J. Korean Soc. Food Nutr.
25(3), 539~549(1996)

한국영양식량학회지

Dietary Fiber and Large Bowel Cancer

-Review-

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Abstract

Large bowel cancer correlates tightly to dietary factors such as dietary fiber and fat. Dietary fiber prevents the large bowel cancer in different modes of action which depend upon physicochemical and fermentable properties. Water-soluble fiber is fermented easily by intestinal microbes producing short chain fatty acids ; in contrast, water-insoluble fiber occurs effectively more rapid transit time due to greater bulk of gut content, though it is unfermentable. Not only short chain fatty acid is utilized in the proximal and distal colon as primary energy source, but also it lowers pH in the colon to normalize cellular differentiation and helps to stimulate peristaltic movement by acting as an osmotic laxative. In particular, butyric acid may also regulate gene expression and cell growth, though it is an important respiratory fuel for the colonocyte. Since dietary fiber and non-digestible oligosaccharides are the major source of butyric acid, this provides a possible link between dietary fiber and oligosaccharide and prevention of large bowel cancer. But, as with many links between dietary fiber and large bowel cancer, a direct casual association has not been established. In addition, RDA of dietary fiber which is 20~25g/day for adult Japanese, appears to be reasonable for the defecation once daily and the prevention of large bowel cancer.

Key words: dietary fiber, large bowel cancer, fermentation, intestinal microbes, short chain fatty acid colon cancer

EPIDEMIOLOGY OF COLON CANCER

It is pointed out by many epidemiological and experimental studies that colon cancer is concerned closely with dietary life. Death rate of stomach cancer is very high and that of colon cancer is low in Japan. While death rate of colon cancer is very high and that of stomach cancer is low in Western developed countries. Fig. 1 shows the mortality rate of colon cancer in various countries(1). The mortality rate of both male and female in Japan is steadily increasing and the speed is very high compared with those of other developed countries, although the death rate still remains lower.

In comparison with the mortality rate of colon and stomach cancers in Japanese, Japanese-Hawaiian and Hawaiian, Kolonel *et al.* demonstrate that death rate of stomach cancer is the highest in Japanese and is the lowest in Hawaiian(2). First- and second-generation Japanese-Hawaiian are the second and the third, respectively. On the contrary, death rate of colon cancer is the highest in Hawaiian and is the lowest in Japanese. That of Japanese-Hawaiian is in the middle. These results suggest that colon cancer is very closely related to dietary factors, because Japanese-Hawaiian and Japanese may have same gene expression on stomach and colon cancers.

DIETARY FACTORS AND COLON CANCER

Colon cancer, in particular, is considered to be related to the intakes of dietary fiber and fat. For instance, fat intake in American is very high, andenergy ratio of fat is about 40% or more. Dietary fiber intake is very low, actually 10~12g per day. On the contrary, fat energy ratio of Japanese is about 25% and dietary fiber intake is about 16 to 17g per day. As a result, death rate of American due to colon cancer is much higher than that of Japanese. Fig. 2 shows the annual changes of dietary fiber and fat intakes in Japan. Fat intake increased greatly from about 18g/day in 1950 to about 60g/day in 1993, while dietary fiber intake decreased markedly from 22g/day or over in 1950 to 16g/day in 1993, corresponding to the decrease of complex carbohydrate intake(3). It appears that the similar tendency, in-

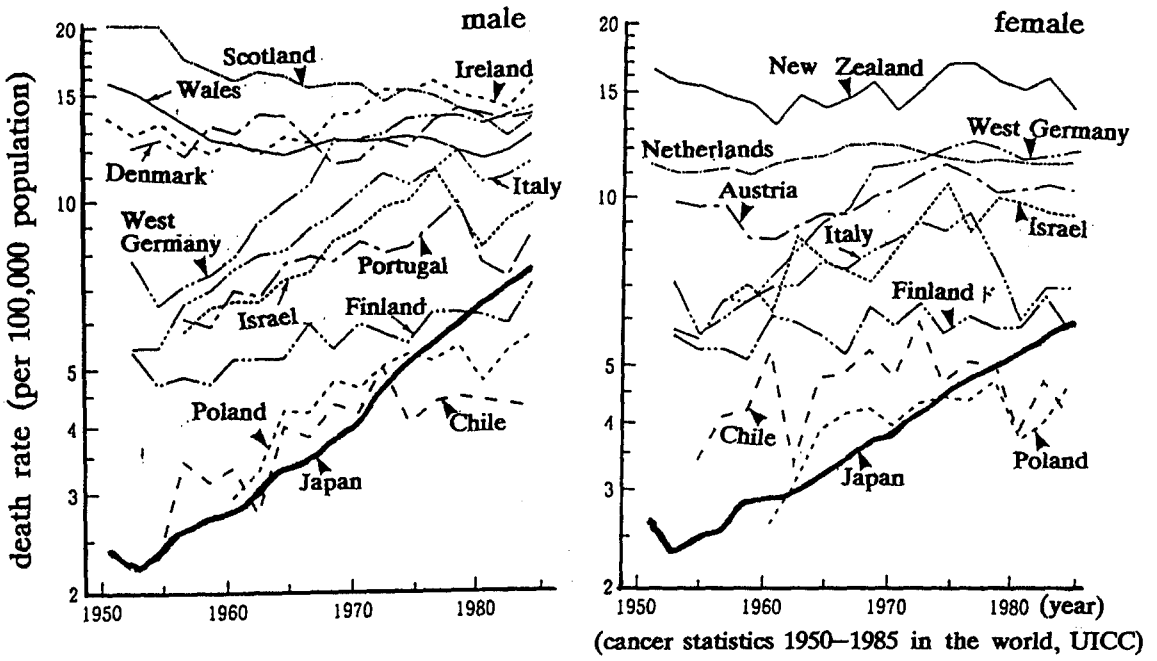


Fig. 1. Annual changes of age-corrected death rate in the world.

creasing of fat intake and decreasing of dietary fiber intake, occurs in Korea recently.

