Cytochalasin H inhibits angiogenesis via the suppression of HIF-1α protein accumulation and VEGF expression through PI3K/AKT/P70S6K and ERK1/2 signaling pathways in non-small cell lung cancer cells

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Our previous studies have isolated cytochalasin H (CyH) from mangrove-derived endophytic fungus in Zhanjiang and have demonstrated that CyH induces apoptosis and inhibits migration in A549 non-small cell lung cancer (NSCLC) cells. In this study, we further explored the effect of CyH on angiogenesis in NSCLC cells and the underlying molecular mechanisms. A549 and H460 NSCLC cells were treated with different concentrations of CyH for 24 h. The effects of CyH on NSCLC angiogenesis *in vitro* and *in vivo* were investigated. The expression of hypoxia inducible factor-1α (HIF-1α) and vascular endothelial growth factor (VEGF) in xenografted NSCLC of nude mice was analyzed by immunohistochemistry. ELISA was used to analyze the concentration of VEGF in the conditioned media derived from treated and untreated NSCLC cells. Western blot was performed to detect the levels of HIF-1α, p-AKT, p-P70S6K, and p-ERK1/2 proteins, and RT-qPCR was used to determine the levels of HIF-1α and VEGF mRNA in A549 and H460 cells. Our results showed that CyH significantly inhibited angiogenesis *in vitro* and *in vivo* and suppressed the hemoglobin content and HIF-1α and VEGF protein expression in xenografted NSCLC tissues of nude mice. CyH inhibited the secretion of VEGF protein and the expression of HIF-1α protein in A549 and H460 cells. Moreover, CyH had a significant inhibitory effect on VEGF mRNA expression but had no effect on HIF-1α mRNA expression, and CyH inhibited HIF-1α protein expression by promoting the degradation of HIF-1α protein in A549 and H460 cells. Additionally, CyH dramatically inhibited AKT, P70S6K, and ERK1/2 activation in A549 and H460 cells. Taken together, our results suggest that CyH can inhibit NSCLC angiogenesis by the suppression of HIF-1α protein accumulation and VEGF expression through PI3K/AKT/P70S6K and ERK1/2 signaling pathways.

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