Quercetin Inhibits 5-HT3A Receptor-Mediated Ion Current by Interacting with Pretransmembrane Domain I

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Abstract

We investigated the effect of quercetin on mouse 5-HT3A receptor channel activity, which is involved in pain transmission, analgesia, vomiting, and mood disorders in nervous system. 5-HT3A receptor was expressed in Xenopusoocytes, and the current was measured using two-electrode voltage clamp technique. Treatment of quercetin itself had no effect on the oocytes injected with H2O as well as on the oocytes injected with 5-HT3A receptor cRNA. In the oocytes injected with 5-HT3A receptor cRNA, co-treatment of quercetin with 5-HT inhibited 5-HT-induced inward peak current (I5-HT) with dose-dependent and reversible manner. The half-inhibitory concentrations (IC50) of quercetin was 64.7 ± 2.2 mM. The inhibitions of I5-HT by quercetin were competitive and voltage-independent. Point mutations of pre-transmembraine domain 1 (pre-TM1) such as R222T and R222A but not R222D, R222E and R222Kabolished quercetin-induced inhibition of I5-HT, indicating that quercetin interacts pre-TM1 of 5-HT3A receptor. These results indicate that quercetin might regulate 5-HT3Areceptor channel activity via interaction with N-terminal domain and these results, further, show that this regulation of 5-HT3Areceptor channel activity by quercetin might be one of pharmacological actions of flavonoids.

References

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