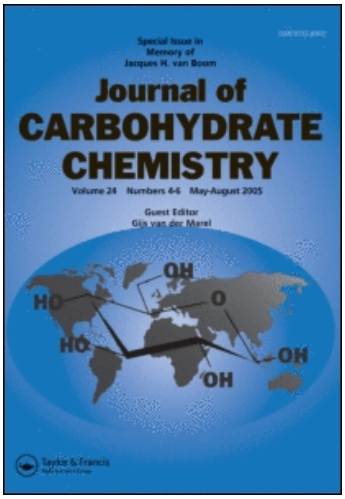

Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

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To cite this Article Hidaka, Hidemasa , Hirayama, Masao and Yamada, Kazuhiko(1991) 'Review Article: Fructooligosaccharides Enzymatic Preparation and Biofunctions', Journal of Carbohydrate Chemistry, 10: 4, 509 — 522
To link to this Article: DOI: 10.1080/07328309108543928
URL: http://dx.doi.org/10.1080/07328309108543928

J. CARBOHYDRATE CHEMISTRY, 10(4), 509-522 (1991)

REVIEW ARTICLE

FRUCTOOLIGOSACCHARIDES

ENZYMATIC PREPARATION AND BIOFUNCTIONS[1]

Hidemasa Hidaka,* Masao Hirayama and Kazuhiko Yamada

Bio Science Laboratories
Meiji Seika Kaisha, Ltd.
5-3-1, Chiyoda, Sakado-shi
Saitama, 350-02 Japan

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I. INTRODUCTION

Recently the study of oligosaccharides has been extensively pursued in Japan after the findings of the remarkable biofunctions and usefulness of fructooligosaccharides for human health, improving the intestinal microflora and importance in livestock nutrition.

The importance of non-digestible dietary fiber has been widely recognized for the prevention of hypercholesterolemia and colon cancer. Non-digestible oligosaccharides (or dietary fiber) pass through the small intestine without digestion after intake, and reach the large intestine where many of the intestinal microorganisms utilize them.

Bifidobacteria, one of the representatives of useful intestinal bacteria, produces acetic acid and lactic acid from these saccharides, and the short chain fatty acids (SCFA) lower the pH of digestive tract and protect from overgrowth of harmful bacteria.

In this paper, we would like to review the fructooligosaccharides as a representative class of the useful non-digestible oligosaccharides. Many studies have shown that fructooligosaccharide administration improves the intestinal flora, which subsequently relieve constipation, improve blood lipids in hyperlipidemia and suppress the production of intestinal putrefactive substances.

II. OLIGOSACCHARIDES AND THEIR ORIGINS

Many kinds of oligosaccharides having biofunctions are commercially produced from various kinds of food materials. Representatives are illustrated in Fig. 1, most of which are obtained by enzymatic transformation. Fructooligosaccharides (FOS, Meioligo®) and isomalturose (IMT, Palatinose®) were prepared from sucrose by β-fructofuranosidase and α-glucosyltransferase, respectively. Cyclodextrin glucanotransferase is successfully applied to produce cyclodextrins (CD) and glucooligosylsucrose (GlcS, Coupling sugar®). Galactooligosaccharides (GOS) are obtained from lactose by β-galactosidase but lactulose (Lact) is prepared from the same material by alkali isomerization. Xylooligosaccharides (XOS) and agarooligosaccharides (AOS) are prepared from the corresponding polysaccharides by enzymatic hydrolysis. In addition, there are several naturally occurring oligosaccharides, for example, raffinose (Raf) and

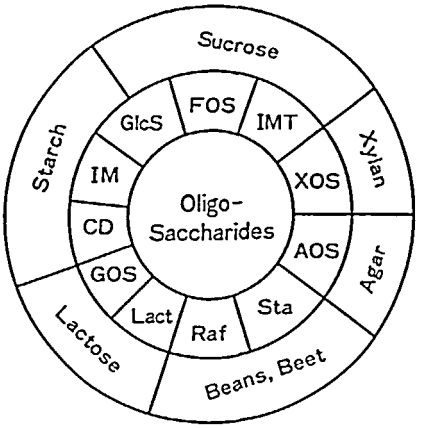

Fig. 1. Oligosaccharides and their origins.

