Curcumin metabolites induce autophagic cell death through PI3K/AKT-mTOR signaling in COLO205 human colon adenocarcinoma cells

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Autophagy, type II programmed cell death, is crucial for maintaining cellular homeostasis and plays a role in many diseases including cancer. Tetrahydrocurcumin (THC), a major metabolite of curcumin, has been demonstrated an autophagy-inducing effect in human HL-60 promyelocytic leukemia cells. In the present study, we found that THC and two other curcumin metabolites, tetrahydrodemethoxycurcumin (THDC) and tetrahydrobisdemethoxycurcumin (THBC), decreased the survival ratio of COLO205 human colon adenocarcinoma cells, but did not increase the sub-G1 cell population, one of the hallmarks of apoptosis. THC and its derivatives, THDC and THBC, induced autophagic cell death in COLO205 cells by increasing acidic vascular organelle (AVO) formation, an autophagy marker. The results also indicated that the numbers of the methoxy groups in the curcumin metabolites were negatively correlated with their autophagy-inducing effects. The amounts of LC3-I/II and beclin-1 increased and the phosphorylation levels of PI3K, AKT, and mTOR decreased with the addition of THBC in a dose-dependent manner. Taken together, these data demonstrated the anticancer efficacy of curcumin metabolites which suggest a potential translational application for the prevention of human colon cancer.

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