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## Anti-proliferative and anti-telomerase activity of black raspberry extract in human colorectal cancer cells

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Berries have attracted considerable attention because of their antineoplastic activities demonstrated in both preclinical and clinical studies. Several mechanisms have been proposed to explain berry anti-tumor effects, which include inhibition of angiogenesis and induction of cell cycle arrest and apoptosis. However, no previously published studies have investigated berry antitelomerase activity in cancer cells. The aim of this research was to examine the antitelomerase effect of blackberry in human colorectal cancer (CRC) cells. Anti-telomerase activity of blackberry juice was analyzed in six human CRC cells, both in cell-free systems and intact cells by TRAP assay. The effect of blackberry on the expression of human telomerase catalytic subunit, hTERT mRNA and methylation status of its gene promoter was also examined by quantitative RT-PCR and MSP analysis, respectively. Blackberry extract significantly inhibited the growth of six CRC cells in a dose-dependent manner. Telomerase activity of CRC cells incubated with IC<sub>50</sub> concentration of berry extract for 48 and 72h decreased by 15-37.5% and 43.23 - 62.5% ( $p < 0.05$ ), respectively. In the cell-free assay, treatment with as little as 7 $\mu$ l/ml of berry juice completely inhibited telomerase activity in all CRC cell lines. Berry treatment caused a significant reduction of hTERT expression in SW480, HT29/219, LS180, and HCT116 cells ( $p < 0.01$ ) and a non-significant reduction in other two cell lines. Berry treatment partially induced hypomethylation of hTERT promoter in CRC cells. Our data indicate that telomerase inhibition is a key mechanism by which blackberry exert its anticancer effect in CRC cells.

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