

Prevention and treatment of colitis and colitis-associated tumorigenesis by Berberine

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Berberine, an isoquinoline alkaloid, is a major active component in the plant genera *Berberis* and *Coptis*. It has been used for treating bacteria-associated diarrhea and intestinal parasitic infections for several decades. Increasing evidence has demonstrated berberine's immunoregulatory effects on inflammation. We have found that berberine promoted recovery of dextran sulfate sodium (DSS)-induced intestinal injury and inflammation in mice, which correlated with its inhibitory effects on inflammatory cytokine production by colonic macrophages and epithelial cells through suppressing signaling pathways.

Chronic inflammation is a risk factor for cancer development, including colitis-associated cancer (CAC). Thus, novel therapies for chronic colitis should target both disease remission and preventing tumorigenesis. Recent studies indicated that berberine suppressed growth of several tumor cell lines in vitro through cell type-dependent mechanisms. We have shown that berberine induced caspase-independent cell death through activation of apoptosis-inducing factor (AIF), and inhibited basal level of and epidermal growth factor (EGF)-stimulated proliferation and down-regulated EGF receptor expression in colon tumor cells. Berberine showed less cytotoxicity on normal colon cells, indicating the relative selectivity for tumor cells. Furthermore, we found that berberine exerted preventive and treatment effects on colorectal cancer in two mouse models of CAC, wild-type mice treated with azoxymethane and DSS and APC^{min/+} mice with DSS treatment.

These studies have potential direct relevance to medicine by identifying the effects of berberine on prevention and/or treatment of CAC. Furthermore, mechanisms of berberine's action will serve as the rationale to support the development of new hypothesis-driven studies to define the clinical efficacy of berberine.

Biography

Fang Yan completed her MD in 1991 in China, Ph.D. in 1997 from University of Louisville and postdoctoral studies from Vanderbilt University in 2011. Currently, she is a research associate professor at Vanderbilt University. Dr. Yan's research focuses on investigating the mechanisms and treatment for intestinal inflammation and inflammation-associated tumor. Dr. Yan's research is supported by National Institute of Health (NIH) and Crohn's and Colitis Foundation of America. She has published 35 papers in peer-review journals. American Gastroenterological Association offered Dr. Yan a Basic Science Research Award in 2008 to honor her studies to understand the mechanisms of probiotic action in human health. Dr. Yan is serving an editorial board member for several journals and a NIH grant reviewer.

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