Introduction to Pharmacognosy
Carbohydrates

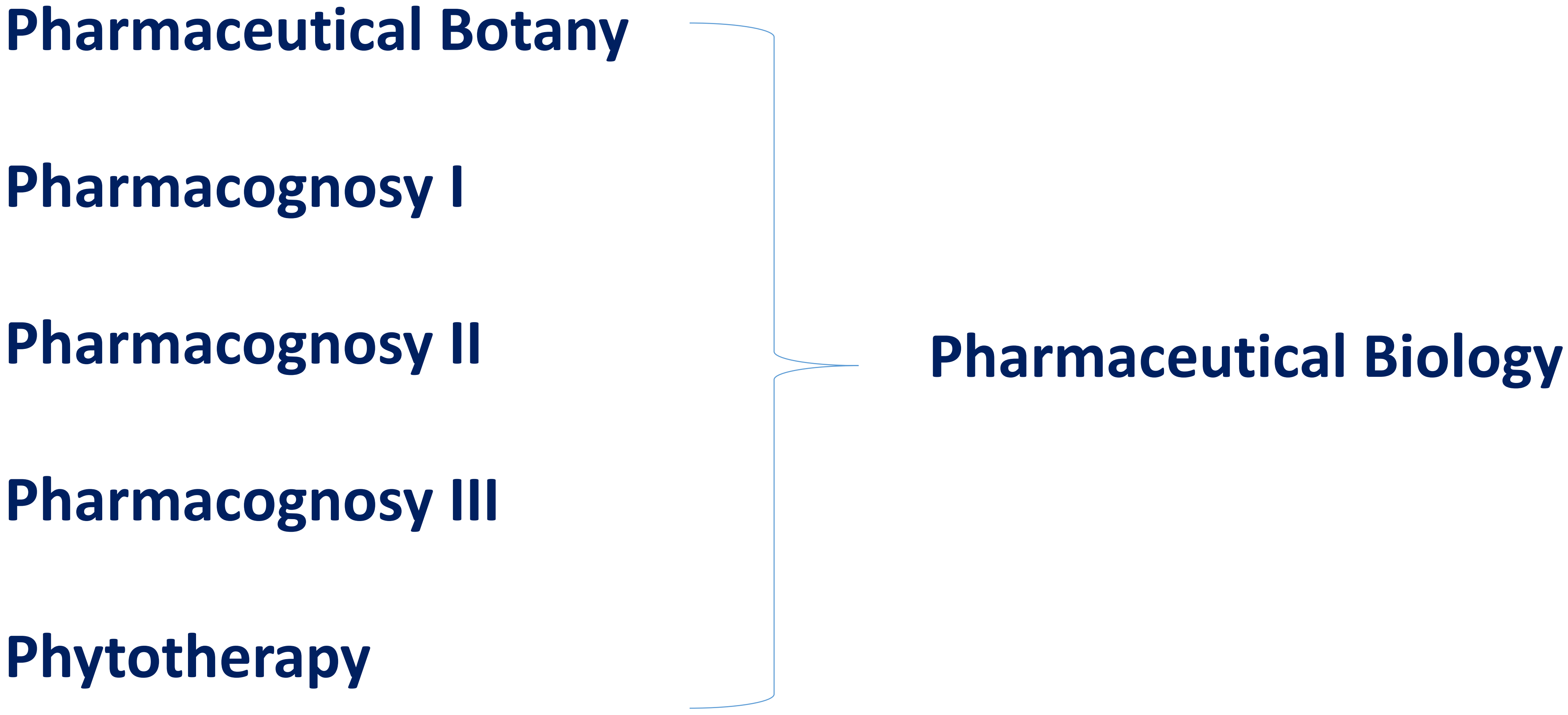
Prof. Dr. Ali Hikmet Meriçli

Etymologically «Pharmacognosy» is the **knownledge** (from the Greek ***gnosis***) of **poisons** (***pharmacon***). **Note that pharmacon not only means poison, but also medication…the difference lies in the dose.** Thus the might legitimately think that pharmacognosy treats alldrug-like substances : that is not the case. Pharmacognosy limits its field of investigation to natural starting materials : it is simply the descendant of «Materia medica», a discipline which, since Dioscorides's treatise by that name, and until the birth of synthetic chemistry, dealt with mineral, animal and plant starting materials, in other words all of the materials aveilable to prepare remedies, since no others were known.

As time passed, mineral substances lost their appeal. Those that are still in use are now covered as well-definied substances, just like synthetic organic substances and in the same texts. Some do not hesitate to include Pharmacognosy Biotechnologie and Genetic Engineering.

Under these conditions, **Pharmacognosy is the study of starting materials and substances intended for therapeutics, and of biological origin, in other words obtained from plants (about 90%), animals, or by fermentation from micro-organisms**.

Beyond the definition of Pharmacognosy, it is important to emphasize what many consider, and they are absolutely correct, one of its major assets : its multydisciplinary character. In pharmacognosy, to study a plant is : to define its identity; to describe its morphology and anatomy (**Pharmaceutical Botany**); to know its origin and production methods; to appreciate their impact on the plant quality: to determine its chemical composition and the factors that may affect it; to know the structure, physico-chemical properties, and pharmacological activity of the active principles; finally to come to grips with all the problems linked to the optimal utilization of plants and plant products : indications, contraindications, side effects and drug interactions. To know plants and their uses is also- and this applies mostly to **Phytotherapy**- to be aware of the limits and the dangers of what must be at times no more than a placebotherapy.



Pharmaceutical Botany

Pharmacognosy I

Pharmacognosy II

Pharmacognosy III

Phytotherapy

Pharmaceutical Biology

Compounds of Primary Metabolism

A **primary metabolite** is a kind of metabolite that is directly involved in normal growth, development, and reproduction. It usually performs a physiological function in the organism (i.e. an intrinsic function). A primary metabolite is typically present in many organism or cell. It is also referred to as a central metabolite, which has an even more restricted meaning (present in any autonomously growing cell or organism).

Conversely, a **secondary metabolite** is not directly involved in those processes, but usually has an important ecological function (i.e. a relational function). A secondary metabolite is typically present in a taxonomically restricted set of organisms or cells (Plants, Fungi, Bacteria...).

Carbohydrates

Lipids

Amino acides and Peptides, Proteins and Enzymes

Carbohydrates

Carbohydrates are universal contituents of living organisms. They are at first approximation, organic compounds with carbonyl (aldehyde or ketone) and multiple hydroxyl functions. The carbohydrate group also encompasses oxidized or reduced derivatives (uronic acids, polyalcohols), their esters, and their amine derivatives (amino sugars)

In plants they are found

- as support elements

- as energy reverses

- as constituents of various metabolites

- as required precursors for all other metabolites

Clasically they are distinguished as :

- Monosaccharides

- Oligomeric and polymeric saccharides

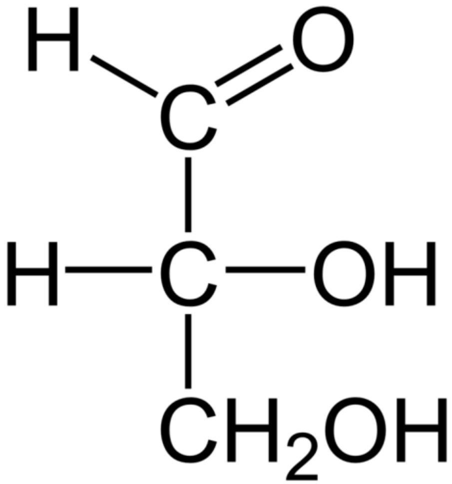
- -Simple or true saccharides

- Glycosides or conjugate saccharides

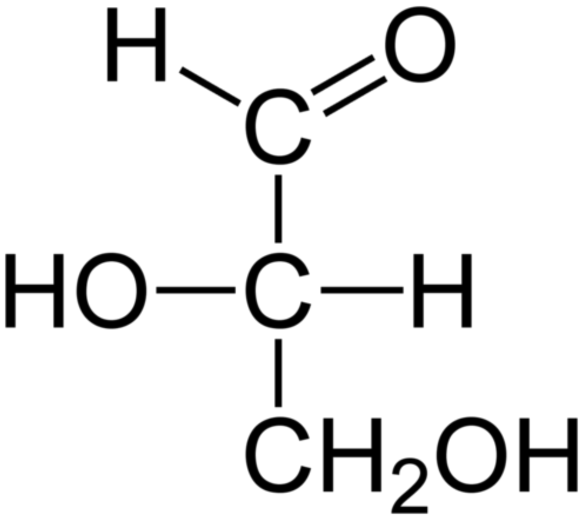
Monosaccharides

Naming : In general the naming of monosaccharides is based on the number of carbon atoms in the molecule : tetroses, pentoses, hexoses, heptoses…., and on the nature of their carbonyl function (for example D-ribose and D-xylose are aldoses, D-ribulose and D-xylulose (for example are ketones). The numbering of carbon atoms begins with the aldehyde carbon, or, for ketone carbon the lower possible number.

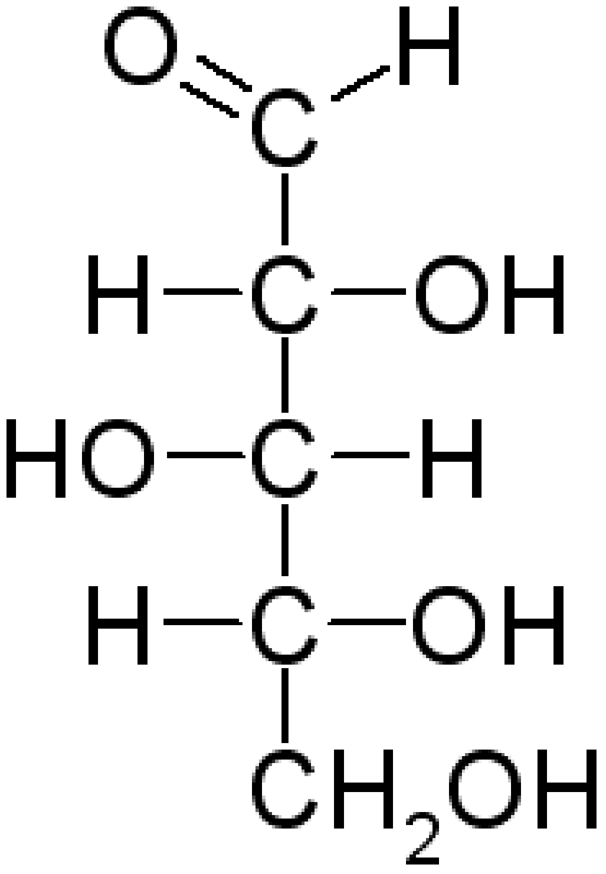
D- and L-Series : Consider the simplest monosaccharide, glyceraldehyde (an aldotriose): it has one asymmetric carbon, so there are two enantiomers, (*R*) and (*S*). D-glyceraldehyde and L-glyceraldehyde are defined arbitrarily and by convention as having the secondary hydroxyl group on the right or on the left side of the molecule, respectively, in the Fischer vertical represantion,aldehyde carbon at the top.



