

Abstract

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In vitro studies on the inhibition of colon cancer by butyrate and carnitine.

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OBJECTIVE: Epidemiologic studies support an association between diet and the incidence of colorectal cancer. Butyrate, a short-chain fatty acid present in dietary fiber and dairy products, is a potential anticarcinogenic compound. We previously showed that **carnitine can enhance the bioavailability of butyrate in vivo**. In the present study, we evaluated the effects of butyrate alone and in combination with carnitine on colon cancer cells in vitro, examining proliferation and apoptosis and the molecular mechanisms by which these nutrients may inhibit colon cancer.

METHODS: Caco-2 cells, a well-established cell model, were incubated with butyrate (2.5-20mM) with or without carnitine (10mM) for various incubation periods. Proliferation was measured by incorporation of (3)H-thymidine, and apoptosis was detected using flow cytometry, and then confirmed by analyzing the presence of single-strand DNA breaks typical of apoptotic cells. Prostaglandin E(2) production was assayed and Bcl-2 and cyclo-oxygenase-2 expressions were examined by western blotting.

RESULTS: **Butyrate and carnitine inhibited Caco-2 cell proliferation (P<0.05) and induced apoptosis (P<0.05)**. Prostaglandin E(2) production was decreased in treated Caco-2 cells. At the molecular level, the expression of proapoptotic Bax and Bak proteins were increased in cells incubated with butyrate and carnitine, whereas expression of antiapoptotic Bcl-x(L) was decreased. Cyclo-oxygenase-2 expression was decreased in cells incubated with butyrate and carnitine.

CONCLUSIONS: **Butyrate and carnitine inhibit human colon carcinoma cell proliferation and induce apoptosis in human colon carcinoma cells**. This is accompanied by an appreciable alteration of the Bax-to-Bcl-x(L) and Bak-to-Bcl-x(L) ratios in favor of apoptosis. This study provides a scientific rationale to study the effects of carnitine and butyrate in colon cancer in vivo.

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