

The drug resistance suppression induced by curcuminoids in colon cancer SW-480 cells is mediated by reactive oxygen species-induced disruption of the microRNA-27a-ZBTB10-Sp axis

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Worldwide, colon cancer is considered as one of the major causes of cancer deaths both in men and women, and is the third leading cause of cancer mortality in the US. Investigations have revealed that natural dietary compounds like Curcuminoids can be used as chemopreventive agents to delay, prevent or even reverse the development of colorectal cancer. Curcuminoids are known to produce chemopreventive actions by modulating the gene expression and signaling cascades, which are important for cell proliferation, differentiation and apoptosis, apart from the suppression of chronic inflammation, metastasis and angiogenesis.

Objective:

To determine whether the chemotherapeutic and chemosensitizing activities of Curcuminoids in colon cancer cells are mediated through modulation of the FGF-dependent miR-27a-ZBTB10-Sp-axis.

Study Design:

In this study, human colon adenocarcinoma HT-29 and SW-480 cancer cells, and the non-cancer colon CCD-18Co fibroblast cells were used

Effect of Curcuminoids, 5-fluorouracil (5-FU) or a combination of Curcuminoids and 5-FU on cell proliferation and cell viability were determined

Varying concentrations of Curcuminoids were evaluated against cellular ROS levels, whereas influence on gene and protein expression was assessed by RT-PCR, transfections with expression constructs and Western blots

Curcuminoids (2.5–10 µg/mL) was found to suppress the growth and viability of cancer cells, SW-480 and HT-29 than non-cancer cells, CCD-18Co, as well as enhanced the anticancer activity of 5-FU by suppressing multidrug resistant gene-1 (MDR1)

In addition, treatment with Curcuminoids resulted in inhibition of Sp transcription factors (Sp1, Sp3, and Sp4), which play a major role in the growth and metastasis of many tumour types, and Sp-regulated genes in SW-480 cells

This was accompanied by suppression of ROS-mediated induction of miR-27a:ZBTB10 pathway, a known mechanism for anticancer activity of NSAIDs like GT-094 and betulinic acid in colon cancer cells

Conclusion:

Overall, Curcuminoids could be effective in treating colon cancer in patients who have developed drug resistance.