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Oligosaccharides

1. Introduction.....	27
2. Disaccharides	28
A. General	28
B. Sucrose, Sucrose-containing Drugs.....	28
Sugar-beet	29
Sugar-cane.....	30
3. Disaccharide Derivatives, Maltitol, Isomalt	30
4. Oligosaccharides	31
5. Cyclodextrins	32
6. Bibliography.....	33

1. INTRODUCTION

* Oligosaccharides result from the condensation of two to ten monosaccharide molecules by formation, between successive pairs, of a glycosidic linkage. The latter is formed, *in vivo*, by the transfer of a sugar radical from a nucleotide glycoside to a receiving molecule. It involves the hemiacetal hydroxyl group on the anomeric carbon of one sugar and any hydroxyl group of, 1. another monosaccharide molecule (disaccharide formation), or 2. of a more or less long carbohydrate chain (oligosaccharide and polysaccharide).

Recall:

- that the glycosidic linkage is easily cleaved by chemical hydrolysis and, with high specificity, by enzymatic hydrolysis;
- that the determination of the sequence and of the linkage type in these small molecules is greatly facilitated by advances in spectroscopic techniques (NMR, MS), although some classical methods also remain in use (see biochemistry textbooks).

2. DISACCHARIDES

A. General

The type of glycosidic linkage allows a distinction to be made between non-reducing disaccharides (linkage between the reducing functions of both sugars) and reducing disaccharides (linkage involving the reducing function of only one sugar).

Only one non-reducing disaccharide is of industrial importance: sucrose. Trehalose (α -D-glucopyranosyl-(1 \rightarrow 1)- α -D-glucopyranoside), a nonreducing disaccharide characteristic of fungi and other nonphotosynthetic organisms, is not used.

Although numerous reducing disaccharides can be detected in plants, they are always present in minute quantities: they are in fact degradation products of oligomers, polymers, or glycosides: maltose (α -D-glucopyranosyl-(1 \rightarrow 4)- α -D-glucopyranoside) and cellobiose (β -D-glucopyranosyl-(1 \rightarrow 4)-D-glucopyranoside) arise from the degradation of starch and cellulose, respectively.

The other disaccharides sometimes characterized in plants are normally constituents of glycosidic combinations, particularly those built upon a phenolic aglycone (see table below, see also flavonoids).

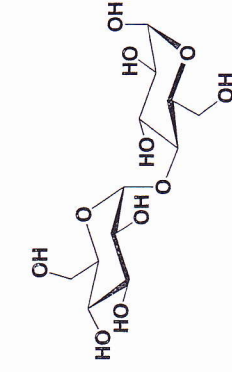
Structure	Trivial Name
<i>O</i> - β -D-Glcp-(1 \rightarrow 4)-D-Glcp	cellobiose
<i>O</i> - α -D-Glcp-(1 \rightarrow 4)-D-Glcp	maltose
<i>O</i> - β -D-Glcp-(1 \rightarrow 2)-D-Glcp	sophorose
<i>O</i> - β -D-Glcp-(1 \rightarrow 3)-D-Glcp	laminaribiose
<i>O</i> - β -D-Glcp-(1 \rightarrow 6)-D-Glcp	gentiobiose
<i>O</i> - β -D-Galp-(1 \rightarrow 4)-D-Glcp	lactose
<i>O</i> - α -L-Rhap-(1 \rightarrow 2)-D-Glcp	neohesperidose
<i>O</i> - α -L-Rhap-(1 \rightarrow 3)-D-Glcp	rungiose
<i>O</i> - α -L-Rhap-(1 \rightarrow 6)-D-Glcp	rutinose
<i>O</i> - β -D-Glcp-(1 \rightarrow 3)- α -L-Rhap	scillabiose
<i>O</i> - β -D-Xylp-(1 \rightarrow 2)-D-Glcp	sambubiose
<i>O</i> - β -D-Xylp-(1 \rightarrow 2)-D-Galp	lathyrrose
<i>O</i> - β -D-Xylp-(1 \rightarrow 6)-D-Glcp	primeverose

