Kirk-Othmer Encyclopedia of Chemical Technology.

SUGAR ALCOHOLS

The sugar alcohols bear a close relationship to the simple sugars from which they are formed by reduction and from which their names are often derived (see Carbohydrates). The polyols discussed herein contain straight carbon chains, each carbon atom usually bearing a hydroxyl group. Also included are polyols derived from disaccharides. Most of the sugar alcohols have the general formula $HOCH_2(CHOH)_n{-}CH_2OH$, where $n = 2 - 5$. They are classified according to the number of hydroxyl groups as tetritols, pentitols, hexitols, and heptitols. Polyols from aldoses are sometimes called alditols. Each class contains stereoisomers. Counting meso and optically active forms, there are three tetritols, four pentitols, ten hexitols, and sixteen heptitols, all of which are known either from natural occurrence or through synthesis (Fig. 1). Of the straight-chain polyols, sorbitol [50-70-4] and mannitol have the greatest industrial significance. However, maltitol, isomalt, and xylitol are finding increasing acceptance in applications in the United States and Canada.

1. Physical Properties

In general, these polyols are water-soluble, crystalline compounds with small optical rotations in water and a slightly sweet to very sweet taste. Selected physical properties of many of the sugar alcohols are listed in Table 1.

Polymorphism has been observed for both D-mannitol (6–9) and sorbitol (10). Three different forms exist for each hexitol. Bond lengths of crystalline pentitols and hexitols are all similar. The average C–C distance is 152 pm; the average C–O distance is 143 pm. Conformations in the crystal structures of sugar alcohols are rationalized by Jeffrey's rule that "the carbon chain adopts the extended, planar zigzag form when the configurations at alternate carbon centers are different, and is bent and nonplanar when they are the same" (9). Conformations are adopted which avoid parallel C–O bonds on alternate carbon atoms. Very little, if any, intramolecular hydrogen bonding exists in the crystalline sugar alcohols, but an extensive network of intermolecular hydrogen bonds has been found. Usually each hydroxyl group is involved in two hydrogen bonds, one as a donor and one as an acceptor (11).

The small optical rotations of the alditols arise from the low energy barrier for rotation about C–C bonds, permitting easy interconversion and the existence of mixtures of rotational isomers (rotamers) in solution (12).

The weakly acidic character of acyclic polyhydric alcohols increases with the number of hydroxyl groups, as indicated by the pK_a values in aqueous solution at 18°C (13).

Alcohol	pK_a	Ref.
glycerol	14.16	13
erythritol	13.90	13
xylitol	13.73	13
sorbitol	13.57	14
mannitol	13.50	14
dulcitol	13.46	13

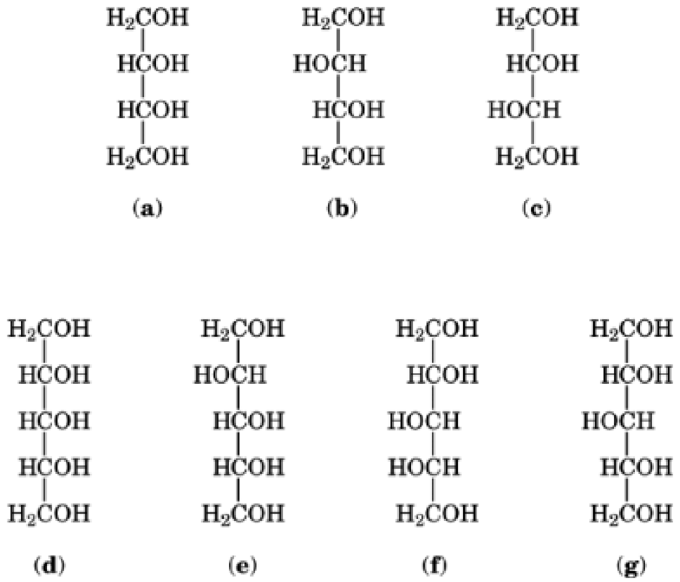


Fig. 1. Structures of the tetritols (**a**) erythritol, (**b**) D-threitol, and (**c**) L-threitol; and the pentitols (**d**) ribitol, (**e**) D-arabinitol, (**f**) L-arabinitol, and (**g**) xylitol.

Table 1. Physical Properties of the Sugar Alcohols

Sugar alcohol	CAS Registry Number	Melting point, °C	Optical activity in $H_2O,[\alpha]^{20--25}{}_D$	Solubility g/100 g H_2O^a	Heat of solution, J/g^b	Heat of combustion, constant vol, kJ/mol^b
			Tetritols			
erythritol	[149-32-6]	120	meso	61.5	23.3^c	−2091.6^d
threitol	[7493-90-5]					
D-threitol	[2418-52-2]	88.5–90	+4.3	very sol		
L-threitol	[2319-57-5]	88.5–90	−4.3			
D,L-threitol	[6968-16-7]	69–70				
			Pentitols			
ribitol	[488-81-3]	102	meso	very sol		
arabinitol	[2152-56-9]					
D-arabinitol	[488-82-4]	103	+131^e	very sol		
L-arabinitol	[7643-75-6]	102–103	−130^e			−2559.4^f
D,L-arabinitol	[6018-27-5]	105				
xylitol	[87-99-0]	61–61.5 (metastable) 93–94.5 (stable)	meso	179	−153.1	−2584.5^g
			Hexitols			
allitol	[488-44-8]	155	meso	very sol		
dulcitol (galactitol)	[608-66-2]	189	meso	3.2^h		−3013.7^d
glucitol	[26566-34-7]					
sorbitol		93 (metastable)	−1.985	235	−111.5	−3025.5^i
(D-glucitol)	[50-70-4]	97.7 (stable)				
L-glucitol	[6706-59-8]	89–91	+1.7			
D,L-glucitol	[60660-56-2]	135–137				
D-mannitol	[69-65-8]	166	−0.4	22	−120.9	−3017.1^i

Table 1. *Continued*

Sugar alcohol	CAS Registry Number	Melting point, °C	Optical activity in $H_2O,[\alpha]^{20--25}_D$	Solubility g/100 g H_2O^a	Heat of solution, J/g[b]	Heat of combustion, constant vol, kJ/mol[b]
L-mannitol	[643-01-6]	162–163				
D,L-mannitol	[133-43-7]	168				
altritol	[5552-13-6]					
D-altritol	[17308-29-1]	88–89	+3.2	very sol		
L-altritol	[60660-58-4]	87–88	−2.9			
D,L-altritol	[60660-57-3]	95–96				
iditol	[24557-79-7]					
D-iditol	[23878-23-3]	73.5–75.0	+3.5			
L-iditol	[488-45-9]	75.7–76.7	−3.5	449		
		Disaccharide alcohols				
maltitol	[585-88-6]	147–150	+90	175	−78.2	
lactitol	[585-86-4]	146	+14		−52.7	
isomalt	[64519-82-0]	145–150		24.5	−38.5	

[a] At 25°C unless otherwise indicated.
[b] To convert J to cal, divide by 4.184.
[c] Ref. 1.
[d] Ref. 2.
[e] In aqueous molybdic acid.
[f] Ref. 3.
[g] Ref. 4.
[h] At 15°C.
[i] Ref. 5.

At 60°C, the pK_a value of sorbitol is 13.00 (15).

In aqueous solution, sugar alcohols influence the structure of water, presumably by hydration of the polyol hydroxyl groups through hydrogen bonding, as indicated by effects on solution compressibility (16), vapor pressure (17), enthalpies of solution (18), dielectric constant (19), and Ag–AgCl electrode potential (20). Compressibility measurements indicate that mannitol in aqueous solution is hydrated with two molecules of water at 25°C (21). Osmotic coefficients are related to the number of hydrophilic groups per molecule, those of sorbitol being larger than those of erythritol (22).

