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The Flavonols Quercetin, Kaempferol, and Myricetin Inhibit Hepatocyte Growth Factor-Induced Medulloblastoma Cell Migration.

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Medulloblastoma, the most common malignant brain tumor in children, is a highly metastatic disease, with up to 30% of children having evidence of disseminated disease at presentation. Recently, the hepatocyte growth factor (HGF) and its receptor, the tyrosine kinase Met, have emerged as key components of human medulloblastoma growth and metastasis, suggesting that inhibition of this pathway may represent an attractive target for the prevention and treatment of this disease. Using immunoblotting procedures, we observed that the dietary-derived flavonols quercetin, kaempferol, and myricetin inhibited HGF/Met signaling in a medulloblastoma cell line (DAOY), preventing the formation of actin-rich membrane ruffles and resulting in the inhibition of Met-induced cell migration in Boyden chambers. Furthermore, quercetin and kaempferol also strongly diminished HGF-mediated Akt activation. Interestingly, the inhibitory effects of quercetin on the tyrosine kinase receptor Met [half-maximal inhibitory effect (IC₅₀) of 12 $\mu\text{mol/L}$] or on the Met-induced activation of Akt (IC₅₀ of 2.5 $\mu\text{mol/L}$) occurred at concentrations achievable through dietary approaches. These results highlight quercetin, kaempferol, and myricetin as dietary-derived inhibitors of Met activity and suggest that this inhibitory effect may contribute to the chemopreventive properties of these molecules.

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