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New Viewpoint on Physiological Property of Dietary Fiber, and the Status of Dietary Fiber Intake in Japan

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The difinition and general physiological functions of dietary fiber has been already described by Dr. Gordon, D.T. elsewhere. Accordingly, I would like to consider about the attention in practical utilization of dietary fiber and the present condition of dietary fiber intake in Japan.

New Viewpoint on Physiological Property of Dietary Fiber

1) Kind and general property of dietary fiber

There are many kinds of dietary fiber (Table 1)[1]. Dietary fiber which the origin is a plant polysaccharide, has important physiological and metabolic effects at all levels of the gastrointestinal tract. The physiological properties of dietary fiber are intimately linked to their physical and chemical properties. These properties are dependent on their composition and structure which vary greatly from one source of fiber to another, and can be altered when dietary fiber is isolated by fractional separation from the plant matrix or food processing.

The biological activity of dietary fiber along the gastrointestinal tract depends on physical properties such as water-holding capacity, ion-exchange activity and gel formation. In particular, these properties are greatly different between water-soluble and water-insoluble. Dietary fiber beneficially influences nutrient digestion and transport rate, glucose, bile acid and other material's absorption, constipation and colonic cancer as discussed on many occasions [2-4].

2) The physiological function is differed by the kind and the source of dietary fiber

It could be pointed out that the physiological functions are differed by the physico-chemical property of dietary fiber, and that one kind of dietary fiber dose not have all those physiological functions. Recognizing the fact is very important in nurition education.

For instance, the effect of dietary fiber on fecal bulk is different from various dietary fiber sources (Fig. 1)[5]. The fermentable dietary fiber such as pectin has a weaker effect on fecal volume and weight. The dietary fiber sources containing cellulose are a great effect on fecal bulk, because it is resistant for the fermentation by intestinal microbes.

Also, the increase of blood glucose level was suppressed significantly by glucomannan, when 50g of glucose was administered orally to heathy subjects with 5g of glucomannan. However, cellulose ingestion could not displayed similar effect[6]. Water-soluble fiber is more effective than water-insoluble fiber on the suppression of increase of blood glucose level[7].

Even if the dietary fiber source is same, the physiological effect is differed by the franctional separation of dietary fiber. The effect of wheat bran on fecal weight is changed by the particle size(Fig. 1)[5]. Thus, coarse wheat bran is more effective than fine wheat bran on fecal bulk and transit time.

Table 1. Chemical composition of fiber

Component	Major constituents		Comments
	Primary chains	Secondary chains	
Cellulose	Glucose	–	Linear polymer with β-(1,4) linkages
Hemicellulose	Mannose, glucose galactose, xylose arabinose	Arabinose galactose glucuronic acid	Mainly β-(1,4) pyranosides
Pectins	Galacturonic acid	Rhamnose, fucose arabinose, xylose	Mainly α-(1,4) galacturans ; varying methylation
Mucilages	Galactose-mannose, glucose-mannose, arabinose-xylose, galacturonic acid	Galactose	
Gums	Galactose, glucuronic-mannose, galacturonic acid, glucose	Xylose, fucose, galactose	
Algal polysaccharides	Mannose, xylose, glucuronic acid	Galactose	Contain sulfate
Lignin	Sinapyl alcohol, coniferyl alcohol, p-Coumaryl alcohol	–	Complex, cross-linked, phenylpropane polymer

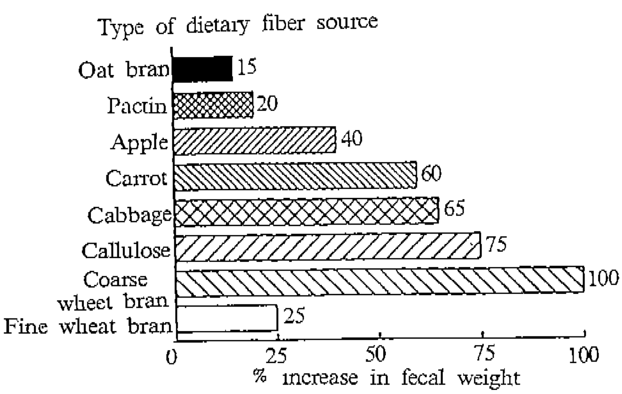


Fig. 1. Effect of various dietary fiber sources on fecal bulk.

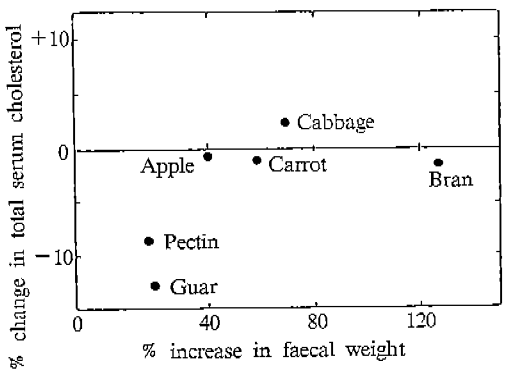


Fig. 2. Effect of various dietary fiber sources on total serum cholesterol and fecal weight in 22 healthy subjects.