2. Occurrence

D-Arabinitol (lyxitol [488-82-4]) (Fig. 1**e**) is found in lichens; in a variety of fungi; in the urediospores of wheat stem rust (23); in the dried herbiage of the Peruvian shrub, pichi, along with D-mannitol, dulcitol, and perseitol (24); and in the avocado (25). It is formed by fermentation of glucose (26–28) and in 40% yields using blackstrap molasses (29). Studies with ^{14}C-labeled glucose show that the yeast converts glucose C–1 to C–1 and C–5 in D-arabinitol and glucose C–2 to C–1, C–2, and C–4 of D-arabinitol (30). D-Arabinitol is formed by catalytic hydrogenation of D-arabinose in the presence of Raney nickel (31) and from the γ-lactones of D-arabinonic and D-lyxonic acids by reduction with sodium borohydride (32, 33). L-Arabinitol (Fig. 1**f**) is synthesized by the reduction of L-arabinose which is abundant in nature (34, 35).

D,L-Arabinitol can be prepared by the action of hydrogen peroxide in the presence of formic acid on divinyl carbinol (36) and, together with ribitol (Fig. 1**d**), from D,L-erythron-4-pentyne-1,2,3-triol, $HOCH_2CHOHCHOHC{\equiv}CH$ (37).

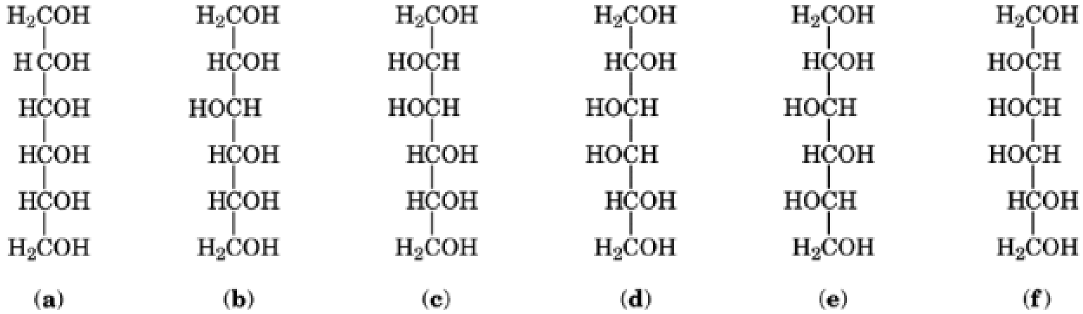


Fig. 2. Structures of hexitols (**a**) allitol, (**b**) sorbitol (D-glucitol), (**c**) D-mannitol, (**d**) dulcitol, (**e**) L-iditol, and (**f**) D-altritol.

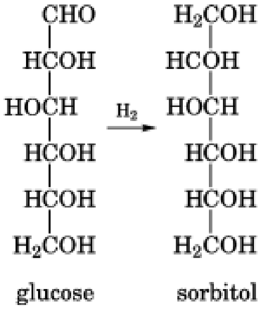
Xylitol (Fig. 1**g**) is found in the primrose (38) and in minor quantity in mushrooms (39). It can be obtained from glucose in 11.6% overall yield by a sequential fermentation process through D-arabinitol and D-xylulose (28).

Xylitol is synthesized by reduction of D-xylose catalytically (40), electrolytically (41), and by sodium amalgam (42). D-Xylose is obtained by hydrolysis of xylan and other hemicellulosic substances obtained from such sources as wood, corn cobs (43), almond shells, hazelnuts, or olive waste (44). Isolation of xylose is not necessary; xylitol results from hydrogenation of the solution obtained by acid hydrolysis of cottonseed hulls (45).

Xylitol also is obtained by sodium borohydride reduction of D-xylonic acid γ-lactone (32) and from glucose by a series of transformations through diacetone glucose (46).

Sorbitol (D-glycitol) (Fig. 2**b**) was discovered initially in the fresh juice of mountain ash berries in 1872. It is found in the fruits of apples, plums, pears, cherries, dates, peaches, and apricots; in the exudate of flowers of apples, pears, and cherries; and in the leaves and bark of apples, plums, prunes, the genus *Fraxinus*, and the genus *Euonymus*. Small amounts are found in the plane tree, the African snowdrop tree, and in various algae. Because sorbitol occurs to a very small extent in grapes, assay of the sorbitol content of wine (qv) has been used to detect its adulteration with other fruit wines or apple cider. An anhydride of sorbitol, polygallitol (1,5-sorbitan), is found in the *Polygala* shrub (47). Sorbitol occurs in the overwintering eggs of the European red mite, the latter affording it protection against freezing (48).

Sorbitol is synthesized commercially by high pressure hydrogenation of glucose, usually using a nickel catalyst. Catalyst promoters include magnesium salts (49), nickel phosphate, and iron (50). Other heterogenous catalysts used for glucose hydrogenation include cobalt, platinum, palladium, and ruthenium (51). Reduction of glucose to sorbitol also can be effected using ruthenium dichlorotriphenyl phosphine as a homogenous hydrogenation catalyst, preferably in the presence of a strong acid such as HCl (52). To form sorbitol, glucose is usually hydrogenated in the pH range of 4–8. Under alkaline conditions, glucose isomerizes to fructose and mannose; hydrogenation of the fructose and mannose yields mannitol as well as sorbitol. In addition, under alkaline conditions the Cannizzaro reaction occurs and sorbitol and gluconic acid are formed. Gluconic acid formation during hydrogenation can be minimized if anion exchange resins in the basic form are the source of alkalinity (53). Although aqueous solutions are customarily used, the monomethyl ethers of ethylene glycol or diethylene glycol are satisfactory solvents (54). Electrolytic reduction of glucose was used formerly for the manufacture of sorbitol (55). Both the γ- and δ-lactones of D-gluconic acid may be reduced to sorbitol by sodium borohydride (32). Sorbitol results from simultaneous hydrolysis and hydrogenation of starch (56), cotton cellulose (57), or sucrose (58).



D-Mannitol is widespread in nature. It is found to a significant extent in the exudates of trees and shrubs such as the plane tree (80–90%), manna ash (30–50%), and olive tree. The manna ash, *Fraxinus rotundifolis*, formerly was cultivated in Sicily for the mannitol content of its sap. Mannitol occurs in the fruit, leaves, and other parts of various plants. This hexitol is present in pumpkin, hedge parsley, onions, celery, strawberries, the genus *Euonymus*, the genus *Hebe*, the cocoa bean, grasses, lilac, *Digitalis purpurea*, mistletoe, and lichens. Mannitol occurs in marine algae, especially brown seaweed, with a seasonal variation in mannitol content which can reach over 20% in the summer and autumn (59). It is found in the mycelia of many fungi and is present in the fresh mushroom to the extent of about 1.0% (60). There is a direct relation between mushroom yield and mannitol content (61). Microbial formation of D-mannitol occurs with fungi (62, 63) or bacteria (64), starting with glucose, fructose, sucrose, or the tubers of Jerusalem artichokes (65). The precursor of mannitol in its biosynthesis in the mushroom *Agaricus bisporus* is fructose (66). Mannitol is produced from glucose in 44% yield after six days by aerobic fermentation with *Aspergillus candidus* (67) and in 30% yield after 10 days with *Torulopsis mannitofaciens* (68). It is formed by submerged culture fermentation of fructose with *Penicillium chrysogenum* in 7.3% conversion (69). Using sodium acetate as the sole carbon source, *Aspergillus niger* forms D-mannitol as well as D-arabinitol, erythritol, and glycerol (70). Small quantities of mannitol are found in wine (71).

Reduction of D-mannose with sodium borohydride or electrolysis leads to D-mannitol in good yield. Pure D-mannose is not yet commercially available but it can be obtained by acid hydrolysis of the mannan of ivory nutmeal in 35% yield (72) and from spent sulfite liquor or prehydrolysis extracts from conifers through the sodium bisulfite mannose adduct or methyl α-D-mannoside (73, 74). Reduction of fructose leads to sorbitol and D-mannitol in equal parts. Sucrose, on reduction under hydrolyzing conditions, also yields the same products in the ratio of three parts of sorbitol to one of D-mannitol. Commercially, D-mannitol is obtained by the reduction of invert sugar. In alkaline media, glucose, fructose, and mannose are interconverted (75, 76). All of the mannose formed can be reduced to mannitol. Mannitol can be prepared by hydrogenation of starch hydrolyzates in alkaline media in the presence of Raney nickel (77). Mannitol, because of its lower solubility, is usually separated from sorbitol by crystallization from aqueous solution. The two hexitols also can be separated chromatographically on a column of calcium poly(styrene-sulfonate), which preferentially retains sorbitol (78). Both the γ- and δ-lactones of D-mannonic acid are reduced catalytically to D-mannitol (79).

