b) Optical isomers: The presence of chiral carbon atom also confers optical activity. An optically active compound has ability to rotate the beam of plane-polarized light to either right or left. All monosaccharides (except dihydroxyacetone) are optically active due to the presence of chiral carbon atoms. They can rotate the beam of plane—polarized light; when the beam of plane-polarized light is rotated to left the sugar is called laevorotatory sugar (Latin 'laevus' means left), whereas, when the beam of plane-polarized light is rotated to right the sugar is called dextrorotatory sugar (Latin 'dexter' means right). The laevorotatory is designated by (l) or (- sign) while dextroromtory is designated by (d) or (+ sign). Glucose and fructose are dextrorotatory (+) and laevorotatory (—) sugars, respectively.

The direction of rotation is independent of the stereochemistry of the sugar, therefore, a sugar with D-configuration may be dextrorotatory, designated by D (+) or laevorotatory, designated by D (—). Similarly, a sugar with L-configuration may be dextrorotatory, designated by L (+) or laevorotatory, designated by L (-). The naturally occurring form of glucose is D (+) isomer and of fructose is D (-) isomer.

A mixture containing equal quantities of dextrorotatory (+) and laevorotatory (—) isomers is found optically inactive and is called racemic mixture or dl mixture. In a racemic mixture, opposite optical activities of both isomers are cancelled by each other. The isolation of optically active pure dextrorotatory (+) or laevorotatory (—) isomer from a racemic mixture is known as resolution.

(c) Epimers: Epimers are isomers that differ in configuration (in stereochemistry) around one specific carbon atom only, e.g. D-glucose and D-mannose are epimers that are formed due to interchange of configuration of 'OH and -H around carbon—2. D-glucose and D-galactose are epimers due to interchange of configuration of —OH and H around carbon-4 (Fig. 4.8).

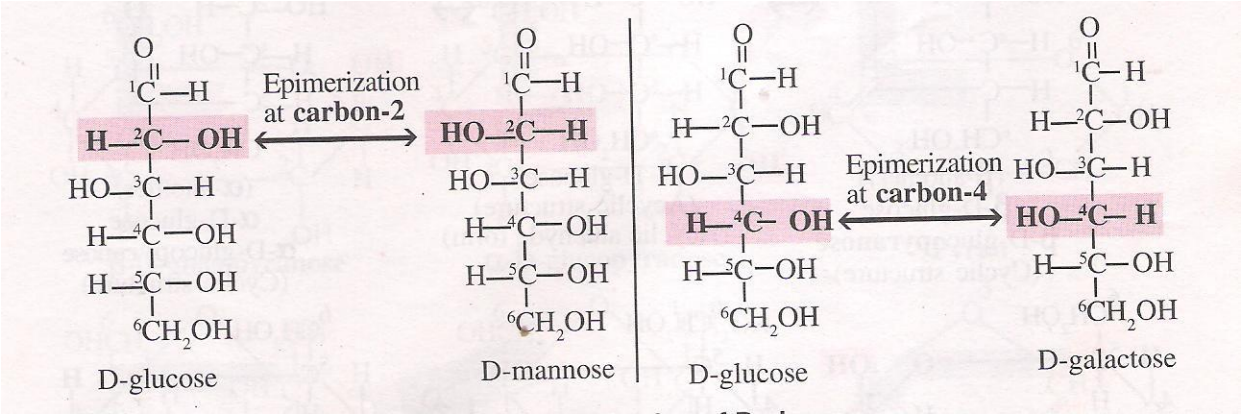


Fig. 4.8 epimerization of D-glucose

(vii) α- and β- anomers: Presence of two reacting groups, a carbonyl group (—CHO on carbon-l in glucose or —CO group on carbon;2 in fructose) and an alcoholic group, on same sugar molecule allows the cyclization of monosaccharides containing five or more carbon atoms. In open chain acyclic) form of glucose, the aldehyde group (—CHO) on carbon-1 condenses with alcoholic —OH group on carbon-5 to form hemiacetal ring, i.e. cyclic structure of glucose (Fig. 4.9). However,

in open chain (acyclic) form of fructose, the keto group (—CO) on carbon-2 condenses with alcoholic —OH group on carbon—5 to form hemiketal ring, i.e. cyclic structure of fructose. If the resulting ring has six atoms in cyclic- ring (5 carbon atoms and l oxygen atom), it is called a pyranose ring (Figs. 4.9 and 4.11). If it is five-member cyclic-ring (4 carbon atoms and l oxygen atom), it is called a furanose ring (Fig. 4.11).