FOS: fructooligosaccharides
GlcS: glucosyl sucrose
IM: isomaltose
CD: cyclodextrins
GOS: galactooligosaccharides
Lact: lactulose
IMT: isomalturose
XOS: xylooligosaccharides
AOS: agarooligosaccharides
Sta: stachyose
Raf: raffinose

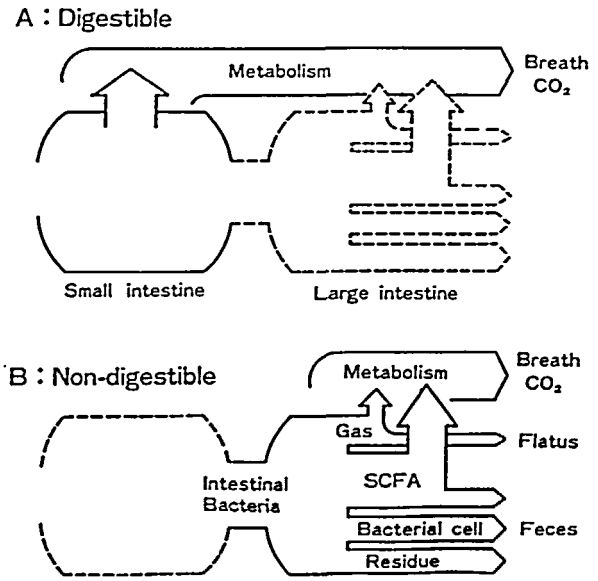

Fig. 2. Two possible pathways of carbohydrate metabolism.
SCFA: short chain fatty acids

Table 1. Physiological functions of oligosaccharides

	Physiological function	Oligosaccharide*
1	Non-digestibility	FOS, Lact, IOS, Raf, GOS
2.	Growth promotion of bifidobacteria	Lact, FOS, GOS, XOS
3.	Cholesterol reduction	FOS, GOS, α-CD
4.	Improvement of constipation	FOS, GOS
5.	Low cariogenicity	IMT, GlcS, FOS

* Abbreviation: see Fig. 1, except ISO, inulooligosaccharides.

stachyose (Sta), which are extracted from plant sources, such as soybeans.

III. PHYSIOLOGICAL FUNCTIONS

From a nutritional aspect, carbohydrates are broadly classified as digestible and non-digestible based on their behavior in the small intestine, as shown in Fig. 2. It is well-known that digestible carbohydrates are used as energy sources through intestinal digestion and absorption. On the other hand, non-digestible saccharides, which pass through the small intestine without digestion, can reach the large intestine where they play an important role in the physiological responses through their bacterial fermentation and physical properties.

As shown in Table 1, these physiological functions include growth promotion of bifidobacteria, cholesterol reduction in plasma and improvement of constipation. The physical and chemical properties of oligosaccharides are so important in determining the response that each of the oligosaccharides has characteristic functions.

In the last decade, the number of people suffering from circulatory organ diseases such as obesity, diabetes, ischemic heart disease and colon cancer have been gradually increasing particularly in developing countries. Non-diges-

tible oligosaccharides and dietary fibers are thought to prevent these diseases by their physiological functions. In the following section, we would like to refer to fructo-oligosaccharides as the representatives of physiologically useful oligosaccharides.

IV. FRUCTOOLIGOSACCHARIDES

IV-a. Enzymatic Preparation. It is known that fructo-oligosaccharides occur naturally in many kinds of plants,[2] such as onion, asparagus root and tubers of Jerusalem artichoke. The fructooligosacchardes can also be prepared from sucrose through the transfructosylating action of enzymes,[3] but no method for their industrial production was established until we developed them as a new sweetener.[4] Fructo-oligosaccharides could be more effectively prepared with a higher concentration of sucrose if use could be made of an enzyme having higher transfructosylating ability. Treatment of 50%(w/v) sucrose with β-fructofuranosidase obtained from Aspergillus niger strain afforded a mixture of fructooligo-saccharides, 1-kestose (GF_2), nystose (GF_3), and 1^F-β-fructofuranoylnystose (Fig. 3).

Fructooligosaccharides were found to be non-digestible by humans and also to be physiologically useful because they improve the intestinal flora.