L-Mannitol does not occur naturally but is obtained by the reduction of L-mannose or L-mannonic acid lactone (80). It can be synthesized from the relatively abundant L-arabinose through the L-mannose and L-glucose cyanohydrins, conversion to the phenylhydrazines which are separated, liberation of L-mannose, and reduction with sodium borohydride (81). Another synthesis is from L-inositol (obtained from its monomethyl ether, quebrachitol) through the diacetonate, periodate oxidation to the blocked dialdehyde, reduction, and removal of the acetone blocking groups (82).

D,L-Mannitol has been obtained by sodium amalgam reduction of D,L-mannose. The identical hexitol is formed from the formaldehyde polymer, acrose, by conversion through its osazone and osone to D,L-fructose (α-acrose) followed by reduction (83).

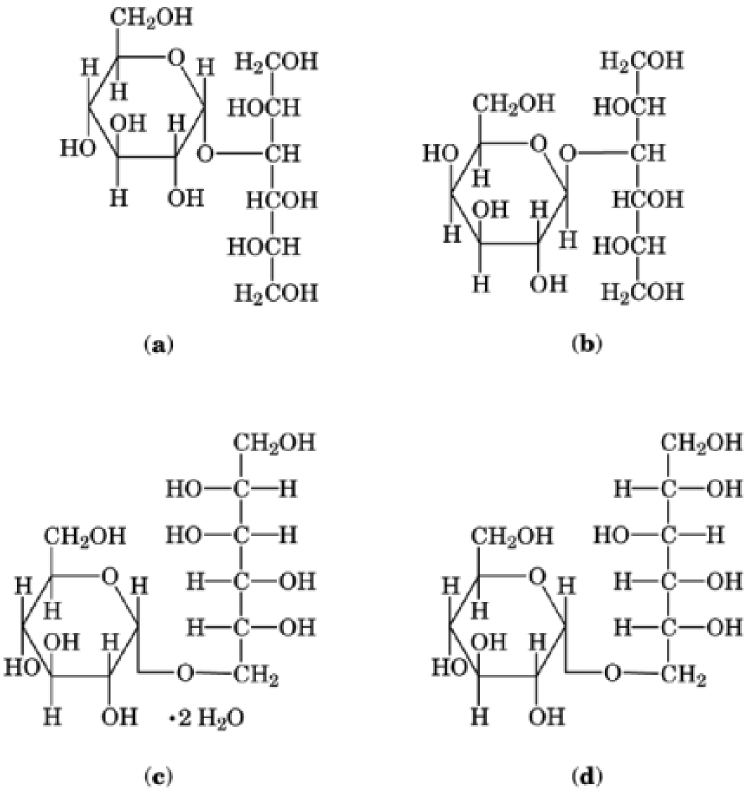


Fig. 3. Structures of disaccharide alcohols (**a**) maltitol, (**b**) lactitol, (**c**) α-D-glucopyranosyl-1,1-D-mannitol(dihydrate), and (**d**) α-D-glucopyranosyl-1,6-D-sorbitol.

Dulcitol (galactitol) is found in red seaweed, in shrubs of the *Euonymus* genus (84, 85), the genus *Hippocratea*, the genus *Adenanthera*, the physic nut, the parasitic herb *Cuscuta reflexa*, and in the mannas from a wide variety of plants. It is produced by the action of yeasts (86) and is found in beer (87). D-Galactose is reduced to dulcitol catalytically (40), electrolytically (88), and chemically (89). Reduction of hydrolyzed lactose leads to the formation of both dulcitol and sorbitol (90, 91). Dulcitol, which is relatively insoluble, is isolated by crystallization from the aqueous reduction mixture. Prehydrolysates of larch wood, which contain large quantities of galactose as well as glucose, arabinose, and xylose, can be simultaneously hydrolyzed and hydrogenated to a product containing 80% dulcitol, affording a pure product after repeated crystallization (92). Dulcitol is formed together with D-galactonic acid by treatment of D-galactose with alkali in the presence of Raney nickel (93). Reduction of D-galactonic acid γ-lactone with sodium borohydride leads to dulcitol (94). Photolysis of 1-deoxy-1-*S*-ethyl-1-thio-D-galactitol, and its sulfoxide in methanol forms dulcitol (95). Oxidation of a mixture and meso and racemic 1,5-hexadiene-3,4-diol with hydrogen peroxide and formic acid (trans addition of hydroxyl) leads predominantly to dulcitol, with some D,L-iditol (36, 96).

Maltitol (4-*O*-α-D-glucopyranosyl-D-glucitol) formed by catalytic hydrogenation of maltose (97), has been obtained both as a noncrystalline powder and a viscous liquid (98). Structures of disaccharide alcohols are shown in Figure 3.

Lactitol (4-*O*-β-D-galactopyranosyl-D-glucitol) is obtained by sodium borohydride reduction (99, 100) or catalytic hydrogenation (101) of lactose. Potentially large quantities of this sugar alcohol are available from lactose obtained from whey.

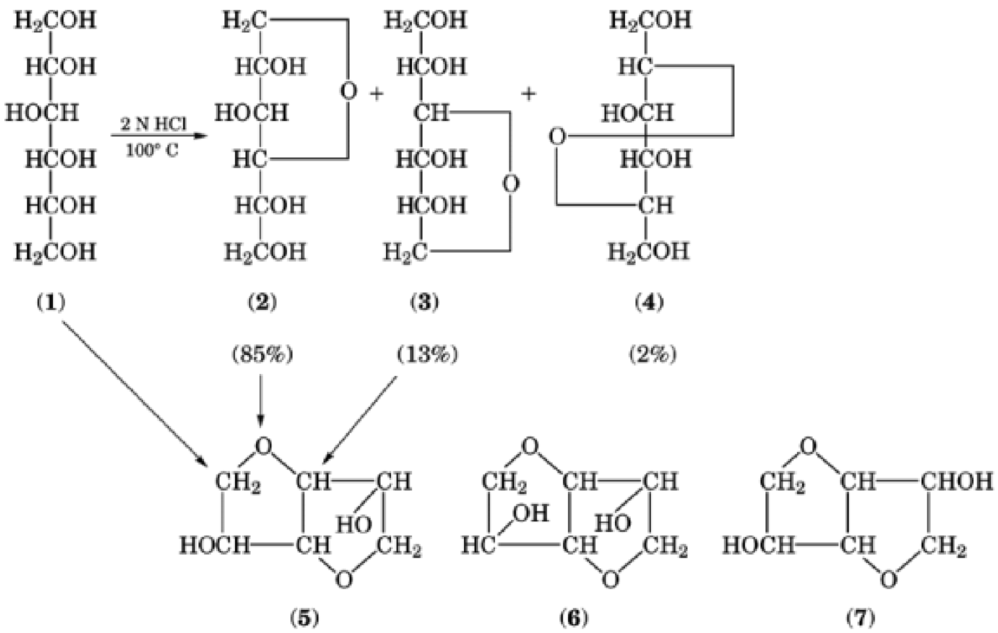


Fig. 4. Anhydrization of sorbitol (**1**) to 1,4-sorbitan (**2**), 3,6-sorbitan (**3**), 2,5-ahydro-L-iditol (**4**), and isosorbide (**5**). Also shown are isomannide (**6**) and isoidide (**7**), which arise from anhydrization of mannitol and iditol, respectively.

Isomalt, a mixture of α-D-glucopyranosyl-1,1-D-mannitol dihydrate and α-D-glucopyranosyl-1,6-D-sorbitol, is obtained by hydrogenating isomaltulose which is enzymatically derived from sucrose (102).

Hydrogenated starch hydrolysates (HSH) is a term used to describe a range of products which do not contain sorbitol or maltitol as a primary component, ie, at least 50%. HSH syrups contain a distribution of sorbitol, maltitol, and other hydrogenated oligo and polysaccharides. Syrups containing maltitol at a level of at least 50% are referred to as Maltitol syrups or Maltitol solutions.