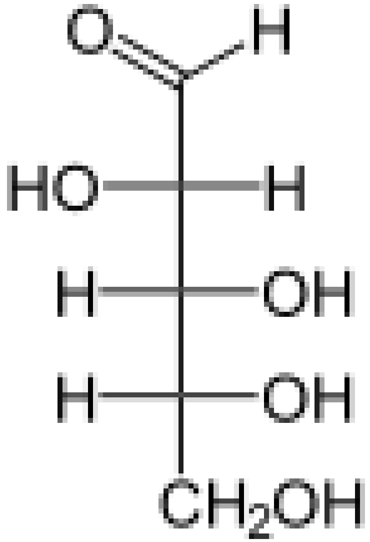
D-Glyceraldehyde



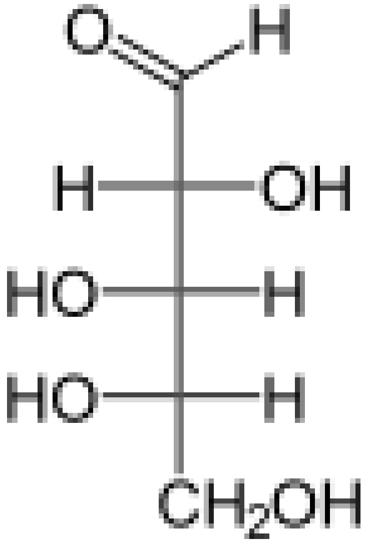
L-Glyceraldehyde



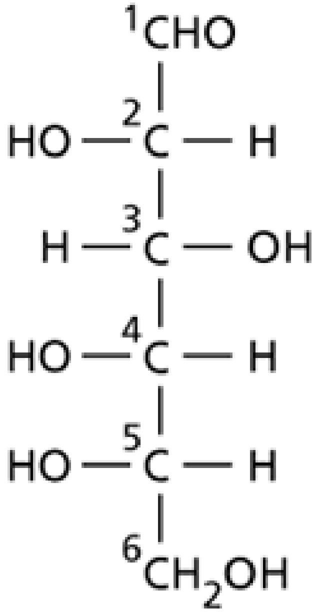
D-Xylose



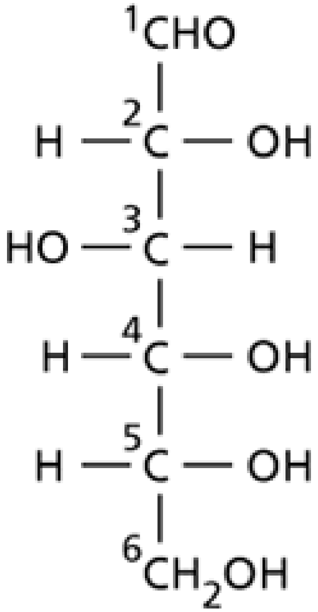
D-Arabinose



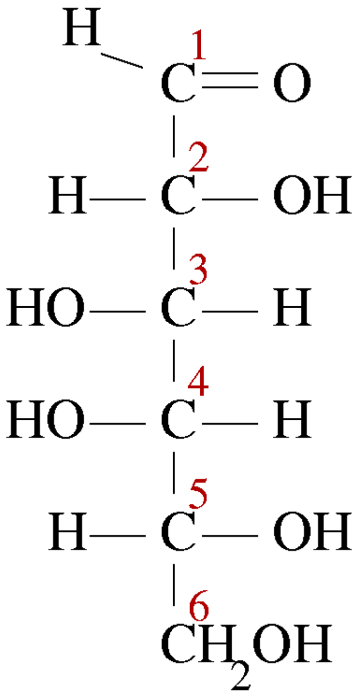
L-Arabinose



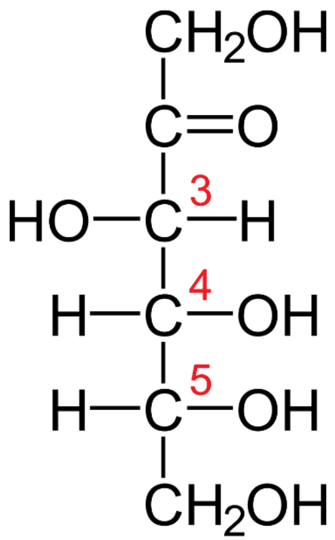
L-Glucose



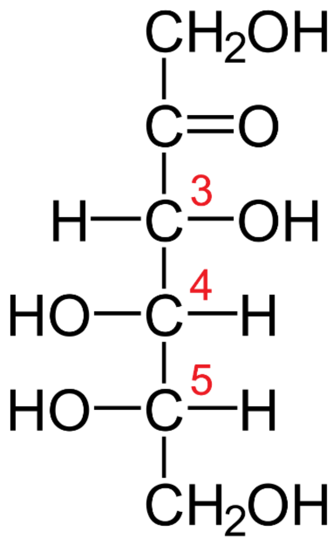
D-Glucose



D-Galactose



D-Fructose

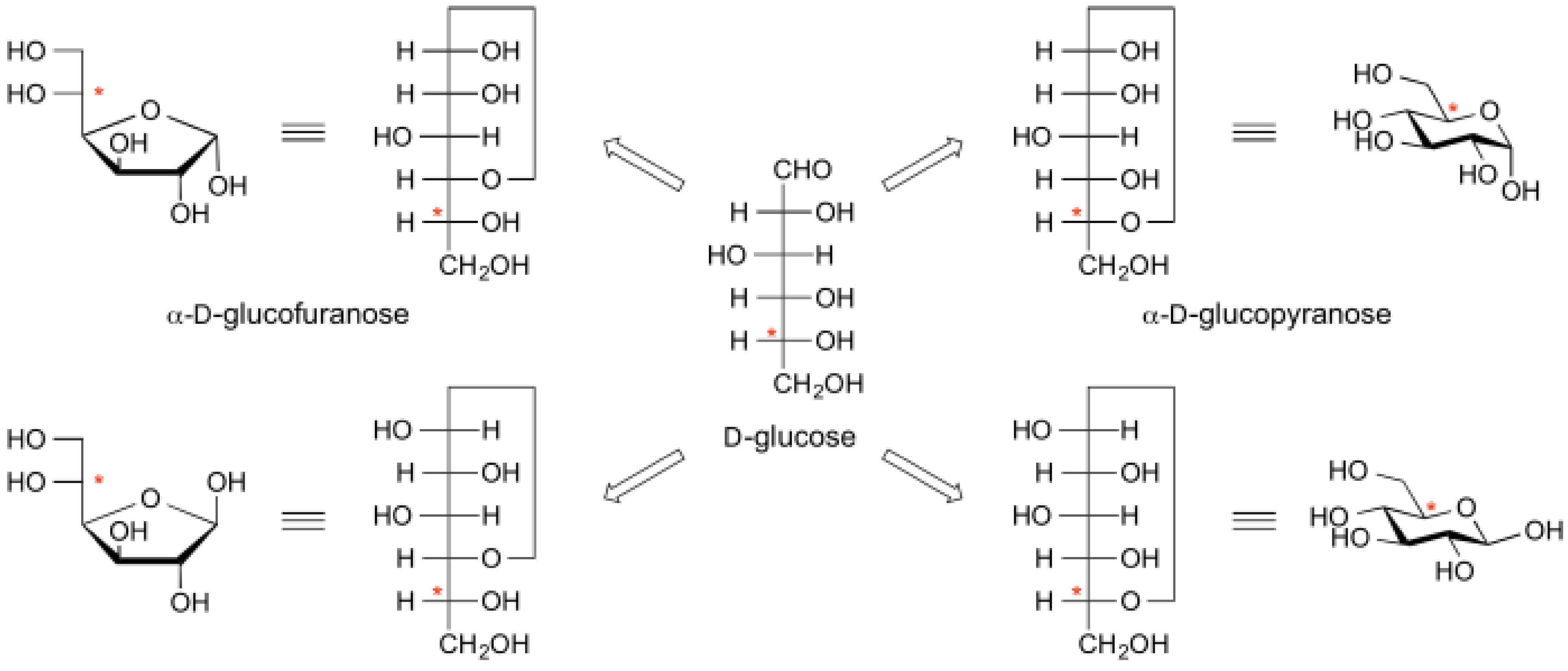


L-Fructose

Again by convention and by reference to glyceraldehyde, it is the orientation of the hydroxyl group most distant from the carbonyl group that determines if a monosaccharide belongs to the D or to L series. Because this rule is arbitrary, the fact that a sugar belongs to either series does not predict its optical activity. The vast majority of natural monosaccharides belong to the D series (exceptions : L-rhamnose, L-arabinose, L-fucose).

Cyclic structure of Monosaccharides: The particular chemical behavior of monosaccharides has led to the postulate that they exist in a cyclic form involving the carbonyl group and one hydroxyl group. The principal consequences are as follows :

- depending on the nature of the bridge (1 → 4 or 1 → 5), the cycle is either a furan or a pyran (furanoses and pyranoses);
- generally, aldohexoses form pyranose rings and ketohexoses form furanose rings
- cyclization leads to two isomeric hemiacetals, α and β,called anomers. The configuriation of the anomeric carbon is α when the hemiacetal hydroxyl group is in the same orientation as the secondary hydroxyl group that determines the series.



α-D-glucofuranose

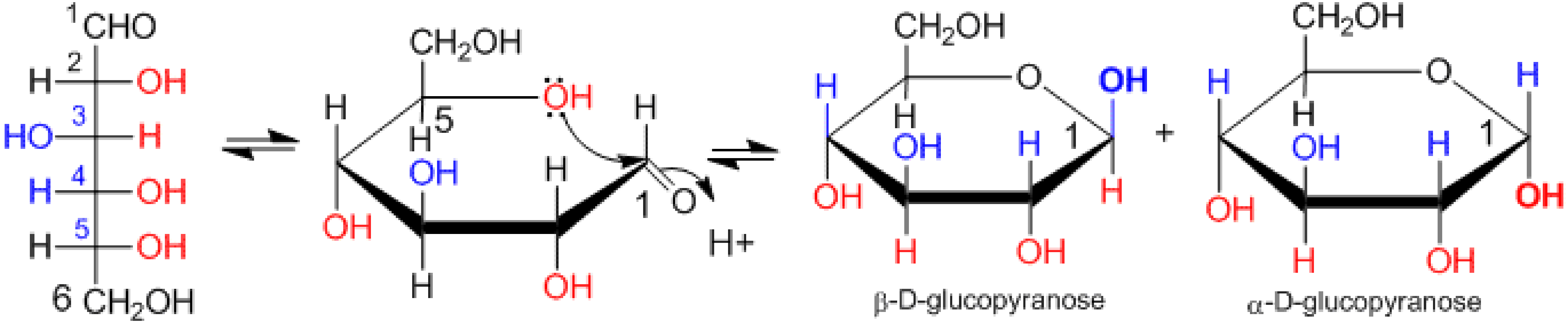
α-D-glucopyranose

D-glucose

β-D-glucofuranose

β-D-glucopyranose

D-glucose

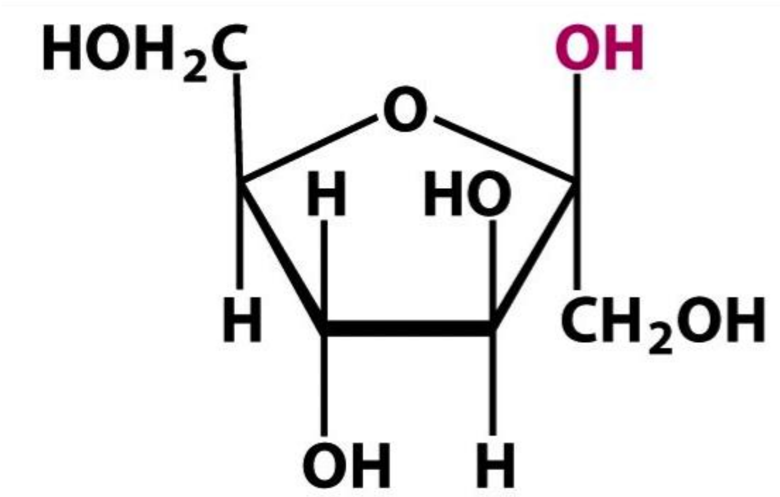


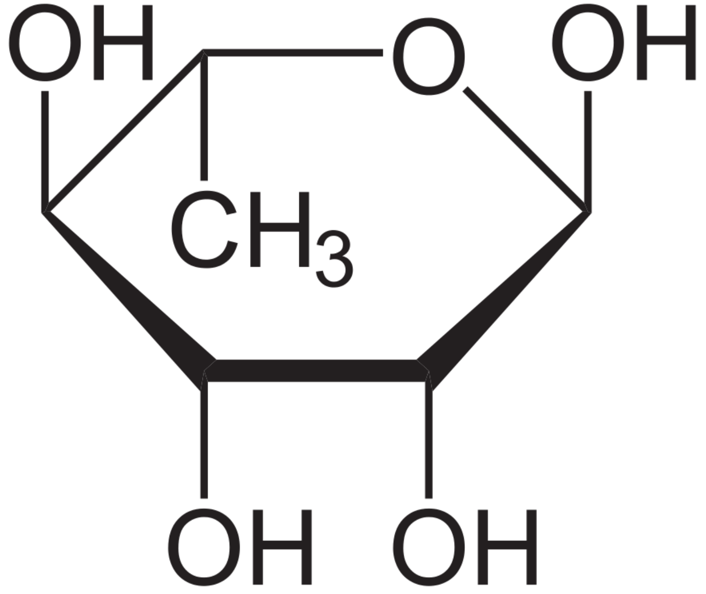
Fischer
Projection

β-D-glucopyranose
OH on C1 point up

α-D-glucopyranose
OH on C1 point down

Haworth Projections





β-D-Fructofuranose

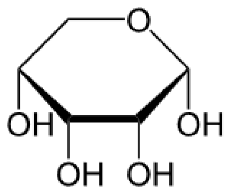
α-L-Rhamnose

Principal Plant Monosaccharides

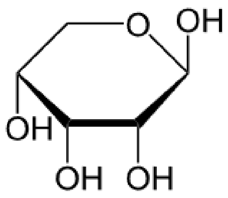
What characterizes plant monosaccharides is their great diversity : pentoses, deoxypentoses, hexoses, deoxyhexoses, dideoxyhexoses, uronic acids, polyalcohols, esters, ethers, and more. Several hundred compounds, some ocur free, others are only known in glycosidic combinations ; very often they are included in polymers.

Tetroses : The four possible isomers of these monosaccharides form two pairs of enantiomers : D- and L-threose on the one hand, D- and L-erythrose on the other hand. They do not occur free. D-erythrose-4-phosphate plays a key role in the genesis of aromaticity.

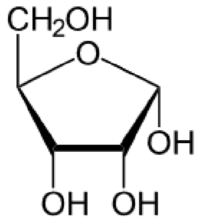
Pentoses : D-ribose is universal (nucleic acid), L-arabinose and D-xylose are common constituents of complex polysaccharides.



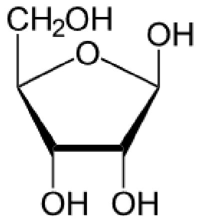
α-D-Ribopyranose



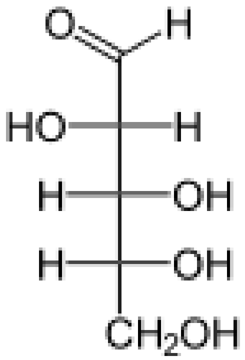
β-D-Ribopyranose



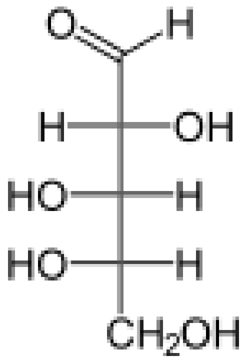
α-D-Ribofuranose



β-D-Ribofuranose

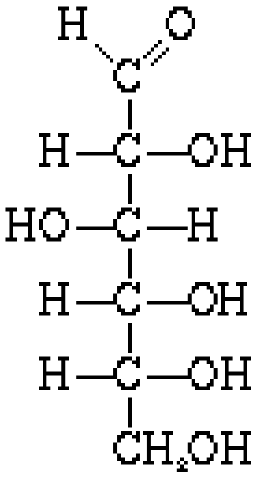


D-Arabinose

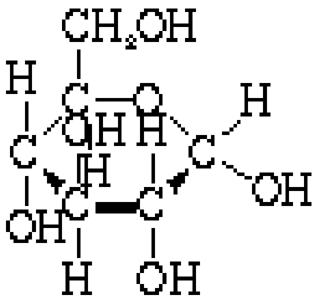


L-Arabinose

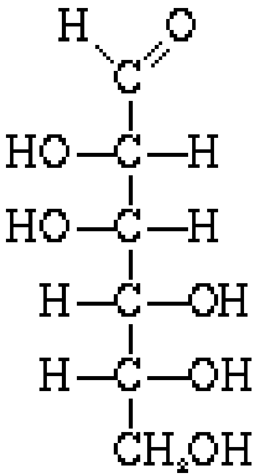
Hexoses : Most are ubiquitous : such is the case for D-glucose and for D-mannose (2-epimer of D-glucose), and also for D-galactose (4-epimer of D-glucose).



