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Relationship between Dietary Fiber and Cancer: Metabolic, Physiologic, and Cellular Mechanisms[1] (42423)

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Abstract. The relationships between fiber consumption and human cancer rates have been examined, together with an analysis of the effects of individual dietary fibers on the experimental induction of large bowel cancer. The human epidemiology indicates an inverse correlation between high fiber consumption and lower colon cancer rates. Cereal fiber sources show the most consistent negative correlation. However, human case-control studies in general fail to confirm any protective effect due to dietary fiber. Case-control studies indicate that if any source of dietary fiber is possibly antineoplastic then it is probably vegetables. These results may mean that purified fibers alone do not inhibit tumor development, whereas it is likely that some other factors present in vegetables are antineoplastic. Experiments in laboratory animals, using chemical induction of large bowel cancer, have in general shown a protective effect with supplements of poorly fermentable fibers such as wheat bran or cellulose. In contrast, a number of fermentable fiber supplements including pectin, corn bran, oat bran, undegraded carageenan, agar, psyllium, guar gum, and alfalfa have been shown to enhance tumor development. Possible mechanisms by which fibers may inhibit colon tumorigenesis include dilution and adsorption of any carcinogens and/or promoters contained within the intestinal lumen, the modulation of colonic microbial metabolic activity, and biological modification of intestinal epithelial cells. Dietary fibers not only bind carcinogens, bile acids, and other potential toxins but also essential nutrients, such as minerals, which can inhibit the carcinogenic process. Fermentation of fibers within the large bowel results in the production of short chain fatty acids, which *in vivo* stimulate cell proliferation, while butyrate appears to be antineoplastic *in vitro*. Evidence suggests that if dietary fibers stimulate cell proliferation during the stage of initiation, then this may lead to tumor enhancement. Fermentation also lowers luminal pH, which in turn modifies colonic microbial metabolic acidity, and is associated with increased epithelial cell proliferation and colon carcinogenesis. Because dietary fibers differ in their physiochemical properties it has been difficult to identify a single mechanism by which fibers modify colon carcinogenesis. Clearly, more metabolic and physiological studies are needed to fully define the mechanisms by which certain fibers inhibit while others enhance experimental colon carcinogenesis.

The concept that dietary fiber is important in maintaining the health of the intestine is not a new one. Hippocrates noted that whole meal bread cleans out the gut and passes through as excrement, while white bread is more nutritious as it makes less feces. Interest in the relationship between dietary fiber, human health, and disease was rekindled with the work of Cleave (1) and subsequently that of Burkitt (2) and Trowell (3). The definition of dietary fiber continues to evolve as a result of the ongoing dialogue among cereal chemists, physiologists, biochemists, nutritionists, and clinicians. One of the more recent definitions to be used is that of the Expert Advisory Committee on Dietary Fibre (Health and Welfare, Canada, 1985) which defined dietary fiber as "the endogenous components of plant material in the diet which are resistent to digestion by enzymes produced by man. They are predominantly nonstarch polysaccharides and lignin and may include, in addition, associated substances." For a more detailed and up-to-date reference source on dietary fiber, its chemistry, physiology, and health-related effects, the reader is referred elsewhere (4, 5). The purpose of the present report is to review the available scientific evidence in both humans and animals, detailing the relationship

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TABLE I. HUMAN COLON CANCER AND DIETARY FIBER: ANALYTICAL EPIDEMIOLOGY SUMMARY OF CORRELATION STUDIES

Correlation/association: Negative	Positive	None
Burkitt (1971)	Hill *et al.* (1979)	Drasar and Irving (1973)
IARC (1977)		Liu *et al.* (1979)
Bingham *et al.* (1979)		Minowa *et al.* (1983)
Rozen *et al.* (1981)		
Krombout *et al.* (1982)		
Jensen *et al.* (1982)		
Cummings *et al.* (1982)		
McKeown-Eyssen and Bright-See (1984)		
Bingham *et al.* (1985)		

between dietary fiber and cancer, in order to define the possible mechanisms by which dietary fibers modify the carcinogenic process.