In cyclic form of glucose, due to formation of hemiacetal ring, the carbon-1 becomes asymmetric carbon with four different groups attached to it and is called anomeric carbon (Fig. 4.9). On the basis of stereochemistry (orientation of ——OH group) at the anomeric carbon atom, two isomers of cyclic structure of glucose are possible.

(i) α-anomer of glucose (α-D-glucose): —OH group on anomeric carbon atom (C1) extends to right (Fig. 4.9).

(ii) β-anomer of glucose (β-D-glucose): -OH group on anomeric carbon atom (C1) extends to left (Fig. 4.9).

Both 0t-D-glucose and B-D-glucose are optically active (dextrorotatory). The **α**- D-glucose and β-D-glucose have specific rotation of $+112^0$ and $+19^0$, respectively (Fig. 4.9). Crystalline glucose exists in a—D-glucopyranose form. When it is dissolved in water, although its cyclic structure is retained in aqueous solution but it undergoes isomerization at anomeric carbon to give rise an equilibrium mixture of both **α** -D-glucopyranose (about 37%) and β-D-glucopyranose (about 62%). The mixture also contains about 1% of glucose in the form of **α**-D-glucofuranose, β-D-gluco-furanose and acyclic aldehyde (open-chain form).

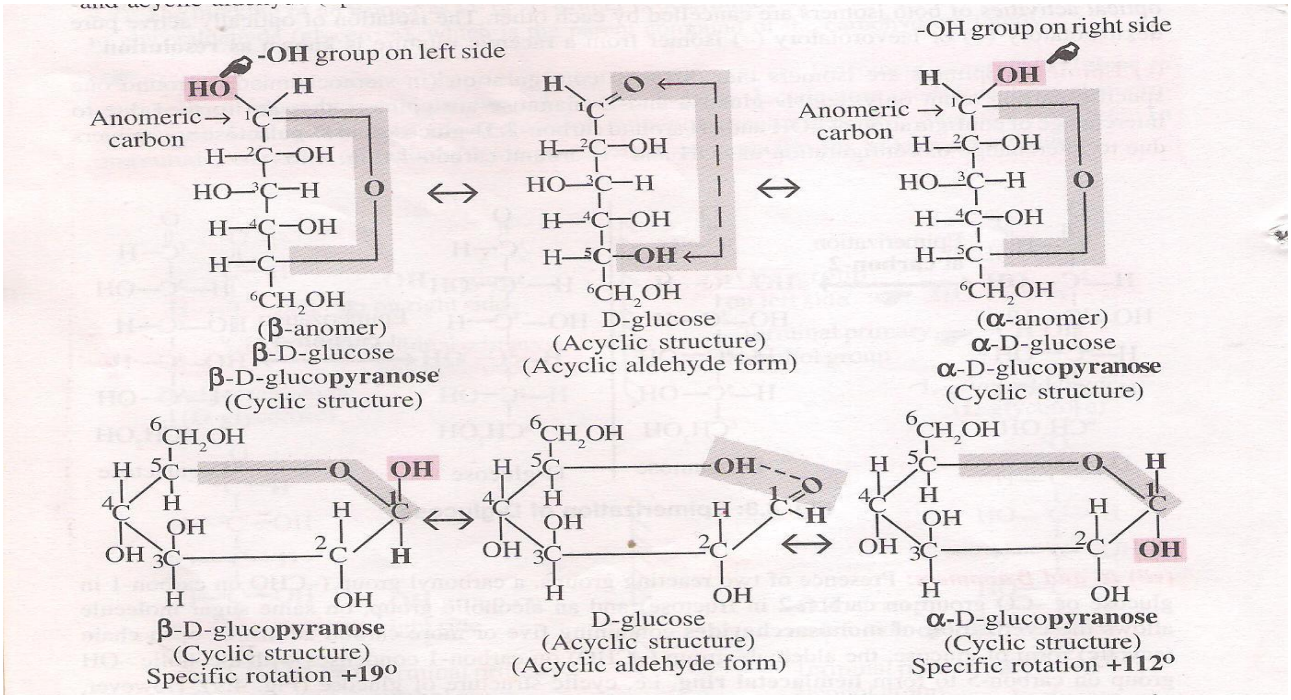


Fig. 4.9 cyclization of acyclic aldehyde form of D-glucose resulting in formation of β-D-glucose (β-anomer) and α-D-glucopyranose (α-anomer)

