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Inhibitory effects of nondigestible carbohydrates of different chain lengths on azoxymethane-induced aberrant crypt foci in Fisher 344 rats

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Abstract

Colon cancer is one of the leading causes of cancer morbidity and mortality in Western countries. The objective of this study was to elucidate the effect of prebiotic carbohydrates of different chain lengths on azoxymethane-induced aberrant crypt foci in Fisher 344 male rats. After an acclimatization period of 1 week, 70 male weanling rats were divided into 7 groups and fed AIN-93G (Control) and 6 experimental diets that contained control + (maltodextrin; Raftiline HP, Raftiline ST, Raftilose P95, Raftilose Synergy1, and Mix; ORAFTI, Tienen, Belgium). All the rats received 16 mg/kg body weight of azoxymethane dissolved in saline subcutaneous at 7 and 8 weeks of age. The rats continued to receive the assigned diets until killed by carbon dioxide asphyxiation at 17 weeks of age. There was a significant ($P < .05$) increase in cecal weight and a decrease in cecal pH in rats fed prebiotic carbohydrates. The highest reduction of colonic aberrant crypt foci, both in total number as well as crypt, multiplicity was seen in the group fed Mix (63.9%). Consumption of diets containing Raftilose Synergy1, Raftiline ST, and Raftiline HP showed a reduction of total colonic crypts by 52.2%, 29.6%, and 46.3%, respectively, as compared with the control diet.

Keywords: Rat; ACFs, aberrant crypt foci; AOM, azoxymethane; Fructo-oligosaccharides; SCFAs, short-chain fatty acids

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1. Introduction

Colon cancer is the second leading cause of cancer-related deaths. Although cancer of the colon is widely believed to be more prevalent in men, it is actually more common in women [1]. Sometimes referred to as colorectal cancer (cancer of the colon and rectum), it is predicted to be responsible for about 56 000 deaths during the year 1999. Several factors are believed to be involved in the generation of cancer. According to the American Institute for Cancer Research, some of the most common causes of cancer include heredity, tobacco use, and high consumption of alcohol.

The link between diet, nutrition, and the risk for cancer is well established [2]. Studies have shown that about 50% of all cancers are the result of poor diet [3]. Diets rich in fat and poor in fiber can increase the incidence of various forms of cancer. For this reason, nutritionists recommend diets rich in largely unprocessed fruits and vegetables, which are generally low in fat and represent the source of naturally occurring dietary fiber and cancer-fighting nutrients such as vitamin A, vitamin C, and carotenoids. These substances are very effective against cancer of the lung, breast, oral cavity, esophagus, stomach, pancreas, cervix, and prostate, especially the colon and rectum [4-6].

Recent research has revealed that certain classes of nondigestible carbohydrates such as inulin, which is extracted from chicory root by processes that are similar to beet sugar processing, have been shown to be chemopreventive in various experimental models [7-13]. These carbohydrates that are not digested or absorbed in the stomach or small intestine arrive almost quantitatively in the colon where they are fermented selectively by certain groups of bacteria (bifidobacteria, lactobacilli, and others). This increased bacterial metabolic activity is thought to be the basis of the anticancer properties of these prebiotic carbohydrates. The effects may be realized through increased production of short-chain fatty acids (SCFAs) through bacterial cell wall interactions with the host (immunologic) and/or reduced production of genotoxic and putrefactive compounds in the intestinal lumen. Fructo-oligosaccharides have been shown to be indigestible by enzymes in the human small intestine but are fermented extensively by large-bowel microflora [14,15]. There is preliminary evidence of the inhibitory effects of inulin in experimental animals [8,12,13,16].

A number of natural and synthetic compounds are being studied as potentially chemopreventive for colon cancer using the induction of aberrant crypt foci (ACFs) as the primary end point. Aberrant crypt foci are preneoplastic lesions in rat colon, and they are induced by all colon carcinogens [17,18].

Aberrant crypt foci are preneoplastic lesions found in most colon cancers [19]. Aberrant crypt foci are characterized by 1 or more crypts that appear as a single focus but are larger than normal crypts, have thickened epithelia, possess altered luminal openings, have an increased pericryptal area between them and normal crypts, and appear elevated compared with normal crypts when viewed under a microscope [20,21]. Each ACF contains numerous crypts per focus that multiply with time after treatment with a carcinogen and can be observed as early as 2 weeks after injection of the carcinogen [22]. These ACF can develop into polyps and eventually into colon cancer.

Foci of aberrant crypts in rat colon are putative cancerous lesions that have been proposed as biomarkers for short-term assays for testing chemical carcinogens and chemopreventive