

PREVENTION OF GLYCERYL TRINITRATE TOLERANCE BY FLAVONOIDS

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Glyceryl trinitrate (GTN) is one of the most widely used anti-ischemic. However, the development of tolerance after continuous application for 24 to 72 hours limits its clinical utility. Tolerance appears to be associated with the oxidative stress induced by GTN in blood vessels. Flavonoids are important components in herbal medicine. They have antioxidative effect and potentiate vascular relaxation. In this study, the potential of nine flavonoids to prevent GTN tolerance were examined. Changes in isometric tension in thoracic aorta of Sprague Dawley rats were studied using organ chamber technique. Aortic rings were treated with GTN (30 μ M) for one hour to induce GTN tolerance. They were incubated with or without flavonoids for 30 minutes before GTN treatment. Afterwards, rings were contracted with phenylephrine (1 μ M) and relaxed with GTN (0.1 nM to 30 μ M). GTN-induced relaxation was reduced by prior incubation with GTN; this reduction was prevented by apigenin (10 μ M), which did not affect the relaxations in the control group (without prior treatment with GTN). On the other hand, luteolin (10 μ M) potentiated relaxations to GTN in both the control and GTNpre-treated groups. Therefore, apigenin may have the potential to prevent the development of GTN tolerance.