Tsuji *et al.* calculated dietary fiber and fat intakes in detail from the materials of national nutrition survey in Japan from 1947 through 1987, and clarified the correlation to age-corrected death rate of colon cancer in Japan(4). The result of the correlation between dietary fiber intake and death rate of colon cancer demonstrates that death rate of colon cancer increased slowly corresponding to the decrease of dietary fiber intake from 1947 through around 1965. And thereafter, it increased markedly corresponding to the slight decrease of dietary fiber intake(Fig. 3).

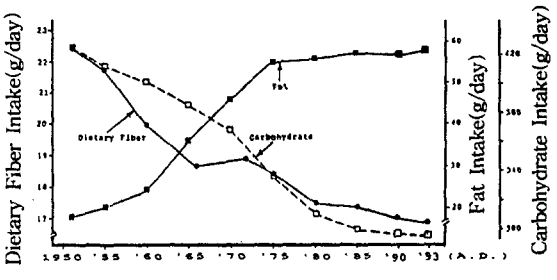
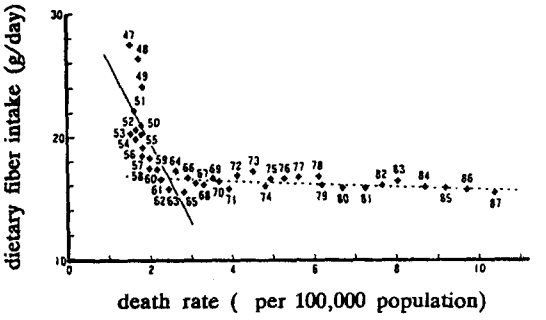


Fig. 2. Relation between dietary fiber and fat intakes.



***: Each number means years (1947–1987) (Tsuji 1990)**

Fig. 3. Correlation between dietary fiber intake and colon cancer in Japan.

Thus, the death rate of colon cancer is correlated inversely with dietary fiber intake, and when the dietary fiber intake reaches less than 17g/day, which 2 lines cross at the point of early 1960s, the death rate of colon cancer starts to increase greatly. Namely, it indicates that dietary fiber intake of 17g/day is a critical point for colon cancer.

Conversely, death rate of colon cancer increased slowly corresponding to fat intake from 1947 through 1970, and thereafter it increased abruptly corre-

sponding to slight increase of fat intake from 1971 through 1987. These results show that death rate of colon cancer and fat intake have a very close correlation, and death rate of colon cancer starts to increase greatly when fat intake is over about 50g/day. Namely, it indicates that fat intake 50g/day is a critical point for colon cancer.

It is generally considered that dietary fiber is concerned with the prevention of large bowel cancer through physicochemical properties. Dietary fiber induces more rapid transit time due to greater bulk of gut contents, and stimulates the defecation. The rapid transit time simulates the excretion of carcinogens which are contaminated in the meals or produced by intestinal microbes during the passing of gastrointestinal tract. If carcinogens are excreted from the colon, the risk of cancer will be lowered. Also, dietary fiber dilutes carcinogens which are contained in the gut contents, and decreases the contact of carcinogen to the epithelial surface of colon. At the same time, dietary fiber decreases the carcinogens produced from bile acids by harmful bacteria in the colon.

Fat intake stimulates the bile acid secretion to promote the digestion and absorption. Therefore, the increase of fat intake enhances the secretion of bile acids. As a result, it increases the amount of bile acids which reach the colon and the production of carcinogens from bile acids by harmful bacteria. In addition, fat intake stimulates to increase harmful bacteria. Colon cancer seems to be induced or promoted by the combination of several dietary factors.

FERMENTATION OF DIETARY FIBER AND COLON CANCER

Products and colonic environment

Recently, it is suggested that the fermentation of dietary fiber may greatly contribute to the prevention of colon cancer. A very important property of dietary fiber is its ability to serve as a substrate for gastrointestinal fermentation by microbes. Fermentable dietary fiber plays an active role in affecting the environment of the lower digestive tract through microorganism and their products(5). The fermentation by intestinal microbes is carried out mainly in the proximal large intestine. Degrees of fermentation depend upon sources of dietary fiber. Highly lignified fibers are less fermentable and remain relatively unfermented. The dietary fiber found in alfalfa and wheat bran is unfermentable, whereas those of cabbage and cauliflower are over 90% fermentable(6). Nondigestible oligosaccharides which are developed actively in Japan, are very fermentable.

Water-soluble dietary fiber and nondigestible oligosaccharides are fermented readily by intestinal microbes in the metabolic pathway as shown in Fig. 4, and short chain fatty acids such as acetic acid, propionic acid and butyric acid, carbon dioxide, methane and hydrogen are produced. Other short chain fatty acids such as lactic acid, succinic acid, valeric acid etc. are also produced in the *in vitro* incubation of nondigestible carbohydrates with colonic contents. But they are not detected in the feces, because they are further metabolized by other microbes in the lower intestine. Short chain fatty acids lower pH in the colon and help to stimulate peristaltic movement by acting as an osmotic laxative (7). Moreover, short chain fatty acids are absorbed from large intestine and metabolized to carbon dioxide to produce energy(8). In particular, butyric acid is utilized in both the proximal and distal colon as primary energy source(9). Therefore, this fatty acid may be an important respiratory fuel distally. Ammonia, a product of fermentation, is converted to urea in the liver and excreted to urine.