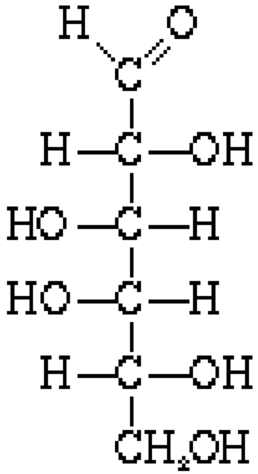
D-Glucose



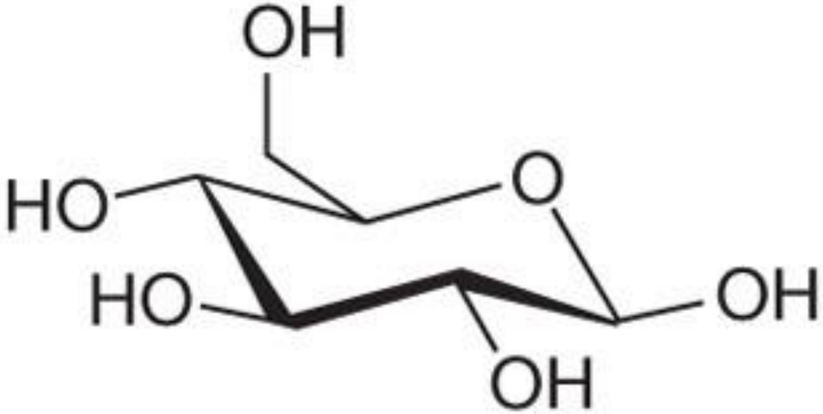
α-D-Glucopyranose



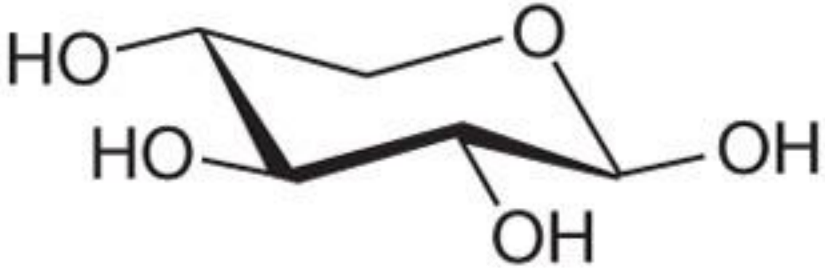
D-Mannose



D-Galactose



D-glucose

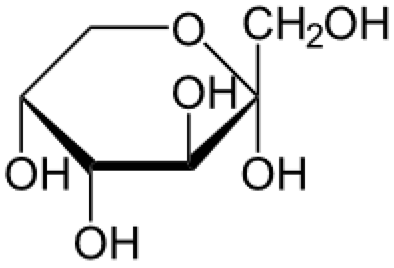


D-xylose

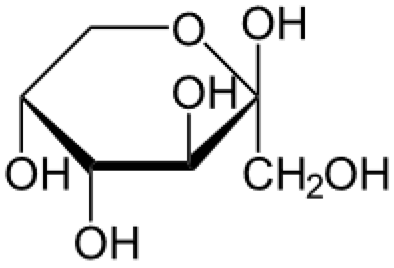
Although glucose is commonly free, as well as combined into polysaccharide structures (starch, cellulose, and other glucans), its 2- and 4-epimers are almost exclusively known as polymers (for example, mannans, gluco- and galactomannans of Fabaceae). D-galactose is rather common in glycosides.

The ketose corresponding to D-glucose and D-mannose is D-fructose. Abundant in the free state in fruits, it is just common as disaccharide (sucrose).

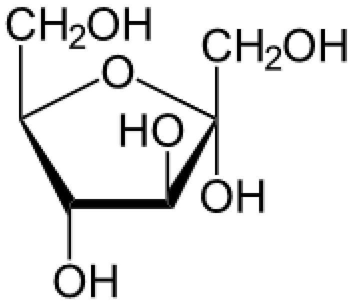
Within oligomers and polymers, D-fructose is present in the form of β-D-fructofuranose, whereas in the free state, the more stable β-D-fructopyranose is favored.



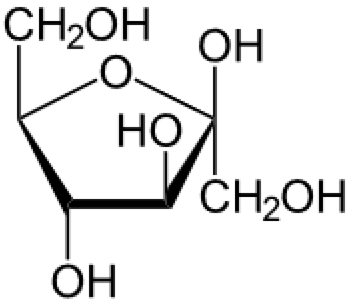
α-D-Fructopyranose



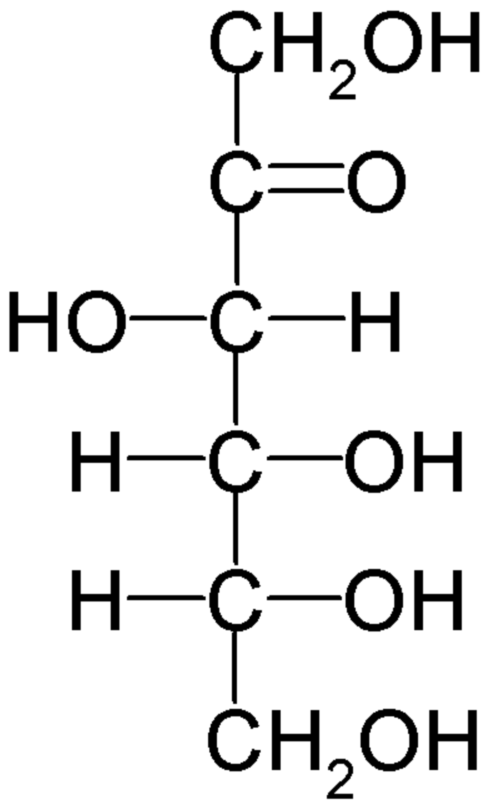
β-D-Fructopyranose



α-D-Fructofuranose



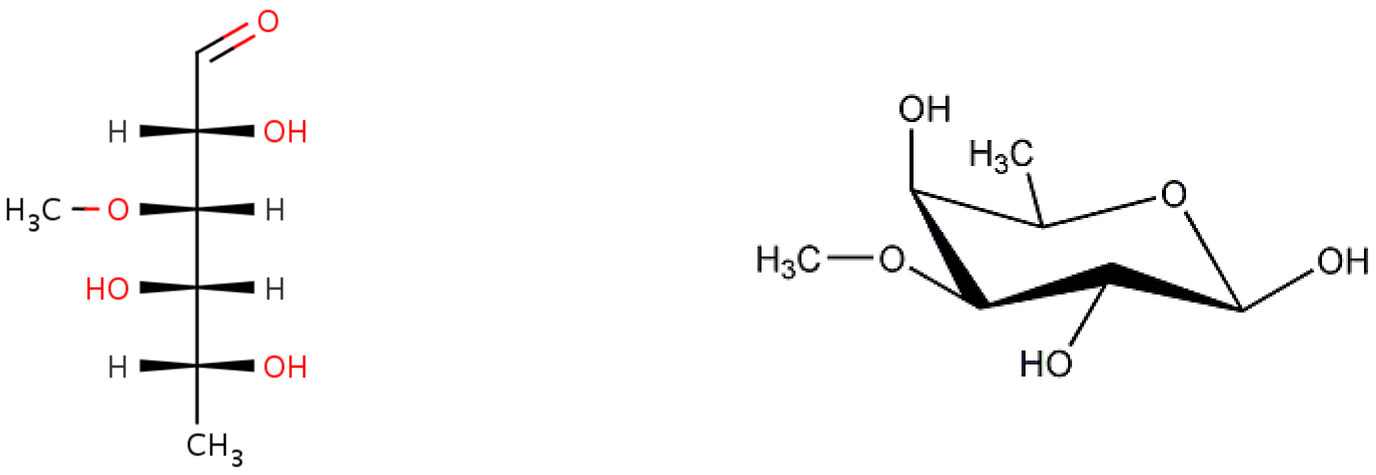
β-D-Fructofuranose



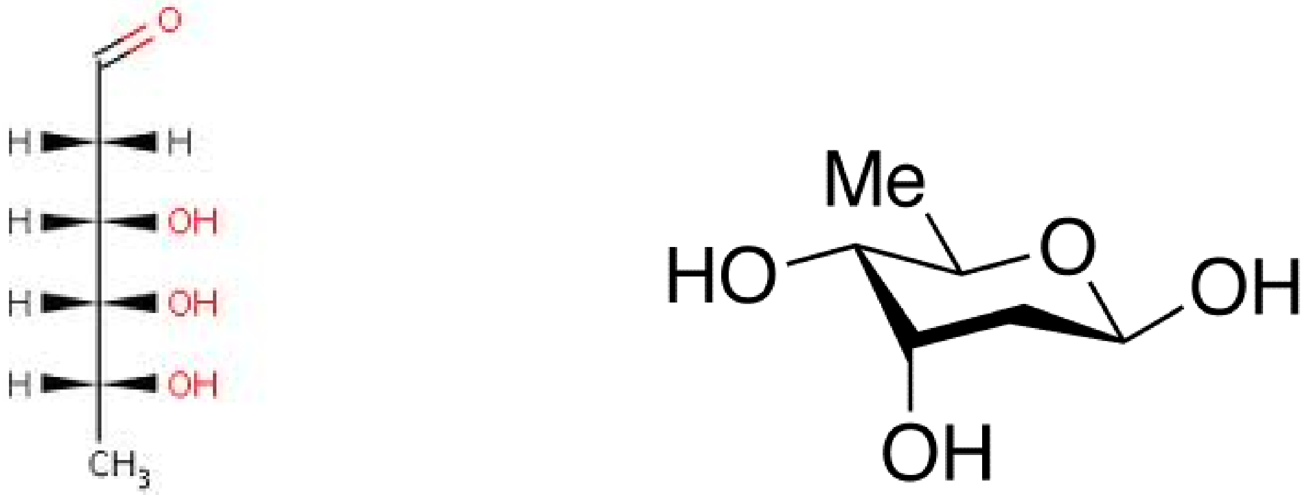
D-fructose

Deoxysugars : Except for 2-deoxyribose, which is ubiquitous as a DNA component, it is mostly in plants that sugars occur in which one or two alcohol functions have been eliminated by reduction; examples are 6-deoxyhexoses and 2,6-dideoxyhexoses.

Some deoxysugars are spesific to cardiotonic glycosides such as
L-thevetose (6-deoxy-3-O-methyl-L-glucose), D-digitalose (6-deoxy-3-O-methyl-D-galactose), D-digitoxose (2,6-dideoxy-D-allose) and
L-oleandrose (2,6-dideoxy3-O-methyl-L-rhamnose).

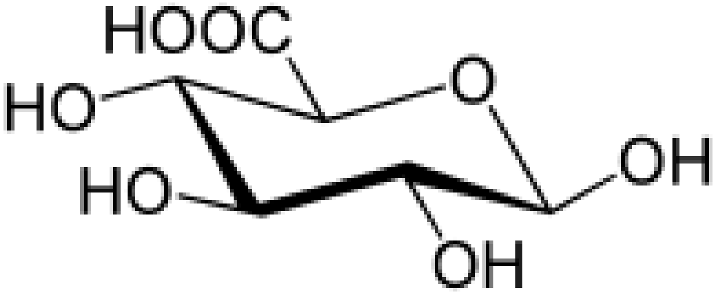


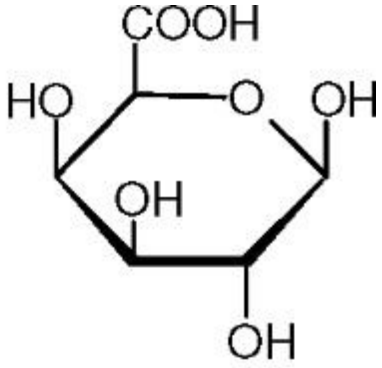
D-Digitalose



D-Digitoxose

Uronic acids : Uronic acids are the products of hexose oxidation by specific dehydrogenases in which the primary alcohol function is oxidized carboxylic acid. D-glucuronic acid and D-galacturonic acid are normal constituents of parietal polysaccharides (particularly pectin), of mucilages (e.g. Marsmallow), and of most polysaccharide-containing secrections (e.g. *Sterculia* gum)

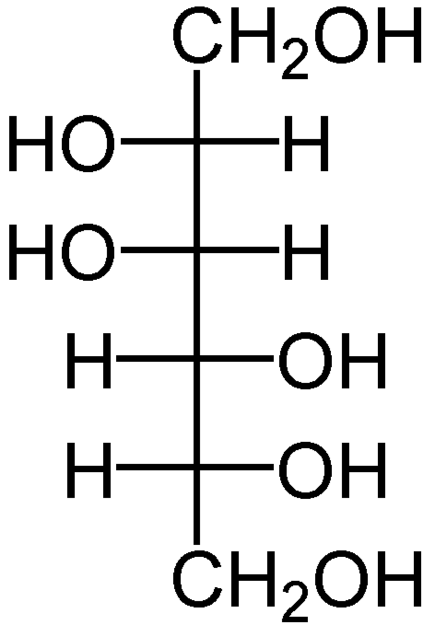




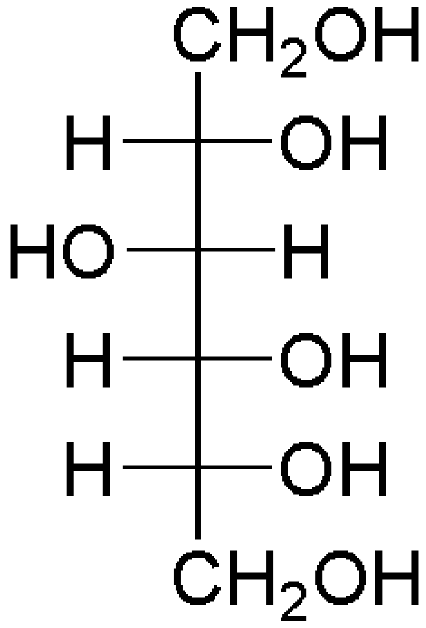
β-D-galacturonic acid

β-D-glucuronic acid

Polyalcohols : Polyalcohols result from the reduction of the carbonyl function of monosaccharides. D-glucitol=D-sorbitol, D-mannitol, and meso-galactiol are fairly widespread.



D-mannitol



D-sorbitol

Amino sugars : Amino sugars are fundamental constituents of bacterial polysaccharides. They are present in some fungi but rare in higher plants.

PRINCIPAL MONOSACCHARIDES USED IN PHARMACY

D-Glucose

Although it is present in substantial quantities in many plant species, glucose is not extracted for commercial use. It is prepared by enzimatic hydrolysis of starch through the combined action of α-amylase and aminoglucosidase.

Glucose is prepared for parenteral administration in aqueous solution. The indications for injectable solutions (at 5 and 10%) are : prevention of intra- and extracellular dehydration; common rehydration (when the water loss exceeds loss of sodium chloride and other electrolytes), prophylaxis and treatment of ketosis in malnutrition.

D-Fructose

Present in pratically all fruits, as well as in honey, D-fructose can be obtained industrially by hydrolizing inulin (a polymer characteristic of certain Asteraceae: Jerusalem artichoke and chicory,among others). It can be used for parenteral feding

MONOSACCHARIDE DERIVATIVES USED IN PHARMACY

D-Sorbitol=D-Glucitol

This polyalcohol occurs naturally in the fruit of various Rosaceae, particularly that of the mountain ash, *Sorbus aucuparia*, as well as in the thallus of certain seaweeds. Industrially, it is obtained by catalytic hydrogenetion under pressure or by electrolytic reduction of D-glucose.

Sorbus aucuparia

In therapeutics, sorbitol is used for its cholecystokinetic properties. It is indicated in the symptomatic treatment of constipation and used in the symptomatic treatment of dyspepsia. Contraindications include organic inflammatory colopathy, occlusion, and undiagnosed abdominal pain. It must not be combined with sodium polystyrene sulfonate (a resin that binds intestinal potassium and is used to treat hyperkalemia).

As a sweetener, sorbitol is used as a substitute for sucrose for diabetics. It is commonly used in pharmaceutical technology, to regulate the moisture content of powders, to stabilize texture in pastes, as a plasticizer for gelatin, and to retard the crystallization of sugars. It is also largely used in food technology.

