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Sulforaphane as a chemosensitizer for standard-chemotherapy in experimental colorectal carcinoma

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An increase in the use of systemic chemotherapy for colorectal cancer has shown to be associated with liver injury (fatty changes to the liver and sinusoidal injury). Further the use of standard chemotherapy results in a high intrinsic multi-drug resistance. Thus the aim of this study was to determine the cytostatic effect of standard chemotherapy with FOLFOX in combination with sulforaphane in an in vitro model using two different metastatic colon adenocarcinoma cell lines from either rats or humans, to compare the observed effect with the effect on normal tissue cells and to investigate the regulation of multi-drug resistance protein-2 expression when treated in with SFN and FOLFOX in combination.

The significant inhibition of cell viability by combined treatment and the time-dependent reduction of the fractional inhibitory sulforaphane concentrations were shown in both cell lines for the first time. The number of human carcinoma cells and fibroblasts was increased by the smaller sulforaphane concentrations in combination with FOLFOX. There was no inhibition of HFF cell viability by the combined treatment (sulforaphane $\leq$ 10 µM) reported. The human colorectal carcinoma cell viability assay results were supported by the results from DNA fragmentation assay, where significant increase of apoptotic cells by the combined treatment starting from SFN concentration 5 µM and significant increase of necrotic cells at the highest SFN concentrations in a dose-dependent manner was revealed. The effect of combined treatment on significant dose-dependent increase expression in mRNA and protein levels of multi-drug transporter protein-2 in this study was determined. The results of rat and human cell viability assays were comparable.

To estimate the benefit of SFN as an additive agent to standard chemotherapy as FOLFOX for colon cancer treatment clinical trials are warranted.