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Rutin alleviates liver damage caused by cold stress through the signaling pathways of PI3K-AKT-mTOR and Nrf2-Keap1 in mice

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Chronic cold exposure induces oxidative damage and inflammatory responses in animals. While rutin demonstrates established health benefits, its therapeutic mechanisms against cold stress remain incompletely characterized. The aim of this study was to investigate the effect and mechanism of oral rutin on the liver of mice under cold conditions. A total of 48 6-week-old male Balb/c mice with similar weight (23±1g) were randomly divided into four experimental groups: Control group (CON), Rutin group (RUT), Cold stress with rutin group (CS+RUT) and Cold stress group (CS). The results showed there was obvious oxidative stress, inflammation and liver damage of mice in the CS group, and oral rutin, significantly increased the activities of various antioxidant enzymes ($P < 0.05$) and the contents of malondialdehyde (MDA) and hydrogen peroxide (H_2O_2) in liver ($P < 0.05$). By mediating the PI3K-AKT-mTOR and Nrf2-Keap1 signaling pathways and the symptoms of cold stress injury were significantly alleviated by rutin. This study demonstrated that the recipe rutin can significantly alleviate liver damage caused by cold stress through PI3K-AKT-mTOR and Nrf2-Keap1 signaling pathways, and lays a theoretical foundation for the application of rutin in cold-stressed animals.

Keywords: *In vivo* test, Antioxidant, Plant extracts, Production applications, Stress response