

A potential Anticancer Agent, Salvianolic Acid B, Inhibits Growth of HNSCC via Cyclooxygenase-2 and Apoptotic Pathways

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Abstract

Cyclooxygenase-2 (Cox-2) is an important mediator of inflammation and overexpression of COX-2 in oral mucosa has been associated with increased risk of head and neck squamous cell carcinoma (HNSCC). Therefore, celecoxib, a selective inhibitor of COX-2, was hailed as a promising chemo-preventive agent for HNSCC. However, its dose-dependent cardiac toxicity limits long term use of celecoxib. The objective of this study is to investigate effective, safer and affordable chemo-preventive agent. Salvianolic acid B (Sal-B) was isolated from *Salvia miltiorrhiza* Bge, which is a well-known Chinese herb medicine for cancer therapy. Anticancer activity of Sal-B was assessed in HNSCC by evaluating the levels of cell growth and COX-2 expression. We found that Sal-B can effectively inhibit HNSCC JHU-022 and JHU-013 cells with IC_{50} of 18 and 50 μ M, respectively. Nude mice with HNSCC solid tumor xenografts were treated with Sal-B (80mg/kg/day) or celecoxib (5mg/kg/day) for 25 days and the tumor volumes in Sal-B treated group were significantly lower than those in celecoxib treated or untreated control groups ($p < 0.05$). In addition, combination treatment of low dose of Sal-B (40mg/kg/day) and celecoxib (5mg/kg/day) in HNSCC significantly enhanced anticancer efficacy compared to single treatment regimens. Interestingly, Sal-B selectively inhibited COX-2 expression and low expression levels of COX-2 protein were found in cultured HNSCC cells and in HNSCC cells isolated from tumor xenografts. Sal-B treatment also caused dose-dependent inhibition of prostaglandin E_2 synthesis, either with or without lipopolysaccharide stimulation. Taken together, these results strongly suggest that Sal-B is a promising multifunctional anticancer agent and the combination of Sal-B with low dose of celecoxib hold potential as a new preventive strategy in targeting inflammatory associated tumor development.