D-mannitol

D-mannitol occurs naturally in the manna of manna ash, and in substantial quantities in the thallus of brown algae (laminaria). It is prepared industrially by the epimerization of D-glucose in alkaline medium, followed by catalytic or electrolytic reduction.

D-mannitol is not readily metabolized and is an osmotic diuretic by parenteral administration. It undergoes rapid glomerular filtration and practically no tubular reabsorption.

Uses : Mannitol is cholecystokinetic agent and a laxative. It is proposed for oral administration in the symptomatic treatment of dyspepsia (gastric dilation, impairment of digestion, nausea) and in the adjunctive therapy of constipation.

Contraindication : biliary tract obstruction. It can also be used for colon preparation before endoscopy , although it increases the risk of colon gases formation.

Fraxinus ornus **Oleaceae**

Manna

Dişbudak **Manna ash**

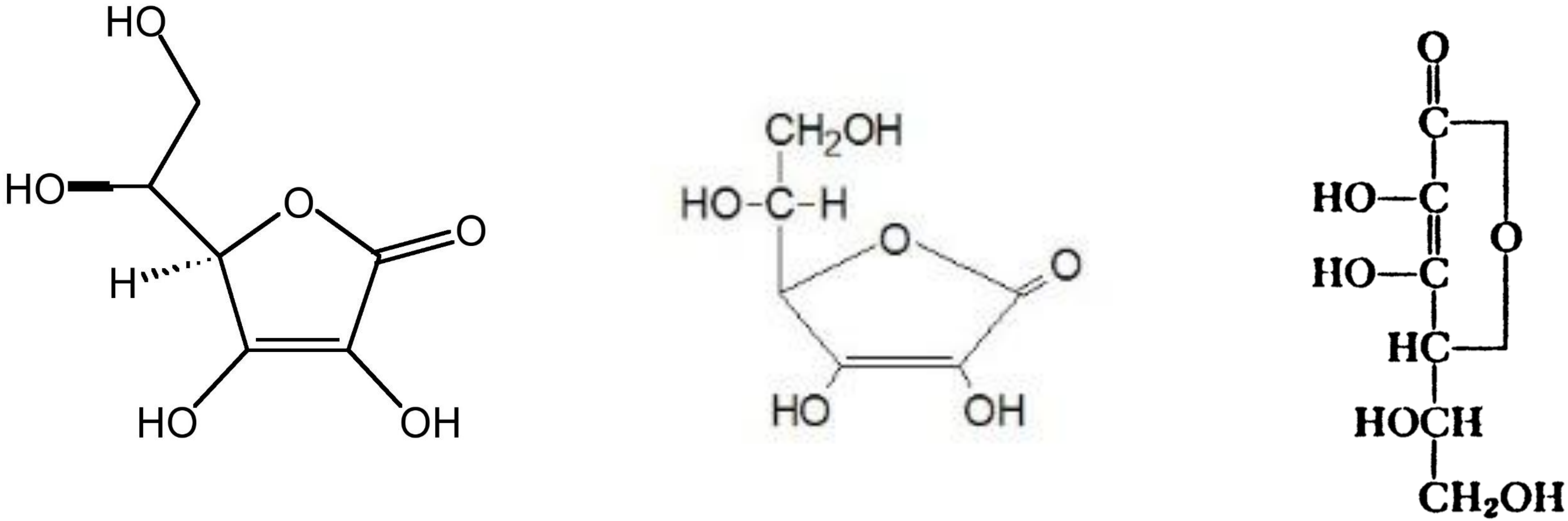
Following the incision of the bark during the warm and dry season an exudate appears : manna. This manna consist of irregular yellowish, and odorless fragments called flake manna, or tears, or sorts.

D-mannitol, the main constituent, occurs alongside D-glucose, D-fructose, and oligosaccharides. The dried exudate of manna ash is classified as a bulk laxative, therefore the phytopharmaceuticals that contain it may claim the following indication: symptomatic treatment of constipation.

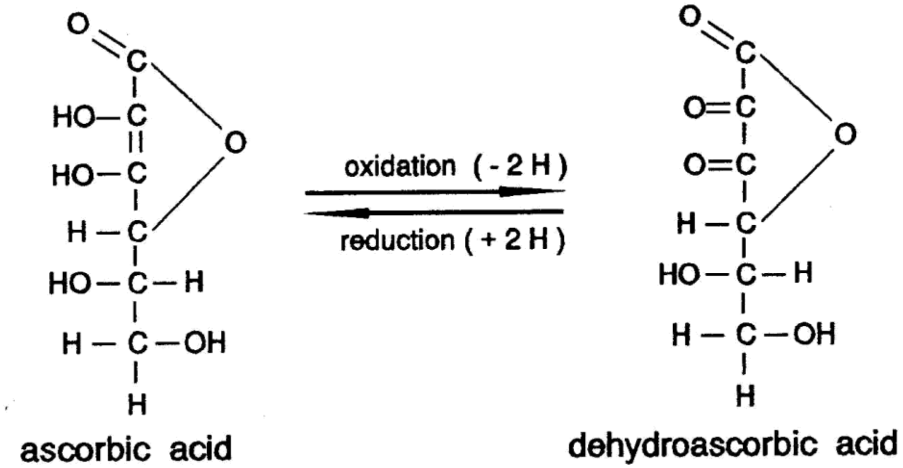
SUGAR DERIVATIVES : ASCORBIC ACID AND OTHER ACIDS

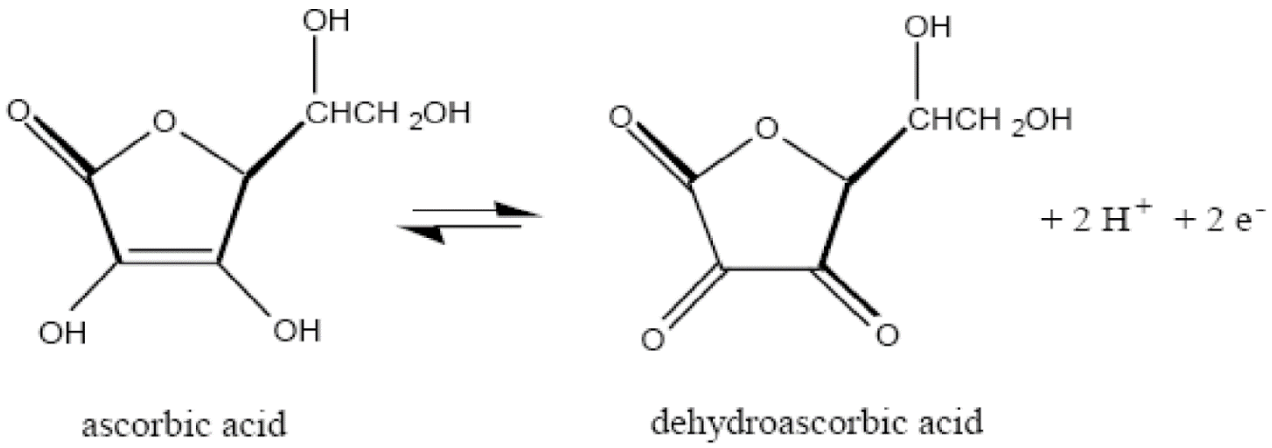
Vitamin C is L-(+)-threo-ascorbic acid. Biosynthetically, it arises -in plants- directly from D-glucose with conservation of the carbon chain sequence. The acidity of the molecule and its reducing character are linked to the fact that its enediol structure is easily oxidized to a bicyclic structure, dehydroascorbic acid.

Properties : Vitamin C can play a role in various oxoreduction reaction. Vitamin C is not synthesized by primates, therefore humans must obtain it from their diet (recommended intake : 80 mg/day).



Ascorbic acid


oxidation (- 2 H)
reduction (+ 2 H)
ascorbic acid
dehydroascorbic acid


ascorbic acid
dehydroascorbic acid
+ 2 H$^+$ + 2 e$^-$

Uses : Vitamin C is indicated at vitamin-like doses (10-50 mg/day) : 1. for the treatment of scurvy 2. for the prophylaxis of vitamin C deficiensis resulting from poorly balanced or insufficient nutrition. At high doses (0.5 g/day), it is used for the treatment of coryza-, flu-, and convalescence-related asthenia.

Ascorbic acid is present in large quantities in various fruits: sea buckthorn (*Hippophae rhamnoides*), kiwi (*Actinidia sinensis*), paprika (*Capsicum annuum*), acerola (*Malpighia punicifolia*). It is particularly abundant in rose hips (*Rosa canina*).

Rosa canina **Rosae caninae fructus** **Rose hips**

Rosaceae

Kuşburnu **Dog rose**

The drug –rose hips- consist of the ripe and dried receptacle cup, as well as the akenes within. It must contain not less than 0.2% ascorbic acid. Rose hips owe their color to carotenoids. They contain tannins, pectin, sugars and D-sorbitol. Vitamin C (up to 1.7%) occurs alongside malic acid and citric acid.

The German Commission E monographs includes a long list of the uses of the drug (treatment and prevention of influenza-type infections, infectious diseases, and vitamin C deficiencies, to facitilate digestion, for arthritis, as a diuretic, as an astringent, and so on)

Malpighia punicifolia
Acerola

Malpighiaceae

Malpighiae fructus
Aserola

Malpighia punicifolia is a bush growing in Central- and South America. The fruits seem like cherries and contain 100 times more ascorbic acid than orange fruits. Acerola is used for the treatment and prevention of influenza-type infections, infectious diseases, and vitamin C deficiencies.

Hibiscus sabdariffa

Hibiskus

Malvaceae

Hibisci sabdariffae flos

Red sorrel

The calyx and calyculus of this subtropical Malvaceae are boiled to prepare a refreshing beverage. The drug contains heterogeneous acidic polysaccharides and is rich in numerous phenolic compounds : 3-glycoside of gossipetine, anthocyanines. It is characterized by a high level of organic acids (15-30%): citric, malic, tartaric acids and the lactone of hydroxycitric acid.

Various properties are attributed to this drug, which seems to be spasmolytic,and by virtue of the presence of anthocyanins, may protect against angina pectoris.

Tamarindus indica

Demirhindi

Caesalpiniaceae

Tamarindi fructus

Tamarind

The pulp of the fruit is reddish-brown, has a mild sweet taste, and is rich in pectins and monosaccharides (20-40%). It also contains 10-15% organic acids such as tartaric acid, malic acid, and citric acid, in the free state and as salts (the main component is potassium hydrogen tartrate).

The commercial «gum» is obtained by crushing the endosperm after elimination of the teguments by treating with heat and pounding. Tamarind gum is used by various non-food industries for its ability to form viscous solutions with pseudoplastic behavior. The cosmetic industry uses polysaccharide fractions from the seed to «stimulate to repair of damaged skin».

Oligosaccharides

Oligosaccharides result from the consideration of two to ten monosaccharide molecules by formation, between successive pairs, of a glycosidic linkage.

DISACCHARIDES

The type of glycosidic linkage allows a distinction to be made between non-reducing disaccarides (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→1)- α-D-glucopyranoside), a non-reducting 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→4)- α-D-glucopyranoside) and cellobiose (β-D-glucopyranosyl-(1→4)- α-D-glucopyranoside) arise from the degradation of starch and cellulose, respectively.

Sucrose, Sucrose-containing Drugs

Sucrose (α-D-glucopyranosyl-(1→2)- β -D-fructofuranoside) is **a non-reducing disaccharide**. It can be obtained from sugar mapple, *Acer saccharum*, a tree native to the eastern part of the North American continent. It is also one of the date palm, *Phoenix dactylifera*. Its two major industrial sources sugar cane, *Saccharum officinarum* and the sugar beet, *Beta vulgaris*, and it has been produced industrially from the sugar beet since the beginning of the 19. century.

Sucrose is used as expicient for tablets and other forms for oral administration, and for the manufacture of syrups. The pharmaceutical industry uses a sucrose modified physically, with or without maltodextrin addition to tender it directly compressible.

Acer saccharum

Phoenix dactylifera

Beta vulgaris **Betae radix**

Şeker pancarı **Sugar beet** **Chenopodiaceae**

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 sucrose crystallizes in successive batches with the final residue constituing molasses. The industry also prepares liquid sugar, invert liquid sugar and invert sugar syrup.

Saccharum officinarum **Sacchari officinari corpi (stem, gövde)**

Şeker kamışı **sugar cane** **Poaceae**

The crushed stems afford a juice (press juice), which after being freed of proteins and naturalized (liming) filtered, decolorized, and concentrated, yields crystallizied raw sucrose (crystallized brown sugar). This sugar can be «rafined» by stirring in concentrated syrup, recovering in a centrifuge, dissolving, concentrating, and crystallizing.

DISACCHARIDE DERIVATIVES

- **Sucrose esters** (Olestra®)
- **Maltitol** (maltitol syrup = Lycasin®
- Isomalt
- The synthetic disaccharide **lactulose** (= β-D-galactopyranosyl-(1→4)-D-fructofuranoside)
- **Lactitol** = The catalytic hydrogenation product of lactulose

OLIGOSACCHARIDES : Higher oligosaccharides (3 to 10 sugars) represent storage forms specific limited species or plant groups, and this explains their interest for chemico-taxonomist. The most common storage oligasaccharides are the nonreducting galactosyl derivatives of sucrose. Like other storage forms, they are primarily stocked in seeds and underground organs.

CYCLODEXTRINS : Cyclodextrins are cyclic oligosaccharides produced by the enzymatic degradation of starch.
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).

POLYSACCHARIDES

Polysaccharides (or glycans) are arbitrarily defined as high-molecular weight polymers resulting from the condensation of a large number of monosaccharide molecules. Each sugar is linked to its neighbor through a glycosidic linkage formed by a theoretical elimination of a water molecule between the hemiacetal hydroxyl group on C-1 of one sugar and any of the hydroxyl groups on the other sugar molecule. They are responsible for the rigidity of cell walls in higher plants (or on the contrary for the flexibility of the thallus of algae), or they are energy storage forms (starch and other polysaccharides in plants, and also glycogen in animals).

STRUCTURE OF POLYSACCHARIDES : homogeneous polysaccharides can be distinguished, resulting from the condensation of a large number of molecules of the same sugar, from heterogenous polysaccharides, which result from the condensation of molecules of different types of sugars.

The following are classically distinguished :

- if β-(1→4), the shape is very elongated ribbon (e.g., cellulose)
- if α-(1→4), the polymer may adopt a helical shape (e.g.,amylose)

BEHAVIOR OF POLYSACCHARIDES : GEL FORMATION : Many polisaccharides are characterized by their ability to form gels, that is solid three-dimensional macromolecular arrays that retain the liquid phase within their lattice. Gel formation is, in a way, the passage from disorder (a true solution) to a certain order created by the partial association of chains or of segments of a chain.

