comparison to the known substrate N7-MeG, hAAG exhibited a decrease in catalytic activity of N7-BnG. Future structural studies, employing X-ray crystallography, will actively uncover the conformational requirements of active-site residues necessary for accommodating bulkier alkyl lesions. Our research actively explores and characterizes the unique processing of alkylated DNA lesions by repair pathways TLS and BER, shedding light on their less conventional roles in repairing lesions of larger size.

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Abstract 2321

The combination of Astragaloside I, Curcumol, and Solasodine synergistically suppressed colon cancer proliferation via Hedgehog signaling

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Keywords: Astragaloside I, Curcumol, and Solasodine, Combination, Hedgehog signaling, Colon cancer

Background: Aberrant Hedgehog (Hh) signaling activation has been reported to be associated with colon cancer, one of the major causes of cancer death. Natural compounds such as phytochemicals have been applied to prevent colon carcinogenesis. However, due to the limited efficacy and the possible toxicity from the high dose of single compound, it is worthwhile to employ the combination of multiple compounds exerting the synergistic effect. Here, we determined the optimal combination ratio of natural compounds showing the significant effect on inhibiting Hh signaling and validated the effect on inhibiting the growth of colon cancer cells. Methods: The effects of natural compounds on Gli1 transcriptional activity were assessed by dual luciferase assay. Robust optimization was used to determine the optimal combination ratio of natural compounds. Colony formation assay and flow cytometry analysis were used to evaluate the effect of compounds on the proliferation and apoptosis of colon cancer cells. The expression of apoptosis-related markers and Hh/Gli1 signaling mediators were examined by Western blot. Results: Based on the results of dual luciferase, 7 compounds were selected for robust optimization, resulting in 3 combinations. After colony formation assay, we found that the combination of Astragaloside I, Curcumol, and Solasodine synergistically inhibited the proliferation of HCT116 and HT29 colon cancer cells than single compound treatments. In addition, compared to the single compound treatment, the combination of Astragaloside I, Curcumol, and Solasodine significantly induced apoptosis as well as regulated the expression of apoptosis-related markers such as cleaved-PARP, Bax, and Bcl-2 of colon cancer cells. Mechanically, the combination remarkably suppressed Hh signaling in colon cancer cells, which is consistent with the effects of Hh inhibitor Gant61. Conclusion: The combination of Astragaloside I, Curcumol, and Solasodine exerted the synergistic effect on suppressing colon cancer proliferation via Hh signaling, suggesting that the combination approach of natural phytochemicals may be a potent strategy against colon cancer.

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