IV-b Physiological Significances

Non-digestibility; The fructooligosaccharides were not hydrolyzed in the rat and human by digestive enzymes such as disaccharidases of intestinal mucosa and α-amylase of pancreatic homogenates.[5] Sugar tolerance tests on healthy subjects confirmed that fructooligosaccharides were neither digestible nor absorbable as their monosaccharide components which are fructose and glucose (Fig. 4). After the ingestion of sucrose, plasma glucosemic, fructosemic and insulin responses were observed rapidly. However, fructooligosaccharides ingestion did not show any increase in the concentration of the above in the plasma.[6]

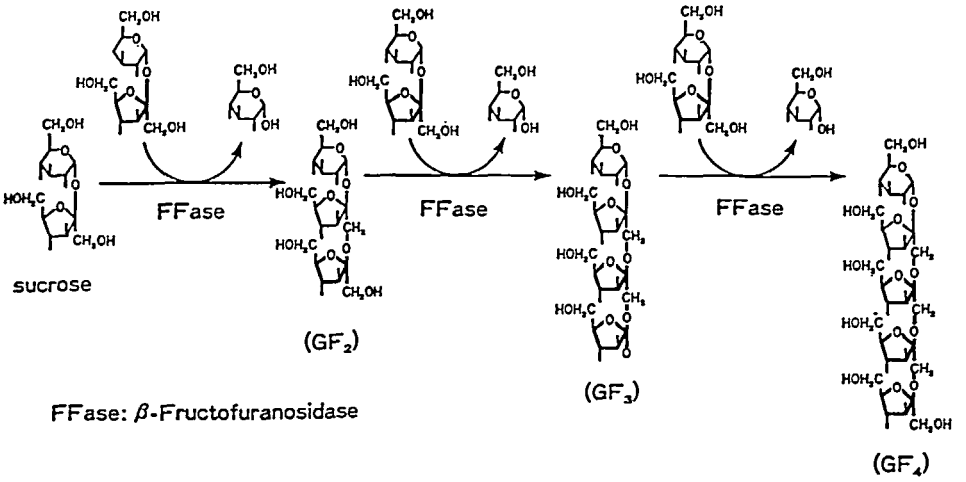

Fig. 3. Enzymatic preparation of fructooligosaccharides, 1-kestose (GF_2), nystose (GF_3) and 1^F-β-fructofuranosylnystose (GF_4).

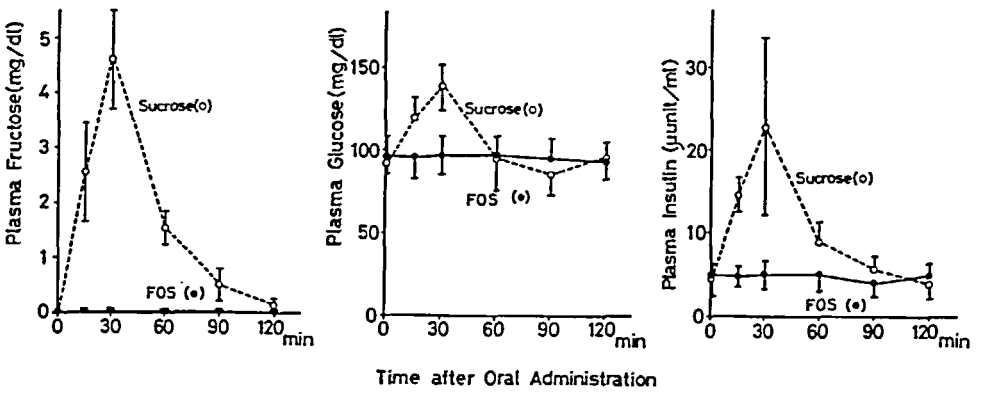

Fig. 4. Plasma glucose, fructose and insulin after oral administration of fructooligosaccharide (25g) or sucrose (25g) to healthy men.

Table 2. Utilization of Several Sugars by Some Intestinal Bacteria[a]

