Low digestibility carbohydrates

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LOW DIGESTIBILITY CARBOHYDRATES

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The workshop was dedicated to Dr A.P. de Groot, formerly head of the Department of Biological Toxicology of the TNO-CIVO Toxicology and Nutrition Institute on the occasion of his retirement.
The theme "Low Digestibility Carbohydrates" was chosen because of his many-sided activities in this field of research.

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OPENING SPEECH

R.J.J. Hermus

TNO-CIVO Toxicology and Nutrition Institute, Zeist, the Netherlands

It is a tradition of TNO-CIVO to yearly organize a scientific meeting to report and discuss important parts of our research programme. Two years ago a symposium on vitamins was held (CIVO, 1985). Last year's symposium (CIVO, 1985a) was devoted to the role of fish (fats) in nutrition. The present workshop will deal with the class of polyols and with dietary fibre, together called "low digestibility carbohydrates". This workshop has been organized to honour Dr. Antoon de Groot on the occasion of his retirement from TNO-CIVO as head of the department of Biological Toxicology. Both the organisational form of a workshop and the subject "low digestibility carbohydrates" pay tribute to the scientist and person de Groot, who has contributed very much to this area. He has never been very keen on presenting the results of his studies in the spot lights of the public media or in front of large audiences. All the more reason to dedicate the workshop to him!

In nutrition we had the protein era, which began with the pioneering work of G.J. Mulder at about 1850 and which lasted about one hundred years. Then came the fat era, which had its peak in the sixties and seventies. It is sometimes said that now the era of the carbohydrates has arrived.

In fact it is true that all dietary guidelines which have been issued during the last 10 years have recommended to reduce fat consumption and to increase carbohydrate consumption, mainly of the complex type and including dietary fibre. Important considerations in this context are that the carbohydrates to be consumed should be: non-cariogenic, eu-glycemic, normolipidemic, favourable for intestinal function, sometimes sweet and sometimes low in energy. They should also provide body and texture to the foodstuffs, especially in low-energy or low-fat foods.

A wide range of products has been and still is under development in recent years, each having one or more of the above-mentioned characteristics e.g. poly-alcohols, modified starches, cyclodextrins. A very classical one is sorbitol, which is sweet and, in so far as it is absorbed, is metabolized by the human body. Its absorption rate is however very slow, such that only small amounts can be ingested at a time. The daily amount should not exceed 35-45 grams. Otherwise sorbitol will enter the distal part of the intestine where it is readily fermented by the microflora present in colon and rectum. Then gases, lactic acid and volatile fatty acids are produced. They are partly absorbed from the colon. The hydrogen thus allows detection in the expired air of the colonic activity. The volatile fatty acids contribute to the energy value of the diet. Grosso modo along similar lines also other polyols are incompletely, partially or not at all digested and absorbed in the upper intestine. They also serve as a substrate to the microflora e.g. xylitol, lactitol, isomalt (formerly called Palatinit). Recently a new sweetener fructooligosaccharide (Neosugar) was reported (Tokunaga et al., 1986). It caused in rats similar phenomena as are well-known for dietary fibre such as a decreased weight gain, caecum and colon enlargement, increased faecal weight and shortening of the intestinal transit time. Faecal sterols and

volatile fatty acids were increased. Diarrhoea was prevalent during the first days but disappeared after adaptation.

These results resemble the early observations from our laboratory by Hellendoorn (1969) who observed that the portion of starch of foods not digested in the small intestine could be fermented by bacteria in the colon as indicated by carbon dioxyde production and the presence of lactic acid, volatile fatty acids and a lowered pH.

The now almost classical TNO-CIVO studies of de Groot et al. (1974) and of Leegwater et al. (1974) about the toxicology of modified starches learned that enlargement of the caecum and other parts of the large intestine, often associated with soft stools and diarrhoea, together with the absence of signs of toxicity should be considered as a physiological response to the presence of products resulting from incomplete digestion. The rapid disappearance of caecal enlargement after removal of the modified starch supports the hypothesis that caecal enlargement is an adaptive phenomenon rather than a pathological condition.
The next step, from modified starch to dietary fibre is only a small one. In recent years many experiments have been carried out at TNO-CIVO, both in rats (Sinkeldam et al., 1985) and with human volunteers (van Dokkum et al., 1982; 1983), about the biological characterization of this heterogeneous class of compounds.
It is evident from the foregoing that there are no essential differences between polyols, Neosugar, modified starches or dietary fibre. They all have in common their more or less complete fermentation by the microflora in the gut.

