measured with Western blots.

Results: APAP induced the death of TIB-73 cells by increasing the level of intracellular ROS (50%) and Ca^{2+}(23%) and decreasing the level of intracellular free and total Mg^{2+} (12.5% and 30%, respectively). Taurine reduced the APAP-induced generation of ROS and activation of JNK and Bax, and increased total and intracellular Mg^{2+} via ERK activation. Increased intracellular ROS promoted JNK and Bax activation, which increased APAP-induced TIB-73 cell death.

Conclusions: Taurine may attenuate APAP-induced cytotoxicity and liver damage by increasing the levels of intracellular Mg^{2+} and activating ERK1/2 activation.

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Melatonin ameliorates alcohol-induced bile acid homeostasis by enhancing miR-497

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Introduction: Alcoholic liver disease is amajor cause of chronic liver disease worldwide that can progress from steatosis to steatohepatitis, cirrhosis, and cancer. Melatonin plays a crucial role in regulating diverse physiological functions and metabolic homeostasis. MicroRNAs are a class of noncoding RNAs and key regulators of various biological processes. Herein, we demonstrate that melatonin improves bile acid homeostasis in the liver of alcohol-fed mice by controlling the expression of miR-497.

Materials and Methods: Wild-type (C57BL/6) mice were fed with Lieber-DeCarli formulas and administered with melatonin, 2-arachidonoyl glycerol (AG) ether, and AM251, a selective cannabinoid receptor type 1 (CB1R) antagonist. Primary mouse hepatocytes were transfected with microRNA mimic (Pre-miR-497) and microRNA inhibitor (anti-miR-497) under both alcohol and melatonin exposure. Gene expression profiles and metabolic changes were measured in the liver and blood of these mice.

Results: Bile acid level and expression of CB1R, b-cell translocation gene 2 (BTG2), Yin Yang 1 (YY1), bile acid synthetic enzymes were significantly elevated in the liver of Lieber-DeCarli alcohol-fed mice. Overexpression of BTG2 enhanced hepatic YY1 gene expression and bile acid homeostasis, whereas disruption of CB1R-BTG2-YY1 cascade protected against bile acid homeostasis caused by alcohol challenge. We identified an alcohol-mediated YY1 binding site on the cholesterol7a-hydroxylase (CYP7A1) gene promoter using promoter deletion analysis and chromatin immunoprecipitation assays. Notably, melatonin markedly attenuated alcohol-stimulated induction of BTG2, YY1 mRNA levels and bile acid homeostasis by promoting miR-497. Interestingly, overexpression of miR-497 mimic dramatically repressed the increase of BTG2 and YY1 gene expression as well as bile acid homeostasis by alcohol, whereas this phenomenon was significantly reversed by miR-497 inhibitor.

Conclusions: These results demonstrate that the up-regulation of miR-497 by melatonin represses alcohol-induced bile acid homeostasis by attenuating the BTG2-YY1 signaling pathway. The melatonin-miR497 signaling network may provide a novel therapeutic approach for the prevention of hepatic metabolic dysfunction caused by the alcohol-dependent pathway.

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Fluoxetine-induced abnormalities of cardiac function

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Introduction: Fluoxetine is a widely used antidepressant compound and its action is primarily attributed to selective serotonin reuptake inhibitor in the central nervous system. However, there are an increasing number of case reports on dysrhythmias, such as atrial fibrillation or bradycardia. Since an intracellular Mg^{2+} concentration ($[Mg^{2+}]i$) should be maintained within a relatively narrow concentration range in order to ensure the proper functioning of the heart, Mg^{2+} is often lost from cardiac cells during the development of heart disease, which may exacerbate the damage caused by disease. Our objective was to investigate an effect of fluoxetine on cardiac functions and to investigate alteration of ionic homeostasis.

Materials and Methods: Left ventricular development pressure (LVDP), maximum velocity of the change in pressure (dP/dt_{max}), minimum velocity of the change in pressure (dP/dt_{min}), heart rate (HR) and Mg^{2+} efflux ($[Mg^{2+}]e$)were measured simultaneously in isolated rat hearts with Langendorff's perfusion system. Fluoxetine blocked that increasing of LVDP by increasing of potassium. Especially, the effect of fluoxetine was prolonged after washout. $[Mg^{2+}]i$