3. Chemical Properties

3.1. Anhydrization

The sugar alcohols can lose one or more molecules of water internally, usually under the influence of acids, to form cyclic ethers. Nomenclature is illustrated by the hexitol derivatives. Monoanhydro internal ethers are called hexitans, and the dianhydro derivatives are called hexides. The main dehydration involves loss of water from the primary hydroxyl groups and the resulting formation of tetrahydrofuran derivatives having the configuration of the starting alditol, as shown for sorbitol **1** in Figure 4 (103–105). Small amounts of the 2,5-anhydrides form at the same time with inversion at the 2- or 5-positions, eg, 2,5-anhydro-L-iditol **4** from sorbitol. Hexitols anhydrize faster than pentitols or tetritols. Rates of dehydration depend on configuration and are slower where a noninvolved hydroxyl can interact with a leaving group.

Loss of a second molecule of water occurs on heating **1** (106, 107), **2**, or **3** (108) with concentrated sulfuric or hydrochloric acid forming 1,4:3,6-dianhydro-D-glucitol (isosorbide) **5**. Mannitol and iditol anhydrize under similar conditions to isomannide **6** and isoidide **7**, respectively. In **6**, both hydroxyl groups are oriented toward each other (endo); in **7**, both are oriented away from each other (exo); and in isosorbide **5**, one hydroxyl is endo and the other exo. Xylitol loses two moles of water to form 1,3:2,5-dianhydroxylitol (109).

3.2. Esterification

Both partial and complete esters of sugar alcohols are known. The most important method for the preparation of partial fatty esters involves the interaction of polyols and fatty acids at 180–250°C (110). During direct esterification of the sugar alcohols, anhydrization occurs to varying degrees depending upon the conditions. Thus, esterification of sorbitol with stearic acid leads to a mixture of stearates of sorbitan and isosorbide as well as of sorbitol. Unanhydrized esters may be prepared by reaction with acid anhydrides or acid chlorides or by ester interchange reactions. In general, use of an excess of these reagents leads to esterification of all hydroxyl groups. Sorbitol hexanicotinate is prepared from the action of nicotinic acid chloride and sorbitol in the presence of pyridine (111). Completely substituted formate esters result from reaction of pentitols and hexitols and concentrated formic acid in the presence of phosphorus pentoxide (112). Primary hydroxyl groups react with esterifying reagents appreciably more rapidly than do secondary hydroxyls. As a consequence, it is possible to prepare ester derivatives involving only the primary hydroxyls, as in the formation of D-mannitol 1-monolaurate and 1,6-dilaurate by reaction of D-mannitol with lauroyl chloride at 100°C (113). The endo hydroxyl of isosorbide, which is involved in intramolecular hydrogen bond formation, is more easily esterified than the exo hydroxyl (114).

Cyclic carbonates result from polyols by transesterification using organic carbonates (115). Thus sorbitol and diphenylcarbonate in the presence of dibutyl tin oxide at 140–150°C form sorbitol tricarbonate in quantitative yield (116).

Mannitol hexanitrate is obtained by nitration of mannitol with mixed nitric and sulfuric acids. Similarly, nitration of sorbitol using mixed acid produces the hexanitrate when the reaction is conducted at 0–3°C and at -10 to $-75^{\circ}\mathrm{C}$, the main product is sorbitol pentanitrate (117). Xylitol, ribitol, and L-arabinitol are converted to the pentanitrates by fuming nitric acid and acetic anhydride (118). Phosphate esters of sugar alcohols are obtained by the action of phosphorus oxychloride (119) and by alcoholysis of organic phosphates (120). The 1,6-dibenzene sulfonate of D-mannitol is obtained by the action of benzene sulfonyl chloride in pyridine at 0°C (121). To obtain 1,6-dimethanesulfonyl-D-mannitol free from anhydrides and other by-products, after similar sulfonation with methane sulfonyl chloride and pyridine the remaining hydroxyl groups are acetylated with acetic anhydride and the insoluble acetyl derivative is separated, followed by deacetylation with hydrogen chloride in methanol (122). Alkyl sulfate esters of polyhydric alcohols result from the action of sulfur trioxide–trialkyl phosphates as in the reaction of sorbitol at 34–40°C with sulfur trioxide–triethyl phosphate to form sorbitol hexa(ethylsulfate) (123).

3.3. Etherification

The reaction of alkyl halides with sugar polyols in the presence of aqueous alkaline reagents generally results in partial etherification. Thus, a tetraallyl ether is formed on reaction of D-mannitol with allyl bromide in the presence of 20% sodium hydroxide at 75°C (124). Treatment of this partial ether with metallic sodium to form an alcoholate, followed by reaction with additional allyl bromide, leads to hexaallyl D-mannitol (125). Complete methylation of D-mannitol occurs, however, by the action of dimethyl sulfate and sodium hydroxide (126). A mixture of tetra- and pentabutyloxymethyl ethers of D-mannitol results from the action of butyl chloromethyl ether (127). Completely substituted trimethylsilyl derivatives of polyols, distillable *in vacuo,* are prepared by interaction with trimethylchlorosilane in the presence of pyridine (128). Hexavinylmannitol is obtained from D-mannitol and acetylene at 25.31 MPa (250 atm) and 160°C (129).

Reaction of olefin oxides (epoxides) to produce poly(oxyalkylene) ether derivatives is the etherification of polyols of greatest commercial importance. Epoxides used include ethylene oxide, propylene oxide, and epichlorohydrin. The products of oxyalkylation have the same number of hydroxyl groups per mole as the starting polyol. Examples include the poly(oxypropylene) ethers of sorbitol (130) and lactitol (131), usually formed in the presence of an alkaline catalyst such as potassium hydroxide. Reaction of epichlorohydrin and isosorbide leads to the bisglycidyl ether (132). A polysubstituted carboxyethyl ether of mannitol has been obtained by the interaction of mannitol with acrylonitrile followed by hydrolysis of the intermediate cyanoethyl ether (133).

3.4. Acetal Formation

In common with other glycols, the sugar alcohols react with aldehydes and ketones to yield cyclic acetals and ketals. Five-membered rings are formed from adjacent hydroxyls and six-membered rings result from 1,3-hydroxyls. From the hexitols, mono-, di-, or triacetals or ketals may be obtained. Acetal formation is extensively used to protect hydroxyl groups during transformations in the polyol and carbohydrate series since conditions for the formation and removal of cyclic acetal linkages are relatively mild and proceed without inversion of configuration at asymmetric centers.

3.5. Oxidation

Sorbitol is oxidized by fermentation with *Acetobacter suboxydans* to L-sorbose, an intermediate in the synthesis of ascorbic acid (134, 135) (see Vitamins). The same organism, *Acetobacter xylinium* and related bacteria convert erythritol to L-erythrulose (136), D-mannitol to D-fructose (137), and allitol to L-ribohexulose (138). These results are generalized in the case of the more specific *Acetobacter suboxydans* (139) by the Hudson-Bertrand rules which state that in a *cis*-glycol having a D-configuration, a secondary hydroxyl adjacent to a primary hydroxyl is oxidized to a ketone (140). A similar stereospecific oxidation is that of an L-secondary hydroxyl adjacent to a primary hydroxyl in a polyol by diphosphopyridine nucleotide, which is catalyzed by L-iditol dehydrogenase; sorbitol is oxidized to fructose, L-iditol to sorbose, xylitol to D-xylulose, and ribitol to D-ribulose (141) (see Microbial transformations).

Careful oxidation using aqueous bromine produces mixtures of aldoses and ketoses. Thus, sorbitol is converted to a mixture of D-glucose, D-fructose, L-glucose, and L-sorbose (142). Aldoses and ketoses also result from ozone oxidation of sorbitol and mannitol (143). Reducing sugars are formed from the action of hydrogen peroxide in the presence of ferrous salts on erythritol, D-mannitol, dulcitol, or sorbitol. Ribitol, D-arabinitol, and xylitol are oxidized by mercury(II) acetate to mixtures of 2- and 3-pentuloses (144, 145). Permanganate, manganese dioxide, chromic acid, and nitric acid completely oxidize polyols to carbon dioxide.