B. Sucrose, Sucrose-containing Drugs

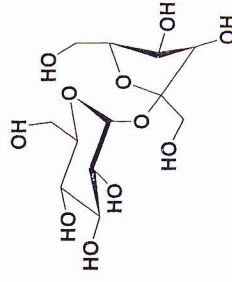
Sucrose (α -D-glucopyranosyl-(1 \rightarrow 2)- β -D-fructofuranoside) is a nonreducing disaccharide. As the principal form of transport and temporary storage of energy in plants, it accumulates in certain fleshy roots. It can be obtained from sugar maple, *Acer saccharum* Marshall, a tree native to the eastern part of the north American continent. It is also one of the main constituents of the date, the fruit of the date palm (*Phoenix dactylifera* L., Palmae). Its two major industrial sources are the sugar cane

and the sugar beet, and it has been produced industrially from the sugar beet since the beginning of the nineteenth century. The world production is greater than 110 million metric tons, including one third from beet and two thirds from sugar cane.

Sucrose from beet root was characterized in the middle of the eighteenth century (Markgraf, 1745). Two centuries later, its total synthesis was published (1953) and its conformational analysis completed (NMR). Meanwhile, the greatest names in chemistry found interest in its structure, its chemical and biological properties, its origin, and its fate. Yet the subject does not appear to have been exhausted: in a review published in 1990 C. Avigad reports that from 1982 to 1986, sucrose triggered approximately 10,000 scientific articles (listed in *Chemical Abstracts*).



α -Maltose



Saccharose

Official sucrose (Eur. Ph., 3rd Ed.) must pass tests very similar to those prescribed for glucose. It is used as excipient for tablets and other forms for oral administration, and for the manufacture of syrups (minimum concentration 45% w/w). The pharmaceutical industry uses a sucrose modified physically, with or without maltodextrin addition, to render it directly compressible. The industry also frequently resorts to a simple syrup (French Pharmacopoeia) obtained by dissolving 650 g of sucrose in 1 L of hot purified water and eventually adding antimicrobial agents ($d = 1.31-1.33$, refractive index 1.449-1.458).

In food technology, sucrose has forever been used as a preservative: when the concentration is sufficient—the maximal solubility at 20°C is 204 g per 100 g water—the development of microorganisms is inhibited.

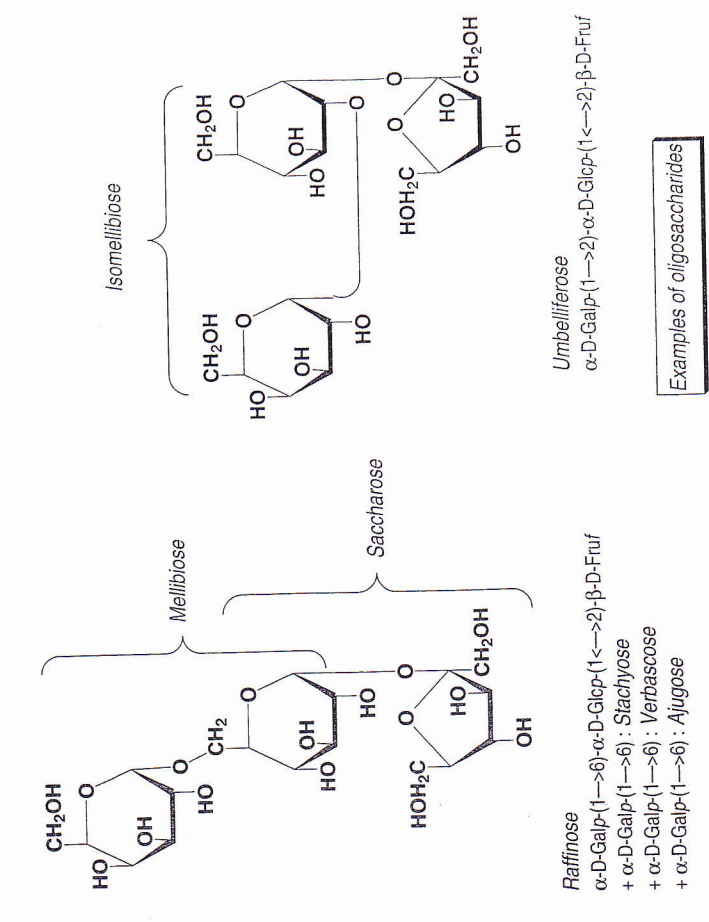
● SUGAR BEET, *Beta vulgaris* L., Chenopodiaceae

The plant is biennial, but is cultivated as annual. Varieties with high need for vernalization do not bloom, consequently the root develops further. It contains around 77% water and 16-17% sucrose. The world production (1997) was 263 million metric tons, including 33 million metric tons in France (FAO, 1998).

