability to escape from predators, however for environmentally relevant concentrations, which are very low, our result suggests that wild fish will not be affected in their early life stages. Despite that, we have to consider also fish exposed to low levels of MDMA for a chronic exposure in the environment and future studies are necessary to understand better this long-term exposure.

Keywords: psychoactive substances; MDMA; Behaviour; Visual Stimuli; *Danio rerio*

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POSTER 129

In vitro neuroprotective effects of dua-acting antiparkinsonians

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Resumo

Introduction: Parkinson Disease (PD) is the second most common neurodegenerative disorder [1], being characterized by the degeneration of dopaminergic neurons of substantia nigra pars compacta [2]. PD is also associated with iron accumulation within the brain, which triggers a specific form of regulated cell death called ferroptosis, further leading to dopamine (DA) depletion [3]. Currently, no effective treatment exists for stopping or delaying PD progression. Instead, the available drugs are predominantly directed to symptoms relief, keeping the course of the disease unchanged [4]. **Objectives:** Thus, the main goal of this study was to evaluate the potential in vitro neuroprotective effects of newly synthetized smart dual-acting molecules (3-hydroxypyridin-4-ones). These compounds were developed in the scope of the FCT-funded project "COMT4brain" and demonstrated the ability of simultaneously chelate iron and inhibit COMT, allowing to restore DA levels. **Material and**

methods: Differentiated SH-SY5Y cells (dopaminergic phenotype) were used as the in vitro model. The compounds cytotoxicity (0-25 µM) was evaluated, 24h after exposure, by the neutral red uptake and resazurin reduction assays, to select non-cytotoxic concentrations. To evaluate the potential neuroprotective effects against iron (III)-induced cytotoxicity, the cells were exposed to ferric nitrilotriacetate (FeNTA, 500 and 1000 µM, 24h), a ferric (Fe3+) iron aggressor, in the presence and absence of compounds. Also, the cells were exposed to MPP+ (500 and 1000 µM), a neurotoxin that induces an in vitro PD model, with or without simultaneous exposure to the tested compounds, and their potential protective effects evaluated 24h after exposure. Moreover, the compounds effects on the activity of P-glycoprotein (P-gp), an efflux transporter impacting several neurodegenerative diseases [5], were assessed through the rhodamine 123 accumulation assay. **Results:** The dual-acting agents demonstrated to be safe towards differentiated SH-SY5Y cells, and with minor effects on P-gp activity, therefore presenting a small potential for pharmacokinetic interactions. Noteworthy, several of the tested derivatives showed a significant protection against MPP+- and FeNTA-induced cytotoxicity, 24h after exposure to the aggressors, highlighting their promising neuroprotective effects. **Conclusions:** In conclusion, the new dual-acting agents tested demonstrated their potential use as a new therapeutic disease-modifying strategy for PD.

Keywords: Parkinson's disease; catechol O-methyltransferase (COMT); dopamine; ferroptosis; hydroxypyridin-4-ones

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POSTER 130

The impactof cannabinoids in Schizophrenia: a systematic review

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Resumo

Introduction: The association between the use of Cannabis and the development of schizophrenia has been a heavily researched and debated topic for over three decades. Due to the high morbidity and mortality of schizophrenia, and to the extensive, widespread use of cannabinoids, it is important to clarify if Cannabis abuse is in fact a component cause or even a direct trigger of the onset of this disease. **Objectives:** The present work aimed at conducting a systematic review of the available literature to determine the likelihood of an association between the consumption of cannabinoids and the incidence of schizophrenia. **Methods:** A thorough research of scientific publications was performed on multiple databases, including PubMed, Scielo, Science.gov, BMC, Cochrane, Google Scholar, and other relevant sources. A total of 6,328 published articles were found through specific combinations of keywords related to Cannabis/cannabinoids and schizophrenia. After application of exclusion criteria (e.g., duplicates; studies in idioms other than English, Portuguese and Spanish; conference abstracts; letters to the Editor; reviews; meta-analysis; articles not fully available; animal, in vitro or in situ studies; studies on the treatment of schizophrenia or cannabis-related complications; studies on schizophrenia remission; postmortem studies; questionnaires), 58 studies were included in this systematic review. **Results:** Most of the studies (52 out of 58) described a close association between Cannabis consumption and the onset of schizophrenia, or at least an increased risk of development of the disease. Some of the studies (4) further