Bacterial species	Isolation from human intestine[b]		No. of strains	Glucose	Lactulose	Raffinose	Fructooligosaccharides
	% positive	Mean					
Bifidobacterium adolescentis	54.6	10.0	4	++	++	++	++
longum	21.3	9.9	3	++	++	++	++
breve	9.9	9.2	3	++	++	++	+
infantis	24.8	9.8	2	++	++	++	++
bifidum	5.0	10.2	2	++	++	−$^{++}$	−
Lactobacillus acidophilus	44.7	9.2	3	++	++	−	−
fermentum	38.3	8.4	4	++	++$^{-}$	V	−
plantarum	29.8	8.8	1	++	++	−	+
Eubacterium aerofaciens	48.9	9.7	1	++	++	−	+
lentum	42.6	9.3	1	−	−	−	−
Bacteroides fragilis	46.1	10.4	4	++	++	++	++
thetaiotaomicron	86.5	10.7	3	++	++	++	++
vulgatus	69.5	10.6	2	++	++	++	++
Escherichia coli	92.9	8.6	2	++	++	V	−
Klebssiella pneumoniae	19.9	7.7	1	++	−	++	++
Enterococcus faecalis	80.1	7.5	1	++	+	−	+
faecium	30.5	7.9	1	++	++	−	+
Streptococcus intermedius	27.7	10.2	2	++	++	−	++
Peptostreptococcus prevotii	16.3	10.0	1	++	−	++	−
Clostridium perfringens	41.1	7.1	4	++	++	+	−
difficile	0.7	4.8	2	++	−	−	−
paraputrificum	9.9	8.5	2	++	+	−	−
clostridiiforme	8.5	9.0	2	++	++	++	+
ramosum	53.2	9.1	2	++	++	+	+
Veillonella dispar	34.0	7.9	2	−	−	−	−
Megasphaera elsdenii	5.0	9.4	1	−	−	−	−

a Judgement of bacterial growth: ++, same level of growth compared to glucose; +, weaker growth compared to glucose; −, no growth; V, variable (strains may be either + or −); superscripts indicate the results of occasional strains in the species.
b Finegold, S.M. et al. (1974).

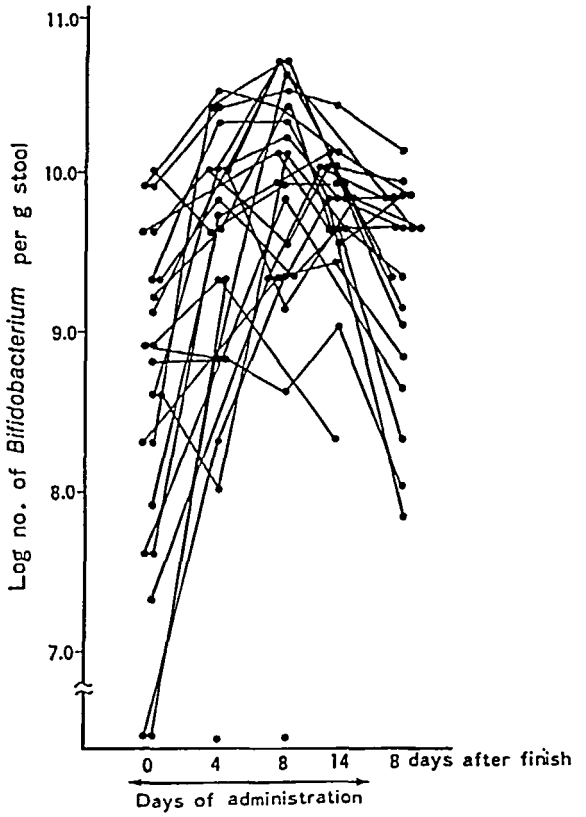

Fig. 5. Changes in individual fecal bifidobacteria by the administration of fructooligosaccharides.

Growth promotion of bifidobacteria; Fructooligosaccharides can be utilized by human intestinal bacteria, predominantly Bifidobacterium sp., species in Bacteroides fragilis group as shown in Table 2.[7] However, they cannot be utilized by undesirable putrefactive bacteria such as Clostridium perfringens, Clostridium difficile or Escherichia coli.

The administration of fructooligosaccharides to senile inpatients for two weeks (8g/day) resulted in a significant increase of the bifidobacterial number in the feces, without increasing the other putrefactive bacteria (Fig. 5).[8]

Table 3. Biological activities of bifidobacteria[9]

Acid production from sugars
Acetic acid & Lactic acid
— Antibacterial effect
— Decrease of absorption of ammonia and amines through intestinal walls
Immunological activation
— Defense from pathogenic bacteria
— Therapy of tumors
Production of vitamins and enzymes
Vitamin B_1, B_6, Folic acid, etc.
Human casein phosphatase, Lysozyme
No production of
Ammonia or amines (indole etc.) from amino acids
H_2S from amino acids
Nitrite (NO_2) from nitrate
(ammonia from urea)

The physiological significance of bifidobacteria are listed in Table 3, based on in vitro and in vivo studies.[9] Additional studies are necessary to prove the usefulness of bifidobacteria in the human intestine. However, many investigators have reported that an increase in the number of bifidobacteria was benefical for good health.