Short chain fatty acids, in particular butyric acid

Butyric acid may also regulate gene expression and cell growth, although it is an important respiratory fuel for the colonocyte. At concentrations typically found in the human bowel, butyric acid has been shown to reduce DNA synthesis *in vitro* at low concentrations and to suppress the proliferation in a variety of cells(10). Virus-induced cellular differentiation can be reversed by butyric acid, while in rat hepatoma cells butyric acid leads the cell to revert to a more normal appearance during cell division(11). The potential for butyric acid to inhibit tumor growth in the large bowel appears to be great. Since

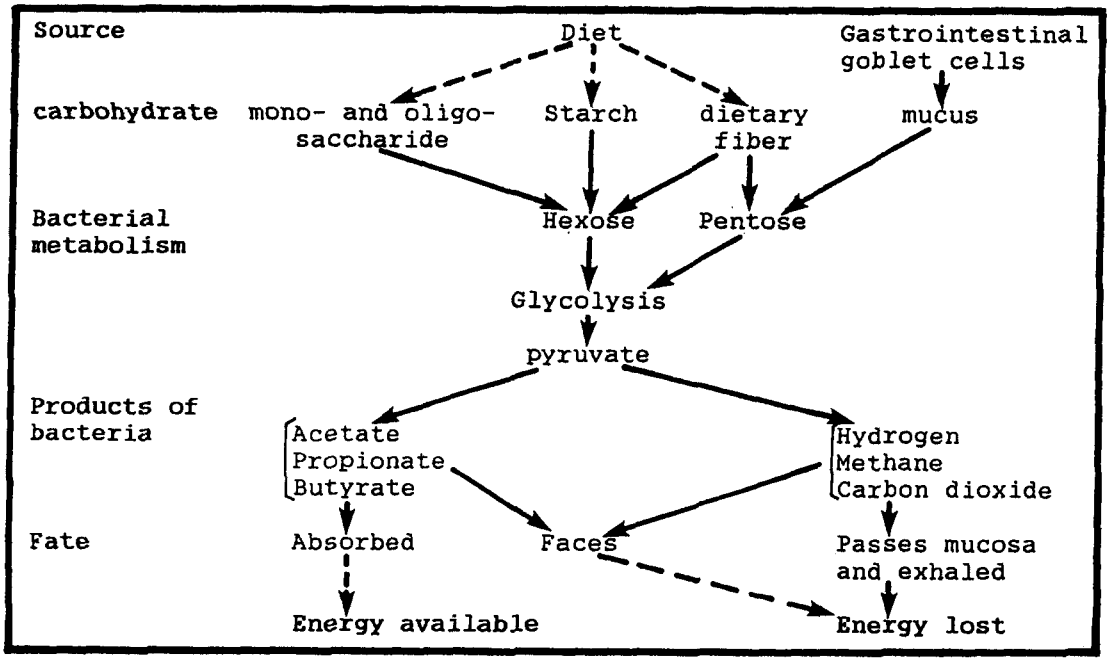


Fig. 4. Metabolism of fermentable carbohydrates in the large intestine.

dietary fiber is known to be the major source of butyric acid, this provides a possible link between dietary fiber and prevention of large bowel cancer(12).

On the other hand, a number of other studies have shown that short chain fatty acids may play a part in the maintenance of mucosal integrity and growth in the colon. Jacobs and coworkers have reported that when dietary fiber of various forms is added to the diets of rats, the colonic epithelial cell cycle is modified(13,14). The fraction of replication cell increases and differentiation of goblet cell mucin and columna cell membrane surfaces occurs. These changes are associated with differences in pH, but short chain fatty acids are likely mediators. In other experiments using rats with an ileal fistula, when a mixture of short chain fatty acids is instilled directly into the colon daily, an increased crypt cell production rate is observed within two days(15).

However, it appears that the trophic effects of dietary fiber is induced by the mechanism which is different from their results on cell proliferation and cell growth in the colon. The interesting results on the trophic effects of dietary fiber will be described later.

pH and colon cancer

Fermentation may also affect pH in the intestine, especially the cecum, and pH plays and important role in the regulation of cell growth(16). Dietary fiber ingestion lowers colonic pH, because short chain fatty acids increase in the colonic contents. An alkaline medium is shown to provide selective growth conditions for epithelial tumour cells in tissue culture(17). But, cancer cells grow over a wide pH range and are not susceptible to pH changes. Contact inhibition between cells is pH dependent. Bile acid degradation also pH dependent. In an acid environment, the initial conversion step of primary to secondary bile acids, 7-α-dehydroxylation, is inhibited(18). This is a key step in the development of bowel cancer.

It has been observed that patients with large bowel cancer have higher fecal pH than controls(19).

Table 1. Effects of dietary fiber feeding and its elimination on nucleic acid and protein compositions in rat cecal mucosa

Feeding periods(weeks)		Groups		
		Control diet	Glucomannan diet	Cellulose diet
4	Mucosal weight(g)	0.148±0.015	0.375±0.042***	0.408±0.034***
	Total DNA(mg)	1.19 ±0.08	2.14 ±0.16***	3.09 ±0.01***
	RNA/DNA	0.92 ±0.04	1.23 ±0.08**	1.38 ±1.00**
	Protein/DNA	19.5 ±0.5	19.9 ±0.3	21.0 ±0.9
5	Mucosal weight(g)	0.192±0.018	0.188±0.017	0.200±0.020
	Total DNA(mg)	1.36 ±0.10	1.32 ±0.10	1.46 ±0.14
	RNA/DNA	1.00 ±0.04	1.05 ±0.07	1.04 ±0.05
	Protein/DNA	21.4 ±0.6	20.2 ±0.6	20.6 ±0.2

After 4 weeks-feeding with the indicated diet, the rats were switched to a control diet and then further fed a week(total 5 weeks) before decapitation. Values given are the means±S.E.
,*Significantly different from the control group at $p<0.01$ and $p<0.001$, respectively

Furthermore, epidemiological studies of high- and low-risk populations for bowel cancer demonstrate that pH in the high-risk groups is higher compared to that in the low-risk groups(20). It seems that an effect of fermentation through pH reduction is a possible protective mechanism for large bowel cancer.