3.6. Reduction

Sorbitol and mannitol are each converted by the action of concentrated hydriodic acid to secondary iodides (2- and 3-iodohexanes). The results of this reduction were used in early proofs of structure of glucose and fructose (146). Catalytic hydrogenolysis of the polyols results in breaking of both carbon-to-carbon and carbon-to-oxygen bonds. Thus, hydrogenolysis of sorbitol leads to the formation of ethylene glycol, propylene glycol, glycerol, erythritol, and xylitol (147, 148). Ethylene glycol, propylene glycol, glycerol, erythritol, and monohydric alcohols are formed by the hydrogenolysis of xylitol (149).

3.7. Metal Complexes

The sugar alcohols form complexes in solution with most metal ions. In aqueous solution, calcium, strontium, and barium are more strongly complexed than are sodium, potassium, and magnesium (150). Solid magnesium complexes of sorbitol and other polyols are prepared with magnesium ethoxide (151); sorbitol alcoholate complexes of sodium and lithium precipitate from anhydrous ethanol (152). Polyol and carbohydrate complexes of alkali and alkaline earth metals have been reviewed (153). The stability of some polyol metal complexes is such that precipitation of the metal hydroxide from solution is inhibited. Thus, addition of sorbitol or D-mannitol to an aqueous solution of sodium ferric tartrate prevents precipitation of ferric oxide (154); D-mannitol prevents precipitation of titanium(IV) hydroxide (155), and at pH values above 12, precipitation of calcium, strontium, and cupric hydroxides is partially inhibited by sorbitol (156). Copper, iron, and cobalt all complex with cellobiitol (157). Tetritols, pentitols, and hexitols complex with copper in aqueous solutions of both cupric acetate and basic cupric acetate (158). Separation of mannitol from a mixture with dulcitol (resulting from reduction of wood sugar mixtures containing mannose and galactose) is achieved by selective complexation of dulcitol with ferric salts (159) (see also Alkoxides metal; Chelating agents).

4. Isomerization

Isomerization of sorbitol, D-mannitol, L-iditol, and dulcitol occurs in aqueous solution in the presence of hydrogen under pressure and a nickel–kieselguhr catalyst at 130–190°C (160). In the case of the first three, a quasiequilibrium composition is obtained regardless of starting material. Equilibrium concentrations are 41.4% sorbitol, 31.5% D-mannitol, 26.5% L-iditol, and 0.6% dulcitol. In the presence of the same catalyst, the isohexides establish an equilibrium at 220–240°C and 15.2 MPa (150 atm) of hydrogen pressure, having the composition 57% isoidide, 36% isosorbide, and 7% isomannide (161).

5. Analysis

Analytical separation of the sugar alcohols from each other and from similar materials, such as carbohydrates, is done chromatographically (see Chromatography). Sorbitol, for example, is readily separated from glycerol, erythritol, and other polyols by chromatography on paper using butanol–water as developing solution (162), and on thin layers of silicic acid using butanol–acetic acid–ethyl ether–water as developing solution (163). Improved separations of sugar alcohols and carbohydrates have been obtained by including boric acid (164, 165) or phenylboronic acid (166) in the solvent, thereby forming esters with the polyols. Paper electrophoresis of polyols and carbohydrates in molybdate (167), tellurate, germinate (168), or stannate (169) also enables the obtaining of some useful separations. Although polyols and carbohydrates can be separated by column chromatography on silicate absorbents (170), partition chromatography on ion exchange resins is of particular value for quantitative separations of these classes of materials (171). Use of cation exchange resins in the lithium form and anion exchange resins in the sulfate (172) or molybdate (173) form permit the separation of pentitols, hexitols, heptitols, and disaccharide alcohols as well as related carbohydrates (see Ion exchange). Direct gas chromatographic determination of free sugar alcohols in biological media such as fermentation (qv) cultures has been reported (174). A mixture of glycerol, erythritol, D-arabinitol, and xylitol can be separated and each polyol determined by this procedure. Erythritol and other sugar alcohols are used as stationary phases for the gas chromatographic separation of volatiles in beer (qv) and wine (qv) (174).

Separated polyols are detected by a variety of reagents, including ammoniacal silver nitrate (175), concentrated sulfuric acid, potassium permanganate (163), lead tetraacetate, and potassium telluratocuprate (176). A mixture of sodium metaperiodate and potassium permanganate can be used to detect as little as 5–8 μg of mannitol or erythritol (177).

Conversion to acetates, trifluoroacetates (178), butyl boronates (179) trimethylsilyl derivatives, or cyclic acetals offers a means both for identifying individual compounds and for separating mixtures of polyols, chiefly by gas–liquid chromatography (glc). Thus, sorbitol in bakery products is converted to the hexaacetate, separated, and determined by glc using a flame ionization detector (180); aqueous solutions of sorbitol and mannitol are similarly separated and determined (181). Sorbitol may be identified by formation of its monobenzylidene derivative (182) and mannitol by conversion to its hexaacetate (183).

The sugar alcohols can be determined by periodate oxidation, followed by measurement of the formaldehyde or formic acid liberated (184) or titration of the excess periodate (185). Small quantities of sorbitol in biological fluids have been determined by this method (186). Measurement of the heat liberated in periodate oxidation of sorbitol in foodstuffs is the basis of a thermometric determination (187). Sorbitol is determined in wine and vinegar by precipitation with *o*-chlorobenzaldehyde forming the tris(*o*-chlorobenzylidene) derivative (188). Sugar alcohols may be analyzed colorimetrically after reaction with *p*-hydroxybenzaldehyde or *p*-dimethylaminobenzaldehyde, thiourea, and concentrated sulfuric acid (189). After complexation with copper, sorbitol and mannitol are determined by iodometric titration of excess cupric ion (190). Enzymatic assays have been described for several polyols, including sorbitol (191), ribitol (192), and erythritol (193). Although nonspecific, one of the most valuable procedures for the quantitative analysis of polyols is the determination of hydroxyl number. This method involves reaction with acetic anhydride, followed by measurement of the acetic acid liberated.

Polarimetric analysis of sorbitol and mannitol in the presence of each other and of sugars is possible because of their enhanced optical rotation when molybdate complexes are formed and the higher rotation of the mannitol molybdate complex under conditions of low acidity (194). The concentration of a pure solution of sorbitol may be determined by means of the refractometer (195). Mass spectra of trimethylsilyl ethers of sugar alcohols provide unambiguous identification of tetritols, pentitols, and hexitols and permit determination of molecular weight (196).

6. Manufacture of Sorbitol, Mannitol, and Xylitol

Sorbitol is manufactured by catalytic hydrogenation of glucose using either batch or continuous hydrogenation procedures. Corn sugar (qv) is the most important raw material, but other sources of glucose, such as hydrolyzed starch (qv), also may be used (197). Both supported nickel and Raney nickel are used as catalysts (198). In the continuous procedure, a 50% solution of dextrose in water is prepared and transferred to a mixing tank. The catalyst, nickel on diatomaceous earth, is added to the glucose solution and the resulting slurry is pumped to the reactor after being heated to about 140°C. Hydrogen is introduced into the reactor at a pressure of approximately 12.7 MPa (125 atm) concurrently with the sugar solution. Spent catalyst is collected on a filter and is separately regenerated for reuse. The sorbitol solution is purified in two steps: (*1*) by passage through an ion-exchange resin bed to remove gluconate as well as other ions, and (*2*) by treatment with activated carbon to remove trace organic impurities. The solution of pure sorbitol is concentrated in a continuous evaporator to a solution containing 70% solids, which is sold under the trademark SORBO (a registered trademark of SPI Polyols, Inc.), meeting USP 23 standards. Crystalline sorbitol is obtained by further concentration and crystallization (qv). It is sold in a variety of particle-size distributions, the one chosen depending on the application.

When invert sugar is used as a starting material, sorbitol and mannitol are produced simultaneously. Mannitol crystallizes from solution after the hydrogenation step owing to its lower solubility in water. It is sold as a white, crystalline powder or free-flowing granules (directly compressible grades) meeting USP 23 standards.

Extraction of mannitol from seaweed is a method of lesser importance commercially. In one method starting with this source, whole seaweed is steeped at 20°C in water which has been acidified to pH 2 with sulfuric acid. After filtration, the extract is neutralized and made alkaline with lime, precipitating calcium and magnesium sulfates together with some colloids. The filtrate or centrifugate from this operation is dialyzed; mannitol and mineral salts pass through the semipermeable membrane. The dialyzate is concentrated and mannitol crystallizes from solution on cooling. If the weight ratio of mannitol to alkali chlorides in the dialyzate is less than 1, this ratio is attained by addition of pure mannitol before crystallization is begun (199, 200).