Epidemiology. Human epidemiological investigations have demonstrated an inverse association between high fiber diets and colonic cancer (Table I) in about 69% of the studies (2, 6–17). More specifically, the availability or intake of cereal fiber is inversely correlated with colon cancer (Table II) rates in 80% of investigations (6, 10, 12, 14, 18–23). On the other hand, fruit and vegetable consumption (Table III) shows no association in more than three-fourths of the reports (7, 10, 12, 14, 18–21, 23, 24). Legume consumption (Table III), however, is negatively associated with colonic cancer rates in about 60% of studies (12, 18, 19, 20, 23). The components of fiber-containing foods that show the best negative correlation with colon cancer include the pentose fraction, cellulose, nonstarch polysaccharide and uronic acids, of which vegetables are a rich source (7, 13).

Case control studies (Table IV), however, do not support the hypothesis that dietary fiber protects against large bowel cancer. None of the reviewed studies show an association between total fiber consumption and colon cancer frequency (25–27). Cereal and rice consumption show no association in four studies (30–33), while one report demonstrated that colon cancer cases consumed more cereals (28) than controls while another found the opposite (29). Consumption of vegetables was lower in cancer cases than controls in five publications (28, 29, 32, 35, 36). Foods identified as being potentially protective include cabbage, lettuce, spinach, broccoli, and Brussel sprouts. However, in five other studies no effect was found (25, 30, 31, 33, 37), while in another the cancer subjects consumed more vegetables (34). Legume and fruit consumption does not appear to be different in case-control studies (25, 32). Thus, there appears to be a lack of consistency in human epidemiological studies, leading to some skepticism about the claims for fiber

TABLE II. HUMAN COLON CANCER AND CEREAL FIBER AVAILABILITY OR INTAKE: SUMMARY OF ANALYTICAL EPIDEMIOLOGY

Correlation/association: Negative	Positive	None
Howell (1975)	Hill *et al.* (1979)	Armstrong and Doll (1975)
Knox (1977)		
Maruchi *et al.* (1977)		
Schrauzer (1976)		
IARC (1977)		
Hirayama (1981)[a]		
Jensen *et al.* (1982)		
McKeown-Eyssen and Bright-See (1984)		

[a] Cohort study.

TABLE III. HUMAN COLON CANCER AND FRUIT AND VEGETABLE INTAKE: SUMMARY OF ANALYTICAL EPIDEMIOLOGY

Correlation/association: Negative	Positive	None
Fruit and vegetables Bingham *et al.* (1979)	Hill *et al.* (1979)	Armstrong and Doll (1975) Howell (1975) Schrauzer (1976) Knox (1977) Maruchi *et al.* (1977) Jensen *et al.* (1982) McKeown-Eyssen and Bright-See (1984) Phillips and Snowdon (1985)[a]
Legumes Howell (1975) Knox (1977) McKeown-Eyssen and Bright-See (1984)		Armstrong and Doll (1975) Maruchi *et al.* (1977)

[a] Cohort study.

preventing colon cancer. However, these data do suggest that a higher consumption of certain vegetables may be associated with lower colon cancer rates. Moreover, the mechanism of any protective effect may be unrelated to the actual fiber in the vegetables, but possibly to some other component present in these foods. Correlation epidemiology can be notoriously misleading. The same data that are used to show a negative correlation between fiber intake and colon cancer also show a highly significant correlation between gastric cancer and fiber consumption (4). However, these same studies have not been used to support the concept that a high fiber diet may enhance the development of stomach cancer. The inherent problems in such studies have been discussed in detail elsewhere (38). Because of the difficulties in accurately measuring nutrient intake and controlling for each dietary variable, retrospective human studies may have many flaws. Therefore in order to carry