ISOLATION : Polysaccharides dissolve in water, possibly in the presence of mineral acids (as for pectin extraction) or of various salts (carbonates in the case of algin). In the laboratory, aprotic dipolar solvents can also be used. The elimination of salts and of low molecular-weight molecules can be done by dialysis, by using ion exchange resins, by molecular gel filtration or by extraction (for example, elimination of oligasaccharides and pigments by ethanol or acetone).

Polisaccharides from microorganisms and fungi

DEXTRANS : Dextrans are glucose polymers or glucans made of α-D-glucopyranosyl residues linked 1→6. These molecules are more or less branched, of high molecular weight (40-50 x 10^6), and synthesized by an exocellular enzyme present in various bacteria of the genera *Leuconostoc, Lactobacillus*, and *Streptococcus*.

Production : Commercial dextran is a polymer containing about 95% α-D-(1→6) and 5% α-D-(1→3) involved exclusively in lateral branching. Its production involves selected strains of *Leuconostoc mesenteroides,* cultivated on sucrose-rich media. Upon completion of the culture, ethanol is added to precipitate the polymer. Because the molecular weight is still quite high, a partial hydrolysis follows to dispose of polymers of 40.000 to 75.000 molecular weight.

This partial depolymerization can be done in acidic medium, by fungal enzymes, or by ultrasonic treatment. After deionization, precipitation with acetone, and recrystallization, «medical dextran» is obtained. **Uses** : Dextrans (of average molecular weight 60.000 [Dextran 60] in solution or of molecular weight 40.000 [Dextran 40] at 3.5 or 10%) are administered intravenously (infusion). **The viscosity and osmolarity of these solutions are close to those of plasma.** Dextran is non toxic, serologically neutral, of prolonged action and completely eliminated. It is a plasma substitute used for the following indications : for plasma volume expansion in shock due to hemorrhage, trauma, and toxiinfection; for preoperative hemodilution.Because it interferes with hemostasis, the maximum dose is set at 1.5 g/kg/day of dextran, or 20 mL/kg.

Dextran 40 has similar indications. Hypersensitivity reactions are rather but always possible, thus the infusion must begin very slowly. Dextran is also used for the formulation of eye drops indicated for the symptomatic treatment of lacrymal insuffiency and designed to improve the comfort of contact lens bearers, by mantaning a lubricating film on the cornea. Dextranomer (INN) is used for mechanical cleansing of wounds through absorption of exudates and tissue debris, for example from wet wounds and with or without infection, such as decubitus eschars or leg ulcers due to venous stasis.

XANTHAN GUM

Origin and preparation : *Xanthomonas campestris* is a bacterium which commonly develops on certain species of Brassicaceae where by using the vegetable substrate, it produces a gummy exudate : **xanthan gum**.

Industrially this gum is produced by bacterial culture on correctly buffered and aereted media containing carbohydrates, a source of nitrogen, and minerals. Upon completion of fermentation, the polymer is recovered by precipitation with isopropanol, filtered, dried and crushed.

Structure : On a backbone similar to that of cellulose (D-glucopyranoses linked β-(1→4)), trisaccharides from branches from the 3-position of the glucose units.

Properties : Soluble in hot and cold water, xantham gum forms aqueous solutions of which the viscosity remains practically unchanged by temperature changes, as well as pH changes.

Uses : A first-choice stabilizer for the formulation of suspensions and emultions, xantham gum is highly prized for the pseudoplasticity of its solutions and its global market is growing rapidly.

Lentinan

Lentinan is a homogenous polymer isolated from a fungus *Lentinus edoles*. Structuraly, it is a glucan containing a principal chain with β-(1→3), linkages, substituded by (1→6) linked glucoses, and of the molecular weight around 500.000. The antitumor properties of lentinan, demonstrated on several experimental models, seem to be due not to any cytotoxic properties, but to an immunogenic activity.

Lentinus edoles

Algal Polysaccharides

Economic Interest of Seaweeds

The main economic interst of seaweeds is that they are an important source of polysaccharides with thickening and gelling properties : **alginates, carrageenans**, and **agar** mostly for use in food technology, and also in pharmacy.

ALGINIC ACID, ALGINATES

According to the 3. edition of the European Pharmacopoeia, alginic acid is a «mixture of polyuronic acids obtained mainly from algae belonging to the Phaeophyceae, it contains not less than 19.0% and not more than 25.0% of carboxyl groups, calculated with reference to the dried substance».

Sources of Alginic Acid : Alginic acid is a virtually constant constituent of Phaeophyceae. *Laminaria* and *Fucus* (Brown algae) are the principal genera currently used for the industrial preparation of alginic acid and alginates.

Fucus **Kelp**

Fucus serratus, Fucus vesiculosus **Fucaceae**

Fucus serratus ***Fucus vesiculosus***

These perennial seaweeds are abundant on the coasts of temparate and cold seas of the northern hemisphere. In the English Channel, they colonize intertidal zone, which extends from the highest wave-splashed rocks down to levels uncovered only by lowest tides.

Alginic Acid Structure : Alginic acid is a linear polymer constructed from two uronic acids, D-mannuronic acid (=M) and L-guluronic acid (=G). The linkage between monomers is of the β-(1→4) type. These acids are present in the polymer under the form of homogeneous poly-M or poly-G blocks separated by regions where they may alternate (G-M-G-M…). In the native state, alginates ocur as mixed salts (Na^+, Mg^+, Ca^{2+}), which must in part be linked to fucans.

Preparation of Alginic Acid and Alginates : Because of a marked poly anionic character, alginic acid is insoluble in water and can form salts: soluble sodium, potassium or ammonium salts, and insoluble calcium salts.

Extraction of the fragmented or crushed thalluses generally begins with a deionized acidified water wash which eliminates soluble mineral salts and sugars. It continues by maceration and stirring of the thallus fragments in hot aqueous alkaline (50° C, sodium carbonte), which solubilizes alginic acid. After filtration and elimination of residues, calcium alginate is prepared by adding a calcium chloride solution to the filtrate : the deodorized precipitate is recovered and can be purified by redissolution and precipitation as alginic acid.

Alginic acid can also be isolated directly by acidifying the alkaline solution : the polymer loses solubility and the carbon dioxide that is formed carries it to the surface.

Properties : Alginates of monovalent cations, and of magnesium, dissolve in water, forming viscous colloidal solutions with pseudoplastic behavior at low concentrations. Progressive adition of divalent cations (calcium) causes the thermally irreversible formation of an elastic gel : the guluronic units with pleated conformation retain calcium ions by coordination, in cooperation with a parallel chain.

Uses of Alginates

In Pharmacy : Alginates and alginic acid are used in digestive pathology. As a general rule they are combined with sodium bicarbonate and with aluminium hydroxide and taken after meals. Gastric acidity frees alginic acid which forms a foamy gel (carbon dioxide is released from bicarbonate) and places a floating barrier over the gastric content. Reflux is limited, if it should occur and the gel protects the mucosa of the esophagus against aggression by the gastric juice. Accordingly, these polysaccharides are incorporated into preparations for the symptomatic treatment of disturbances due to pathogenic acidity : reflux and other esophagitis, hiatal hernias and pyrosis.

The sodium salt of β-poly-D-mannuronic acid is proposed as an adjunct in resrictive diets for the treatment of obesity.

Calcium alginate is also commercialized in the form of hemostatic wool or gauze : upon contact with blood and exudates, alginate forms a fibrillate gel, thus causing a rapid hemostasis.

In pharmaceutical technology, alginates are valued for their thickening, binding (stabilization of emultions, suspensions, and more), and disintegrating properties (tablet formulations); they are also used for slow-release formulations and formulations resistant to gastric acidity (capsules with enteric coating).

Laminaria **Laminarya**

Laminaria digitata, Laminaria hyperborea

Laminariaceae

Laminarias are abundant on the coast of the English Channel where they occupy the subtidal zone, between the low tide and a depth of about twenty meters. They are harvested mechanically on the coast Brittany and constitute the bulk of the raw material consumed by the colloid industry.

CARRAGEENANS

Carrageenans, often referred to as carrageenates, are obtained from various Rhodophyceae seaweeds from the Gigartinaceae, Solieraceae, Hypneaceae, and Furcellaiaceae families after treatment with hot water and precipitation by ethanol, methanol, 2-propanol or potassium chloride; they must contain not less than 15% and not more than 40% sulfur, expressed as sulfates.

Chondrus

Chondrus crispus

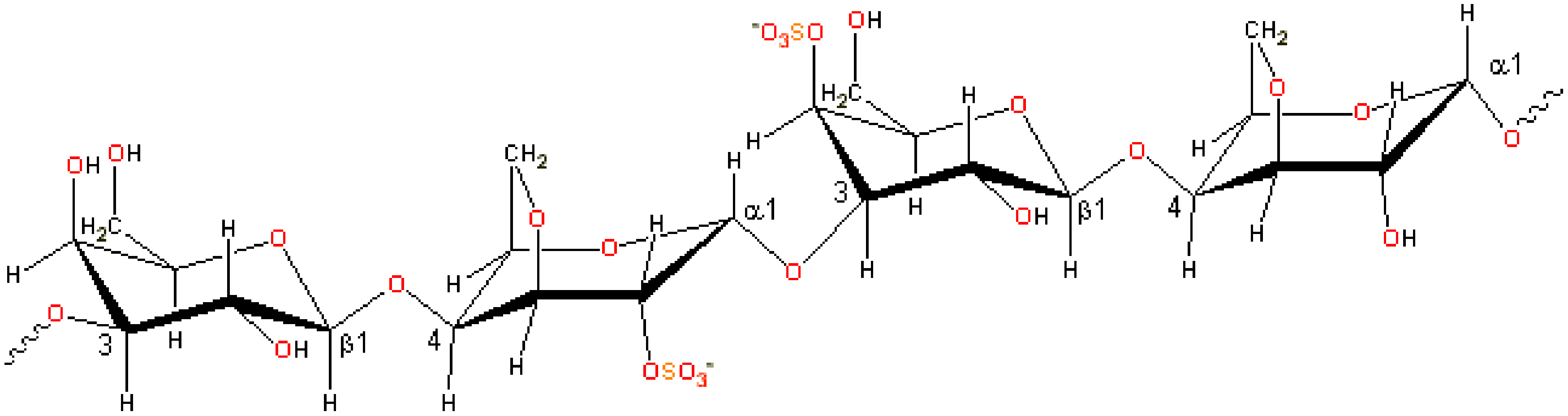
Gigartinaceae

This seaweed, also known as Irish moss, is a small species, with a ramified thallus. It grows affixed to rocks on the coasts of the Atlantic Ocean and of the English Channel, where it can be harvested manually. This species can also be cultivated in basins.

Structure of Carrageenans : Carrageenans are galactans or polymers of D-galactose, are heavily sulfated, and are anions with multiple electrolytes of molecular weight ranging from 10^5 to 10^6. All carrageenans have a linear structure of the $(AB)_n$ type, with alternating 1→3 and 1→4 bonds, types of carrageenans are distinguished as these repeating units : (ι,k, λ, μ, ν, θ,ξ).

Properties of Carrageenans : Gel forming capability and the properties of the resulting gels depend on the structure of the carrageenan.

I and k carrageenans dissolve readily in warm water. λ - carrageenan solutions do not gel. Carrageenans interact with galactomannans which reinforce gel cohesion. They also interact with proteins, particularly those of milk which they form specific ionic interactions. They have few incompabilities (gelatin in acidic medium, quaternary ammonium salts) and their gel stability is good.



General carrageenan structure

Preparation of Carrageenans :

Although the principle of the extraction in simple, its technological inplementation demands substantial know-how. After a wash that eliminates debris and minerals, the seaweeds are extracted by slightly alkaline warm water. The residual thalluses, filtered under pressure, are discarded. The supernatant is partially concentrated and an alcohol is added (for example 2-propanol) to precipitate the polysaccharide. Carrageenans are wrung, dried, and milled. If necessary, carrageenan can be fractionated (in the laboratory) by selective precipitation of k carrageenan by potassium chloride, leaving λ fraction in solution.

Uses of carrageenans :

The pharmaceutical industry takes advantage of the properties of the gels for applications in pharmaceutical technology (e.g., formulations of pastes, creams and emulsions), as well as for therapeutic or diabetic applications : symptomatic treatment of constipation, protection of mucosae in proctology, use as an adjunct in restrictive diets. Carrageenans also enter in the formulation of hygiene and cosmetic products : toothpastes, shampoos, ointments, creams, gels , lotions etc.

AGAR (Gelose)

According to the 3rd edition of the European Pharmacopoeia, agar consist of the polysaccharides from various species of Rhodophyceae mainly belonging to the genus *Gelidium*. It is prepared by treating the algae with boiling water, the extract is filtered whilst hot, concentrated and dried.

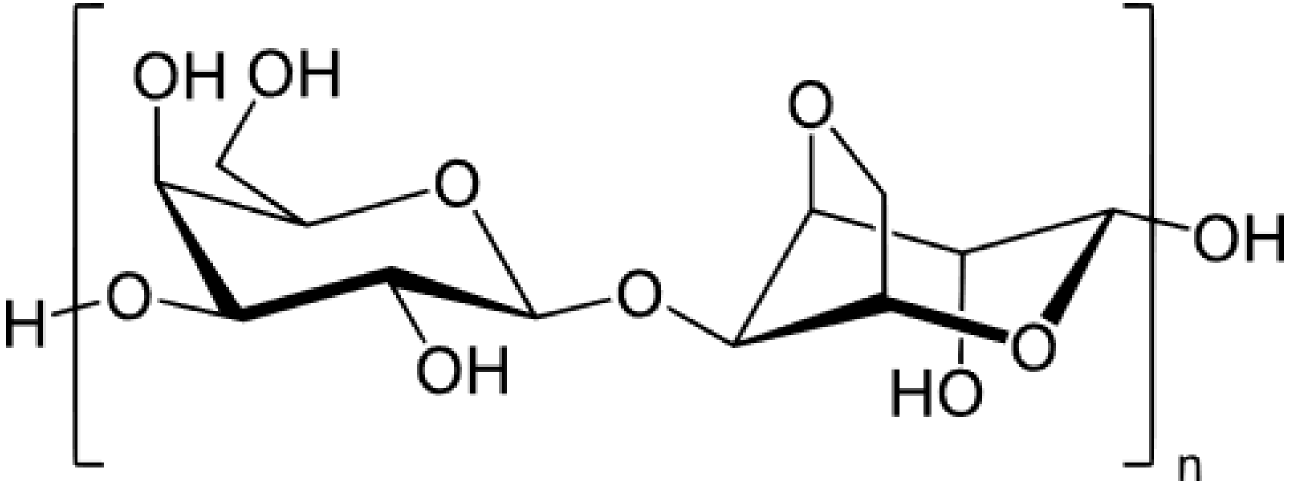
Sources of Agar : Like carrageenans, agar is extracted from thalluses of various Rhodophyceae, especially red algae (*Gelidium corneum, Gelidium amansii, Gracilaria confervoides, Gracilaria lichenoides*, as well as a few species of the genera *Gelidiella* or *Pterocladia*.