Xylose is obtained from sulfite liquors, particularly from hardwoods, such as birch, by methanol extraction of concentrates or dried sulfite lyes, ultrafiltration (qv) and reverse osmosis (qv), ion exchange, ion exclusion, or combinations of these treatments (201). Hydrogenation of xylose is carried out in aqueous solution, usually at basic pH. The Raney nickel catalyst has a loading of 2% at 125°C and 3.5 MPa (515 psi) (202, 203).

7. Economic Aspects

The 1995 Canadian and United States sugar alcohol (polyol) production is shown in Table 2. The market share of each is also given. Liquids comprise 48%; crystalline product comprises 39%; and mannitol comprises 13% of the polyol market. An estimate of total U.S. sorbitol capacity for 1995 on a 70% solution basis was 498,000 t. ADM, Decatur, Ill., produced 68,200 t; Ethichem, Easton, Pa., 13,600 t; Lonza, Mapleton, Ill., 45,400 t; Roquette America, Gurnee, Ill., 68,200 t; and SPI Polyols, New Castle, Del., 75,000 t (204). Hoffman-LaRoche, which produces sorbitol for captive usage in the manufacture of Vitamin C (see Vitamins), produced about 27,300 t in 1995.

Table 2. 1995 United States and Canada Polyols Product Market Share

Products	Quantity, $t \times 10^3$	Sales, $\$ \times 10^6$	Market share, %
liquids	171	98.4	47.7
crystalline	51.0	80.9	39.2
mannitol	7.1	27.1	13.1
Total	229.1	206.4	100.0

The 1995 estimate of polyol market share by industry is shown in Table 3. The volume of polyols used in confectionery and oral care products is almost equivalent, at 24% and 26%, respectively. These two applications alone comprise 50% of the polyol usage (see Dentifrices).

Table 3. 1995 Polyols Market Share by Industry

		Sales	
Market segment	Volume, $t \times 10^3$	$\$ \times 10^6$	%
confectionery	55.6	84.6	41.0
oral care	58.5	30.3	14.7
pharmaceutical	21.7	25.4	12.3
food	15.4	15.7	7.6
vitamin C	30.0	15.0	7.3
industrial	20.8	13.3	6.4
surimi	9.0	11.6	5.6
surfactants	17.1	9.4	4.6
cosmetic	1.6	1.1	0.0
Total	*229.9*	*206.4*	*100.0*

8. Biological Properties

8.1. Toxicity

Sugar alcohols are classified as relatively harmless. Acute oral toxicity values in mice for mannitol and sorbitol (5) are given in Table 4. The acute oral LD_{50} value for xylitol in mice is 25.7 g/kg (205). Ingestion of 10 g/d of either mannitol or sorbitol by a normal human subject for one month resulted in no untoward effects (206). Xylitol given to healthy humans for 21 d in increasing doses up to 75 g/d produced no adverse effects (207). The limiting dose of xylitol for production of diarrhea in humans is 20–30 g (4), but tolerance usually develops on continued administration (207).

Table 4. Acute Oral Toxicity in Mice, LD_{50}, g/kg

Mice	Mannitol	Sorbitol
male	22.2	23.2
female	22.0	25.7

8.2. Laxation Thresholds

All sugar alcohols have the potential to cause diarrhea or flatulence owing to their slow absorption from the small intestine. Sorbitol and mannitol have laxation thresholds of 50 and 20 g/d, respectively, and where it is reasonably foreseeable that consumption will exceed these levels, foods must bear the statement “Excess consumption may have a laxation effect”, per 21 CFR 184.1835 (Sorbitol) and 180.25 (mannitol). Maltitol, isomalt, lactitol, maltitol solution (syrup), and hydrogenated starch hydrolysates (HSH) are reported by manufacturers to have laxation thresholds of 100 g/d, 50 g/d, 20 g/d, 75 g/d, and 75 g/d, respectively. These sugar alcohols are not FDA-regulated as of 1996.

8.3. Blood Glucose and Insulin Response

In humans, ingestion of sugar alcohols has shown a significantly reduced rise in blood glucose and insulin response, owing to slow absorption by the body. As a result, many foods based on sugar alcohols have been used safely in the diets of diabetics (208).

Absorption of mannitol (209), sorbitol (210), and xylitol (4) from the intestinal tract is relatively slow, compared to that of glucose. In humans, approximately 65% of orally administered mannitol is absorbed in the dose range of 40–100 g. About one-third of the absorbed mannitol is excreted in the urine. The remainder is oxidized to carbon dioxide (211).

After an oral dose of 35 g of sorbitol, normal or mildly diabetic human subjects excreted 1.5–2.7% in the urine and oxidized 80–87% to carbon dioxide (212). Human subjects, after oral ingestion of up to 220 g of xylitol per day, excreted less than 1% of the dose in the urine (207), indicating efficient metabolism similar to that shown in the results of animal experiments (213). The first metabolic product from mannitol and sorbitol is fructose (214), and from xylitol it is D-xylulose (213). Fructose, sorbitol, and xylitol are principally metabolized in the liver, independent of insulin (215). Although fructose, sorbitol, and xylitol are used as glucose precursors by the liver (and the subsequent metabolism of glucose requires insulin), blood glucose concentration is increased only slightly following oral or intravenous administration of the substances (216).

8.4. Anticariogenicity

Sugar alcohols are not fermented to release acids that may cause tooth decay by the oral bacteria which metabolize sugars and starches (208). As a result, use of sugar alcohols in sugar-free chewing gum, pressed mints, confections, and toothpaste has been widely accepted.

8.5. Caloric Values

Absorption and metabolism data for each of the sugar alcohols has been reviewed by the Federation of American Societies for Experimental Biology (FASEB). Caloric values are lower than 4 cal/g (16.7 J/g), the caloric value of sugar. The values reported for each of the sugar alcohols are sorbitol, 2.6 cal/g (10.9 J/g); mannitol, 1.6 cal/g (6.7 J/g); maltitol, 3.0 cal/g (12.6 J/g); lactitol, 2.0 cal/g (8.4 J/g); isomalt, 2.0 cal/g (8.4 J/g); xylitol, 2.4 cal/g (10.0 J/g); and hydrogenated starch hydrolysate (HSH), 3.0 cal/g (12.6 J/g) (217). Manufacturers have received no letters from the FDA objecting to the use of these reduced caloric values.

9. Uses

The hexitols and their derivatives are used in many fields, including foods, pharmaceuticals (qv), cosmetics (qv), textiles (qv), and polymers.

Aqueous sorbitol solutions are hygroscopic and are used as humectants, softeners, and plasticizers in many different types of formulation. The hygroscopicity of sorbitol solutions is less than that of glycerol but greater than that of sugar solutions. In crystalline form, sorbitol does not absorb moisture greatly below the level of about 70% relative humidity. Above this level, sorbitol is deliquescent and dissolves in absorbed water. Mannitol is considerably less hygroscopic in its crystalline form. Many applications of mannitol take advantage of its low hygroscopicity and its resistance to occlusion of water.

Sweetness is often an important characteristic of sugar alcohols in food and pharmaceutical applications. The property of sweetness is measured in a variety of ways and has a corresponding variability in ratings (218). Based on one or more test methods, erythritol and xylitol are similar to or sweeter than sucrose (218, 219). Sorbitol is about 60% as sweet as sucrose, and mannitol, D-arabinitol, ribitol, maltitol, isomalt, and lactitol are generally comparable to sorbitol (see Sweeteners).

The partial fatty acid esters of the hexitols, usually anhydrized, find extensive use in surface-active applications, such as emulsification, wetting, detergency, and solubilization. Anhydrized sorbitol or mannitol moieties are versatile building blocks which confer hydrophilic properties on surfactants containing them. The less expensive sorbitol derivatives are used more extensively than the analogous mannitol compounds. Fatty acid esters of hexitans tend to be oil-soluble and to form water-in-oil (w/o) emulsions. Hydrophilic character of sorbitan fatty esters is enhanced by attachment of poly(oxyethylene) chains. As the poly(oxyethylene) chain length is increased, the tendency for water-solubility increases and oil-solubility decreases. Hexitan fatty esters having long poly(oxyethylene) chains tend to form o/w emulsions.