Their application in the human diet will depend upon their specific toxic effects, if any, and their effect or properties such as: cariogenicity, energy value, appetite stimulant or depressant, eu-glyceamia, blood lipids, composition and metabolic activity of intestinal flora, intestinal transit time, faecal bulking capacity, binding of toxins and xenobiotics. However, also potential adverse effects should be considered, such as flatulence provoking effect, binding of minerals and trace elements and erosion of the mucous membrane of the intestine and consequently proliferation of intestinal cells and possible enhancement of carcinogenesis.
Especially the lactitol and lactose-induced hyperplasia of Leydig cells, as well as the hyperplastic and neoplastic changes of the adrenal medulla deserve further scrutiny as was done in a 1986 FASEB evaluation of sugar alcohols and lactose.

Recently the interest of de Groot into acid-base disturbances due to fermentation products from the colon, was aroused in connection with calcium metabolism and hyperplasia of the urinary bladder epithelium. He will unfold his ideas in this workshop.

The programme of these two days was deliberately set up in accordance with the abovementioned philosophy of a similarity in the mechanism of action of polyols and dietary fibre. However, because the legislative and industrial implications are different, we will deal with the polyols separately. I hope the mutual effects will become apparent as well as the gaps in our knowledge when Dr. H. Blumenthal from FDA will summarize and discuss topics for the future. Besides having these two days of very critical and constructive discussions, I trust we also will have a lot of fun and that, I am convinced, will please Antoon de Groot very much. That is why we have dedicated this workshop to him and invited a number of his

good friends, among them the founding fathers of the TNO-CIVO Institutes: Dr. M. van Eekelen and Dr. C. Engel.

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LOW DIGESTIBILITY CARBOHYDRATES — CHEMICAL AND BIOCHEMICAL ASPECTS

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Introduction

The theme of the workshop is 'low digestibility carbohydrates'. This paper deals with the chemical nature of the most important representatives of such compounds and with biochemical mechanisms underlying the phenomenon 'low digestibility'. Aim is to provide a chemical basis for the topics to be covered in the next papers.

The overview has been kept concise; more detailed information is to be found in textbooks of carbohydrate chemistry (e.g. Pigman & Horton, 1970, 1972) and in the papers cited in the next sections.

Structural features of carbohydrates

Carbohydrates, or (poly)saccharides, have been defined as compounds that are composed of polyhydroxy aldehydes (aldoses), polyhydroxy ketones (ketoses), polyhydroxy alcohols (sugar alcohols), polyhydroxy acids (among which the uronic acids), their simple derivatives, and their polymers in which the monosaccharidic units are interconnected by hemiacetal linkages (the 'glycosidic bonds').

The (stereo)chemical structure of some of the monosaccharidic units present in low digestibility carbohydrates is shown in Fig. 1.
The compounds in the top row have a cyclic structure with an oxygen atom in the ring. Glucose and glucuronic acid have been depicted with a six-membered 'pyranose' ring; fructose with a five-membered 'furanose' ring.

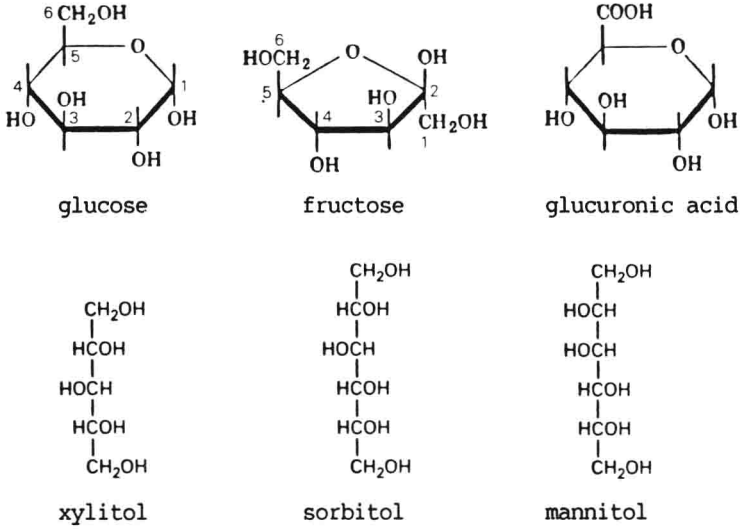


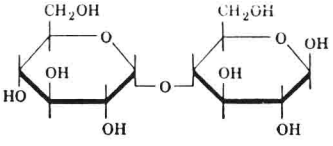
Fig. 1. Monosaccharidic units present in low digestibility carbohydrates.