Methane and colon cancer

Methane is one of the principal end-products of fermentation in anaerobic system and methanogenic bacteria have been found in feces. Methane instilled into the colon appears rapidly in breath. A patient group with unexpectedly high amount of methane in breath is those with large bowel cancer. Haines *et al.* found that 80% of large bowel cancer patients had detectable breath methane compared with only 39% of control(21). In other study, the proportion of methane producers were increased in patients with premalignant bowel conditions such as polyps or ulcerative colitis(22). Physiologically methane production has been associated with slow-gut transit, low fecal weight and high fecal pH, although consistant results have not been obtained.

As with many links between bowel cancer and gut function, a direct casual association has not been established.

TISSUE ENLARGEMENT BY DIETARY FIBER AND COLON CANCER

The whole tissue weight and mucosa weights of cecum and colon are increased greatly in rats fed cellulose or glucomannan for 6 weeks compared with that of fiber-free diet group. Also, total DNA and ratio of RNA/DNA of cecal mucosa are increased significantly in enlarged tissues, whereas protein/DNA ratio is not changed significantly in any groups fed dietary fiber(23-25)(Table 1). Therefore, the tissue enlargement can be attributed to hyperplasia, with an increase in the number of cells. It suggests that the prolonged ingestion of dietary fiber stimulates cell proliferation in the cecal and colonic mucosa. But, these results don't demonstrate that dietary fiber stimulates or promotes large bowel cancer.

In the scanning electron microscope image of the cecum of a rat fed fiber-free control diet or the glucomannan diet for 2 weeks, the cell size is not different between both groups. But, the surface of epithelial cell is more smooth in the case of glucomannan group than in the case of dietary fiber-free group. Furthermore, the microvilli of the cecum of glucomannan group is distributed orderly and smoothly compared with that of the fiber-free group. These results suggest that a suitable intake of dietary fiber is essential to maintain the function and form of the large bowel.

In addition, the hyperplastic cecal and colonic enlargement induced by dietary fiber is readily reverted by the elimination of dietary fiber from diets. Rats were raised on fiber-free control diet, glucomannan diet and cellulose diet, respectively. After,

4 week-feeding, rats in both glucomannan feeding and cellulose feeding were switched to a fiber-free control diet, and further raised on the same diet for additional 4 weeks. Total feeding period was 8 weeks. Rats were killed 0, 1, 2 and 4 weeks after switch of diet.

The whole tissue and mucosal weights of the rat cecum increased greatly by glucomannan or cellulose feeding for 4 weeks, and the enlarged cecum decreased dramatically within a week after the diet was switched to the fiber-free control diet(25)(Fig. 5). Also, total DNA and ratio of RNA/DNA were increased significantly by glucomannan or cellulose feeding for 4 weeks. And they returned readily to the level of fiber-free control group a week after the switch over to the fiber-free diet(Table 1). Furthermore, the activity of (Na+K)ATPase in the cecal mucosa increased significantly in both glucomannan and cellulose groups compared to that of the fiber-free control group for 4 weeks-feeding. After the diet was switched to the fiber-free diet, the stimulated (Na+K)ATPase activity returned readily to the level of control group within a week(Fig. 6). These results demonstrate that the hyperplastic enlargement of cecum and colon which is induced by dietary fiber ingestion, is readily reverted by elimination of dietary fiber.

The cell proliferation is also active in the large bowel with carcinoma. But, the stimulation of cell proliferation and cell growth is limited at the portion

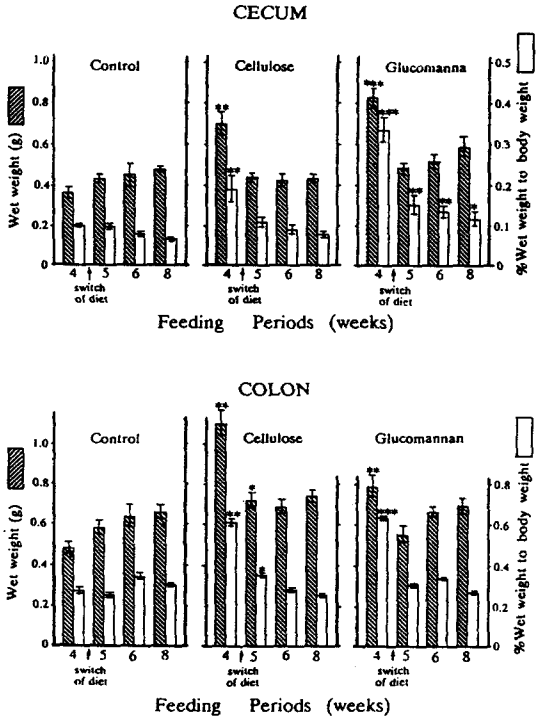


Fig. 5. Effect of feeding and elimination of dietary fiber on the weight of rat cecum and colon.
Male Wistar rats, initially weighing 50g were raised on control(fiber-free), 20% glucomannan and 20% cellulose diets for 4 weeks, respectively. And then glucomannan diet and cellulose diet were switched to a control diet and further raised on the same diet for additional 4 weeks(total 8 weeks). Rats were killed 0, 1, 2 and 4 weeks after switch of diet, respectively. Each point represents means+SEM of 6 rats.
*,**Indicate significant difference from that of 4 weeks-feeding at $p<0.05$ and $p<0.01$, respectively.

