Luteolin, quercetin and ursolic acid are potent inhibitors of proliferation and inducers of apoptosis in both KRAS and BRAF mutated human colorectal cancer cells.

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Abstract
KRAS and BRAF mutations are frequent in colorectal carcinoma (CRC) and have the potential to activate proliferation and survival through MAPK/ERK and/or PI3K signalling pathways. Because diet is one of the most important determinants of CRC incidence and progression, we studied the effects of the dietary phytochemicals quercetin (Q), luteolin (L) and ursolic acid (UA) on cell proliferation and apoptosis in two human CRC derived cell lines, HCT15 and CO115, harboring KRAS and BRAF activating mutations, respectively. In KRAS mutated HCT15 cells, Q and L significantly decreased ERK phosphorylation, whereas in BRAF mutated CO115 cells the three compounds decreased Akt phosphorylation but had no effect on phospho-ERK. Our findings show that these natural compounds have antiproliferative and proapoptotic effects and simultaneously seem to act on KRAS and PI3K but not on BRAF. These results shed light on the molecular mechanisms of action of Q, L and UA and emphasize the potential of dietary choices for the control of CRC progression.

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