

PROTECTIVE EFFECT OF FLATERONE ON MPTP OPENING IN RAT HEART MITOCHONDRIA UNDER OXIDATIVE STRESS

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Cardiovascular diseases (CVDs) remain the leading cause of mortality worldwide. Oxidative stress plays a crucial role in the pathogenesis of myocardial infarction by promoting excessive generation of reactive oxygen species (ROS), which triggers the opening of the mitochondrial permeability transition pore (mPTP). Sustained mPTP opening leads to mitochondrial dysfunction, impaired ATP production, and cardiomyocyte death. Therefore, inhibition of mPTP opening has emerged as a promising strategy for cardioprotection. Due to their antioxidant properties, flavonoids may protect mitochondria by preventing mPTP opening.

This study aimed to investigate the effect of flaterone on mPTP opening in rat heart mitochondria under oxidative stress conditions *in vivo*. Flaterone, a flavonoid preparation isolated from *Thermopsis alterniflora*, was used as the test compound in this study.

In the experiment, laboratory rats (220±30 g) were randomly divided into experimental groups (n = 4). All groups except the healthy control group were pretreated with flaterone (100 mg/kg and 50 mg/kg) for 21 days, after which myocardial infarction (MI) was induced using isoproterenol (ISO 85 mg/kg). Serum cardiac troponin I (cTnI) levels were analyzed to confirm MI induction. To assess the change in cardiac mitochondrial membrane permeability under ISO-induced oxidative stress, mitochondrial swelling was monitored at 540 nm.

Since oxidative stress is a major trigger of mPTP opening, we investigated the effect of Flaterone on the mPTP status of rat heart. As shown in Figure 1, mitochondria from isoproterenol (ISO)-treated rats showed a rapid decrease in absorbance at 540 nm, indicating increased Ca²⁺-dependent mitochondrial swelling and increased mPTP opening compared to the control group. Pretreatment with Flaterone significantly attenuated these changes in a dose-dependent manner, with the 100 mg/kg dose providing greater protection than the 50 mg/kg dose.

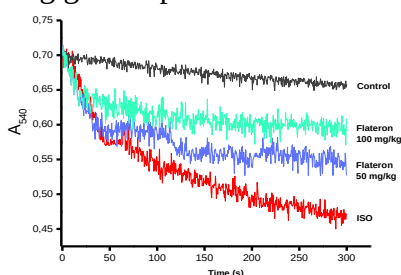


Figure 1. Representative kinetic traces of mitochondrial permeability transition pore (mPTP)-associated swelling in isolated rat heart mitochondria from control, isoproterenol (ISO)-treated, and Flaterone-pretreated groups. Mitochondrial swelling was assessed as the decrease in absorbance at 540 nm (A_{540}) over 300 s.

Flaterone protected rat heart mitochondria against oxidative stress-induced dysfunction by inhibiting Ca²⁺-dependent mPTP opening and preserving mitochondrial membrane integrity. These findings indicate that flaterone exerts cardioprotective effects through the maintenance of mitochondrial function and suggest its potential as a natural therapeutic agent for preventing oxidative stress-related myocardial injury.