3) One kind of dietary fiber dose not act equally several physiolosical functions

Furthermore, one kind of dietary fiber dose not act equally several physiolosical functions. Guar gum has a great hypocholesterolemic effect, but its effect is very small on the increase of fecal volume. On the contrary, wheat bran has a strong effect of fecal bulk, but dose not have a hypocholesterolemic effect(Fig. 2)[8].

We use easily and conveniently "dietary fiber" as a general term. However, as mentioned above, the physiological function is different from the kind and the source, in particular physicochemical property of dietary fiber. We have to consider about the kind and the source of dietary fiber, when we talk about the physiological function of dietary fiber or when we advise dietary fiber in nutrition education.

4) The physiological function is differed from the degree of polymerization of dietary fiber

Recently, dietary fiber which was isolated and purified from plant matrix or synthesized artificially, is added to many kinds of beverage and other food items to supplement dietary fiber in Japan and probably in Korea. In particular, soft drinks containing dietary fiber are developed actively, and the consumption is more than 4 hundred million bottles per year in Japan. The soft drinks containing dietary fiber are a unique food and can easily supplement dietary fiber.

Polydextrose is used mainly as fiber source. But, some other dietary fibers with small molecule are developed recently by some companies and used to fiber-containing drinks. However, the bioavailability of dietary fiber added into drink is not as same as that of intact natural dietary fiber.

In general, dietary fiber isolated from natural plants has a high molecular weight, so that it forms easily a gel and becomes sticky. Accordingly, the partially hydrolyzed dietary fiber or artificially synthesized polysaccharide is used in the soft drink as the source of dietary fiber. In principle, the physiological activity of dietary fiber declines in proportion to the decrease of degree of polymerization, because water-holding capacity and gel formation activity decrease(Fig. 3).

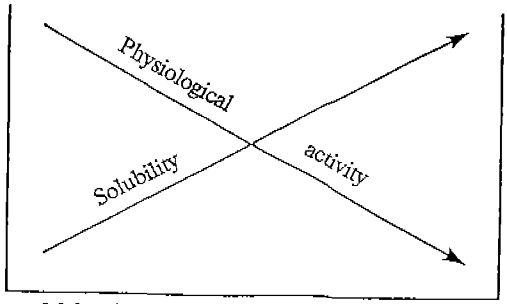


Fig. 3. Relationship between molecular weight and physiological properties of dietary fiber.

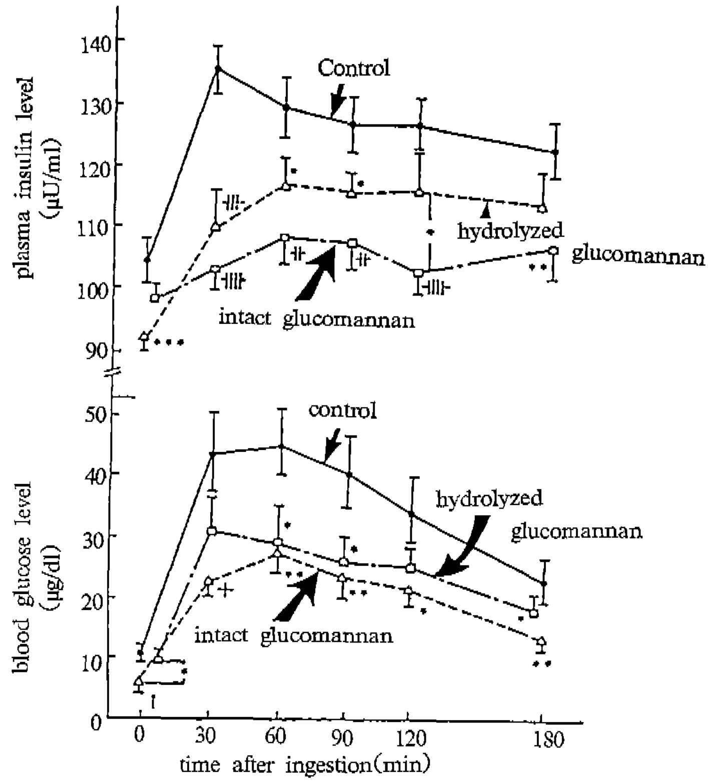
Fig. 4 shows the comparative effect of intact and partially hydrolized glucomannan on blood glucose level[9]. The effect of partially hydrolized glucomannan on blood glucose level is significantly lower than that of intact glucomannan, though the molecular weight of partially hydrolized glucomannan used in those experiments is not clear. If glucomannan is completely hydrolized, the suppression of blood glucose level shold be lost nearly. In fact, it has been demonstrated that glucomannan of small molecular weight loses mostly hypocholesterolemic effect[10].

The nutritional significance of isolated dietary fiber which is actively added to food items, is clearly different from that of intact dietary fiber obtained from natural foods. Therefore, in order to bring out the expected physiological effect of dietary fiber, we have to select the kind or the source of dietary fiber, if it is isolated.

5) Polydextrose increases fecal weight and volume

As mentioned above, the bioavailability of dietary fiber added to the soft drink is different from that of other fiber-rich food items with intact natural fiber. The physiological function is limitted, but not zero.

Polydextrose is a polysaccharide which is synthe-



* : p<0.05, ** : p<0.025, *** : p<0.01,
+ : p<0.01, ++ : p<0.005, +++ : p<0.0025,
++++ : p<0.0005.