9.1. Foods

Sugar alcohols can replace sugar as a bulking agent in foods. As a result, sugar alcohols have increased the number and variety of sugar-free foods which utilize their functional advantages of anticariogenicity, insulin-independent metabolism, and lower caloric values. Approvals for the use of intense sweeteners in a variety of foods from beverages to confectionery products has enabled sweetness levels of sugar-free foods, utilizing sugar alcohols, to be increased for consumer acceptance.

Sorbitol is affirmed Generally Recognized As Safe (GRAS) by the FDA. Usage levels in foods, outlined by 21 CFR 184.1835, include 99% in hard candy and cough drops, 75% in chewing gum, 98% in soft candy, 30% in baked goods and baking mixes, 17% in frozen dairy desserts and mixes, and 12% in all other foods. The labels of foods where the reasonably foreseeable consumption may result in a daily ingestion of 50 g/d of sorbitol shall bear the statement, "Excess consumption may have a laxative effect". In these applications, sorbitol provides bulk, texture, and sweetness to the system.

Mannitol is a food additive permitted in food on an interim basis. Usage levels in foods, outlined by 21 CFR 180.25, include 98% in pressed mints and 5% in all other candy and cough drops, 31% in chewing gum, 4% in soft candy, 8% in confections and frostings, 15% in nonstandardized jams and jellies, and 2.5% in all other foods. The label of food where the reasonably foreseeable consumption may result in a daily ingestion of 20 grams of mannitol shall bear the statement "Excess consumption may have a laxative effect". Because mannitol is nonhygroscopic, it has been the bulking agent of choice for sugar-free chocolate-flavored coatings and compound coatings. Where the cooling effect of mannitol is undesirable, maltitol is used as a replacement. Mannitol is also used as a plasticizer in sugar-free chewing gum and as a dusting agent on the gum to prevent it from sticking to the wrapper.

Xylitol is approved, according to 21 CFR 172.395, for special dietary uses at levels not greater than that required to produce its intended effect. Xylitol is used in sugar-free chewing gum to provide sweetness, softness and a cooling effect.

Maltitol, lactitol, isomalt, maltitol solutions (syrups), and hydrogenated starch hydrolysates (HSH) have GRAS petitions filed with the FDA and are being sold commercially under self-determined GRAS status. Maltitol, owing to its lower negative heat of solution, is often preferred over mannitol as the bulking agent for sugar-free chocolate-flavored coatings and compound coatings. Isomalt, maltitol solutions (syrups), and HSH are used in sugar-free candies produced by conventional roping and stamping equipment.

Sugar alcohols have also found application in foods containing sugars. Sorbitol is an effective cryoprotectant in surimi, preventing denaturation of the muscle protein during frozen storage.

In artificially sweetened canned fruit, addition of sorbitol syrup provides body. Sorbitol has the property of reducing the undesirable aftertaste of saccharin (220). It sequesters metal ions in canned soft drinks as well as iron and copper ions in wines, thereby preventing the occurrence of cloudiness in compounds of these metals (221). Spray-drying a solution of mannitol and acetaldehyde gives a nonhygroscopic powder useful as a flavor-enhancer for fruit-flavored gelatins or beverages (222). D-Arabinitol has been formulated in jams and other foods as a sweetening agent of low caloric value (223). Maltitol and lactitol increase viscosity and confer sweetness in beverages and other foods (98, 224). Carotenoids (225) and edible fats (226) are stabilized by sorbitol, which also prolongs the storage life of sterilized milk concentrates (227). Mixtures of sorbitol or mannitol and a fat, applied as an aqueous syrup to snacks and cereals, confer a rich mouth-feel and keep these foods crisp when they are immersed in milk (228). Both mannitol and sorbitol, at 1% concentration, inhibit the growth of *A. niger* in an intermediate-moisture (15–40%) food system containing raisins, peanuts, chicken, and nonfat dry milk (229). Freezer burn of rapidly frozen livers is prevented or greatly reduced by dipping in 25% sorbitol solution (230). Incorporation of sorbitol into frankfurter meat improves color, taste, shelf life, and facilitates removal of the casings (231). Sorbitol, sometimes in combination with propylene glycol (232), texturizes pet foods by its humectant properties (see Feeds and feed additives).

In candy manufacture, sorbitol is used in conjunction with sugars to increase shelf life. It is used in making fudge, candy cream centers, soft and grained marshmallows, and in other types of candy where softness depends upon the type of crystalline structure. The function of sorbitol in this application is in retarding the solidification of sugar often associated with staleness in such candy. In butter creams, an additional benefit is involved in flavor improvement by virtue of the sequestering action it has on trace metals. Sorbitol may be used in diabetic chocolates. Crystalline sorbitol or crystallized blends of sorbitol and mannitol constitute a sugarless confection (233), as does sorbitol containing up to 5% citric acid (234).

Sorbitol is used as a humectant and softener in shredded coconut, where it has a decided advantage over the invert sugar often used, because darkening of the product does not occur. A small quantity of sorbitol, as the 70% aqueous solution, added to peanut butter has been shown to reduce dryness and crumbliness and improve spreadability. Nuts coated with a blend of mannitol and sorbitol, from an aqueous solution or slurry of the hexitols, are roasted at 177–205°C. The hexitol coating on the nuts immobilizes salt applied during cooling and does not flake off (235, 236). No oxidative degradation of the hexitols occurs on prolonged heating, and there is no significant decrease in hexitol content. Only traces of mannitans and sorbitans are formed (237).

Sorbitan fatty esters and their poly(oxyethylene) derivatives are used as shortening emulsifiers. In cakes and cake mixes, emulsification of the shortening is improved, resulting in better cake volume, texture, grain, and eating qualities. These emulsifiers are used in icings and icing bases as well as in pressure-packed synthetic cream-type toppings. In ice-cream, they confer improved body and texture and provide dryness and improved aeration. Poly(oxyethylene(20)) sorbitan monooleate and the corresponding tristearate are used as emulsifiers either separately or as blends in ice cream and other frozen desserts. Crystallization of cane sugar is accelerated, the fluidity of the crystallizing mass improved, and the sugar yield increased by addition of poly(oxyethylene(20)) sorbitan monostearate.

9.2. Pharmaceuticals

Mannitol finds its principal use in pharmaceutical applications (see Pharmaceuticals). It is used as a base in chewable, multilayer, and press-coated tablets of vitamins, antacids, aspirin, and other pharmaceuticals, sometimes in combination with sucrose or lactose. It provides a sweet taste, disintegrates smoothly, and masks the unpleasant taste of drugs such as aspirin. Tablets containing mannitol retain little moisture because of the low affinity of mannitol for water, making it an excellent excipient and thus suitable for use with moisture-sensitive actives. Mannitol is available as a powder for wet granulation tableting and in a granular form for direct compression tableting.

Sorbitol solution finds use as a bodying agent in pharmaceutical syrups and elixirs. The use of sorbitol in cough syrups reduces the tendency of bottle caps to stick because of crystallization of the sugar present (238). Sorbitol solution is also used as the base for sugar-free cough syrups, which have increased in popularity, particularly in the pediatric market. Enhanced stability is conferred by sorbitol in aqueous preparations of medications such as vitamin B_{12} (239), procaine penicillin (240), and aspirin (241). Stable suspensions of biologicals, such as smallpox vaccine, are obtained in a medium containing polydimethylsiloxane, mannitol, and sorbitol (242). Inclusion of sorbitol in aqueous suspensions of magnesium hydroxide prevents flocculation and coagulation, even when they are subjected to freeze–thaw cycles. A gel base in which other ingredients can be incorporated to make w/o creams is produced by combining 70% sorbitol solution with a lipophilic surfactant. Crystalline sorbitol is used as an excipient, where it gives a cool and pleasing taste from its endothermal heat of solution. Use of crystalline and powdered sorbitol enables preparation of troches with different degrees of hardness, by direct compression (243). Sorbitol is used in enema solutions (244).