The numbering of the carbon atoms of the glucose molecule is given as an aid to understand the way the monosaccharides are interconnected in carbohydrates composed of more than one saccharide unit.
The three compounds shown in the bottom row are sugar alcohols. They contain only hydroxyl groups and are always present in an open chain configuration.

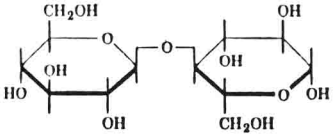
A feature of special interest in the cyclic carbohydrates is the position of the hydroxyl group next to the oxygen atom in the ring. This hydroxyl group may be positioned above or under the plane of the ring. A hydroxyl group pointing downwards, with the oxygen atom in the ring pointing backwards, is called an α-hydroxyl group. When the hydroxyl group is pointing upwards, it concerns a β-hydroxyl group. In Fig. 1 glucose and glucuronic acid have been depicted in the α-configuration and fructose in the β-configuration.
If the oxygen atom in the ring is pointing forward, then an α-hydroxyl group is above and a β-hydroxyl group under the plane of the ring.

Carbohydrates are classified, dependent on the number of saccharide units present in the molecule, as monosaccharides, disaccharides, oligosaccharides and polysaccharides. Oligosaccharides may contain from three up to ten or twelve monosaccharidic units per molecule. Some polysaccharides contain over one million of such units per molecule.

In di-, oligo-, and polysaccharides the monosacharide units are linked by glycosidic bonds. This is illustrated in Fig. 2. for maltose and cellobiose, both 1,4-linked glucosyl-glucoses. It depends on the position of the hydroxyl group next to the oxygen in the ring, whether it is an α- or a β-linkage.



maltose (α-1,4-linked)



cellobiose (β-1,4-linked)

Fig. 2. Alpha- and beta-glycosidic linkages.

It is particularly the type of glycosidic bond that determines whether the carbohydrate hydrolyzing enzymes in the small intestine are capable to break down large molecules to smaller fragments.

Low digestibility carbohydrates

- Monosaccharides

The sugar alcohols, shown in Fig. 1. are commercially important low digestibility monosaccharides. Xylitol has five hydroxyl-groups, sorbitol and mannitol have six. The difference between sorbitol and mannitol is in the position of the hydroxyl group on C2 (the second carbon atom from the top of the molecule).

Xylitol (synonym: xylit) is prepared by catalytic hydrogenation of xylose. Sorbitol (synonyms: glucitol, sorbol, sorbit) and mannitol (synonyms: mannit, mannite) are produced by catalytic hydrogenation of

glucose or fructose. All three compounds are used as food additives or as sweeteners.

Both xylitol, sorbitol, and mannitol have been detected in vegetables or fruits. Moreover, xylitol and sorbitol are normal intermediates in carbohydrate metabolism in mammals. Most probably, this also applies to mannitol. Why these three sugar alcohols are, nevertheless, to be considered as low digestibility carbohydrates, is discussed in the last part of this paper.

- Disaccharides

The structural formulae of some well-known low digestibility disaccharides are shown in Fig. 3.

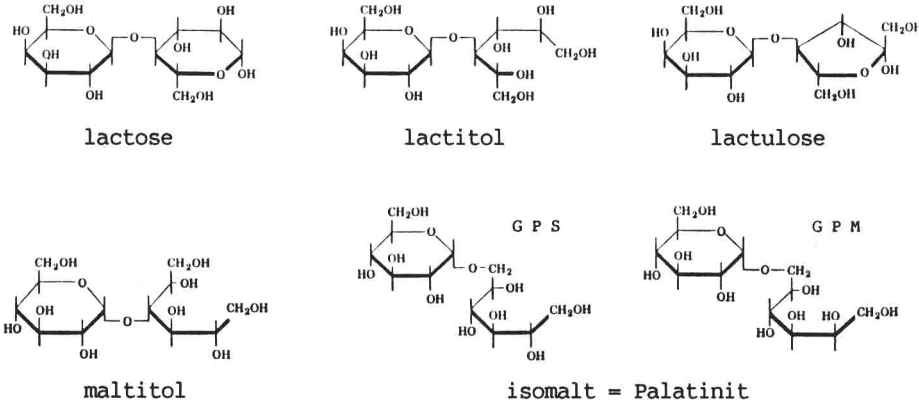


Fig. 3. Low digestibility disaccharides.

Lactose is an important component of milk and is a β-glycoside (β-1,4-linked galactosyl-glucose). Some of the most typical and earliest effects observed in rats fed with low digestibility carbohydrates (namely diarrhoea, "potbellies", and caecal enlargment) have been known for a long time from feeding studies with this very compound.