Fig. 4. Effect of intact and partially hydrolyzed glucomannan on blood glucose and insulin levels in healthy subjects.

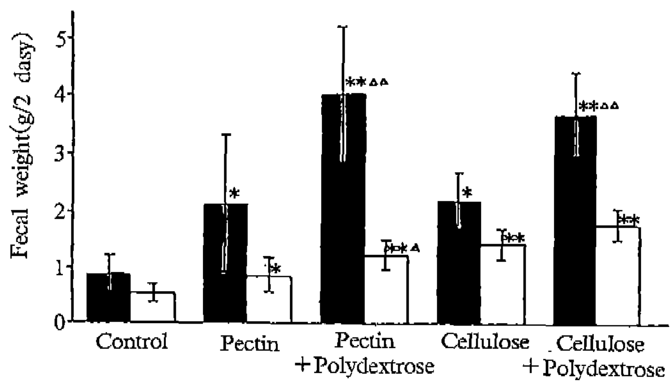


Fig. 5. Effect of polydextrose on wet and dry fecal weights in the rat. Data represent means of 10 rats/group ; and vertical bars, SD. ■ wet weight(g/2 days) ; □ dry weight(g/2 days). *,** Significantly different from control group at p<0.05 and p<0.01, respectively. △,△△ Significant difference between Polydextrose-nonsupplemented and -supplemented groups at p<0.05 and p<0.01, respectively.

sized artificially from glucose, sorbitol and citric acid (89 : 10 : 1), and is consisted of heterogeneous molecular weights, but it is smaller than that of natural dietary fiber. Polydextrose with bigger molecular weight is resistant for digestive enzymes. Therefore, the available energy is about 1kcal/g. Polydextrose with these properties can partially display similar physiological function as dietary fiber. Polydextrose increases significantly both wet and dry fecal weight and shortened transit time in rats(Fig. 5)[11].

6) Available energy of dietary fiber is not zero kcal/g

The available energy of dietary fiber is used as 0kcal/g in the United States[12]. But, it is not correct, because dietary fiber, in particular water-soluble fiber, is fermented in part by intestinal microbes and produced short chain fatty acids. The short chain faty acids are absorbed from the large intestine and contributes to the host as energy source.

Dietary fiber is not digested by the small intestine or escape the absorption and reach the large intestine to be metabolized in part or completely by the intestinal microbes in the pathway of Fig. 6. The products are short chain fatty acids such as acetate, propionate and butyrate, carbon dioxide, methane, and hydrogen. Only the short chain fatty acid of them is absorbed from the lower intestine and further metabolized to carbon dioxide and water by the organs such as liver, kidney and muscle. Therefore, dietary fiber contributes partially to the host as energy source, although the available energy is dependent on the fermentability of dietary fiber.

It is very difficult to evaluate exactly the available energy of dietary fiber, because the fermentability of dietary fiber is greatly varied by the physical and chemical properties, in particular between water-soluble and water-insoluble fiber. Here, I would like to show a method to estimate the available energy of dietary fiber.

It is possible to estimate the potential energy of fermentable dietary fiber, if the quantitative relationship between the substrate and product in the fermentation is made evident. Fig. 7 shows several fermentation equation proposed previously by several researchers[13-16]. When the combustion energy (acetate 209.0, propionate 370.4, butyrate 528.7 kcal/mol) of each short chain fatty acid is inserted into the molecule of short chain fatty acids in these

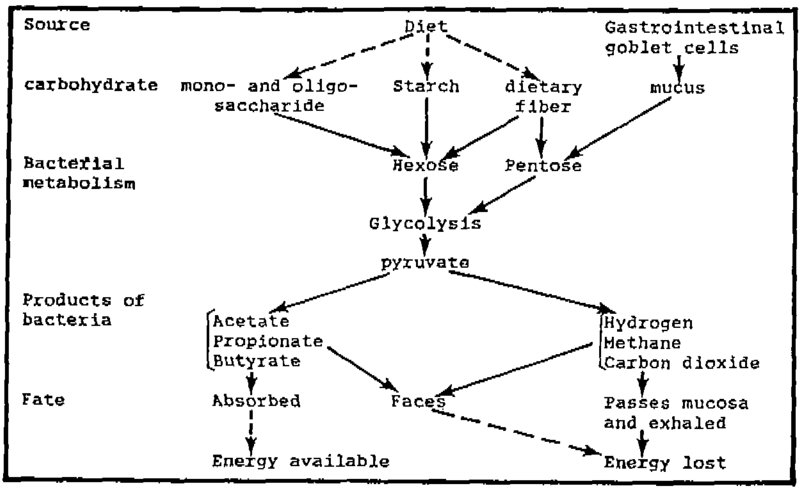


Fig. 6. Carbohydrate metabolism in the large intestine.

Fig. 7. Proposed equations for colonic fermentation of carbohydrates.