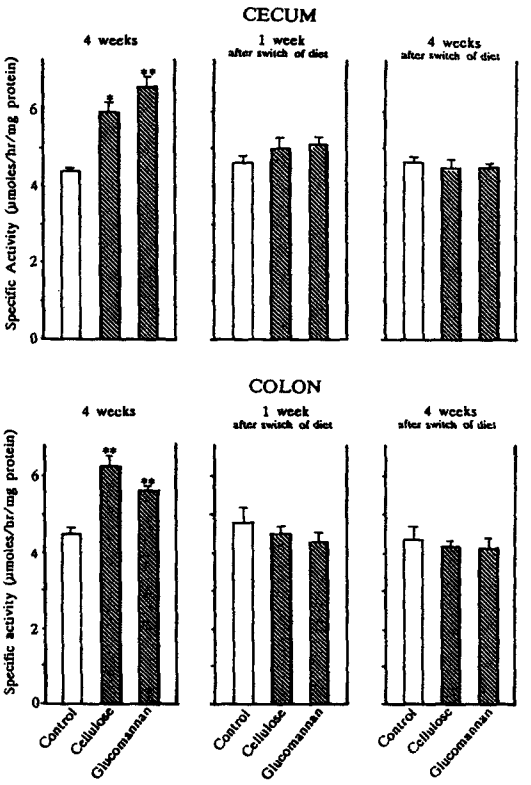


Fig. 6. Effect of feeding and elimination of dietary fiber on (Na+K)ATPase activity of rat cecal and colonic mucosa.
Rats were the same as described in Fig. 5. Each point represents means+SEM of 6 rats.
*,**Indicate significant difference from that of 4 weeks-feeding at $p<0.05$ and $p<0.01$, respectively.

of tissue with carcinoma, and cell growth progresses actively so that the increased cell number or enlarged tissues cannot revert readily to the ordinary levels. Therefore, the trophic effect of dietary fiber for cell proliferation and cell growth in large bowel is clearly different from active proliferation of carcinoma cells in large bowel. It seems that the cecal and colonic enlargement induced by the ingestion of dietary fiber or nondigestible oligosaccharides is an adaptive response to the variable environment in gastrointestinal tract.

The short chain fatty acids which are produced by fermentation of dietary fiber, may stimulate cell proliferation of large bowel. But, it can not explain that kaolin and polyethylene glycol also stimulate mucosal weight and cell proliferation in cecum and colon as same as dietary fiber(26,27). Both kaolin and polyethylene glycol cannot produce short chain fatty acids.

OLIGOSACCHARIDE AND COLON CANCER

Galactosylsucrose(other name lactosucrose) is a trisaccharide and has about a half of sucrose in sweetness. It is not hydrolyzed by digestive enzymes and fermented easily by colonic bacteria. when rats are injected subcutaneously with dimethylhydrazine(DMH) twice a week during raising of control diet for 4 weeks, and then the control diet was switched to 2% cellulose diet or 2% cellulose plus 2% lactosucrose diet for 34 weeks, the carcinoma was not found in the non- DMH group fed a control diet and carcinoma incidence in the DMH group fed a control diet was 46.7%. Thus, carcinoma incidence was increased to about 50% by DMH injection. However, carcinoma incidence in the DMH group fed a lactosucrose diet was 16.7%(28) (Table 2). Lactosucrose decreased significantly carcinoma incidence. In addition, the number of carcinoma per rat was 0 in the non-DMH group fed a control diet. That in the DMH group fed a control diet was 0.47, and that in the DMH group fed a lactosucrose diet was 0.17, respectively. The number of carcinoma per rat was also decreased by lactosucrose ingestion.

Cecal microflora was improved by lactosucrose ingestion. In the DMH group fed a lactosucrose diet, beneficial bacteria such as *Bifidobacterium* increased significantly, and harmful bacteria such as *Bacteriodaceae* decreased significantly. Furthermore, short chain fatty acids in the cecal contents increased significantly in the DMH group fed a lactosucrose diet compared with that of DMH group fed a diet without lactosucrose. In particular, the increase of n-butyric acid and acetic acids was remarkable(28).

These results demonstrate that lactosucrose may protect large bowel against cancer through pH reduction, increase of short chain fatty acids and improvement of large bowel microflora.

RECOMMENDED DIETARY ALLOWANCE OF DIETARY FIBER

The recommended dietary allowance(RDA) of dietary fiber was established in 1994 in Japan(29). RDA is revised every 5 years in Japan. The present RDA is the 5th revision, and was started to use officially from April, 1995. RDA of dietary fiber was established first in the present amendment. Probably, RDA of dietary fiber is not yet established officially in the world.

When RDA of dietary fiber is established, the standard tables of dietary fiber contents in foods

Table 2. Incidence of carcinogenesis induced 1,2-dimethylhydrazine(DMH) in rats

Group	Number of rats with tumors	Carcinoma incidence(%)	Number of carcinoma per rat
Cellulose, DMH(−)	0(0/18)	0.0	0.00
Cellulose, DMH(+)	14(14/30)	46.7	0.47
Cellulose+lactosucrose, DMH(+)	5(5/30)	16.7*	0.17

Tumor incidence is expressed as a percentage of animals with tumors. Parentheses contain number of animal with tumors/number of animal in dietary group. A vehicle control group was received equal volumes of normal saline. Carcinoma was not observed in saline-treated rats. Significantly different from the cellulose, DMH(+) group(*$p<0.05$)

must be ready to estimate dietary fiber from diets. In Japan, the Science and Technology Agency published the standard tables officially in 1992(30). Because they were very complicate and time-consuming, the analytical method of dietary fiber was not authorized till the recent. However, the Prosky's enzymatic-gravimetric method(31) was established to measure dietary fiber content in foods. This method can measure total fiber and water-soluble and -insoluble fibers rapidly. The modified method was used for the standard tables of dietary fiber in foods in Japan.