Gelidium amansii

Gracilaria lichenoides

Structure of Agar : This polysaccharide is a complex galactan, formerly considered to be a mixture of two fractions, agarose and agaropectin. The major part, agarose is a barely sulfated linear polymer, constructed as a linear structure of the $(AB)_n$ type with alternate 1→3 and 1→4 bonds, where the A units are partially methylated D-galactoses and the B units are enantiomers of galactose, almost always of the 3,6-anhydro-L-galactose type.

Agar consist of colorless to pale yellow, translucent and resilient ribbons or flakes. Agar dissolves in hot water and forms thick gels upon cooling. It cannot be assimilated, will not ferment, and is non toxic, thus it is a mechanical laxative because it increases the bulk and hydration of feces, and makes transit regular. A classic culture medium in bacteriology, agar can be used for the in vitro production of plants.



Agarose

Homogeneous Polysaccharides

STARCH

The main reserve substance in plants, starch is an energy source indispensable humans and countless animals. Present in all vegetable organs, it is concentrated preferentially in the following:

- In the seeds of cereals (oats, wheat, corn ,rice, rye…)
- In fruits : breadfruit (*Artocarpus communis*), plantain (*Musa paradisiaca*)
- In the subterranean parts : potato, manihot..

Starch-Producing Cereals

WHEAT (*Triticum* sp) BUĞDAY RICE (*Oryza* sp) PİRİNÇ
CORN (*Zea mays*) MISIR Poaceae

Triticum aestivum

Oryza sativa

Zea mays

These extensively cultivated plants are of interest to pharmacy for their starch, and also for their lipidic fraction (wheat germ oil, official corn oil), for their fibers (wheat bran) or their fiber content (brown rice), for gluten or zein (tablet coatings), for the unsaponifiable matter of corn oil (proposed for the treatment of periodontitis), for corn styles (traditionally used to enhance the renal and digestive elimination functions,to faciliate the renal elimination of water, and as an adjunct in weight loss diets), and for the transformation products of starch : dextrins, sugars, polyalcohols, and by-products that are raw materials for fermentation or for chemical industry.

Starches from Tubers and Rhizomes

Potato

Solanum tuberosum

Patates

Solanaceae

Manihot **Manihot**

Manihot esculenta **Euphorbiaceae**

Potato tubers constitute, after corn, the second worlwide source of starch. The rusping of tubers and successive washings yield a starch slurry. Enzyme enriched potato starch gives a gel of texture comparable to that of fats.

Manihot is a major starch-containing food of tropical zones of the globe on all continents. After peeling, chopping, and rosting-which substantially decreases the cyanogenic glycoside content- it is used to prepare main dishes.

Production of Starch

Starch is chiefly extracted from corn and from potato tubers and secondarily from wheat.

Corn starch is prepared as follows (wet process) : After elimination of impurities by sifting and ventilating, the grain is softened by steeping for 30 to 48 hours in water brought to 50°C with sulfur dioxide in the cattle field market added. The steepwater, loaded with proteins, soluble carbohydrates, lactic acid, vitamins, and minerals, is recovered : it will serve as the basis of the composition of culture media for industrial fermentation such as antibiotic production by microorganisms (corn steep liquor). The excess, mixed with hulls, finds an outlet in the cattle feed market (corn gluten feed).

Milling degermination of the softened grain in aqueous medium allows the elimination based on differences in density, of the germs, which are the source of an oil of dietery interest. The residual pasty mix, composed of germ-free grain fragments, it is finely milled; after sieving, centrifuging separates proteins (corn gluten) and starch.

At this stage, starch is in a milky suspension on starch slurry. The poor conservation of this form and the cost of its transportation explain why the major part of the product is immediately transformed on site. The remainder is dried. One quintal of corn produces around 63 kg of starch.

Starchs are identified by their ability to form colloidal solutions and colored **deep blue** in the presence of iodine.

Structure and Composition : Amylose and Amylopectin

The saccharide fraction of starch is a mixture of two polymers : amylose, which is essentially linear, and amylopectin, a ramified molecule. Starches are clearly differentiated by their respective amylose content (16-17% in rice, 20% in the potato, 25-28 wheat, and 60-65% corn)

Amylose consists of D-glucose units exclusively by α-(1→4) bonds. Note the existence of a small number of short α-(1→6) branched chains.

Amylopectin,the major constituent of starches, is one of the largest known polysaccharides, as its molecular weight can reach, in certain cultivars,10^7 to 10^8. Its structure is ramified into a three-like shape : linear α-(1→4) chains of 15 to over 60 units, following a trimodal distribution, are grafted to one another by α-(1→6) linkages that represent about 5-6% of all bonds.

Uses of Starches

In pharmacy, the main use of starches and derivatives is as adjuncts in tablet formulation : diluents, binders, desintegrants, anticaking agents. Starch is also a starting material for the reaction that yields dextrins and cyclodextrins, polyalcohols, gluconates, and more generally, bio-industrial products (e.g., fermentation, xanthan gum production).

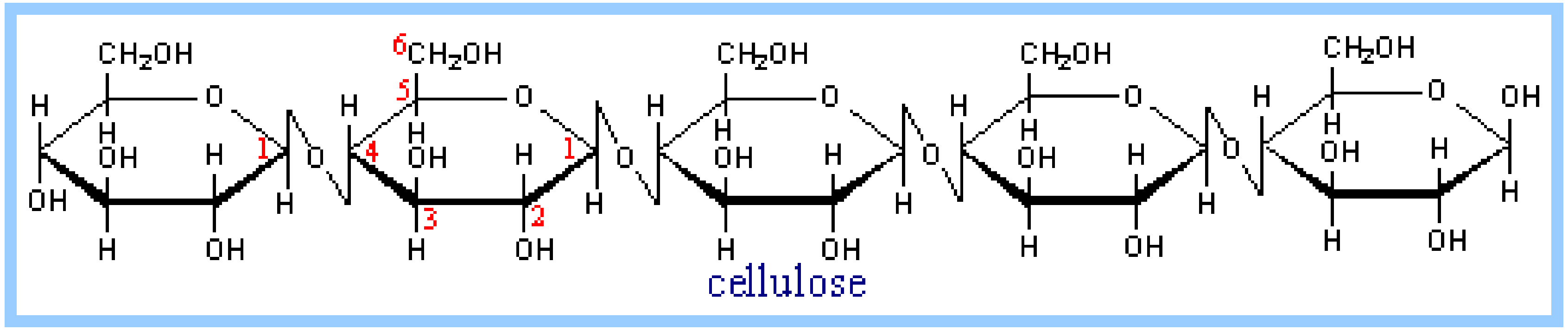
Besides multiple uses in food technology, starches find innumerable applications in other sectors : paper production, the textile industry, glues and adhesives, water and ore treatment, drilling and more

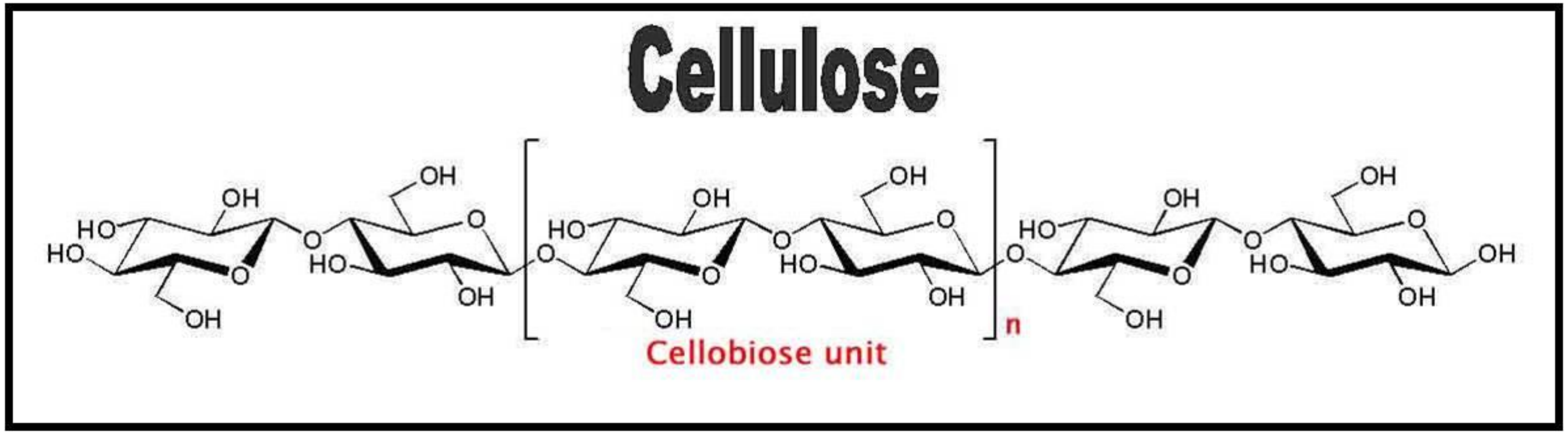
CELLULOSE

Sources and Structure

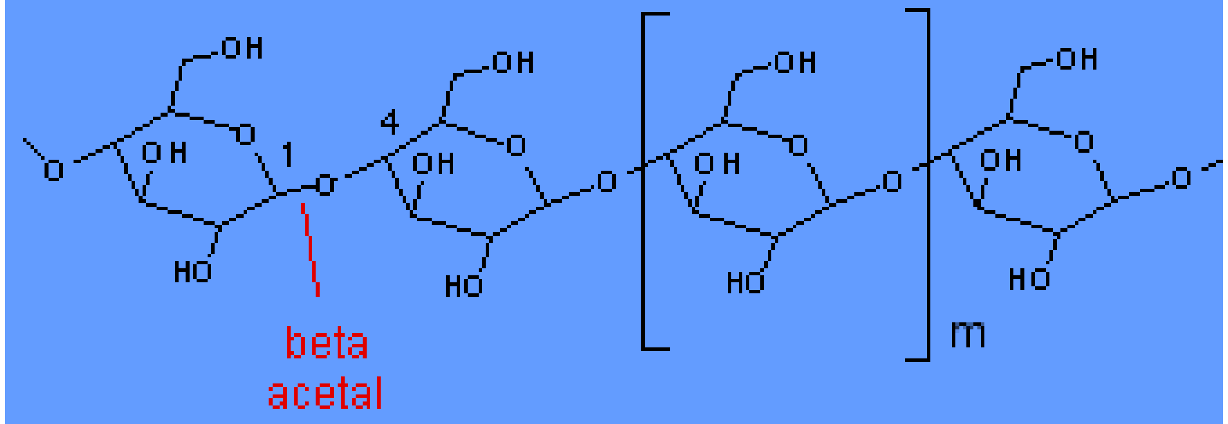
Cellulose is undoubtedly the most universal biological polymer. The cellulose currently used comes from delignifying wood in acetic acid or alkaline medium (for the paper industry) and from cotton linters (for the chemical industry), degradation products of straw can also be used. Cotton fiber is used directly by the textile industry. Other processes, currently being developed as pilot experiments, allow recovery of cellulose and other wood constituents (hemicellulose, lignin). Such in the case of extraction by hot methanol followed by methanolic sodium hydroxide treatment, and of the explosion process, very brief treatment by water vapor at 200-250^{o}C under 35-40 bar pressure followed by brutal return to normal pressure. This process yields a good quality of cellulose.

Structure : Cellulose is a linear polymer, made of β-(1→4) linked D-glucose units.





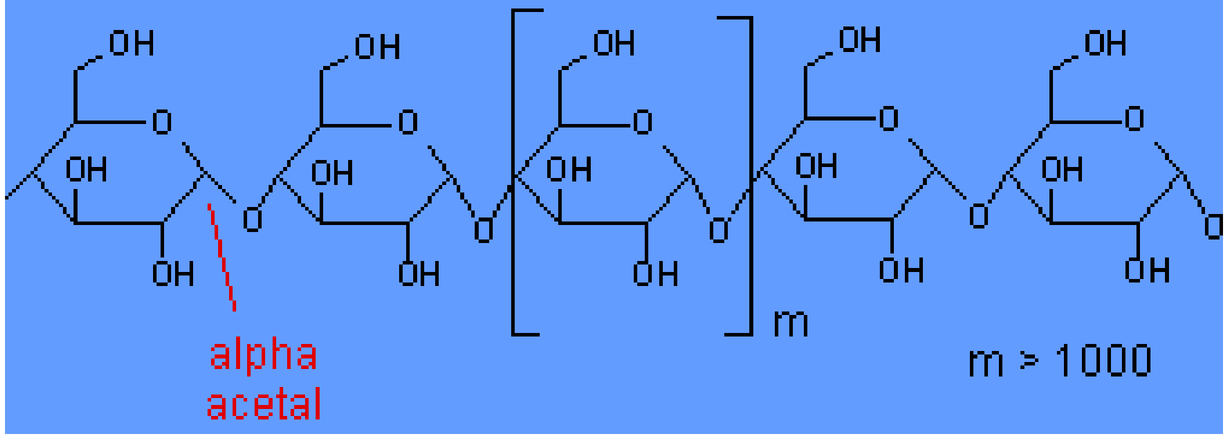
Cellulose



beta acetal

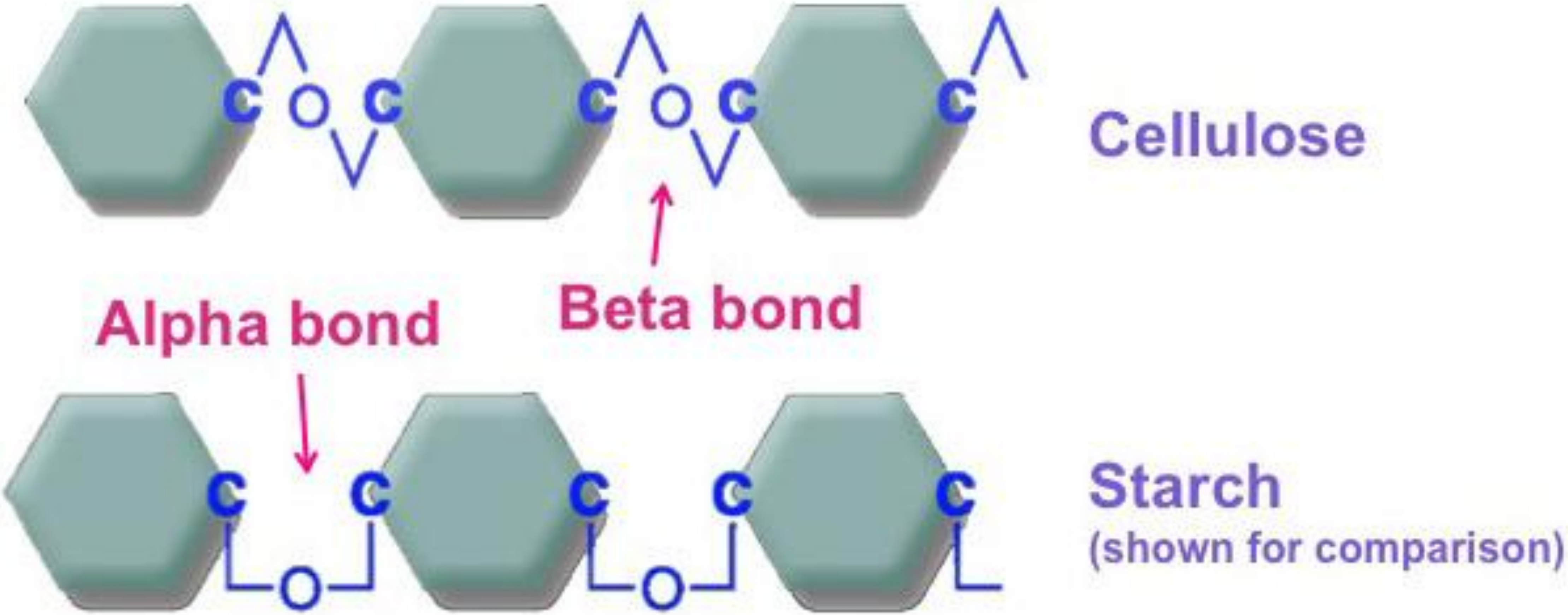
m = 2000 -26,000

Starch



alpha acetal

m > 1000


C
O
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C
Cellulose
Beta bond
Alpha bond
C
C
C
C
C
O
O
Starch
(shown for comparison)