(viii) Mutarotation: The phenomenon of change in specific rotation (of beam of plane-polarized light) shown by some sugars such as glucose, fructose, etc. is called mutarotation. For example, when crystalline α-D-glucose (α-D- glucopyranose), which has initial specific rotation of $+112^0$, is dissolved in distilled water its specific rotation gradually changes with time and attains a stable value of +5250. Similarly, when crystalline ['§»D-glucose (B~D-glucopyranose), which has initial specific rotation of +190, is dissolved in distilled water its specific rotation gradually changes with time and attains the same specific rotation of +5250. Such change in specific rotation is called mutarotation (Fig. 4.10)

The mutarotation results from interconversion of α-D-glucose (α-D-glucopyranose) and β-D- glucose (β-Dqglucopyranose) in an aqueous solution. The on-and β-anomers of D-glucose interconvert in aqueous solution due to isomerization at anomeiic carbon atom as shown in Fig. 4.9. Whenever α-D-glucose or β-D-glucose is dissolved in distilled water, each spontaneously produces an equilibrium mixture of both (α—D-glucose and β-D- glucose. At equilibrium, the mixture contains about 62% B-D- glucopyranose, 37% on-D-glucopyranose ‘and 1% glucofuranose and acyclic aldehyde form of glucose. At equilibrium, such mixture has stable specific rotation of +5250.

β-D-glucopyranose		D-glucose		α-D-glucopyranose
Cyclic structure	→	acyclic st.	←	Cyclic st.
approx.62%		<1%		approx. 37%
Specific rotation +19°	→	s.r + 52.5°	←	s.r +112°