The standard tables of dietary fiber have 227 foods which were selected from 1621 foods in the standard tables of food compositions in Japan, and gives the values of total fiber and water-soluble and -insoluble fibers. But, only total fiber is shown in Algae, because this method cannot measure separatively water-soluble and -insoluble fibers in these foods. The Japanese standard tables of dietary fiber is very unique in the world, because it is analyzed by a single method, listed important selected foods of 227 and entries separatively total fiber, water-soluble and water-insoluble fibers. However, no animal foods such as meats, fishes and shellfishes are measured for this standard table of dietary fiber.

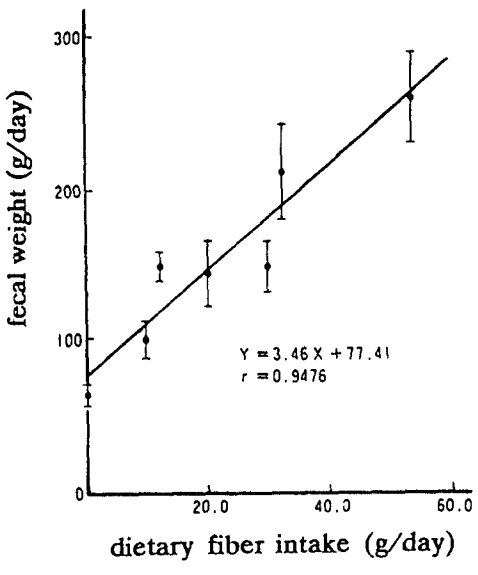


Fig. 7. Relation between fecal weight and dietary fiber intake.

In the decision of RDA of dietary fiber, one defection per day was used as a standard which normal daily life is kept and chronic diseases are not caused. Innami and his colaborators(32) have demonstrated that dietary fiber intake is correlated well with fecal weight in the experiments using Japanese subjects (Fig. 7). And the regular defecation, once a day needs about 150g of feces. As a result, they suggest that 18~20g of dietary fiber must be ingested to make 150g of feces per day. Also, Nakaji *et al.*(33) have reported that when normal Japanese women ingested 20g of dietary fiber per day, they excreted 151g of feces per day. Ohta *et al.*(34) reported that the patients with large bowel cancer took 15g of dietary fiber per day, while the patients without gut diseases took 20g of dietary fiber per day. As described earlier, Tsuji *et al.* suggest that the optimal intake of dietary fiber to avoid colon cancer is more than 17g per day.

In addition, Spiller *et al.*(35) have found that the transit time decreases until a fecal weight of 150g/day was reached, but beyond this point there was only a slight additional decrease in transit time. Cummings *et al.*(36) suggests that in order to reduce the risk of large bowel cancer and constipation in a Western country, the stool weight should be increased to 150g/day. Therefore, dietary fiber intake should be increased to about 21g/day in the popular meal, or 18g/day in starch rich-diet.

From the results of these reports, 30g or more of dietary fiber per day may be better to expect certain effects. However, it is impossible for present Japanese to take 30g per day, because present dietary fiber intake is less than 17g per day. Therefore, 20~25g per day was obtained as RDA of dietary fiber for Japanese adults with safety margin and personal variation considered(Table 3)(29). The value corresponds to 10g of dietary fiber per 1000kcal intake. As energy intake of Japanese adult male is 2500kcal, its RDA of dietary fiber becomes 25g. As that of Japanese adult female is 2000kcal, its RDA of dietary fiber becomes 20g. This 10g/1000kcal can use in RDA of dietary fiber for elderly and children which energy intake is lower than adult. For instance, it is calculated as 15g/day, if energy intake is 1500kcal.

Table 3. RDA of dietary fiber for Japanese

20~25g/day for adults
10g/1000kcal intake

FDA in USA recommends 20~35g of dietary fiber per day(37). But Dr. Prosky talked to us in his special lecture in Tokyo on May 22, 1996 that FDA recommends to take 25g of dietary fiber for 2000kcal intake and 30g for 2500kcal intake. These values are slightly higher than those of Japanese.

The physiological functions of dietary fiber are significantly different between water -soluble and water-insoluble dietary fiber. Furthermore, they are affected by physicochemical properties dependent on the compositions of dietary fiber. Therefore, RDA of dietary fiber must be established for water-soluble and -insoluble dietary fiber separately in the near future. In addition, if possible, RDA of dietary fiber should be provided in detail on the components such as cellulose, hemicellulose, pectin, gum etc. In the present RDA of dietary fiber, the rough values are obtained for only adults, in spite of detailed RDA needs for each life stage, because we don't have enough materials to solve these problems.

In the results of nutrition survey of female students in Tokyo, total fiber, water-soluble and -insoluble fibers were calculated using dietary fiber tables for Japanese foods. Total fiber intake was 13.6g per day and those of water-soluble and -insoluble fibers were 2.5g and 10.8g per day, respectively (38). The fiber intake per 1000kcal was 8g. Total fiber intake was very low compared with RDA. Energy and protein intakes were 1700kcal and 61g, respectively. These values are general in young females in Tokyo. Water-soluble fiber intake was about one-fourth of water-insoluble fiber. As similar values are obtained in other nutrition surveys, water-insoluble fiber intake seems to be more than 4-fold of water-soluble fiber intake in daily life.

The processed foods containing enrich-dietary fiber are developed actively to supply dietary fiber in Japan. At present, 69 foods are permitted by the Ministry of Health and Welfare as Food for Specified Health Uses, so called Functional Food(39). Seven of them are fiber-containing foods which the functions of dietary fiber are emphasized and are as cereal, soft drinks and wiener sausage(Table 4). There are many processed foods such as cookie, bread, soft drinks, yoghurt etc. containing enriched-fiber but these foods are not permitted as Functional Food.