$58\ C_6H_{12}O_6 \longrightarrow 62$ acetate $+ 22$ propionate $+ 16$ butyrate $+ 60.5\ CO_2 + 33.5\ CH_4 + 27\ H_2O$ (Hungate, 1966)

2.78 kcal/g

$34.5\ C_6H_{12}O_6 \longrightarrow 48$ acetate $+ 11$ propionate $+ 5$ butyrate $+ 34.25\ CO_2 + 23.75\ CH_4 + 10.5\ H_2O$ (Miller & Wolin, 1979)

2.70 kcal/g

$58\ C_6H_{12}O_6 + 36\ H_2O \longrightarrow 60$ acetate $+ 24$ propionate $+ 16$ butyrate $+ 92\ CO_2 + 256[H]$ (Livesey & Elia, 1988)

2.86 kcal/g

$37.73\ C_6H_{12}O_6 \longrightarrow 34.5$ acetate $+ 9.7$ propionate $+ 8.6$ butyrate $+ 38.2\ CO_2 + 18.8\ CH_4\ 6.13\ C_6H_{10}O_3$

2.51 kcal/g (Smith & Bryant, 1979)

equations, total cumbustion energy of short chain fatty acids produced from fermentable substrate is calculated between 2.51 and 2.86kcal/g. The average value is 2.71kcal/g. Thus, it means that the total combustion energy of short chain fatty acids is about 2.71kcal, when 1g of dietary fiber is fermented completely by intestinal microbes. But, this potential energy is not utilized fully by the host.

The tentative utilization efficiency of short chain fatty acids is calculated as 69% from the combustion energy(3.48kcal/g) and the available energy(2.40kcal/g) of acetic acid. This available energy, 2.40 kcal/g is used in the standard table of food compositions is the U.S. and Japan[17] The total available energy produced from 1g of fermentable dietary fiber is calculated as 1.87kcal by multiplication of 69% by 2.71kcal/g. Therefore, this result indicates that the available energy is about 2kcal/g, but no zero kcal/g, if dietary fiber is fermented completely by intestinal microbes. Fermentable dietary fiber contributes partially as energy source.

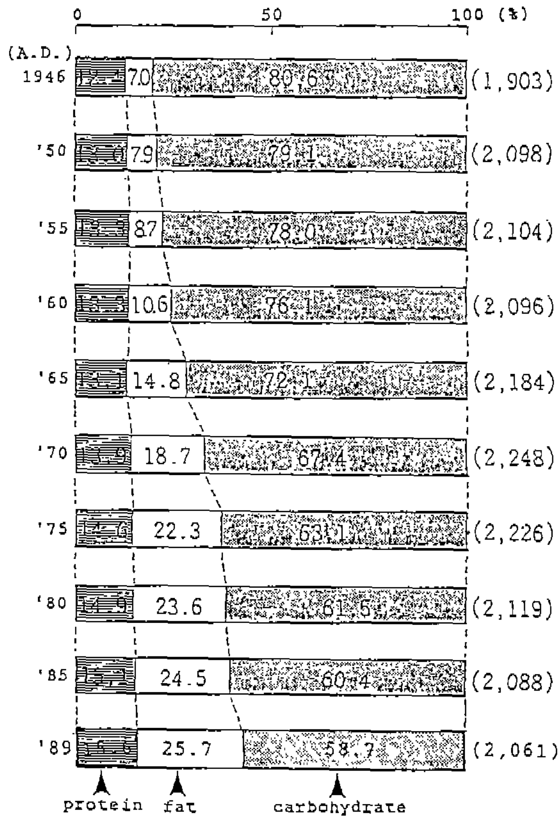
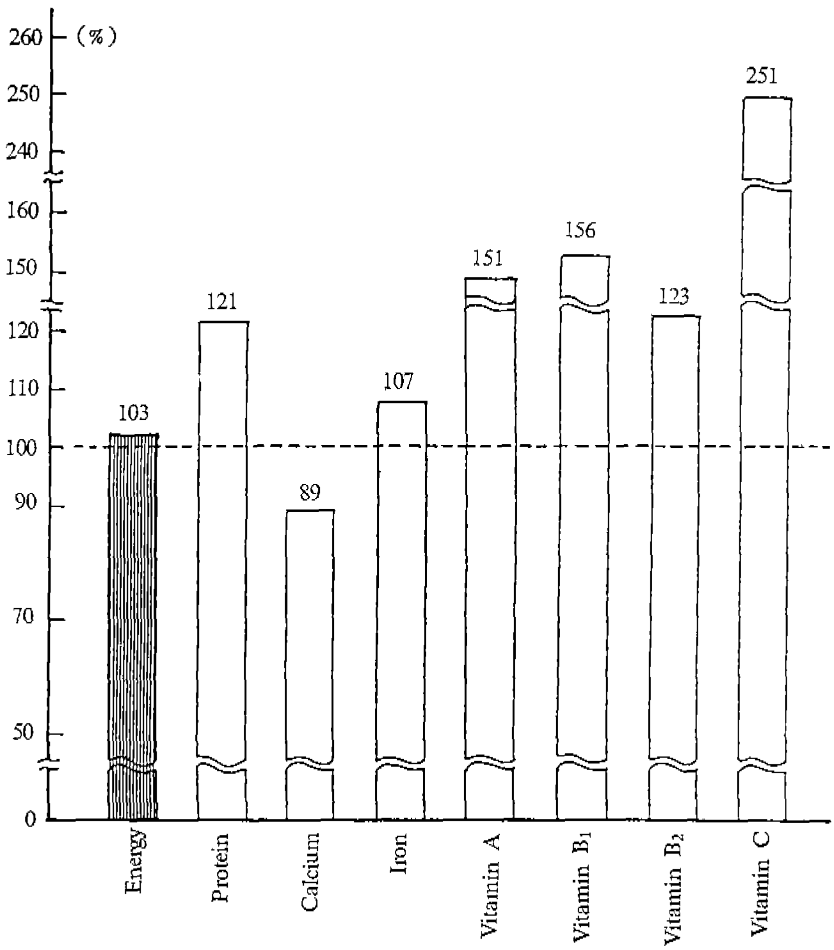


Fig. 8. Annual change of ratio of nutrients for energy intake in japan.

