

Relaxant Effects of Flavonoids in Isolated Guinea Pig Trachea and Their Structure-Activity Relationships

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摘要

Abstract

The structure-activity relationships between flavonoids and their tracheal relaxant action are not very well known. In the present study, 26 natural and synthetic flavonoids, divided into the 5 classes of flavones, flavonols, flavanones, isoflavones and chalcones, were tested, and their IC₅₀ values were determined. The IC₅₀ values of these 5 classes indicated that flavones were more potent than flavonols. Flavones were also more potent than flavanones, suggesting that the presence of a double bond between C-2 and C-3 is important. However, flavones were similar to isoflavones in potency. Chalcones, a class with an open C-ring, appeared to be the least potent among these 5 classes. Introduction of a hydroxy group at position C-6 of flavones increased their relaxant activities; so did adding a hydroxy group at position C-7 of flavones. The optimum number of hydroxy groups introduced to the A-ring of flavones was one. As more hydroxy groups were introduced to positions at C-5, C-6, and/or C-7 of flavones, the IC₅₀ values increased. Flavones or flavonols with a pyrogallol moiety either in the A- or B-ring, respectively, had no activity. Flavonols with ortho-hydroxy groups in the B-ring were more potent than those with meta-hydroxy groups. The activity of 6-hydroxyflavone disappeared when the C-6 hydroxy group of the A-ring was methoxylated. If the C-4 hydroxy group of the B ring was methoxylated, the relaxant effect of these flavones was also attenuated or disappeared. Therefore, the hydroxy group on either the A- or B-ring of flavones and flavonols being methylated resulted in lower potency of the tracheal relaxant effects. However, when all hydroxy groups on both the A- and B-rings of flavones or flavonols were methoxylated, higher potency was observed. Therefore, the influence of methoxylation in flavones may be similar to that in flavonols. However, if the C-3 hydroxy group on the C-ring of flavonols, but not flavones which lack this hydroxy group, was methoxylated, the relaxant effects may increase. Glycosylation of the hydroxy group at position C-7 of flavones or flavanones attenuates the relaxant effects.