The roots are washed, cleaned of stones and straw, minced into small slivers known as cossettes, and sucrose is extracted by simple diffusion in hot water. The resulting juice is purified by liming followed by carbon dioxide treatment. After filtration, the clarified juice is concentrated under vacuum. From the syrup, the

stimulates intestinal peristalsis. The lowering of the colon pH by the acids arising from its degradation by the microflora decreases the intestinal absorption of ammonia (as NH₃), and enhances its diffusion out of the blood and its trapping and elimination (as NH₄⁺). Indications: constipation, hepatic encephalopathies. If needed (e.g., in a coma), the product may be used by nasogastric administration or by enema.

• **Lactitol**, the catalytic hydrogenation product of lactulose—not a sugar of plant origin—claims the same indications and the same potential side effects (flatulence, abdominal cramps, diarrhea).



4. OLIGOSACCHARIDES

Higher oligosaccharides (3 to 10 sugars) represent storage forms specific to limiter species or plant groups, and this explains their interest for the chemo-taxonomist. Some are also involved in the formation of glycosides (linear or branched trisaccharides of flavonoids, oligosaccharides of saponins... see the example of gypsoside below).

The most common storage oligosaccharides are the nonreducing galactosyl derivatives of sucrose. Like other storage forms, they are primarily stocked in seeds and in underground organs. Although they are sometimes present in plants to which

sucrose crystallizes in successive batches with the final residue constituting molasses. Drying by centrifugation allows recovery of the purified product (crystallized white sugar). The average yield is about 130 kg of sucrose and 35-40 kg of molasses at 48% sucrose per thousand kg of beets. The industry also prepares liquid sugar, invert liquid sugar, and invert sugar syrup.

• SUGAR CANE, *Saccharum officinarum* L., Poaceae

S. officinarum in the broad sense of the term comprises at least three subspecies and numerous varieties. Like corn, sugar cane is a high yield C4-type plant. It is a tall perennial reed of debatable origin (India, Melanesia?), its stem is solid between the joints, and ends in large panicle of inflorescences. The crushed stems afford a juice (press juice), which after being freed of proteins and neutralized (liming), filtered, decolorized, and concentrated, yields crystallized raw sucrose (crystallized brown sugar). This sugar can be "refined" by stirring in concentrated syrup, recovering in a centrifuge, dissolving, concentrating, and crystallizing. Asia (e.g., India, China, Thailand, Pakistan), South America (e.g., Brazil, Colombia), and the Caribbean islands plus North and Central America (e.g., Cuba, Mexico, Guatemala) are the main production zones. The world production was 1.24 billion metric tons in 1997 (FAO, 1998).

3. DISACCHARIDE DERIVATIVES

• **Sucrose esters** (Olestra®). This mixture of hexa-, hepta-, and octaesters of sucrose and of fatty acids obtained from dietary oils is a fat substitute. These esters are not digested nor absorbed and their use in some foods was approved in 1995 in the United States by the FDA. The only undesirable effects initially attributed to Olestra were a potential for abdominal cramps and anal discharge in some subjects and at high doses.

• **maltitol** (maltitol syrup = Lycasin®). This polyalcohol does not occur naturally, it is produced by synthesis from glucose syrups rich in maltose. In France, it is an authorized sweetener.

• **isomalt** This is the product of the catalytic hydrogenation of isomaltulose, itself the product of the enzymatic transformation (by *Protaminobacter rubrum*) of sucrose. It is a mixture of α -D-glucopyranosyl-(1 \rightarrow 6)-sorbitol and of α -D-glucopyranosyl-(1 \rightarrow 6)-mannitol (Palatinit®). It too is an authorized sweetener (see above, meso-xylitol).