Cholesterol reduction: As shown in Table 4, serum total cholesterol, HDL-cholesterol, triglycerides and apolipoproteins were measured before and after the fructooligosaccharides administration (8g/day) to the hypercholesterolemic subjects with Type IIa hyperlipoproteinemia.[10] Total cholesterol and apoprotein B were decreased, although this reduction was not significant. HDL-cholesterol and triglycerides remained unchanged. Apoprotein E was significantly increased. The daily intake of fructooligosaccharides lowered the total serum cholesterol, which would be mainly due to the reduction in LDL-cholesterol contents.

Table 4. Effect of fructooligosaccharides (FOS) on serum lipids

Serum components	Initial[a]	After FOS
Total cholesterol	277.6±15.1	260±29.0
HDL-cholesterol	57.3±11.5	57.7±13.4
Triglycerides	119.8±41.8	119.6±51.8
Apo A-I	138.3±14.3	145.2±22.1
Apo B	160.3±20.7	152.2±24.0
Apo E	3.6±1.0	4.8±1.6[b]

a) Expressed as Mean±SD of mg/ml of serum

b) Significantly different from initial value at $p<0.05$(paired t-test)

Constipation improvement; Fructooligosaccharides had a beneficial effect on constipation. Fifteen functionally constipated subjects ranging from 20 to 82 years old were administrated fructooligosaccharides for 28 days. After ingestion of fructooligosaccharides, 11 subjects (73%) were improved in terms of constipation, and all the subjects could defecate more than once in 3 days (Fig. 6).[11] It is considered that the alleviation of constipation by non-digestible saccharides is partly due to the high osmotic pressure of short chain fatty acids produced by intestinal bacteria and consequently accelerated peristaltic movement.

V. METABOLISM OF DIGESTIBLE AND NON-DIGESTIBLE SACCHARIDES

Digestion of ingested carbohydrates goes through the processes of luminal breakdown of polysaccharides to oligosacharides and disaccharides. These are hydrolysed at the brush border membrane to monosaccharides which are absorbed by active transport, facilitated or passive diffusion systems (Fig. 7). Food, however, also contains other saccharides which are not digested by the small intestinal enzymes and thus reach the large intestine. A large part of these substances are subsequently fermented there mainly

