Early and Late Apoptosis Events in Human Transformed and Non-Transformed Colonocytes are Independent on Intracellular Acidification

Abstract:
Intracellular acidification is discussed to play a pivotal role in the process of programmed cell death by providing an intracellular environment optimal for the activation of caspases and the execution of apoptosis. Using three human colon epithelial cell lines we tested whether effects on early and late apoptosis markers can be related to changes in intracellular pH (pHi). Caspase-3-like activity and plasma membrane disintegration served as measures of early apoptosis whereas nuclear fragmentation served as indicator of late apoptosis events. The pHi was measured using the pH-sensitive dye 2’, 7’-bis (2-carboxyethyl-5-(6)-carboxyfluorescein. Six flavonoids differing in apoptosis inducing activity were employed as tools. In HT-29 cells, quercetin and flavone proved to potently increase apoptosis without altering pHi. In Caco-2 cells, quercetin and flavone increased early and late apoptosis parameters associated with a concomitant decline in pHi. However, addition of imidazole prevented the acidification without altering the apoptotic response to the flavonoids. In NCOL-1 cells, only quercetin was able to induce apoptosis and changes observed correlate with the observed initial intracellular acidification rate. Here too, imidazole prevented the pHi decline but failed to affect apoptosis execution. In conclusion, apoptosis in human colonocytes is not affected by alterations in pHi.