Japanese Health Status and Dietary Fiber Intake

1) Status of Japanese nutrient intake

The National Nutrition Servcy is carried out every year since the second world war in Japan. In the part, it was carried out two of four times in a year. Intake of plant foods, in particular rice and sweet potato is decreasing. By contrast, animal food intake



(Source : National Nutrition Survey)

Fig. 9. Adequacy of nutrient intake in japan.

is increasing[18]. The decrease of plant food intake suggests that dietary fiber intake is decreaseing gradually. Intake of animal fat and animal protein increased greatly, and carbohydrate intake decreased clearly[18]. This animal fat dose not include fish oil, because fish oil is composed mainly with polyunsaturated fatty acids, and the physiological function is simillar to that of plant oil rather than fat in beef and pork.

On the ratio of each untrient in total energy intake, after 1946, the energy contribution from carbohydrates decreased significantly, but still was about 60%. In contrast, energy contribution from fat rose from 7% of 1946 to 25.3% of 1989(Fig. 8). Especially, the intake of animal fat with saturated fatty acid is increaseing. Although 25% is considered the optimal level of fat energy contribution, the average fat intake of Japanese exceeded the optimum level in 1989[19].

Fig. 9 shows the ratio of nutrient intake to the recommended dietary allowance for Japanese. Currently Japanese attained adequate intake of most components, except for calcium intake of which was slightly below the adequacy levels[18]. However,

Table 2. Annual change of daily intake of dietary fiber per capita in japan

A.D.	Total Intake (g/day)	Except animal foods (g/day)	Concentration (g/1000 g of diet)
1951	22.42	21.95	20.48
1955	21.75	21.23	19.77
1960	19.95	19.39	17.68
1966	18.69	18.03	15.05
1972	18.92	18.09	13.28
1975	18.42	17.60	13.05
1980	17.46	16.62	12.92
1985	17.34	16.50	12.89

These values were calculated from the ingested food groups in Nationa Nutrition Survey using the table of dietary fiber contents published by the Association of Prefectural and Municipal of Public Health Institutes.

this result does not mean that all individual Japanese attained nutrient adequacy.

2) Dietary fiber intake of Japanese

Although dietary fiber intake of Japanese was researched in many studies in the past, the values fluctulated with time and researchers. The most trustworthy table of dietary fiber content of 255 food items was published in 1989 after a nationwide study was conducted in a cooperative project of 53 local public health institutes[20]. The dietary fiber content in the study was measured by the AOAC method according to Prosky[21].

In order to estimate the change of dietary fiber intake of Japanese, dietary fiber values of foods in the table were plugged to food intake record collected in National Nutrition Surveys. Dietary fiber intake decreased with time, from 22.4g in 1951 to 17.3g in 1985, an approximately 22% total decrease in 35 years(Table 2)[20]. This is because, with time, more refined foods and more animal foods have been consumed by the Japanese. Dietary fiber intake of American is 13.1g/day. The main fiber sources of Japanese were rice and other cereals,

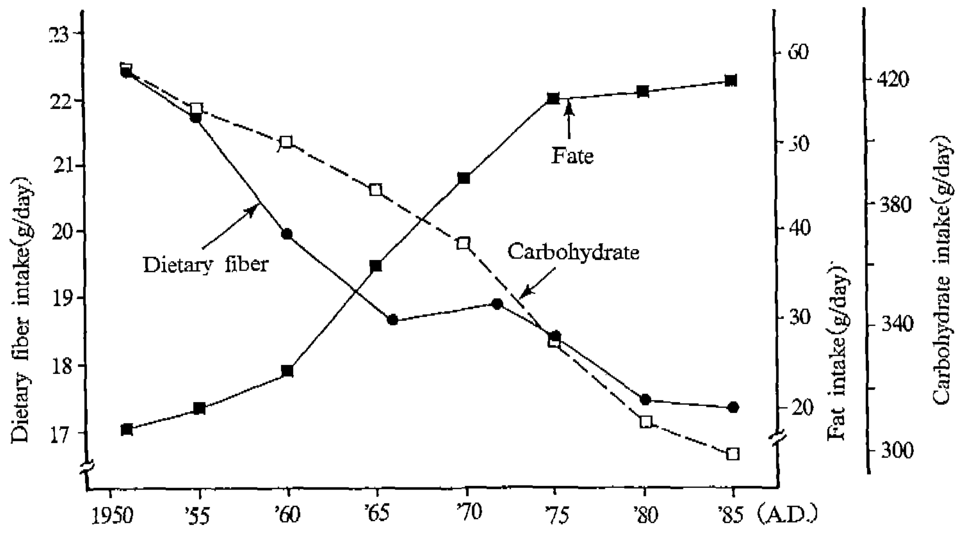


Fig. 10. Relation between dietary fiber intake and fat and carbohydrate intake.