Cotton Pamuk
Gossypium herbaceum G. hirsutum, G. barbadense
Malvaceae

Gossypium hirsutum

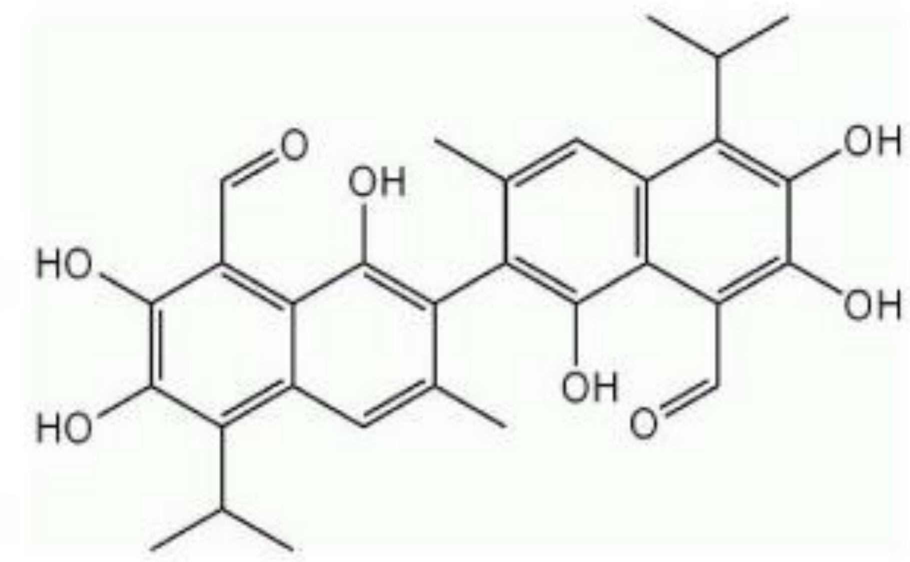
Gossypium herbaceum

Cotton plants : The different breeds and varieties of cotton plants currently cultivated belong to four species : two Asian diploid ones with thick and short fibers (*Gossypium arboretum, G. herbaceum*) and two American tetraploid ones (*G. hirsutum* with medium fibers and *G. barbadense* with long fibers).

Fibers : They arise at the surface of the seed and may be accompanied by a short hair down. The fiber color is white, creamy, light brown, or sometimes greenish. They are very elongated (the lenght varies from 15 to 40 mm), have a thin wall covered by a waxy cuticle, and are folded several times within the capellate volume. Chemically, the fiber is composed of cellulose (95-99%), proteins, waxes, and pectins.

Cellulose powder is used as a pharmaceutical aid, as a self binding tablet diluent and disintegrant is compression, and as stabilizer for suspensions.

The cottonseed oil contains gossypol, an infertility agent, and it must be eliminated from the oil.



Gossypol

DIETARY FIBERS

The phrase «dietary fibers», universally adopted by nutritionists and dieticians, is difficult to define, since it represents a nutritional and physiological concept, rather than a defined category of chemical substances.

The current tendency is to classify dietary fibers according to their solubility in water : insoluble fibers (e.g., cellulose) and soluble fibers.

The concept of soluble fiber includes complex polysaccharides such as pectins (which are glycogalacturonans) and other hydrocolloids capable of forming viscous solutions or gels (e.g., guar galactomannans, plantain heteroxylans).

Fiber intake in a normal diet comes chiefly from the cell walls of the vegetables that are part of our nutrition : fruits, vegetables, and various seeds and cereal products.

Main Constituents of Dietary Fibers of Parietal Origin

a- Polysaccharides

- cellulose
- pectins
- hemicelluloses : xylans, xyloglucans, glucuronoxylans…

b- Lignin : heteropolymers formed of phenylpropane units

c- Other elements :glycoproteins, hydroxyproline

Wheat bran : Wheat bran represents approxymately 18% of the weight of the caryopsis. Bran corresponds to the envelopes of the fruit and to the fraction of the kernel that milling does not manage to detach. Although it is rich in minerals (potassium, phosphorus as phytate, magnesium, and more) and in fibers (45% on average), it also contains proteins (17%), starch (15-20%) and carbohydrates (7-8%) : the caloric intake is far from nil.

Biological Effects on Dietary Fibers

Since the composition of fibers varies, they do not all have the same biological value, and it is very difficult to establish a precise relationship between the composition of fibers and the biological properties that are attributed to them.

Three groups of effects can be distinguished for dietary fibers : the action on intestinal transit, the suspected effect on the frequency of colorectal cancers, and the metabolic activity.

Action on intestinal Transit : There is a dual effect. First there is an effect on the bulk of feces which is often increased in substantial proportions (127% after ingestion of 20 g of wheat bran). This action takes place especially with insoluble fibers and seems linked, among other things, to the capacity of the fraction of the fibers that is not degraded in the colon to absorb water and to fiber size.

Uses of Dietary Fibers

Usage forms : Bakery flours are very poor in fiber, especially because the extraction % is low. There exist on the market, however, flours with high extraction yield (whole grain breads) and bran enriched flours (bran bakery products).

The forms most often used in dietetics are, some breads and fiber-enriched cookie products (cakes, tea cakes). Also used are pharmaceutical forms, for example granulated forms and tablets.

Indications : The main use is for normalization of intestinal transit. Cereal fibers (coarse bran), which absorb much water and will not ferment, seem preferable to soluble fibers that sometimes cause flatulence : they may be taken as 10-20 g/day in two or three servings with sufficient water intake.

Fiber based products are also used in weight loss diets : fibers do not partipiciate in providing energy and, while diluting the ingested nutrients, they permit the feeling of satiation sooner.

Other uses are in diets, particularly in diabetics : fibers are then frequently associated with a low-calorie diet where the major part of the energetic intake is covered by polysaccharides of starch type.

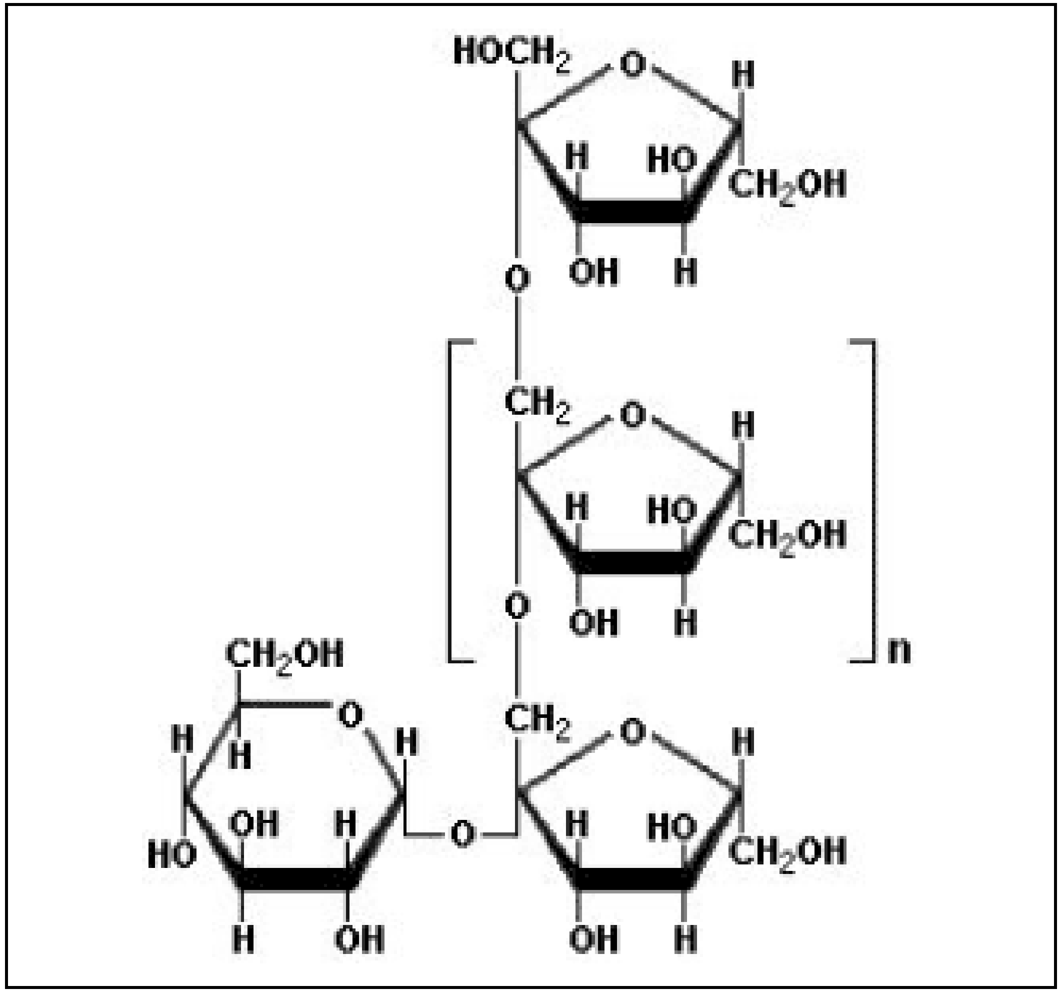
The daily fiber intake is 20-25 g in most industrialized countries, whereas it appears desirable to bring it to 35 g.

FRUCTANS

Fructans are fructose polymers linked by a β-(2→1) bond to a terminal glucose molecule : they can be considered as higher homologs of sucrose.

Especially inulin-type fructans are important. They can be found in Asteraceae and Boraginaceae, and they are concentrated in subterranean organs (roots, bulbs, tubers, and rhizomes) and their content, which varies with the seasons, can be substantial (50% and more).

In the inulin type fructans, the basic unit is β-(2→1) D-fructofuranosylpattern.



General structure of inulin

Inulin (inulins), when injected intravenously, is not metabolized and is not bound by plasma proteins. It is eliminated by the kidney, it is neither excreted nor absorbed in the tubule, and it undergoes glomerular filtration; it increases the osmotic pressure of the tubular liquid. It can be of interest for the exploration of renal function. When administered orally, it reaches the colon without having been adsorbed or degraded.

Especially the roots of *Cichorium intybus* (Chicory, hindiba, Asteraceae) and *Taraxacum officinale* (Dandelion, kara hindiba, Asteraceae) are rich in inulin.

Cichorium intybus *Taraxacum officinale*

Heterogeneous Polysaccharides

GENERALITIES : GUMS AND MUCILAGES

The terms gums or mucilages commonly designate polysaccharide macromolecules that dissolve more or less upon contact with water to form colloidal solutions or gels.

A certain number of criteria have been put forward to distinguish gums and mucilages. Gums are complex molecules, are always heterogeneous and branched , and contain uronic acids. They flow on the outside of the plant and are **generally considered to result from a trauma**. Gums concrete by desiccation, they are insoluble in organic solvents, and the differentiates, them from resins (which are most often terpenoid).

Mucilages on the other hand **are considered to be normal cell constituents**, preexisting in specialized histological formations (cells or canals) that are common in the external tegument of seeds. Fairly widely distributed, they are common in Malvales (acidic mucilages) and Fabales (neutral mucilages of the endosperm). Water-retaining agents, they would have an active role in germination; their formation would involve the Golgi apparatus.

GUMS (EXUDATES)

The analysis of the structure and distribution of gums in the vegetable kingdom has led some authors to classify them into four groups :

1. Group A : This group, which includes *Acacia* gums, is based on a galactan-type backbone substitued by L-arabinose units, and by branched oligosaccharides containing another monosaccharide (L-rhamnose, D-xylose), and D-glucuronic acid.
2. Group B : It includes gums similar to pectins : (1→4) linked D-galacturonic acid chains substituted by short chains containing L-arabinose, D-glucuronic acids, and D-galacturonic acids.
   L-rhamnose occurs in the main chain.

3. Group C : Gums in this group are uncommon 1→4-β-linked xylans and are highly substituted by miscellaneous monosaccharides (L-arabinose, L-galactose, D-glucuronic acid…
4. Group D : The central chain results from alternating (1→4-1→2D-glucuronic acid and D-mannose)

Most gums dissolve in water to form viscous solutions; some are completely insoluble and form gels. Dilute solutions of these gums (%1 or less) generally precipitate upon adition of ethanol. They are optically active, and this is an important element in their identification.

Karaya gum **Karaya gummi** **Karaya zamkı**

***Sterculia* sp.** **Sterculiaceae**

Karaya gum is the air-hardened product of the natural or incision-induced viscous exudate from the trunk and branches of *Sterculia* species growing in Africa. The gum preferably collected before,and after the monsoon season, is obtained after tapping or else blazing or charring . The exudate is collected, freed of residual bark, and sorted by foreign matter content and color.

The drug consists of irregular, translucent, and pinkish-white to brownish masses which smell of acetic acid. This gum is sparingly soluble in water forming a highly viscous suspension.

The gum is of type B (glycanorhamnogalacturonan). Karaya gum has many advantages that explain its extensive use in pharmacy Its ability to form viscous dispersions while swelling considerably make it a bulk laxative; it will not ferment, and is not absorbed, degraded, or toxic.

Gum arabic Arabici gummi (Gummi arabicum) Arap zamkı

Acacia Senegal Mimosaceae

Gum arabic is the air-hardened, gummy exudate which flows, naturally upon tapping, from the trunk and brances of *Acacia senegal*, and other *Acacia* species of African origin.