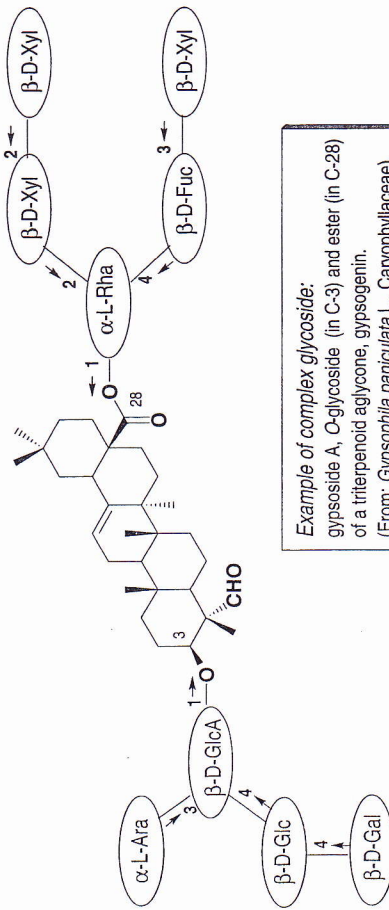
• The synthetic disaccharide **lactulose** (= β -D-galactopyranosyl-(1 \rightarrow 4)-D-fructofuranoside) which acts as an osmotic laxative, reduces blood ammonia, and

tradition attributes medicinal properties, they do not seem to play a key role in their activity (e.g., ombelliferose of Apiaceae roots, planteose of various plantain seeds).

We shall cite as example the most important series, formed by the addition, *via* galactinol (i.e., 1-L-O- α -D-galactopyranosyl-myo-inositol) of D-galactose to sucrose through (1 \rightarrow 6)- α linkages, resulting in raffinose, stachyose, verbascose, and ajugose. The first few in the series are common in Fabaceae seeds: they are in part responsible for the flatulence experienced after consumption of dried vegetables (for example dried beans, chick peas). Stachyose also accumulates in the edible tubers of a Lamiaceae, the Japanese artichoke, *Stachys tuberosa* Nand.

The only oligosaccharides used in food technology are non-reducing fructo-oligosaccharides (prepared enzymatically, see p. 85). They have a reputation for being capable of increasing bifidobacteria and they may, in countries such as Japan, appear in the composition of "medicinal foods" (sugars, beverages, candy). Like the oligosaccharides of the soybean, they may claim alleged indications such as "contribute to maintaining good gastrointestinal health".

Known reducing oligosaccharides are essentially products of partial hydrolysis of polysaccharides: such is the case of maltodextrins from the partial hydrolysis of starch (see above).



Example of complex glycoside:
 gypsoside A, C-glycoside (in C-3) and ester (in C-28)
 of a triterpenoid aglycone, gypsogenin.
 (From: *Gypsophila paniculata* L., Caryophyllaceae).

5. CYCLODEXTRINS

Cyclodextrins are cyclic oligosaccharides produced by the enzymatic degradation of starch. The enzyme, cyclodextrin glycosyl transferase, is produced by different bacilli (e.g., *Bacillus macerans*, *B. circulans*). Structurally, α -, β -, and γ -cyclodextrins consist of six, seven, and eight glucose units, respectively, linked by α -(1 \rightarrow 4) bonds. These molecules are water soluble, hydrolysis-proof, and shaped like a torus. Their cavity has an average diameter of five to eight Å and is relatively hydrophobic (skeleton carbon atoms and ether bridges), whereas on the outside, they are very hydrophilic (primary alcohols on the narrow part of the torus, secondary alcohols on the wide part). Their main interest resides in their ability to form

noncovalent inclusion compounds with numerous molecules of compatible size, and therefore to permit "molecular encapsulation" to increase stability (thermally, chemically), to modify solubility and dissolution rate, to improve bioavailability, to inhibit chemical interactions, to avoid gastric or ocular degradations, to mask taste and smell, and so on. There are many possible applications: complexation of active principles, of pesticides, of detergents, stabilization of flavors and colors. Their great resistance to enzymatic hydrolysis by α -amylase leads to limiting the daily dosage to 3% of the food intake.

For chemists, cyclodextrins and their derivatives constitute a very interesting chromatographic stationary phase: they allow stereoselective separation (and quantitation) of chiral molecules (for example in essential oils).

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