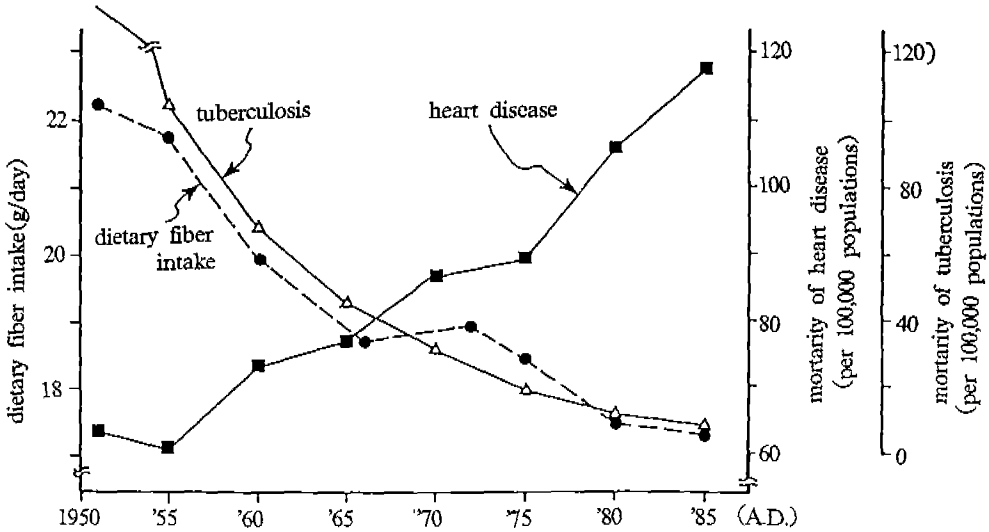


Fig. 11. Relation between dietary fiber intake and mortality of heart disease and tuberculosis.

Table 3. Effect of the chronic intake of Neosugar on fecal weight and gastrointestinal transit time in rats. Animals are the same as described in Fig. 1. Food intake and fecal weight are averaged for the three-day period at the beginning of the sixth week. Transit time was determined using carmine red as marker as described in Methods. Each value represents the mean± SEM.

Groups	Food intake (g/day)	Fecal weight (g/day)	Transit time (h)
Control	16.78± 0.86	0.58± 0.05	27.7± 3.4
10% Neosugar	16.74± 0.96	0.83± 0.05**	20.5± 8.2
20% Neosugar	15.59± 1.00	1.15± 0.22**	14.0± 6.7**
Glucomannan	15.52± 1.17	1.77± 0.25**	9.2± 0.9**

**Significantly different from the control group at $p<0.01$.

pulses and vegetables including fungl.

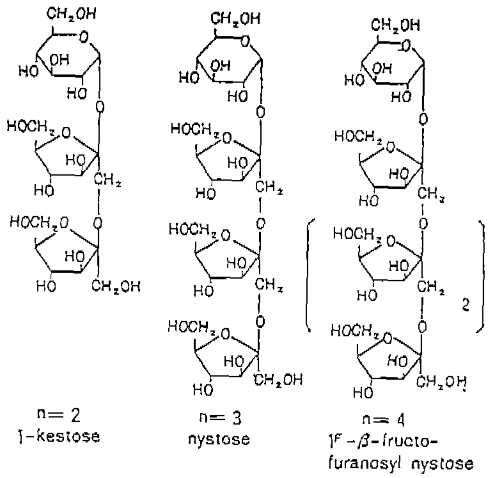
3) Dietary fiber intake and disease death rate in Japan

Malignant neoplasms is the second in disease death rate of Japanese. Colon cancer which is concerned with dietary fiber intake, is increasing gradually, although the level is low. Contraversly, stomach cancer is decreasing.

The result of nutritional servey in Japan demonstrates that the decrease in dietary fiber intake and the increase in fat intake are inversely related. Also, the decrease in dietary fiber intake corresponds with the decrease in carbohydrate intake(Fig. 10). When people become better off economically, they tend to consume more animal foods which are tastier but contain less dietary fiber, and less plant foods which contain more dietary fiber but not as tasty. Therefore, unless efforts are made to eat more plant foods, an increase in dietary fiber intake is difficult to attain.

4) Recommended dietary level of dietary fiber

Dietary changes in Japan have led to the change in disease pattern. The change in disease death rates relates closely to the change in dietary fiber intake. Tuberculosis and heart disease are looked upon as diseases that have been affected as the result



1^F (1-β-fructofuranosyl)$_{n-1}$—sucrose

Fig. 12. Chemical structure of fructooligosaccharides.

of dietary improvement(Fig. 11). The decrease in tuberculosis death rate clearly corresponds with the decrease in dietary fiber intake.

