

Poster 23

Comparing Cytotoxic Effects of Synthetic Cathinones and Methamphetamine on Cardiac AC16 Cell

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Abstract

Background Synthetic cathinones are psychoactive derivatives of the natural drug cathinone. Despite being sold as safer than traditional drugs, over the years there has been a rise in fatalities associated with the cardiotoxic effects of synthetic cathinones [1]. Still, few studies address the mechanisms underlying this toxicity. Objective: This work aimed to study the cardiotoxicity of synthetic cathinones (mephedrone, 3,4-DMMC, ethcathinone, α-PHP, 4-CEC, 4-MEC and α-PVP) in the AC16 human cardiomyocyte cell line and compare it with the toxicity of methamphetamine. Methods: The human cardiomyocyte cell line AC16 was differentiated using horse serum for 24 hours [2]. After differentiation, they were exposed for 48 hours to different concentrations of methamphetamine (1-10 mM), and to the following synthetic cathinones: mephedrone (0.1-10 mM), 3,4-DMMC (0.05-5 mM), ethcathinone (1-10 mM), α-PVP (0.5-5 mM), α-PHP (0.5-5 mM), 4-CEC (0.5-5 mM) and 4-MEC (0.5-5 mM). After the exposure period, two cytotoxicity tests were performed: the MTT reduction and neutral red uptake assays. Results: All the cathinones, (mephedrone, 3,4-DMMC, ethcathinone, α -PHP, 4-CEC, 4-MEC and α -PVP) as well as methamphetamine presented significant cytotoxicity in differentiated AC16 cells, with their cytotoxic effects escalating proportionally with higher concentrations. In the MTT reduction assay, significant cytotoxicity was observed with 3,4-DMMC at a concentration as low as 0.1 mM, mephedrone at 0.25 mM, α -PHP and 4-CEC at 0.5 mM, α -PVP and 4-MEC at 1 mM, while methamphetamine exhibited meaningful toxicity starting at 2.5 mM, and ethcathinone at 5 mM. Over all, the results obtained in the NR uptake assay revealed that higher concentrations were needed to induce cytotoxicity. Conclusions: Although synthetic cathinones are sold as safer than methamphetamine, some have an equal or even greater potential to cause cytotoxicity in this cell model. However, further studies are needed to determine the impact of these cathinones on cellular processes.

Keywords: cardiotoxicity; cathinones; cytotoxicity; AC16 cells

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References

- 1. Radaelli, D.; Manfredi, A.; Zanon, M.; Fattorini, P.; Scopetti, M.; Neri, M.; Frisoni, P.; D'Errico, S. Synthetic Cannabinoids and Cathinones Cardiotoxicity: Facts and Perspectives. Curr Neuropharmacol (2021), 19(11), 2038-2048.
- Davidson, M.M.; Nesti, C.; Palenzuela, L.; Walker, W.F.; Hernandez, E.; Protas, L.; Hirano, M.; Isaac, N.D. Novel cell lines derived from adult human ventricular cardiomyocytes. J Mol Cell Cardiol (2005), 39(1), 133-47.

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