fig. 4.10 mutarotation shown by glucose

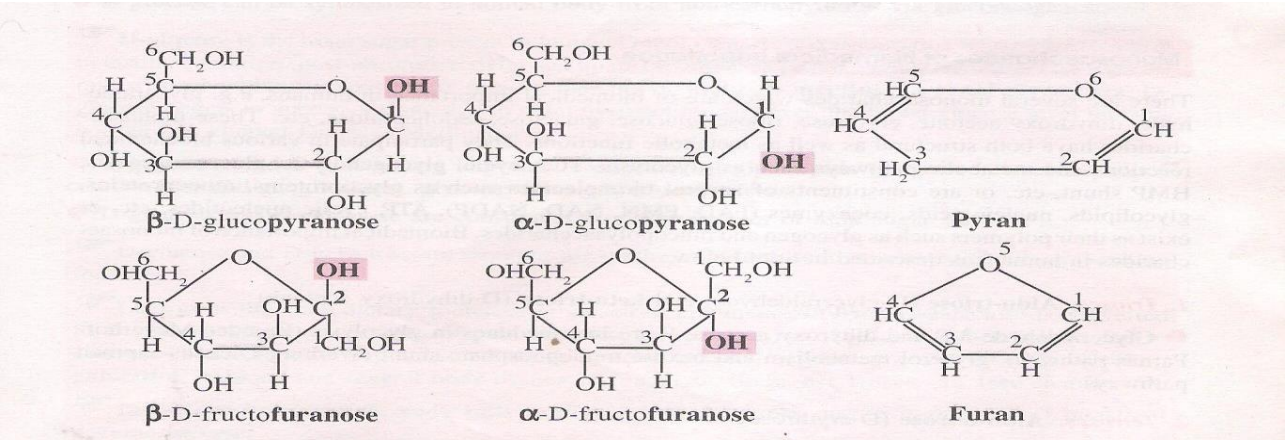


Fig. 4.11 pyranose and furanose form of D-glucose and D-fructose respectively

(ix) pyranose and furanose ring structures: Haworth (1929) proposed that condensation of aldehyde group (on carbon-l) or keto group (on carbon-2) of hexoses with alcoholic-OH group (carbon 5) of same molecule results in formation hemiacctal ring or hemiketal ring, respectively.according to Haworth, if the resulting ring/cycle has six atoms in cyclic-ring (5 carbon and 1 oxygen) it is called a pyranose ring because it resembles the six—membered ring compound pyran (fig.4.11). If it is five memhered cyclic-ring (4 carbons and l oxygen), it is called a furanose ring because it resembles the five~membered ring compound furan (Fig. 4.11) Monosaccharides con- taining five or more carbon atoms can only form cyclic structures. Aldo—hexoses mostly exist in pyranose form, whereas keto-hexose (fructose) and pentoses occur in furanose form. Glucose can exist in both D-glucopyranose and D-glucofuranose forms.

(x) Glycosidic/glucosidic bond: Two monosaccharides are linked together through an oxygen bridge known as O-glycosidic or O-glucosidic bond. The O-glucosidic bond is formed between -OH of the two monosaccharide units by elimination of one water molecule (Fig. 4.12). If the bond is formed between α-anomers, the bond is called **α-glycosidic** bond and if it is formed between the **β-anomers**, it is called **β-glycosidic** bond.

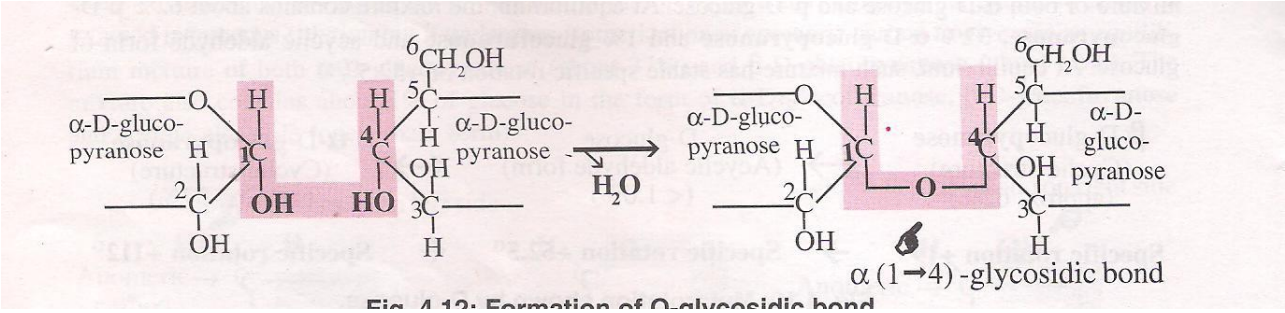


Fig. 4.12 formation by glycosidic bond

monosaccharides of biomedical importance: There are several monosaccharides which are of biomedical importance in humans, e.g. glyceraldehyde, dihydroxy acetone, erythrose, ribose, glucose, galactose, sedoheptulose, etc. These monosaccharides have both structural as well as metabolic functions. They participate in various biochemical reactions and metabolic pathways such as glycolysis, TCA cycle, glycogenolysis, gluconeogenesis,HMP shunt, etc. or are constituents of several biomolecules such as glycoproteins, mucoproteins, glycolipids, nucleic acids, coenzymes (FAD, FMN, NAD, NADP), ATP, cyclic nucleotides, etc. or exist as their polymers such as glycogen and mucopolysaccharides. Biomedical importance of monosaccharides in humans is described in brief below.