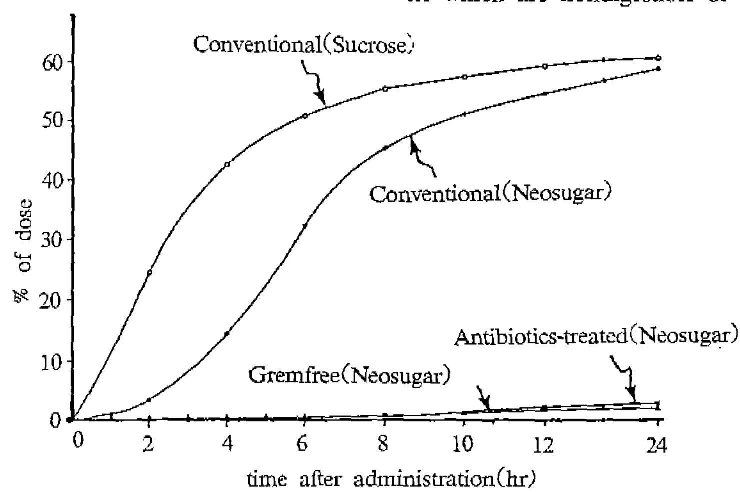
The kinds of diet which are low in dietary fiber, helped preventing the infection of tuberculosis, conversely the same diet increased heart disease. Respective relationships of dietary fiber and other chronic diseases such as diabetes mellitus, hypertention and malignant neoplasms are similar to the relation of dietary fiber intake and heart disease. It may be said that a low dietary fiber diet impacts more on tuberculosis infection than on other diseases. Therefore, the adequate level of dietary fiber intake as part of an optimum diet for the prevention of both chronic diseases and acute diseases must be decided.

FDA of the U.S. recommended 20~35g of dietary fiber per day[22]. Japanese investigators recommend 20~25g of dietary fiber per day, depending on the relationship between dietary fiber intake and chronic disease mortality.

Dietary Fiber-Like Function of Nondigestible Sugar Substitute

1) Metabolism of nondigestible sugar substitute, Neosugar

In recent Japan, new types of sugar substitutes are developed actively(Table 4). Most of sugar substitutes which are nondigestible or partially digestible,



^{14}C-Neosugar(2μci/4 mg/0.4ml) was administered orally to conventional, antibiotics-treated(neomycine and bacitoracine) and gremfree rats(B.W. 230g).

Fig. 13. Cumulative excretion of expired ^{14}C-Carbon dioxide after oral administration of ^{14}C-Neosugar to conventional, antibiotics-treated and germ free rats.

Table 4. Dietary carbohydrates with beneficial effects for health

1. Polysaccharides	
Dietary fiber — water-soluble / — water-insoluble	
2. Oligosaccharides	(sweetness ; % of sucrose)
1) Neosugar	(30~60)
a mixture of fructo-oligosaccharides such as kestose($G_{\alpha1}-{}_2F_1-{}_{2\beta}F$), nystose ($G_{\alpha1}-{}_2F_1-{}_{2\beta}F_1-{}_{2\beta}F$) and fractofuranosyl nystose ($G_{\alpha1}-{}_2F_1-{}_{2\beta}F_1-{}_{2\beta}F_1-{}_{2\beta}F$)	
2) Galacto-oligosaccharides : 2 types	(20~40)
basic bond : ($-{}_4Gal_{\beta1}-{}_4Gal_{\beta1}-{}_4G$)	
($-{}_6Gal_{\beta1}-{}_6Gal_{\beta1}-{}_4G$)	
3) Xylo-oligosaccharide ($Xyl_{\beta1}-{}_4Xyl_{\beta1}-{}_4Xyl_{\beta1}-$)	(ca.50)
4) Isomalto-oligosaccharide	(ca.50)
a mixture of isomaltotriose ($G_{\alpha1}-{}_6G_{\alpha1}\ {}_6G$), panose ($G_{\alpha1}-{}_4G_{\alpha1}-{}_6G$), isomaltose ($G_{\alpha1}-{}_6G$), maltose ($G_{\alpha1}-{}_4G$) and glucose (G)	
5) soybean oligosaccharide	(ca.70)
a mixture of raffinose ($Gal_{\beta1}-{}_6G_{\alpha1}-{}_2F$), stachyose ($Gal_{\beta1}-{}_6Gal_{\beta1}-{}_6G_{\alpha1}-{}_2F$), sucrose ($G_{\alpha1}-{}_2F$) and monosaccharides	
6) Lactosucrose ($Gal_{\beta1}-{}_4G_{\alpha1}-{}_2F$)	(35~60)
7) Lactulose ($Gal_{\beta1}-{}_4F$)	(60~70)
8) Coupling sugar	(50~60)
a mixture of glucosyl-sucrose ($G_{\alpha1}-{}_4G_{\alpha1}-{}_2F$) and maltosyl-sucrose ($G_{\alpha1}-{}_4G_{\alpha1}-{}_4G_{\alpha1}-{}_2F$)	
9) palatinose ($G_{\alpha1}-{}_6F$)	(37~45)
3. Disaccharide alcohols	
1) Maltitol ($G_{\alpha1}-{}_4Sol$)	(80~95)
2) Lactitol ($Gal_{\beta1}-{}_4Sol$)	(30~40)
3) Palatinit	(30~40)
a equivalent mixture of isomaltitol ($G_{\alpha1}-{}_6Sol$) and glucopyranosyl$-\alpha1,6-$mannitol ($G_{\alpha1}-{}_6Man$)	
4. Mono-saccharides	
1) Erythritol (tetrose alcohol)	(75~85)
2) Sorbitol (hexose alcohol)	(60~70)
3) Mannitol (hexose alcohol)	(ca.50)
4) Sorbose (hexose)	(55~75)

have in part the physiological property as well as dietary fiber.