A major pharmaceutical use of poly(oxyethylene) sorbitan fatty acid esters is in the solubilization of the oil-soluble vitamins A and D. In this way, multivitamin preparations can be made which combine both water- and oil-soluble vitamins in a palatable form.

Sorbitan sesquioleate emulsions of petrolatum and wax are used as ointment vehicles in skin treatment. In topical applications, the inclusion of both sorbitan fatty esters and their poly(oxyethylene) derivatives modifies the rate of release and promotes the absorption of antibiotics, antiseptics, local anesthetics, vasoconstrictors, and other medications from suppositories, ointments, and lotions. Poly(oxyethylene(20)) sorbitan monooleate, also known as Polysorbate 80 (USP 23), has been used to promote absorption of ingested fats from the intestine (245).

Manufacture of vitamin C starts with the conversion of sorbitol to L-sorbose. Sorbitol and xylitol have been used for parenteral nutrition following severe injury, burns, or surgery (246). An iron–sorbitol–citric acid complex is an intramuscular hematinic (247). Mannitol administered intravenously (248) and isosorbide administered orally (249) are osmotic diuretics. Mannitol hexanitrate and isosorbide dinitrate are antianginal drugs (see Cardiovascular agents).

9.3. Cosmetics

Sorbitol is widely used in cosmetic applications, both as a humectant, in which case it retards the loss of water from o/w type creams, and as an emollient (see Cosmetics). Spreadability and lubricity of the emulsions are enhanced by aqueous sorbitol solution (250). Sorbitol is useful in both brushless and lather-type shaving creams as a humectant and plasticizer. It is incorporated in many toothpaste formulas of both regular and fluoride types, to the extent of 25–35%. This usage is based on its ability to act as an economic, viscous vehicle, and on its alkali stability, humectant, and plasticizing properties. Xylitol has been used as a humectant in toothpaste, both alone and in combination with sorbitol and glycerol (251) (see Dentifrices). Sorbitol solutions are used in mouthwash formulations. Because sorbitol resists fermentation by oral microorganisms, its use as a mouthwash does not increase the incidence of dental caries. Tests on patients having carious lesions have shown that sorbitol resists fermentation longer than glycerol.

Emulsions of fatty- and petroleum-based substances, both oils and waxes, of the o/w type are made by using blends of sorbitan fatty esters and their poly(oxyethylene) derivatives. Mixtures of poly(oxyethylene(20)) sorbitan monostearate (Polysorbate 60) and sorbitan monostearate are typical examples of blends used for lotions and creams. Both sorbitan fatty acid esters and their poly(oxyethylene) derivatives are particularly advantageous in cosmetic uses because of their very low skin irritant properties. Sorbitan fatty ester emulsifiers for w/o emulsions of mineral oil are used in hair preparations of both the lotion and cream type. Poly(oxyethylene(20)) sorbitan monolaurate is useful in shampoo formulations (see Hair preparations). Poly(oxyethylene) sorbitan surfactants are also used for solubilization of essential oils in the preparation of colognes and after-shave lotions.

9.4. Textiles

Sorbitol sequesters iron and copper ions in strongly alkaline textile bleaching or scouring solutions (see Textiles). In compositions for conferring permanent wash-and-wear properties on cotton fabrics, sorbitol is a scavenger for unreacted formaldehyde (252) and a plasticizer in soil-resistant and soil-release finishes (253).

Sorbitan fatty acid esters and their poly(oxyethylene) derivatives are used both to emulsify textile-treating chemicals and, by themselves, as finishes for textile processing. Poly(oxyethylene(20)) sorbitan monolaurate and its homologues are used as antistatic agents on textiles. Friction of yarns and fibers can be controlled by applying blends of sorbitan fatty acid esters with other surfactants. Sorbitan monopalmitate, monooleate, and monostearate, together with other surfactants, serve as fabric softeners and textile size plasticizers. The condensation product of sorbitol and epichlorohydrin, after reaction with the diethylene triamine diamide of stearic acid, is a component of a textile-softening composition (254). Poly(oxyethylene) derivatives of sorbitol and other polyols are used in viscose spinning baths to improve the properties of viscose rayon, extruded in the form of filaments and films. Sorbitan monooleate is used in dry-cleaning detergents, often in conjunction with an anionic surfactant.

9.5. Polymers

In combination with various metal salts, sorbitol is used as a stabilizer against heat and light in poly(vinyl chloride)(qv) resins and, with a phenolic antioxidant, as a stabilizer in uncured styrene–butadiene rubber (qv) compositions and in polyolefins (see Heat stabilizers; Olefin polymers; Rubber compounding). Heat-sealable films are prepared from a dispersion of sorbitol and starch in water (255). Incorporation of sorbitol in collagen films greatly restricts their permeability to carbon dioxide (256).

Sorbitol, together with other polyhydric alcohols such as glycerol or pentaerythritol, can serve as the polyol component of alkyd resins and rosin esters for use in protective coatings and core binders (see Alkyd resins). The poly(oxypropylene) derivatives of sorbitol have found extensive use as polyol components of polyurethane resins, particularly for rigid urethane foams. In this application, sorbitol derivatives having short poly(oxypropylene) chain lengths, eg, poly(oxypropylene(10)) sorbitol, are combined with a diisocyanate such as toluene dissocyanate, together with blowing agents, catalysts, and other additives, to prepare foams. As the number of poly(oxypropylene) units attached to sorbitol increases above about 14, the products become suitable for use in semirigid and resilient foams, coatings, and elastomers (see Urethane polymers). Sorbitan fatty esters may be used as plasticizers, lubricants, and antifog agents for vinyl resins and other polymers. In suspension polymerization of vinyl chloride, use of sorbitan monolaurate, monopalmitate, and monostearate makes the primary particles of poly(vinyl chloride) more spherical, and controls their size and specific surface, as well as the porosity of the polymer.

9.6. Miscellaneous Uses

Sorbitol is used in flexible glues, cork binders, and printers' rollers, frequently in combination with glycerol, to confer strength and flexibility, as well as stability to humidity change. The high viscosity imparted by sorbitol in these applications is often desirable because it improves the mechanical strength and temperature resistance of the products (257). Glue-type products in which sorbitol is used include bookbinding and magazine and paper tape adhesives. Sorbitol, in conjunction with sugars, glycerol, or propylene glycol, has been used in tobacco as a component of casing solutions, to add moisture-retention properties. Sorbitol solution is used as a moistening agent in synthetic sponges. Clouds and fog disintegrate on introduction of finely divided sorbitol, usually together with inorganic substances such as silica or calcium phosphate (258). As a component in alkaline etching baths for aluminum, sorbitol helps eliminate scale formation on the surfaces of aluminum and aluminum alloys (see Dispersants).

Mannitol and dulcitol are used as components of bacteriological media. Blood is protected during freezing, storing, and thawing by adding 15–20% of mannitol (259). Dulcitol, mannitol, and sorbitol protect freeze-dried bacterial cultures during storage (260), and animal semen is preserved by the addition of small quantities of sorbitol and mannitol together with other materials (261).

Poly(oxyethylene) derivatives of sorbitol and sorbitan fatty acid esters, usually in blends with anionic surfactants, are used as emulsifiers for insecticides, herbicides (qv), and other pesticides (qv). Blends of sorbitan surfactants are also used to suspend pigments in water-based paints and, in pigment pastes, to keep the dispersions uniform. Sorbitan monooleate functions as a corrosion inhibitor. Poly(oxyethylene(20)) sorbitan monopalmitate and monostearate sprayed on glass jars minimize breakage and surface damage (262). Glass fibers are protected by a coating containing poly(oxyethylene(20)) sorbitan monooleate (263). Oil slicks on sea water are dispersed when sprayed with mixtures of sorbitan monooleate and poly(oxyethylene(20)) sorbitan monooleate (102) (see Surfactants).

Organogels can be formed from ethylene glycol, nitrobenzene, vegetable oils, and other organic liquids, using di- or tribenzylidene–sorbitol as gelling agents. In the explosives industry, mannitol hexanitrate is used as an initiator in blasting caps. Nitration of glycerin–ethylene glycol solutions of sorbitol yields low freezing, liquid, high explosive mixtures of value for dynamite formulas (see Explosives and propellants).

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