1. **Triosess**: **Aldo-triose** (D-glyceraldehyde) and keto-triose (D-dihydroxy acetone)

- **Glyceraldehyde-3-P** and **dihyroxy acetone-P** are intermediates in glycolysis (Embden-Meyerhof-Parnas pathway), glycerol metabolism and hexose monophosphate shunt (Warburg-Dickens-Lipman pathway). '

2. **Tetroses**: **Aldo-tetroyse** (**D-erythrose**)

- **Erythrose-4-P** is an intermediate in hexose monophosphate shunt (HMP shunt).

3. **Pentoses**: Aldo-pentoses (D-1ibose, D-2- deoxyribose, D-lyxose, D-xylose, L-fucose) and keto pentoses (D-ribulose, L-xylulose, D-xylulose)

-D-ribose and D-2 deoxyribose are important constituents of nucleotides and nucleic acids D-ribose and D-2-deoxyribose are present in RNA and DNA, respectively.

-D-ribose is also constituent of several coenzymes such as NAD^+ (Nicotinamide adenine dinucleotide), $NADP^+$ (Nicotinamide adenine dinucleotide phosphate) and FAD (flavin adenine dinucleotide).

-AMP, ADP and ATP have D-ribose as structural component.

-D-ribose is constituent of cyclic nucleotides, cAMP and cGMP, which serve as 'second messenger in signal transduction.

-D-ribulose-5-P and D-xylulose-5-P are intermediates in HMP shunt.

-L-xylulose is an intermediate in glucuronic acid pathway.

L-xylulose appears in urine of patients of essential pentosuria. Pentosuria is an inborn error of glucuronic acid pathway and results from inherited deficiency of enzyme L-xylitol dehydrogenase.

- D-xylose and L-fucose are constituents of glycoproteins.

4. **Hexoses**: Aldo-hexoses (D-glucose, D-galactose) and keto-hexose (D-fructose)

- D-glucose is also known as 'dextrose' due to its dextrorotatory nature and is chief source of energy especially for brain cells, erythrocytes, growing fetus, lens and cornea of eyes.

- D-glucose is stored as glycogen in liver and muscles.

- D-glucose can be synthesized in human body from non-carbohydrates via gluconeogenesis.

-**D**-glucose is the main sugar present in human blood; its normal concentration being 70-110 mg/dl in fasting condition (post-absorptive state) and up to 140 mg/dl in post prandial condition. Hyperglycemia with or without glycosuria is seen in patients of diabetes mellitus. In renal glycosuria, D- glucose begins to appear in urine due to renal dysfunction; however, the blood glucose level remains normal.

-**D**-galactose and D-glucose are important constituent of glycolipids (galactocerebrosides, gluco-cerebrosides and gangliosides), glycoproteins and mucoproteins.

-**D**-glucose and D-galactose are constituent rnonosaccharides of milk sugar 'lactose'.

-**D**-glucose and D-galactose are required for synthesis of lactose in mammary glands of lactating mothers.

Lactose is the main dietary source of D-galactose in humans. In liver, D-galactose is converted to D-glucose. However, patients of galactosemia, an inborn error of galactose metabolism, fail to convert D-galactose to D-glucose resulting in accumulation of galactose and its sugar-alcohol, glactitol, in blood and several body tissues such as liver, brain, eye lenses, etc.

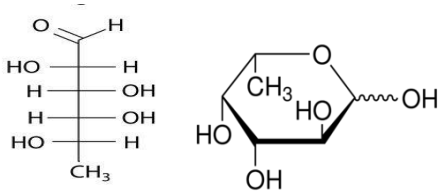
D-fructose is metabolized in liver. However, patients of fructose intolerance, an inborn error' of fructose metabolism, fail to utilize the D-fructose resulting in clinical conditions characterized by fructosuria and hypoglycemia.

E. Heptoses: Keto-heptose (D—sedoheptulose)

Sedoheptulose-7-phosphate is an intermediate in hexose monophosphate shunt (HMP shunt).