TABLE IV. HUMAN COLON CANCER AND DIETARY FIBER: CASE-CONTROL STUDIES

	Differences between cases and controls		
Fiber source	Cases > controls (Enhance)	Cases < controls (Protective)	None
1. Total fiber estimate			Phillips (1975) Dales *et al.* (1978) Jain *et al.* (1980)
2. Cereals and rice	Haenszel *et al.* (1980)	Bjelke (1980)	Higginson (1966) Wynder and Shigematsu (1967) Manousos *et al.* (1983) Bristol *et al.* (1985)
3. Vegetables	Haenszel *et al.* (1973)	Modan *et al.* (1975) Graham *et al.* (1978) Bjelke (1980) Haenszel *et al.* (1980) Manousos *et al.* (1983)	Higginson (1966) Wynder and Shigematsu (1967) Wynder *et al.* (1969) Phillips (1975) Bristol *et al.* (1985)
4. Legumes			Phillips (1975) Manousos *et al.* (1983)
5. Fruit			Phillips (1975) Manousos *et al.* (1983)

TABLE V. DIETARY WHEAT BRAN AND DIMETHYLHYDRAZINE-INDUCED COLON CANCER

Animal	Strain	Sex	% Bran	Effect	Reference
Mice	CF_1	F	40	P	39
	Balb/C	M	20 SWW	E	40
		M	20 HSW	E	40
Rats	Wistar	F	20	N	41
	Sprague–Dawley	F	20	N	42
		M	20	P	42
		M	20	P	43
		M	20	P	44
		M	20	N	45
		M	20	P	46
		M	20	P	47
		M	20	E	47
	Chester Beatty	M	28	P	48
	Fischer 344	M	20	P	49

Note. E, enhancement; P, protective; N, no effect; SWW, soft winter wheat; HSW, hard spring wheat.

out better controlled studies and to examine mechanisms of action, animal models for colon cancer have been developed.

Animal studies. One of the most commonly used colonic carcinogens is 1,2-dimethylhydrazine dihydrochloride (DMH). This is administered systemically, following which it is metabolized to a DNA-methylating agent. Administration of this compound to rodents produces both benign adenomas and malignant carcinomas of the large bowel. Because of the large number of animal studies using defined fiber sources, it is possible to analyze results according to the type of fiber fed. Wheat bran has been the most widely studied fiber supplement. Animal experiments using the carcinogen 1,2-dimethylhydrazine are summarized in Table V. Two out of three experiments using mice showed tumor enhancement with wheat bran (39, 40), whereas in the studies with rats 7 out of 11 experiments showed evidence of protection against tumor induction (41–49). The effects of wheat bran on tumor induction using three other carcinogens are summarized in Table VI. With the carcinogen azoxymethane (AOM), a metabolite of DMH, four out of five experiments demonstrated evidence of protection against tumor development (50–52). On the other hand, using methylnitrosourea (MNU), a direct acting carcinogen, no effect was seen (51), whereas with 3,2′-dimethyl-4-aminobiphenyl (DMAB) there was evidence of protection (53). In summary, it appears that in the majority of experiments in which wheat bran was fed to rodents there was evidence of decreased tumor development. It is of interest, however, that other forms of bran do not exhibit the same tumor modifying effect. As shown in Table VII, there are four published studies (40,

TABLE VI. DIETARY WHEAT BRAN AND EXPERIMENTAL COLON CANCER

Carcinogen	Animal	Strain	Sex	% Bran	Effect	Reference
Azoxymethane	Rats	Sprague–Dawley	M	10	N	50
			M	20	P	50
			M	30	P	50
		Fischer 344	F	15	P	51
		Fischer 344	M	15	P	52
Methylnitrosourea	Rats	Fischer 344	F	15	N	51
3,2′-dimethyl-4-aminobiphenyl	Rats	Fischer 344	M	15	P	53

Note. E, enhancement; P, protective; N, no effect.