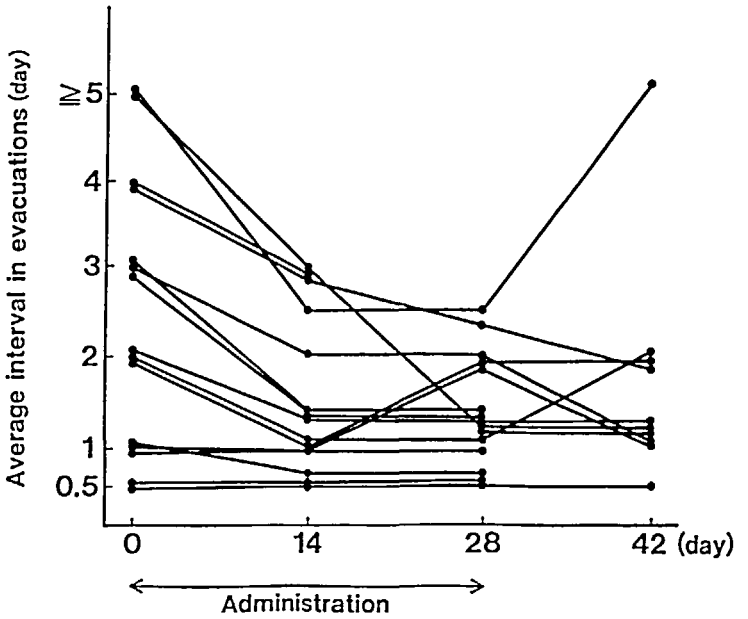

Fig. 6. Improvement of constipation by intake of fructo-oligosaccharides

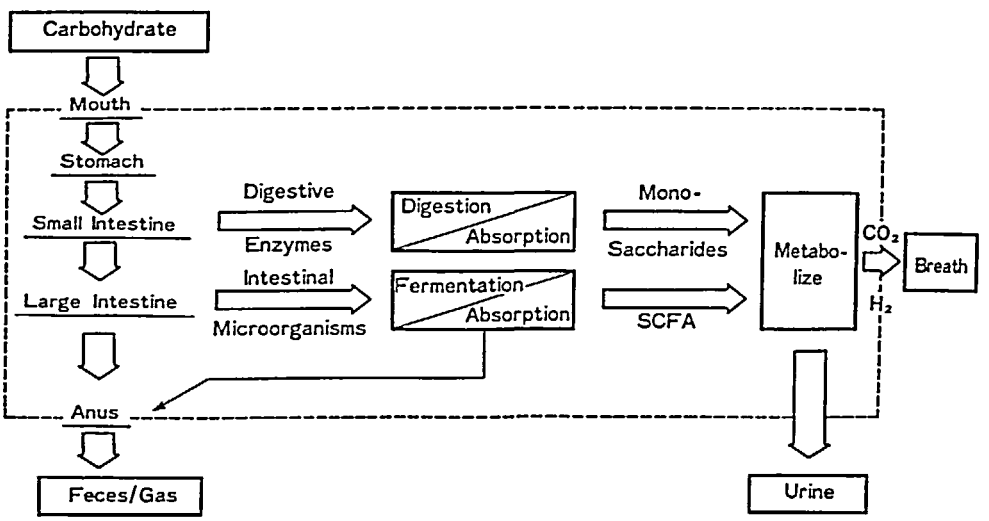

Fig. 7. Metabolic path of digestible and non-digestible saccharides

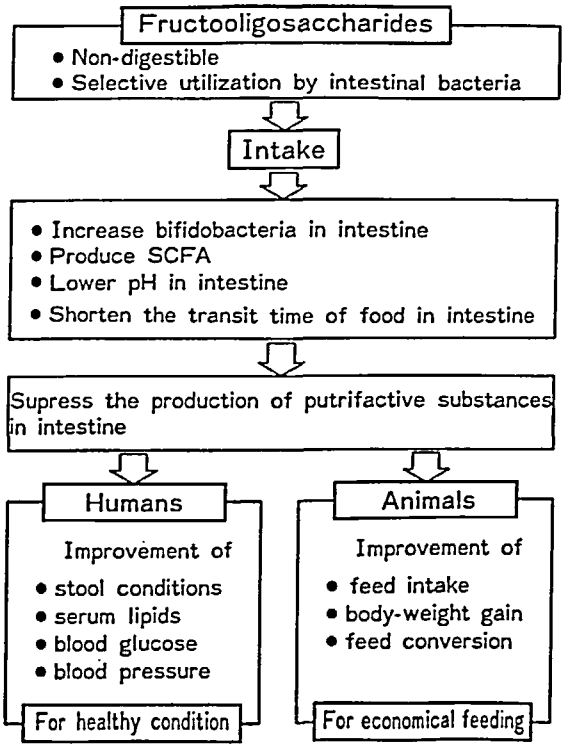

Fig. 8. Physiological action of fructooligosaccharides

to short chain fatty acids by the gut microorganisms. These short chain fatty acids have very important roles or usefulness on digestive tract, intestinal microorganisms and activities of other organs such as the liver. Fermentation and absorption of SCFA are quite different from non-digestible saccharides with respect to physiological effects.

By in vivo experiments using ^{14}C labeled sample,[12, 13] it was shown that fructooligosaccharides were fermented into other substances by intestinal microorganisms and the fermented products, namely short chain fatty acids such as acetic acid, propionic acids and butyric acids, were absorbed, thereafter metabolized, finally to carbon dioxide.

VI. CONCLUSION

Fructooligosaccharides have two characteristic properties, their non-digestibility and selective utilization by intestinal bacteria. The beneficial effects of fructooligosaccharides on humans and animals are thought to be derived from these two properties, as shown in Fig. 8. The non-digestible saccharides are utilized as nutrients by beneficial bacteria in the large intestine, and this selective utilization results in an increase in bifidobacteria, followed by production of short chain fatty acids, lowered pH in the large intestine, and suppression of putrefactive substances.

Further studies are needed to unravel the still unclear physiological significance of non-digestive saccharides. However, fructooligosaccharides have useful properties as described above, and they are now widely applied to foodstuffs and animal feeds.

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