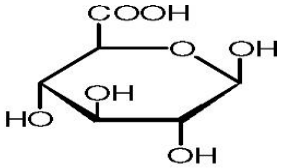
Derivatives of monosaccharides (deoxy sugar, sugar acids, amino sugars and amino sugar acids)

- In deoxy sugars, one of the hydroxyl group (—OH) of sugar is replaced by hydrogen (—H). The D-2'-deoxyribose is constituent of deoxy-ribonucleic-acid (DNA).
- L-fucose (methyl pentose) is constituent of glycoproteins that determine the blood groups.



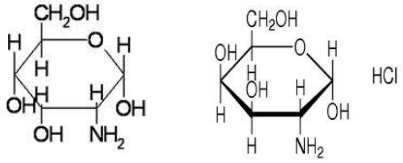
L-fucose (6-deoxy L- galactose)

-In sugar—acids such as D-glucuronic acid (Fig. 4.3) and L-iduronic acid, primary alcoholic group (-CHZOH) of hexoses is oxidized to carboxylic group (—COOH). The sugar acid may also be further sulphated (e.g. sulphated glucuronic acid).



β-D-glucuronic acid

-In amino—sugars such as D-glucosamine, D-galactosamine and D-mannosamine, one of the hydroxyl group (—OH) of the hexoses is replaced by an amino group (—NH2). The amino-sugars may also be acetylated and sulphated, e.g. Naacetylglucosamine and Nacetylgalactosamine sulphate are acetylated and sulphated amino-sugars, respectively.



D-glucosamine D-galctosamine

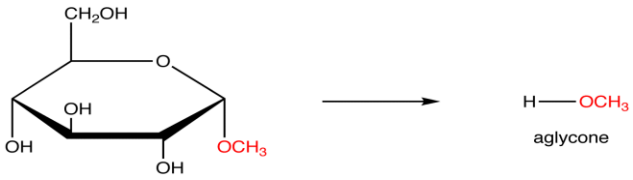
The sugar-acids and amino-sugars are constituent monosaccharides of mucopolysaccharides (glycosaminoglycans) such as hyaluronic acid, keratan sulphate, dermatan sulphate, chondroitin, heparin (natural blood anticoagulant), etc. Mucopolysaccharides are present in cartilage, cornea, skin, tendons, heart valves, synovial fluid, arota, bone, etc. '

D-glucuronic'-acid conjugates bilirubin to convert it into diglucuronide derivative; a soluble form which is excreted in urine. In liver, glucuronic acid also conjugates toxic substances and drugs for their elimination outside the body.

Amino-sugars are also constituents of **proteoglycans** (conjugated proteins containing glycosaminoglycans and core protein), **gangliosides**, **glycoproteins** and **aminoglycoside antibiotics**, e.g.erythromycin, gentamicin, streptomycin, etc. Amino-sugar-acids, e.g. sialic acid (also known as N-acetyl neuraminic acid) and muramic acid are important constituents of glycoproteins, gangliosides and some mucopolysaccharides.

Glycosides

Glycosides are composed of carbohydrate and a non-carbohydrate residue that may be a sterol, a nitrogenous base (e.g. adenine), phenol, glycerol, etc. The non-carbohydrate residue of a glycoside is termed as **aglycone**. The glycosides are formed by condensation between the —OH group of anomeric carbon of carbohydrate residue and —OH or other group of aglycone. If the linkage is formed between two OH groups the bond is called an O-glycosidic bond and if it is formed between -OH group of carbohydrate residue and amine group of adenine then the bond is termed as N-glycosidic bond. If a glycoside contains glucose as carbohydrate residue, it is known as glucoside or glycoside and if the sugar residue is galactose then it is termed as galactoside.



Glycosides are widely distributed in nature. The cardiac glycosides and iminoglycosides are most important glycosides being used as therapeutic agents in medicine. Cardiac glycosides, digoxin and digitoxin, contain the aglycone steroid and are used as drugs in treatment of cardiac insufficiency (heart failure): Cardiac glycosides inhibit Na, K'%ATPase and have positive inotropic effect on cardiac muscles. The aminoglycoside antibiotics such as gentamicin, streptomycin, etc. are used to treat various bacterial infections