Lactulose is β-1,4-linked galactosyl-fructose. The compound is prepared from lactose by means of a process that involves conversion of the glucose moiety of lactose into a fructose unit. It has found application as a laxative.

The other compounds in Fig. 3 are the man-made sugar alcohols lactitol, maltitol, and isomalt. All three products are finding increasing use as sweeteners; lactitol also as a laxative.

Lactitol (synonyms: lactit, lactositol, lactobiosit) is prepared by reduction of lactose and is β-1,4-linked galactosyl-sorbitol.

Maltitol (synonym: Malbit) is produced by catalytic hydrogenation of maltose and is α-1,4-linked glucosyl-sorbitol.

Isomalt (synonyms : isomaltitol, hydrogenated isomaltulose, hydrogenated palatinose, Palatinit) is produced by reduction of palatinose (synonym: isomaltulose). It is a mixture of two α-1,6-linked compounds. Both have a glucose unit at the tail end, but one contains sorbitol and the other one mannitol in front. The one with sorbitol is called 'glucopyranosyl

sorbitol' or GPS; the other one with mannitol 'glucopyranosyl mannitol' or GPM.

- Oligosaccharides

Recently, interest has arisen in the technological properties of cyclodextrins, a group of cyclic oligosaccharides composed of α-1,4-linked glucose units. There are at least three types: α, β, and γ-cyclodextrin; containing 6,7, or 8 glucose-units, respectively.

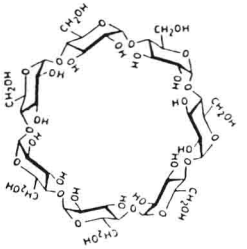


Fig. 4. Structural formula of β-cyclodextrin.

Cyclodextrins can form inclusion complexes with e.g. drugs, food colours, and food flavours. The complexes are often more stable or better water soluble than the compounds themselves.

Data on the physiological properties of cyclodextrins are still scarce. It is known that they are only slowly hydrolyzed by salivary and intestinal enzymes. Therefore, they are likely to induce in mammals at least some of the typical effects that are common to all low digestibility carbohydrates.

Three oligosaccharide containing products have been proposed to be used as 'low-calorie sweeteners' It concerns polydextrose, Lycasin, and Neosugar.

Polydextrose is prepared by melting together, under vacuum, glucose and sorbitol in the presence of citric acid. The composition and chemical identity of the various components of the product are not well defined.

Lycasin is a hydrogenated glucose syrup. It contains sorbitol, maltitol, and a number of oligosaccharidic sugar alcohols (Whitmore, 1985).

The third product, Neosugar, is a mixture of β-2,1-linked (poly)fructo-furanosyl-sucroses. A commercial product may contain approximately 28% trisaccharide, 60% tetrasaccharide, and 12% pentasacharide (Tokunaga et al., 1986).

Still little is known of the physiological and toxicological properties of the above oligosaccharide mixtures.

- Polysaccharides

The most important group of polysaccharides, at least from a nutritional point of view, are the starches, a group of α-linked polyglucoses. There are two types: amyloses and amylopectins. Amyloses consist of α-1,4-linked polyglucose chains; amylopectins contain in addition α-1,6-linked branches (Fig. 5).

Native (not pre-heated) starches may behave like low digestibility carbohydrates, as will be discussed in the last part of this paper.

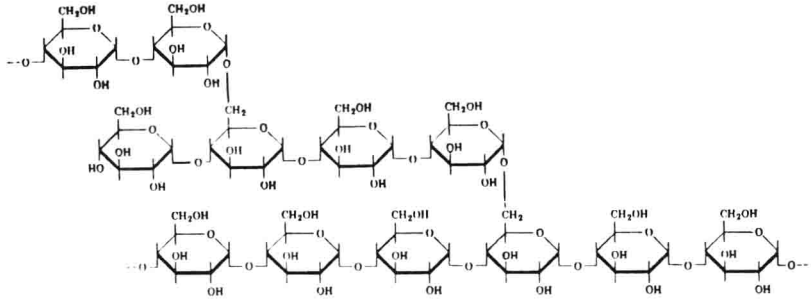


Fig. 5. Structural formula of amylopectin.

Industrially, starches are chemically modified to yield products with improved properties. Such 'chemically modified starches' form a large group of products. The products used in the food industry are prepared by treating native starch with reagents such as acetic anhydride or vinyl acetate (yielding acetylated starches), phosphoric acid derivatives (yielding phosphated starches), propylene oxide (yielding hydroxypropyl starch) or phosphorus oxychloride (yielding cross linked products), see Fig. 6. Some of these products are only partly digestible.