Table 4. Foods for specified health uses(functional foods) containing diet fiber licensed by the Ministry of Health and Welfare

1) Cereals	wheat bran
2) Soft drinks	
Juice	polydextrose
Tea	nondigestible dextrin
Special(?)	polydextrose
3) Wiener sausage	nondigestible dextrin
4) Powder for soft drink	partially hydrolyzed guar gum
5) Jelly	polydextrose

SUMMARY OF MECHANISM OF DIETARY FIBER TO PREVENT LARGE BOWEL CANCER

The mechanism of dietary fiber to prevent large bowel cancer is summarized in Fig. 8. Water-soluble fiber is fermented readily by intestinal microbes. In this process, the colonic environment is improved by increase of beneficial microbes and decrease of harmful bacteria. The improved environment decreases the synthesis of carcinogens from endogenous and exogenous materials such as bile acids. Short chain fatty acids produced by fermentation lower colonic pH and regulate to revert to a normal appearance during cell division. On the other hand, water-insoluble fiber which has a bulking effect increases gut contents and dilutes carcinogen. The increase of gut contents shortens transit time and stimulates defecation. Rapid transit time decreases production of carcinogens and also reduces the contact of carcinogen to epithelial surface. Dietary fiber may protect against large bowel cancer in the combination of several factors. Fermentation of fiber in the large intestine provides a mechanism for protection which occur in the colon after ingestion of dietary fiber. But, it is not enough to explain the relation between dietary fiber and large bowel cancer. Further observations should be provided.

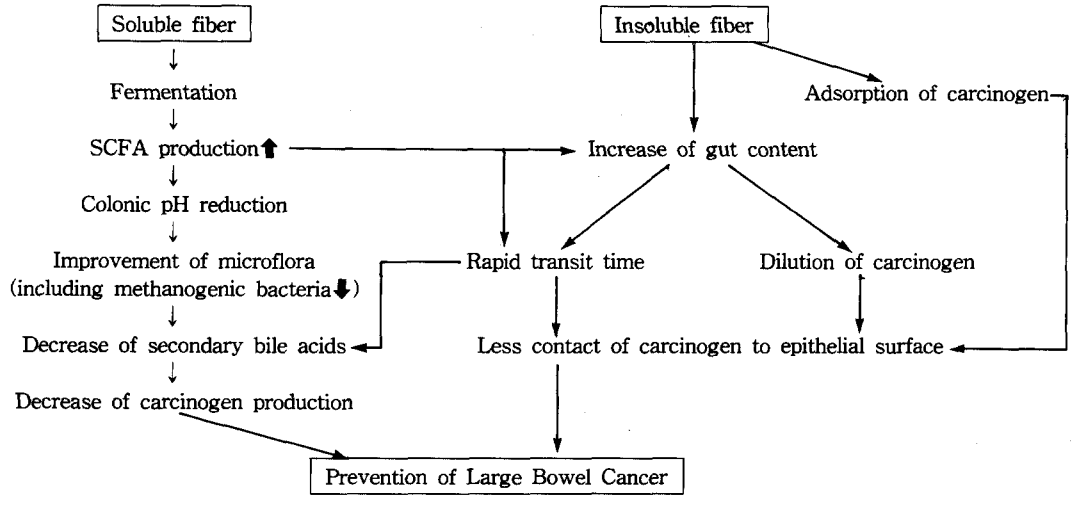


Fig. 8. Preventive mechanism of dietary fiber against large bowel cancer(hypothesis).

REFERENCES

1. Kirihara, M., Aoki, K. and Hisamichi, O. : Cancer mortality statistics in the world. The University of Nagoya Press, Nagoya, p.68(1989)
2. Kolonel, L. N., Hankin, J. H. and Nomura, A. M. Y. : Multiethnic studies of diet, nutrition and cancer in Hawaii. In "*Diet, nutrition and cancer*" Hayashi, Y. et al.(eds.), Japan Sci. Press, Tokyo, p.29(1986)
3. The Ministry of Health and Welfare : Reports of the national nutrition survey for Japanese in 1993. Daiichi-Shuppan, Tokyo(1995)
4. Tsuji, K. : Dietary fiber prevents colonic cancer. Healthiest, No.98, p.26(1993)
5. Cummings, J. : Cancer of the large bowel. In "*Dietary fiber, fiber-depleted foods and diseases*" Trowell, H., Burkitt, D. and Heaton, K.(eds.), Academic Press, London, p.161(1985)
6. Tokunage, T., Oku, T. and Hosoya, N. : Utilization and excretion of a new sweetener fructooligosaccharides(Neosugar) in rats. *J. Nutr.*, **122**, 553(1989)
7. Van Soest, P., Horvath, P., McBurney, M., Jeraci., J. and Allen, M. : Some *in vitro* and *in vivo* properties of dietary fibers from noncereal sources. In "*Unconventional sources of dietary fiber*" Furda, I.(ed.), American Chemical Society, Washington, D.C., p.135 (1983)
8. Hellendoorn, E. W. : Fermentation as the principal cause of the physiological activity of ingestible food residue. In "*Topics dietary fiber research*" Spiller, G. A. and Amen, R. J.(eds.), Plenum Press, New York, p.127(1978)
9. Roediger, A., W.E.W. : Utilization of nutrients by isolated epithelial cells of the rat colon. *Gastroenterology*, **83**, 424(1982)
10. Smith, P. J. : n-Butyrate alters chromatin accessibility to DNA repair enzymes. *Carcinogenesis*, **7**, 423(1986)
11. Hagopian, H. K., Riggs, M. G., Swartz, L. A. and Ingram, V. M. : Effect of n-butyrate on DNA synthesis in chick fibroblasts and Hela cells. *Cell*, **12**, 855(1977)
12. Freeman, H. J. : Effects of differing concentrations of sodium butyrate on 1,2-dimethylhydrazine-induced rate intestinal neoplasia. *Gastoenterology*, **91**, 596(1986)
13. Jacobs, L. R. and Lupton, J. R. : Effect of dietary fiber on rat large bowel mucosal growth and cell proliferation. *Am. J. Physiol.*, **246**, 6378(1986)
14. Lupton, J. R., Coder, D. M. and Jacobs, L. R. : Long-term effects of fermentable fibers on rat colonic pH and epithelial cell cycle. *J. Nutr.*, **118**, 840(1988)
15. Sakata, T. : Stimulatory effect of short-chain fatty acids on epithelial cell proliferation in the rat intestine : a possible explanation for trophic effects of fermentable fiber, gut microbes and luminal trophic factors. *Br. J. Nutr.*, **58**, 95(1987)
16. Hillman, L., Peters, S., Fisher, A. and Pomare, E. W. : Differing effect of pectin, cellulose and lignin on stool pH, transit time and weight. *Br. J. Nutr.*, **56**, 349(1983)
17. MacDonald, I. A., Webb, G. R. and Mhony, D. E. : Fecal hydroxysteroid dehydrogenase activities in vegetarian Seventh-Day Adventists, control subjects and bowel cancer patients. *Am. J. Clin. Nutr.*, **31**, S233 (1978)
18. Malhotra, S. L. : Faecal urobilinogen levels and pH of stool in population groups with different incidence of cancer of the colon, and their possible role in its aetiology. *J. Roy. Soc. Med.*, **75**, 709(1982)
19. Pikovski, M. A. : Differentiated mammary gland tumour tissue grown in an alkaline medium *in vitro*. *Exp. Cell Res.*, **7**, 52(1954)
20. Midtvedt, T. and Norman, A. : Parameters in 7-@-dehydroxylation of bile acids by anaerobic lactobacilli. *Acta Path. Micro. Scand.*, **72**, 313(1968)
21. Haines, A., Metz, G., Dilawari, J., Blendis, L. and Wiggins, H. : Breath methane in patients with cancer

