題名:Chrysin induces G1 phase cell cycle arrest in C6 glioma cells through inducing p21Waf1/Cip1 expression: Involvement of p38 mitogen-activated protein kinase

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上傳時間:2009-10-02T08:59:17Z

摘要:Flavonoids are a broadly distributed class of plant pigments, universally present in plants. They are strong anti-oxidants that can inhibit carcinogenesis in rodents. Chrysin (5,7-dihydroxyflavone) is a natural and biologically active compound extracted from many plants, honey, and propolis. It possesses potent anti-inflammatory, anti-oxidant properties, promotes cell death, and perturbing cell cycle progression. However, the mechanism by which chrysin inhibits cancer cell growth remains poorly understood. Therefore, we developed an interest in the relationship between MAPK signaling pathways and cell growth inhibition after chrysin treatment in rat C6 glioma cells. Cell viability assay and flow cytometric analysis suggested that chrysin exhibited a dose-dependent and time-dependent ability to block rat C6 glioma cell line cell cycle progression at the G1 phase. Western blotting analysis showed that the levels of Rb phosphorylation in C6 glioma cells exposed to 30 microM chrysin for 24h decreased significantly. We demonstrated the expression of cyclin-dependent kinase inhibitor, p21(Waf1/Cip1), to be significantly increased, but the p53 protein level did not change in chrysin-treated cells. Both cyclin-dependent kinase 2 (CDK2) and 4 (CDK4) kinase activities were reduced by chrysin in a dose-dependent manner. Furthermore, chrysin also inhibited proteasome activity. We further showed that chrysin induced p38-MAPK activation, and using a specific p38-MAPK inhibitor, SB203580, attenuated chrysin-induced p21(Waf1/Cip1)

expression. These results suggest that chrysin exerts its growth-inhibitory effects either through activating p38-MAPK leading to the accumulation of p21(Waf1/Cip1) protein or mediating the inhibition of proteasome activity.