Toxicity of synthetic cathinones in human kidney (HK-2) cells

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Abstract: Synthetic cathinones, also known as bath salts, emerged in the recreational drug market in the mid-2000s as alternatives to illicit drugs such as amphetamines and cocaine and represent nowadays a large class of new popular drugs of abuse. The use of synthetic cathinones is associated with adverse health effects, including renal injury, although the underlying mechanisms are not yet understood. The aim of this study was to evaluate the potential nephrotoxic effects of five commonly used cathinone synthetic derivatives, namely 3,4-methylenedioxypyrvalerone (MDPV), methylene, pentedrone, 3,4-dimethylmethcatinone (3,4-DMMC) and 4-methylethcatinone (4-MEC), using the human kidney (HK-2) cell line as an in vitro model. The HK-2 cells were exposed to a wide range of concentrations, specifically 0.01–3 mM for 3,4-DMMC and 0.1–10 mM for all the others synthetic cathinones, for 24 and 48 h. Cytotoxicity was evaluated by measuring mitochondrial reduction of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) and by assessing lysosomal uptake of neutral red (NR). It was observed that all tested compounds induced cell death in a concentration- and time-dependent manner. 3,4-DMMC was found to be the cathinone derivative that exhibited the highest toxicity for HK-2 cells, followed by MDPV, pentedrone, methylene, and 4-MEC. To the best of our knowledge, this is the first study to demonstrate the in vitro nephrotoxic potential of synthetic cathinones.

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Protective effects of SIRT1 antagonist on diabetic-induced renal fibrosis

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Abstract: Chronic kidney disease (CKD) is a leading cause of mortality in patients with diabetes mellitus (DM). Recent studies have shown that SIRT1 is closely related to the occurrence and development of diabetic nephropathy. Silent information regulator 2 (Sir2) is a nicotinamide adenine dinucleotide- (NAD⁺-) dependent deacetylase. The homology of SIRT1 and Sir2 has been extensively studied. SIRT1 deacetylates target proteins using the coenzyme NAD⁺ and is therefore linked to cellular energy metabolism and the redox state through multiple signaling and survival pathways. In the kidneys, SIRT1 may inhibit renal cell apoptosis, inflammation, and fibrosis. Therefore its activation may also become a new therapeutic target in the patients with CKD including diabetic nephropathy. Here, we evaluated the roles of SIRT1 on the kidney fibrosis in diabetic animal model. We found that acetylation of p65 and STAT3 was increased in the kidney of high fat diet-induced ZDF rats. The expression of a-SMA, collagen I, and fibronectin levels were markedly increased in diabetic-induced ZDF rats. Furthermore, SIRT1 inhibitor attenuated the diabetic-induced kidney fibrosis. Our findings strongly support that SIRT1 inhibitor may use as a protective agent for renal fibrosis in chronic hyperglycemia condition.

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Effects on cigarette smoke extract on cell proliferation and apoptosis in mouse embryonic stem cells via reactive oxygen species-induced endoplasmic reticulum stress signaling pathways

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Abstract: Cigarette smoke contains thousands of chemicals, and many components have reproductive and developmental toxicity that is harmful to humans and animals. Previous studies have reported that cigarette smoke or cigarette smoke extract (CSE) have negative effects on embryo development through in vivo and in vitro studies. However, there is no mechanism study on how CSE affects the cellular signaling pathway for apoptosis and oxidative stress in embryonic cells, or how the two pathways cross-link. Therefore, we investigated the effects of CSE on apoptosis and oxidative stress...