TABLE VII. DIETARY BRANS AND EXPERIMENTAL COLON CANCER

Carcinogen	Animal	Strain	Sex	% Bran	Effect	Reference
3,2'-dimethyl-4-aminobiphenyl	Rats	Fischer 344	M	15% corn	E	54
1,2-dimethylhydrazine	Rats	Fischer 344	M	20% corn	E	49
	Rats	Wistar	M	4.5% corn	P	55
	Mice	Balb/c	M	20% corn	E	40
	Rats	Fischer 344	M	20% rice	N	49
	Rats	Fischer 344	M	20% soybean	N	49
	Mice	Balb/c	M	20% soybean	E	40
	Rats	Sprague–Dawley	M	20% oat	E	56

Note. E, enhancement; P, protective; N, no effect.

49, 54, 55) using corn bran, of which three-fourths show evidence of tumor enhancement when corn bran was fed at a 15–20% level (40, 49, 54). On the other hand, rice and soybean bran had no effect in two rat experiments (49), whereas soybean bran enhanced tumor development in mice (40). In one study a 20% oat bran diet also enhanced tumor development (56). The mechanisms by which certain types of cereal bran inhibit while others enhance tumorigenesis has not been well defined. Clapp *et al.* (40) found a positive correlation between tumor incidence and the percentage of neutral detergent fiber in the brans, but not between the individual components of cellulose, hemicellulose, or lignin. Jacobs showed that dietary wheat bran stimulates colonic epithelial cell growth and when fed only during the stage of carcinogen exposure enhances tumor development (47). Paradoxically, the wheat bran supplement was found to inhibit tumor development when fed only during the post carcinogen exposure stage (47). However, tumor enhancement with oat bran correlated with its pH lowering effect, a measure of its fermentability, and not with any effect on cell proliferation (56).

Results using dietary cellulose are summarized in Table VIII. When the carcinogen AOM was used, two out of five experiments showed evidence of protection while the rest showed no effect. This was less than the effect found when using DMH, where four out of five experiments showed evidence of protection against colon cancer development. These studies with cellulose suggest that the type of carcinogen used may be important in determining whether a particular fiber, in this case cellulose, inhibits tumorigenesis.

The studies examining the effect of pectin on experimental colon cancer are summarized in Table IX. When using the carcinogen AOM, one study showed evidence of tumor protection (51). This is in contrast to those studies using DMH (45, 56, 59, 61) where four out of six experiments showed evidence of tu-

TABLE VIII. DIETARY CELLULOSE AND EXPERIMENTAL COLON CANCER

Carcinogen	Animal	Strain	Sex	% Fiber	Effect	Reference
Azoxymethane	Rats	Fischer	M	20	N	57
		Fischer	M	40	N	57
		Sprague–Dawley	M	10	N	50
		Sprague–Dawley	M	20	P	50
		Sprague–Dawley	M	30	P	50
1,2-dimethylhydrazine	Rats	Wistar	M	4.5	P	58
		Wistar	M	4.5	P	59
		Wistar	M	9.0	P	59
		Sprague–Dawley	M	22	P	60
		Sprague–Dawley	M	10	N	56

Note. E, enhancement; P, protective; N, no effect.

TABLE IX. DIETARY PECTIN AND EXPERIMENTAL COLON CANCER

Carcinogen	Animal	Strain	Sex	% Fiber	Effect	Reference
Azoxymethane	Rats	Fischer 344	F	15	P	51
1,2-dimethylhydrazine	Rats	Sprague–Dawley	M	6.5	E	45
		Wistar	M	4.5	N	59
		Wistar	M	9.0	N	59
		Sprague–Dawley	M	5.0 HM	E	61
		Sprague–Dawley	M	5.0 LM	E	61
		Sprague–Dawley	M	10	E	56
Methylnitrosourea	Rats	Fischer 344	F	15	N	51

Note. E, enhancement; P, protective; N, no effect; HM, high methoxylated; LM, low methoxylated.

mor enhancement (45, 56, 61). When the direct-acting carcinogen MNU was used, there was no modulation of tumor development (51).