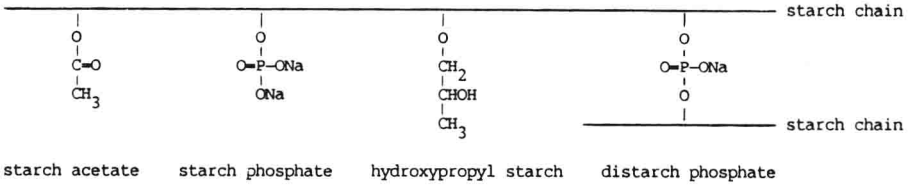


Fig. 6. Schematic formulae of chemically modified starches.

Other low digestibility polysaccharides, although not from a nutritional point of view, are cellulose and hemicellulose, both β-linked polysaccharides.

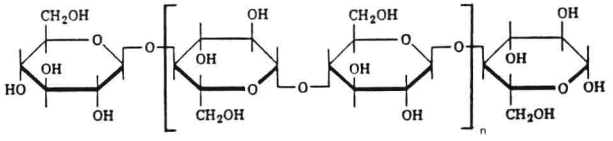


Fig. 7. Formula of cellulose.

Cellulose is β-1,4-linked polyglucose (Fig 7). In plants it is the basic structural component of cell walls.

The hemicelluloses are a group of complex polysaccharides. In plants they surround the cellulose microfibrils in the cell wall. A general formula for these compounds cannot be given. It concerns polymers with different types of monosaccharidic residues; some are shown in Fig. 8.

The hemicelluloses are subclassified on the basis of the principal monosaccharidic units into: xylans (composed of β-1,4-linked xylose

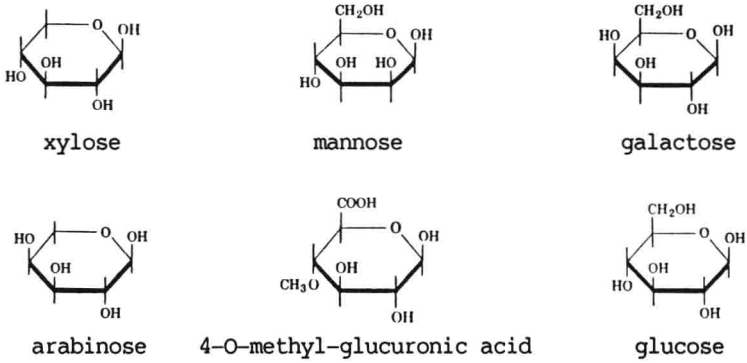


Fig. 8. Structural units present in hemicelluloses.

residues; usually with α-1,2-linked 4-O-methyl-glucuronic acid and/or α-1,3-linked arabinose residues as side chains), mannans (composed of β-1,4-linked mannose residues), gluco-mannans (composed of β-1,4-linked chains of glucose and mannose residues, sometimes with α-1,6-linked galactose residues as a side chain), arabino-galactans (with a framework of β-1,3 and β-1,6-linked chains of arabinose and galactose), a.s.o..

Cellulose and hemicellulose belong to the type of products that make up the bulk of 'dietary fibre', another topic of this workshop. Such products may also contain pectin, a polysaccharide containing uronic acids. A part of a pectin molecule is shown in Fig. 9, along with the structural formula of an alginate, another product containing a uronic acid.

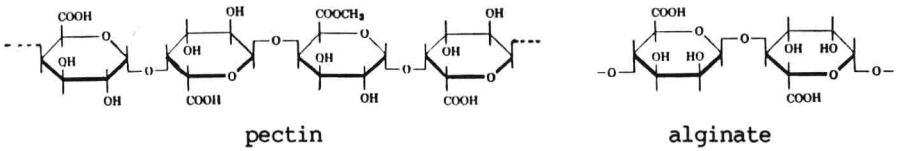


Fig. 9. Structural formulae of pectin and alginate molecules.

Pectins contain α-1,4-linked, partially methylated, galacturonic acid residues; alginates are composed of β-1,4-linked mannuronic acid units. Feeding studies have shown that both products may provoke effects in animals comparable to those observed with other low digestibility carbohydrates.

Mechanisms underlying the phenomenom 'low digestibility'

The term 'low digestibility carbohydrates' is somewhat misleading. In common parlance a carbohydrate is considered to be 'lowly digestible' when the energy it contains is not completely available to an animal or man. This does not imply that the compound in question is excreted as such but rather that it is not completely absorbed and utilized by a mammal. Actually, it might very well be that the compound is fully utilized within the animal body, but then not by the animal itself, but by the intestinal microflora in the large intestine.