The work on acacias takes place during the dry season, as the leaves fall. Both the gum that exudates naturally, and that formed after tapping, are collected. The gum is odorless, tasteless, and adheres to the tongue. As a powder, it is more or less yellowish-white and dissolves very slowly in twice its mass of water to form a solution that is viscous, adhesive, weakly acidic, and rotates polrized light (levarotatory).

The raw gum contains 10-15% water, some tannins, oxidases, **but no starch**. The chief constituent is an acidic polysaccharide, which occurs in native state as a salt. The basic structure is that of a 1→3 galactan substituted by arabinose units (isolated or in short chains) and by complex oligosaccharides comprising D-galactose, L-arabinose, L-rhamnose, and D-glucuronic acid.

The viscosity of its solutions and their fairly good stability in acidic conditions make it an intersting pharmaceutical aid : a stabilizer for suspensions, but also an emulsifier, an agent for encapsulation of fragrances by nebulization, and in additive for the preparation of solid formulations designed for oral administration.

Traganth gum   Tragacantha   Tragacanthae gummi
Tragakantha
Astragalus gummifer   **Fabaceae**

The 3. edition of the European Pharmacopoeia specifies that this gummy air-hardened exudation that flows naturally or by incision from the trunk and branches of *Astragalus gummifer* may also arise from certain other species from Western Asia (In Turkey especially *A. gummifer* and *A. microcarpus*).

In the present case, the gummosis is centripetal and the gum accumulates in the medullary rays, the cell walls of which later disappear : an incision of the branch provokes immediate exudation of the gum which is thrust outward as a viscous ribbon, worm-shaped (accidental trauma) and fan-shaped (incision). Traditionally the basis of the main stem is exposed out of earth and deeply incised: after at least 48 hours the exudates are collected, gathered, and sorted. The least colored batches are considered of highest quality.

Astragalus gummifer

Astragalus microcephalus

Tragacanth gum is odorless and tasteless, consists of thin ribbons (30x10x1 mm) that are flattened, white, translucent, horny, finely, striated longitunally and ondulate in the transverse direction. The stratified cellular membranes that surround the starch grains are stained purple by a zinc chloride and iodine solution.

Chemical Composition : **In contrast to gum arabic, tragacath gum does not contain oxidases, but comprises about 3% starch and 3-4% minerals**. The raw gum is considered to be a mixture of two polysaccharides : tragacanthin (30-40%), which is natural and soluble in water and alcohol mixtures., and dissolves in water to form a colloidal solution, and bassorin (60-70%), which is acidic, precipitates in the presence of ethanol, and swells in the presence of water to form a gel.

Tragacanthin is a arabinogalactan (1→6, 1 →3), is almost neutral, and has a galactose backbone. Bassorin (or tragacanthic acid) on the other hand is a partially methylated glycanogalacturonan, built from four monosaccharides : D-galacturonic acid, D-galactose, D-xylose, and L-fucose.

Uses : A very ancient drug, tragacanth is indicated for the symptomatic treatment of constipation. Dilute solutions (0.5-1%)are very viscous, stable in acid and heat, compatible with most plant hydrocolloids, and easy to conserve; they have a pseudoplastic behavior which together with their anionic character, make them good stabiliziers for suspensions. The product can also be used to form and stabilize emulsions.

POLYSACCHARIDES DERIVED FROM MANNOSE : NEUTRAL MUCILAGES

Mannose is a monosaccharide that occurs frequently in polymers.

Heterogeneous polysaccharides comprising mannose are more frequent

1. **Glucomannans**
2. **Galactomannans**
3. **Galactoglucomannans**

Carob tree **Keçi boynuzu, harnup**

Ceratonia siliqua **Ceasalpiniaceae**

Carob «gum» is composed of an almost pure D-galacto-D-mannan (90-95%). The fruit pulp is poor in lipids (0.4-0.8%) of the dry weight, and proteins (3%), contains 40-50% soluble sugars , cyclitols, and condensed tannins (20%). After pulverization and roasting, it develops a cocoa odor (it is a potential cocoa subsyitute).

Properties of the gum : Partially soluble in cold water, locust bean gum dissolves well in hot water (80^0C) and gives, upon cooling, pseudoplastic solutions of high viscosity that withstand large chances in pH (3-11) and the addition of mineral salts . It acts in synergy with carrageenans to form elastic gels.

Uses :

In therapeutics : carob flour (dried and ground mesocarp pulp) associated with the aleurone of sunflower and rice (or with treated starch) constitutes an absorbent preparation proposed in the symptomatic treatment of diarrheas in the infant and the small child. In the first 24 hours when carob or its combinations are administered, the only other substance taken should be water, to fulfill the need for hydration; later feding is restarted progressively. Carob may be diluted in water or milk, but must not be boiled.

The mucilage extracted from the endosperm is a thickening preparation can be given to infants subject to vomiting.

In dietetics : Devoid of nutritional value, locust bean gum thickens rations without modifying the caloric intake. Thus it can be used traditionally as an adjunct in weight loss diets.

In the industry : Due to their adhesive and thickening properties, locust bean gum solutions find many uses in food technology, mainly in the formulation of fresh or frozen milk products (creams, ice creams), and in bakery products

Guar plant **Guar**

Cyamopsis tetragonolobus **Fabaceae**

Although it is common to speak of guar gum, this is an incorrect use of the word gum, since this product does not result from an exudation subsequent to some trauma, but from grinding the seed albumen. The pharmaceutical industry and food technology also use «guar galactomannan» widely; this product results from the grinding of the (seed) albumen followed by partial hydrolysis.

Cyamopsis tetragonolubus is an annual herb cultivated in India and Pakistan.

The polymer is a D-galacto-D-mannan.

Uses : Although guar gum may be included in the composition of diets for diabetics, it is of interest mostly in diets designed to decrease serum levels of cholesterol, a risk factor in cardiovascular disease. Combined with a diet low in lipids and high in carbohydrates, it can help remedy a moderetely eleveted serum cholesterol level temporarily.

Fenugreek Çemen Foeni-graeci semen

Trigonella foenum-graecum **Fabaceae**

Trigonelle foenum-graecum is a Mediterranian plant, growing and cultivated also in Turkey.The odor of the seeds is linked to numerous volatile constituents (sesquiterpeneoid hydrocarbons, alkanes, lactones)The seeds contain proteins (30%), lipids (7%), C-flavonoids, and many sterols. Carbohydrates are particularly abundant : fibers (cellulose, hemicellulose) and soluble galactomannan (galactose : mannose ratio 1.5 : 1). The seed is also a potential source of sapogenins.

The seeds are recognized as being devoid of toxicity and known for their antidiabetic, blood cholesterol-lowering, and blood-lipid lowering properties.

ACIDIC HETEROGENEOUS POLYSACCHARIDES «ACIDIC MUCILAGES»

Mucilage-containing Plantaginaceae

Several species in the genus *Plantago* provide drugs used in pharmacy : plantago seed, psyllium seed, plantain seeds, or ispaghula owe their laxative properties to very hydrophylic polysaccharides, and the leaves of certain plantains are used in phytotherapy.

Properties :

Ispaghula seed (*Plantago ovata*) and psyllium (*Plantago afra*) are categorized as «bulk laxatives». Their effect confirmed by several clinical studies, is purely mechanical and linked to their mucilage : the polysaccharide macromolecules, which ferment only to a small extent, absorb a large volume of water and form, in the colon, a voluminous gel that increases the bulk, water content, and acidity of the stool, stimulates peristalsis, and facilitates bowel movements with virtually no alteration of the transit period (in the absence of constipation). The mucilage is not depolymerized in the small intestine and is barely degraded by colon bacteria.

The German Comission E monograph specifies that the use of *Plantago ovata* is contra-indicated in patients whose diabetes is difficult to control and that diabetic patients who use insulin may need to reduce the dose.

Uses : Different forms of *Plantago* drugs are currently commercialized : Mucilage extracted from the seeds :The seeds are taken by the tablespoon (1-2) and their administration must be followed by that of an adequate volume of water (150 ml or 5 g, according to the German Commission E monograph). The mucilage itself be it a powder or granules – not to be chewed – is also be taken with a sufficient quantity of liquid. It is generally used alone but sometimes included in combinations (sorbitol, citrate). *Plantago* seeds may also be used in the adjunctive therapy of the painful component of spasmodic componentolitis.

All preparations based on *Plantago* are contraindicated in case of pyloric stenosis. They are to be used with caution in case of megacolon by alteration of colon motility.

Several *Plantago* species including *Plantago ovata, Plantago afra* and *Plantago lanceolata* are growing wildly in Turkey and Cyprus. They are known as «sinirliot, karnıyarık, bağa)» in the folk medicine.

Psyllium Plantago psyllii semen Karnıyarık tohumu

Plantago afra = P. psyllium, Plantago indica

Plantaginaceae

Plantago afra = Plantago psyllium

Ispaghula Plantago ovatae semen karnıyarık tohumu

Plantago ovata = Plantago ispaghula

Plantaginaceae

Plantain Plantago lanceolatae herba sinirliot

Plantago lanceolata, Plantago major **Plantaginaceae**

The leaves also contain iridoids and phenolic compounds

Plantago lanceolata

Polysaccharides of Malvales

High mallow : ***Malva sylvestris***
Marsmallow : ***Althaea officinalis***

Marshmallow dried root or dried suber-frre root and the dried flower of high mallow have been used as drugs (**Altheaea radix, Malvae flos**)

All marshmallow organs contain mucilage. In the case of the roots, it has a highly ramified xtructure composed of D-galactose, L-rhamnose, D-glucuronic acid and D-galacturonic acid. Globally Malvaceae polysaccharides have a close structural similarity to peçtin polysaccharides. The root contains, as do the leaf and flower flavonoids and phenolic acids.

Properties and Uses : Malvae flos and Althaeae radix (High mellow flower and marsmallow root) are approved for the indication «symptomatic treatment of constipation. They are also traditionally used :

by the oral route : adjunctive therapy of the painful component of spazmodic colitis and symptomatic treatment of cough.

topically : a-adjunctive emollient and itsch-relieving treatment of dermatological conditions, protective trophic in the treatment of cracks, abrasions, chaps, and insect bites b- antalgic in conditions affecting the buccal cavity, the oropharynx or both (in collutoria or lozenges)

High mallow **Malvae flos** **Ebegümeci çiçeği**

Malva sylvestris **Malvaceae**

Marsmallow **Althaeae radix** **Hatmi kökü**

Althaea officinalis **Malvaceae**

Lime, Linden **Tiliae flos** **ıhlamur**

Tilia cordata, Tilia platiphyllos **Tiliaceae**

Lime tree inflorescences or linden flowers are rich in phenolic compounds : Phenolic acids, proanthocyanidins, tannins and especially flavonoids. The odor is linked to a small amount of essential oil with the localization that from bracts is rich in phenylacetaldehyde and other aldehydes, whereas that from flowers is dominated by monoterpenoid hydrocarbons. Both contain oxygenated mono- and sesquiterpenes (e.g., linalool, geraniol, farnesol (free and acetylated), camphor, carvone, cineole).

The drug also contains a mocilage composed of five fraction dominated by D-galactose, L-arabinose, L-rhamnose and uronic acids.

Tiliae flos is traditionally used in the symptomatic treatment of neurotonic states in adults and children, especially for minor sleep disturbances. Topically linden flower preparations are used as an adjunct in the emollient and itch-relieving treatment of dermatological conditions, and as a trophic protective agent for cracks, abrasions, frost bites, and insect bites. The German Commission E monograph attributes to linden flowers diaphoretic properties.

Flax **Lini semen** **Keten tohumu**

Linum usitatissimum **Linaceae**

Lini semen (Flaxseed or linseed) contains oil (35-45%), proteins, and mucilage (6-10%); of note is the occurrence of cyanogenic glycosides (linustatin, neolinustatin, traces of linamarin). The mucilage can be fractionated into a neutral fraction, ramified arabinolactan and an acidic fraction. Linseed oil is a highly unsaturated oil, thereforethe ground seeds spoil in storage (oleic acid 10-18%, linoleic acid 23-24%, α-linoleic acid 35-50%).

Properties and Uses : The occurence of mucilage justifies the use of Lini semen as a bulk laxative. The seeds must be taken with a sufficient quantity of fluids to avoid any risk of obstruction of the digestive track. The German Commission E monograph acknowledges that the drug is capable of increasing the volume of the bowel contents, therefore it stimulates peristalsis, and it protects the mucous membrane in case of inflammation (colitis). Obese patients are advised to swallow the seeds without chewing them, to avoid releasing the oil, a source of calories (1g of seeds = 4.7 kcal). The occurence of cyanogenic glycosides does not preclude the consumption of the seeds, as lon as their level does not exceed 5%.

PECTINS

Generalities : Pectins may be difined as a group of polymers built around 1→4 linked α-galacturonic residues associated with arabinan and galactan units. They are glycanogalacturonans in which the nature of the monosaccharides linked to galacturonan varies with the botanical origin. Pectins are chiefly localized in the middle lamella of the vegetable cell wall where they are associated with cellulose. These polymers are particularly abundant in unripe fruits .

Commercially and traditionally, pectic acids with carboxylic functions that are not (or almost not) methylated are distinguished from salts or pectates. Pectinic acid is reserved for partially methylated derivatives.

Practically pectins are classified in function of their degree of methylation (DM), also called degree of esterification (DE).

Production of pectins : Industrial pectin extraction starts from citrus waste (2.5-4% of the fresh pulp weight) and apples (0.5-1.6% of the fresh weight), in other words from the residual pulp leftover from manufacturing fruit juices. After inactivating the enzymes by boiling, pectin is dissolved in hot acidic aqueous solutions. The extract, filtered or centrifuged, and if needed freed from starch (by digestion by amylases), is treated with isopropanol : pectin precipitates. The precipitate is filtered, dried and ground. The temparature, pH, and duration of acidic treatment determine the final DM.

Properties : Pectic acid is insoluble in water but its solubility in water increases with the DM. Alkaline pectates are soluble in water. Pectin solutions are very viscous and their behavior is pseudoplastic. In specific conditions, solutions prepared hot gel upon cooling. The structure of pectins of low DM is not without similarity to that of alginic acid. In case of pectins of high DM, gelification takes place slowly in acidic medium and in the presence of sucrose.

Uses of Pectins : Pectins are of interest in pharmacy above all because of their hydrophilicity : by absorbing the water, they act as a thickening preparation on the gastric contents and regularize transit; they ferment fairly rapidly and enhance bacterial growth, therefore they increase the feces volume. They are used for the symptomatic treatment of vomiting in the infant, and for diarrhea.

In dietetics, the regular use of pectins has proved efficacious in the control of blood cholesterol levels and the prevention of cardiovascular diseases.

Useful in pharmaceutical technology, pectins are mostly used in food technology as stabilizers and gelifiers in jams, jellies, candies, frozen desserts, and sauces.

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