A number of miscellaneous fibers and the results of their effect on colon tumor development are summarized in Table X. Using AOM, undegraded carageenan produced tumor enhancement (62), whereas a high level of alfalfa produced protection (50). Experiments with DMH showed that guar gum, agar, and Metamucil all produced enhancement of tumor development (56, 63, 64), whereas Konjac mannan was protective (65). Using the direct-acting carcinogen MNU, alfalfa was found to enhance tumor development (51). With the carcinogen DMAB, a lignin supplement inhibited tumor development (54).

Based on these studies we begin to see that the effect of a particular fiber on tumor development is related to its physiochemical properties. In general, those fibers that are more insoluble and less fermentable such as lignin, cellulose, and some of the hemicelluloses tend to inhibit tumor development. This is in contrast to the viscous or more soluble and fermentable fibers such as the pectins and gums, which have been associated with increased tumor production. For these reasons it is important to study the metabolic and physiological effects of dietary fibers on the intestine, in order to gain further insight into

TABLE X. DIETARY FIBERS AND EXPERIMENTAL COLON CANCER

Carcinogen	Animal	Strain	Sex	% Fiber	Effect	Reference
Azoxymethane	Rats	Fischer 344	F	15% carageenan	E	62
		Sprague–Dawley	M	10% alfalfa	N	50
		Sprague–Dawley	M	20% alfalfa	N	50
		Sprague–Dawley	M	30% alfalfa	P	50
		Fischer 344	F	15% alfalfa	N	51
1,2-dimethylhydrazine	Rats	Sprague–Dawley	M	20% carrot	N	45
		Sprague–Dawley	M	5% guar gum	N	61
		Sprague–Dawley	M	10% guar gum	E	56
	Mice	CF_1	M	7% agar	E	63
		CF_1	M	9% agar	E	63
		Swiss, albino	M	20% Metamucil	E	64
		Swiss, albino	F	20% Metamucil	N	64
	Rats	Fischer 344	M	20% Konjac mannan	P	65
Methylnitrosourea	Rats	Fischer 344	F	15% alfalfa	E	51
3,2'-dimethyl-4-aminobiphenyl	Rats	Fischer 344	M	7.5% lignin	P	54

Note. E, enhancement; P, protective; N, no effect; Metamucil, psyllium hydrophilic mucilloid.

the mechanisms by which high fiber diets modify tumor development.

Mechanisms of action. The earlier work of Burkitt (2) and Walker (66) indicated that high fiber diets are associated with increased fecal bulk and faster rates of intestinal transit. These observations prompted the hypothesis (2) that these changes would dilute out any carcinogens or promoters present within the intestinal lumen, while also decreasing the time available for their interaction with the intestinal epithelium. However, human and animal studies do not support the concept that transit times are important in the prevention of colon cancer (11, 56). A number of *in vitro* studies have demonstrated that different fibers are able to bind carcinogens (67, 68) and potential tumor promoters (69); however, the relative importance of these actions in humans and animals has not been clearly defined.

The effects of different dietary fibers on the colonic microflora have been studied extensively. Earlier investigations attempted to measure the effects of high fiber diets on individual bacterial species. However, more recently the emphasis has shifted toward studying the functional impact by measuring microbial enzyme activity considered to be important in carcinogen activation. Enzymes measured include β-glucuronidase, which appears to be important in activating AOM in the rodent experimental model, possibly by hydrolyzing the conjugate of methylazoxymethanol in the intestinal lumen. Similarly, β-glucosidase appears to convert glucosides to toxic aglycones. Azoreductase and nitroreductase both form nitroso and *N*-hydroxy compounds from azo and aromatic nitro compounds, respectively. 7-α-Dehydroxylase is important in the degradation of primary to secondary bile acids. These degraded bile acids are considered by some to be the main promoters of colon cancer (70). Bile acids may also be converted from dihydroxy bile acids to carcinogenic polynuclear hydrocarbons. Although dietary fibers clearly modulate cecal and fecal bacterial enzyme acidity, the relationship between enzyme activity and tumor development is less clear.

