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Effects of an Ingredient of Bupleurum On Dopamine D2 Receptor-mediated Signaling in Human Neuroblastoma Cell Line

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Introduction:Dopamine D2 receptors (D2R) are the primary target of antipsychotic drugs and have been shown to regulate Akt/glycogen synthase kinase-3b (GSK-3b) signaling through scaffolding protein b-arrestin 2.

Objective: In the present study, we researched the effects of saikosaponin B1 on the b-arrestin 2-mediated Akt/GSK-3b pathway in human neuroblastoma cell lineSH-SY5Y cells.

Aims: To determine whether saikosaponin B1 affected neuronal morphology in human neuroblastoma cell line SH-SY5Y cells.

Methods: We investigated the effects of saikosaponin B1 on neurite outgrowth using immunostaining. We examined the effects of saikosaponin B1 on Akt and GSK-3b and its well-known downstream regulators, cAMP response element-binding protein (CREB), brain-derived neurotrophic factor (BDNF), and Bcl-2 levels using Western blot analysis.

Results: Saikosaponin B1 was found to enhance neurite outgrowth. Small interfering RNA (siRNA) for b-arrestin 2 knockdown blocked the increase in saikosaponin B1-induced neurite outgrowth. Furthermore, saikosaponin B1 increased the levels of Akt and GSK-3b phosphorylation. The elevation of Akt phosphorylation induced by saikosaponin B1 was reduced by b-arrestin 2 siRNA.Moreover, saikosaponin B1 effectively increased the levels of phospho-CREB, BDNF, and Bcl-2.

Conclusion:Together, these results suggest that regulation of the b-arrestin 2-dependent pathway via blockade of the D2R in SH-SY5Y cells is one mechanism underlying the neuroprotective effect of saikosaponin B1.

Keywords: saikosaponin B1, Dopamine D2 receptors, b-Arrestin 2, Akt/glycogen, Synthase kinase-3b signaling, Neurite outgrowth