of the large bowel. *Lancet*, **2**, 481(1977)
22. Pique, J. M., Pallares, M., Cuso, E., Vilar-Blendis, L. and Gassull, M. A. : Methane production and colon cancer. *Gastroenterology*, **87**, 601(1984)
23. Oku, T., Konishi, F. and Hosoya, H. : Effect of various unavailable carbohydrates and administration periods on several physiological functions of rats. *J. Jpn. Soc. Nutr. Food Sci.*, **34**, 437(1981)
24. Konishi, F., Oku, T. and Hosoya, N. : Hypertrophic effect of unavailable carbohydrate on cecum and colon in rats. *J. Nutr. Sci. Vitaminol.*, **30**, 373(1984)
25. Oku, T. : Reversible cecal and colonic enlargement induced by dietary fiber in rats. *Nutr. Res.*, **15**, 1355 (1996)
26. Goodlad, R. A. and Wright, N. A. : Effects of addition of kaolin or cellulose to an elemental diet on intestinal cell proliferation in the colon of rats. *Br. J. Nutr.*, **51**, 91(1983)
27. Loeschke, K. and Resch, W. : Nucleic acid and protein content of rat cecum mucosa in dietary adaptation-growth by cellular hyperplasia. *Pflugers Arch.*, **372**, 91(1977)
28. Katayama, Y. : Effects of lactosucrose on colonic cancer and colonic environment in rats. (personal communication(1996)
29. The Ministry of Health and Welfare : Recommended dietary allowances for Japanese (5th revision). Daiichi-Shuppan, Tokyo(1994)
30. Resources Council, Science and Technology Agency, Japan : Standard tables of food composition in Japan-Dietary fiber-. Publisher of the Ministry of Finance, Tokyo(1992)
31. Prosky, L., Asp, N. G., Schweizer, T. F., DeVries, J. W. and Furda, I. : Determination of insoluble, soluble, and total dietary fiber in foods and food products : Interlaboratory study. *J. Accoc. Off. Anal. Chem.*, **71**, 1017(1988)
32. Saito, T., Hayakawa, T., Nakamua, K. and Inmami, S. : Fecal output, gastrointestinal transit time, frequency of evacuation and apparent excretion rate of dietary fiber in young men given diets containing different levels of dietary fiber. *J. Nutr. Sci. Vitaminol.*, **37**, 493(1991)
33. Nakaji, S., Murakami, H., Tamura, K., Iwane, S., Fukuda, S., Ohta, M., Munakata, A. and Yoshida, Y. : Examination on fecal weight and effect of cellulose ingestion in patients with constipation. *J. Jpn. Soc. Gastroenterology*, **86**, 2104(1989)
34. Ohta, M., Ishiguro, M., Iwane S., Nakaji, S., Sano, M., Tsuchida, S., Aizawa, N. and Yoshida, Y. : Examination of dietary fiber intake in patients of colon cancer. *J. Jpn. Soc. Gastroenterology*, **82**, 51(1985)
35. Spiller, G. A., Chernoff, M. C., Shipley, E. A., Beigler, M. A. and Briggs, G. M. : Can fecal weight be used to establish a recommended intake of dietary fiber (plantix). *Am. J. Clin. Nutr.*, **30**, 659(1977)
36. Cummings, J. H., Bingham, S. A., Heaton, K. W. and Eastwood, N. A. : Fecal weight, colon cancer risk, and dietary intake of nonstarch polysaccharides (dietary fiber). *Gastroenterology*, **103**, 1783(1992)
37. Pilch, S. M. : Physiological effects and health consequences of dietary fiber. FDA, Washington D. C., p.112(1987)
38. Oku, T., Okazaki, M. and Konishi, S. : Comparison of two dietary fiber tables published by Science and Technology Agency Japan and Japan Association of Prefectural and Manucipal Public Health Institutes. *Jpn. J. Nutr.*, **53**, 25(1995)
39. The Ministry of Health and Welfare : Report on license of Food for Specified Health Uses (published on May 31(1996)

(Received June 16, 1996)