Fibers chelate chemicals that may be promoters or carcinogens and thereby decrease their toxic effects. The cation-exchange capacity of fibers leads to binding of minerals such as calcium, magnesium, iron, and zinc. Mineral binding may be further increased by the phytic and oxalic acids which are present in fiber-containing foods. However, the fermentation of soluble fibers within the large bowel liberates bound minerals which are then free to be absorbed by the colon. Raising the concentration of intraluminal calcium has been shown to bind fatty acids and free bile acids, thereby reducing their mitogenic activity (71). Phytic acid, which is present in cereals, has been shown to complex with iron, preventing hydroxyl radical formation and lipid peroxidation, events thought to be important in the process of tumor development (72).

When dietary fiber or any other nonabsorbed polysaccharide enters the large bowel it is fermented by anerobic microorganisms, resulting in the production of short chain fatty acids (73, 74). Studies have shown that *in vivo* infusions of short chain fatty acids (SCFA) will stimulate colonic cell growth (75) and that butyrate is an important substrate for the colonic epithelial cell (76). *In vitro* studies, using human colon cancer cell lines have also shown that butyrate is antineoplastic, inhibiting tumor cell growth and producing a less malignant phenotype (77, 78). During fermentation, pH falls (56, 73), the greater acidity inhibiting bile acid and carcinogen metabolism (79). The increase in luminal acidity has also been shown to reduce the concentration of ammonia, a bacterial metabolite of protein, and possible also a tumor promoter (79). When pH drops, the solubility of free fatty acids and free bile acids is diminished, thereby theoretically decreasing their potential promoter activity (71). The colonic fermentation of fiber and the resultant changes in luminal metabolism and cell physiology appear to play an important role in determining which fibers inhibit and which fibers enhance colon carcinogenesis.

According to the bile acid hypothesis, there should be an inverse correlation between fecal bile concentration and colon carcinogenesis. The experimental rodent cancer data reviewed earlier have been summarized and plotted in Fig. 1 to determine if this relationship holds true. While cellulose and wheat bran reduce both fecal bile acid concentration and tumor development, corn bran and oat bran increase fecal bile acid excretion and enhance tumor-

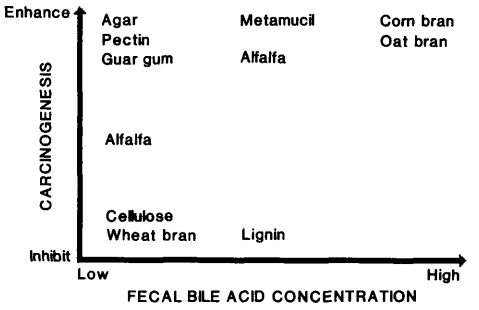

FIG. 1. Relationship between experimental large bowel tumorigenesis and fecal bile acid concentrations in rats fed different fiber supplements.

igenesis. However, exceptions to this relationship include pectin, agar, guar gum, psyllium, and alfalfa, which enhance carcinogenesis without increasing rat fecal bile acids and may even lower bile acid concentrations (80). This is in contrast to the relationship between fiber fermentability and colonic tumorigenesis (Fig. 2). Fibers demonstrated to inhibit tumorigenesis such as cellulose, wheat bran, and lignin are poorly fermented. This is in contrast to those fibers reported to enhance experimental colon carcinogenesis, including pectin, guar gum, oat bran, agar, corn bran, carageenan, and Metamucil, which are all highly fermentable. Thus, while the effect of fibers on bile acid metabolism and excretion is a significant factor, the fermentability of fibers would appear to be an even more important determinant of which fibers inhibit and which enhance colon tumor development.

Lignans are a group of estrogen-like compounds that have antineoplastic properties and can inhibit DNA synthesis (81). Lignans are constituents of certain higher plants and may also be synthesized by the colonic bacteria from fiber-rich foods. The role of lignans in colon carcinogenesis has not been adequately explored and requires further investigation.

