3-O-Methylquercetin more selectively inhibits phosphodiesterase subtype 3

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摘要

Abstract

Rhamnus nakaharai Hayata (Rhamnaceae), has been used as a folk medicine in Taiwan for treating constipation, inflammation, tumors and asthma. 3-O-methylquercetin (3-MQ), a main constituent of the plant, has been reported to inhibit total cAMP- and cGMP-phosphodiesterase (PDE) of guinea pig trachealis. Therefore we were interested in investigating the inhibitory effect of 3-MQ on various PDE isozymes from guinea pig lungs and hearts. Isolated guinea pig lungs and hearts were homogenized and centrifuged. The supernatant was chromatographed over a column of Q-sepharose, and eluted with various concentrations of NaCl. In the following order, PDE subtypes 1, 5, 2, 4 from lungs, and 3 from hearts were separated. The IC 50 values of 3-MQ on these isozymes were 31.9, 86.9, 18.6, 28.5 and 1.6 microM, respectively. 3-MQ (10-100 microM) non-competitively inhibited PDE2, but competitively inhibited PDE4. 3-MQ (1-10 microM) also competitively inhibited PDE3. However, 3-MQ (10-100 microM) did not competitively inhibit PDE1 and 5, although it had a tendency to competitively inhibit PDE1 at concentrations of 10 - 30 microM. The present results showed that K i value of 3-MQ was similar to that of milrinone in PDE3, and was not significantly different from that of Ro 20 - 1724 in PDE4, respectively. In conclusion, 3-MQ was revealed to be a selective and competitive PDE3/PDE4 inhibitor, although its inhibitory effect on PDE4 was not potent. Therefore, 3-MQ may have a potential in the treatment of asthma beside its antiviral activity.