The representative of nondigestible and fermentable sugar substitutes is Neosugar. Neosugar is a mixture of fructooligosaccharides such as 1-kestose, nystose and fructofuranosyl nystose(Fig. 12), and is contained in plants such as asparagus root, edible burdock, onion, wheat and so on. It is manufactured enzymatically from sucrose. The sweetness is about 50% of sucrose[23)].

GF_2 and GF_3 which are components of Neosugar, were not hydrolyzed by the diegestive enzymes of small intestine[24)]. Furthermore, ^{14}C-Neosugar administered intravenously was not degrated by any other organ's enzymes, and was readily excreted into the urine. These results suggest that Neosugar ingested is not utilized apparently in the body.

However, contrary to my expectation, when ^{14}C-

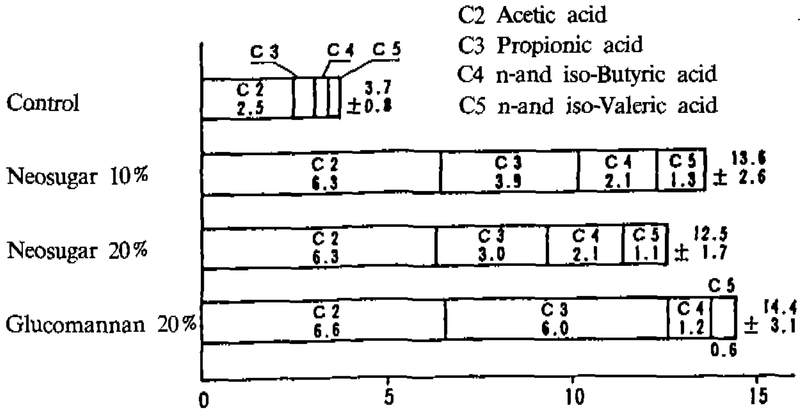


Fig. 14. Effect of neosugar intake on the fecal excretion of volatile fatty acids in rats. The feces, which were obtained from the animals as described in Fig. 2, were used for the determination of volatile fatty acids after extraction with diethyl ether from the supernatant of fecal homogenate. Volatile fatty acids were analyzed by gas chromatography as described in methods. The results are expressed as the mean of 6 rats.

Neosugar was orally administered to conventional rats, about 60% of total radioactivity administered was excreted as expired carbon dioxide, as was the administration of ^{14}C-sucrose. However, when ^{14}C-Neosugar was administered to germfree or antibiotics-treated rats, the conversion of Neosugar to carbon dioxide was strongly inhibited(Fig. 13)[25].

Namely, these results suggest that Neosugar escaped from digestion and absorption in the small intestine reaches the large intestine and is fermented by intestinal microbes. The produced short chain fatty acids are further metabolized to carbon dioxide by the host. Neosugar which is nondigestible and fermentable, is utilized in part as energy source.

2) Effect of Neosugar ingestion on large intestine

Fecal weight was increased significantly by Neosugar ingestion, and transit time was shortened, although the effects are not as significant as water-soluble dietary fibers such as glucomannan and pectin(Table 3)[26].

Also, dietary fiber causes a hyperplasia of cecum and colon of rats. Neosugar ingestion induced significantly the cecal and colonic enlargement, although the effect was smaller than that of glucomannan[26].

3) Fermentation of Neosugar and improvement of intestinal microbes

Dietary fiber increases fecal short chain fatty acid. Also, Neosugar increased greatly fecal excretion of short chain fatty acids. Acetic acid content was highest among short chain fatty acids(Fig. 14)[26]. When ^{14}C-Neosugar was incubated with cecal content of conventional rats in vitro, about 65% of total Neosugar added to the incubation medium were converted to the production of short chain fatty acid and about 12% were to carbon dioxide[25].

From these findings, Neosugar is easily fermented by intestinal bacteria. As a results, Neosugar increases total number of intestinal microbes. At same time, Neosugar stimulates markedly the multiplication of beneficial intestinal microbes such as *Bifido-*

bacterium, and decrease the harmful intestinal microbes such as *Clostridium*[27].

These results demonstrate that Neosugar possesses in part dietary fiber functions. Various kinds of nondigestible sugar substitutes such as galactoologosaccharides, xylooligosaccharide, lactosucrose, raffinose, maltitol, lactitol, palatinit and so on are developing in Japan and the physiological properties are similar to Neosugar. As these sugar substitutes are potentially to be used in a wide range of food items, their presence should be taken into consideration, when dietary fiber intake is evaluated in the country.

Conclusion

Dietary fiber is various physiological properties. However, the physiolosical function is differed from the kind and the source, in particular physicochemical property, of dietary fiber. Furthermore, even if the source of dietary fiber is same, the physiological function is differed by the degree of polymerization and the fractional separation of dietary fiber. Therefore, we have to recognize these facts, when we talk about physiological property of dietary fiber in nutrition education. Also, we have to consider the dietary fiber-like function of nondigestible sugar substitute when we evaluate the dietary fiber intake, because fermentable sugar substitute intake is gradually increasing in the developed conuntries.

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