Dietary fibers modify intestinal epithelial cell morphology and proliferation. In the large bowel, wheat bran, pectin, and guar all stimulate mucosal cell proliferation, wheat bran and guar producing the greatest effect (82, 83). Maximal growth effects of fibers occur in the cecum and proximal colon, the major sites for SCFA production (84), while in the distal colon, where SCFA are metabolized and absorbed (84), growth effects are less but still present (82, 83). Similarly, in carcinogen-exposed rats, dietary wheat bran, pectin, and guar have each found to stimulate colonic cell proliferation, whereas cellulose and oat bran produce no significant response (56, 85). The mechanism by which specific fibers stimulate colonic cell proliferation appears to be mediated through large bowel fermentation. When dietary fiber passes into the large intestine, it is fermented by anerobic microflora resulting in the production of SCFA (73, 74) and a lower luminal pH (56). Both SCFA (75) and an acidic luminal pH (86) have each been demonstrated to stimulate colonic cell proliferation. These trophic effects of dietary fibers and colonic fermentation products appear to play an important role in the stimulation of colon carcinogenesis. Growth factors in general have been shown to promote or enhance tumor development (87). This may explain why a substantial number of experimental and human studies have failed to demonstrate any protective effect with fiber supplements.

In a recent study (56) designed to examine the relationship between colonic cell proliferation, large bowel fermentation, and experimental colon carcinogenesis, we found that fermentation of dietary fiber was associated with a reduction in the pH of large bowel luminal contents. Furthermore, the level of luminal acidity was inversely correlated with tumor frequency (56). Thus, as luminal contents became more acid, the frequency and yield of tumors increased. Although soluble fibers such as pectin and guar stimulated cell proliferation, no consistent relationship between cell prolif-

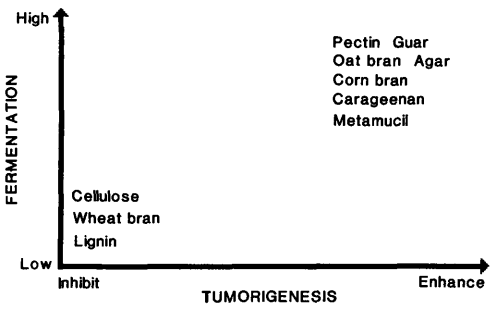

FIG. 2. Relationship between chemically induced large bowel tumorigenesis and fiber fermentability in rats fed different fiber supplements.

eration and colon cancer frequency could be shown (56). Having demonstrated an inverse relationship between pH and colon tumorigenesis in animals fed high fiber diets, we then examined the effect of lowering colonic pH using dietary sorbitol, a nonfattening sweetner, and lactulose, a synthetic disaccharide, used as a laxative and in the treatment of hepatic encephalopathy. In an earlier study it was demonstrated that the addition of either 10% sorbitol or lactulose to the diet reduced the pH of large bowel contents and stimulated mucosal cell proliferation (86). In a series of recently completed experiments it was demonstrated that chronic acidification of colonic luminal contents with either sorbitol (88) or lactulose (89) was associated with increased distal colon tumors. This is in contrast to the tumor enhancement seen with soluble fibers, where increased colon carcinogenesis occurred primarily in the proximal colon (56). Thus, the relationships between colonic epithelial cell proliferation, large bowel fermentation, luminal pH, SCFA's, fecal bile acid levels, and experimental colon carcinogenesis are of a complex nature and require further investigation in both animals and most importantly in humans.

In summary, there is growing evidence that while certain nonfermentable fibers may inhibit experimental colon carcinogenesis, soluble fibers can enhance tumor development. One mechanism for the tumor-enhancing effect of soluble fibers appears to be through large bowel microbial fermentation, the production of SCFA, and reduction in extracellular colonic pH. These effects appear to constitute an important mechanism whereby fibers stimulate colonic cell proliferation. In addition, a number of soluble fibers have been shown to increase the fecal concentration of bile acids, which are known to be tumor promoters. Thus, the fermentation of dietary fibers within the large bowel and the subsequent metabolic and physiological events appear to be important factors to consider when defining the mechanisms by which dietary fibers modify the development of large bowel cancer.

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