

02/12/2022  
Friday

# CHEMISTRY OF CARBOHYDRATES

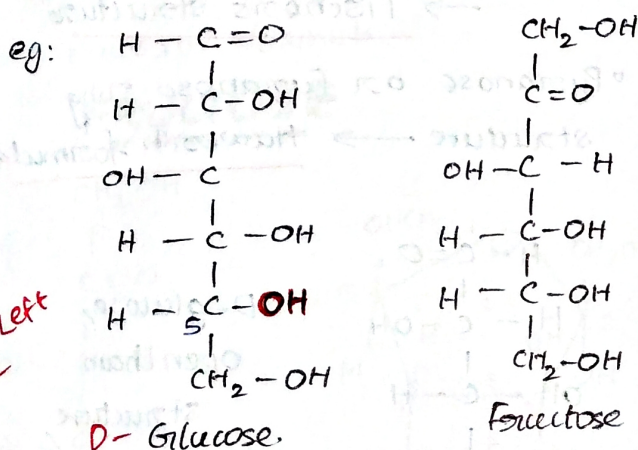
Dr. Genga 8-9 am.

Study of biochemical in our body.

- Defn
- Classification
- Rn
- Biomedical importance / fn
- Isomerism

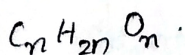
## Carbohydrates

They are polyhydroxy aldehydes or ketones (or) comp. which yield these on hydrolysis.



OH-Left  
→ L

• contain C, H & O with gen. formula



•  $\text{C}_n(\text{H}_2\text{O})_n$  - hydrates of C.  
(for every C → 1 H<sub>2</sub>O)

• All sugars can't be represented by this gen. formula.

except  
↓

eg: Deoxy ribose -  $\text{C}_5\text{H}_{10}\text{O}_4$

• All comp. having H & O in ratio of 2:1 are not carbohydrates

eg: Acetic acid -  $\text{CH}_3\text{COOH}$  -  $\text{C}_2(\text{H}_2\text{O})_2$

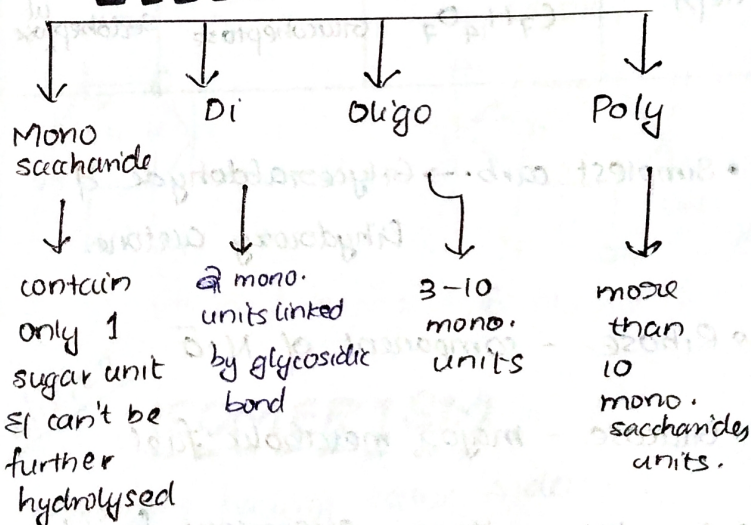
• Apart from C, H & O, many sugars contain N, S, P etc.

eg: Amino sugars, phosphosugars etc.

## Functions

- Main source of energy
  - Glucose 4 Kcal/gm
- Storage form of energy
  - starch & glycogen
- components of cell membrane, receptors - glycoproteins & glycolipids
- structural basis of organs - mucopolysaccharides as ground substance [keratin sulphate, eg!]
- Shock absorber - hyaluronic acid (mucopolysacch.) ↓ seen in synovial fluid.
- Anticoagulant - Heparin (mucopolysacch.)

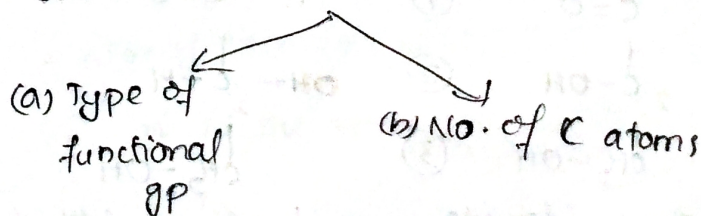
## CLASSIFICATION



## MONOSACCHARIDES

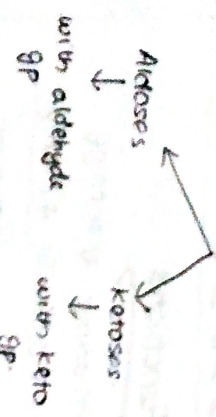
• Molecules having 1 potential sugar gp are mono. they can't further hydrolysed into smaller units.

subclassified based on





They are categorised into two.



eg. ketose

Based on no. of C atoms.

| Mono.    | Mol. formula   | Aldose         | Ketose            |
|----------|----------------|----------------|-------------------|
| Trioses  | $C_3H_6O_3$    | Glyceraldehyde | Dihydroxy acetone |
| Tetroses | $C_4H_8O_4$    | Erythrose      | Erythrulose       |
| Pent     | $C_5H_{10}O_5$ | Ribose         | Ribulose          |
| Hex      | $C_6H_{12}O_6$ | Glucose        | Fructose          |
| Hept     | $C_7H_{14}O_7$ | Glucosamine    | Sedoheptulose     |

Simplest carb. → Glyceraldehyde & Dihydroxy acetone.

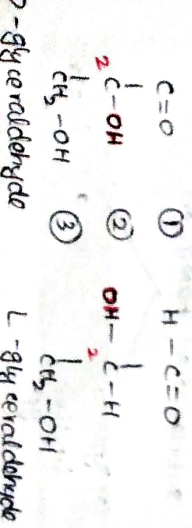
Ribose - component of N.A  
Glucose - major metabolic fuel

Fructose - honey, sugarcane, fruit juice

Galactose - comp. of milk sugar (lactose)

Mannose - const. of glycoproteins

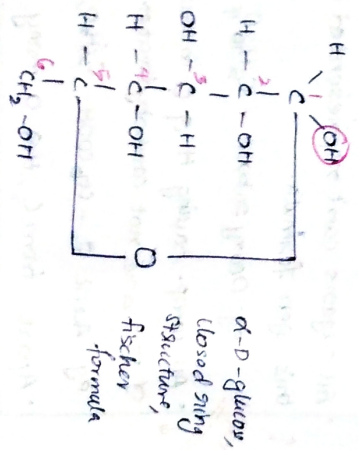
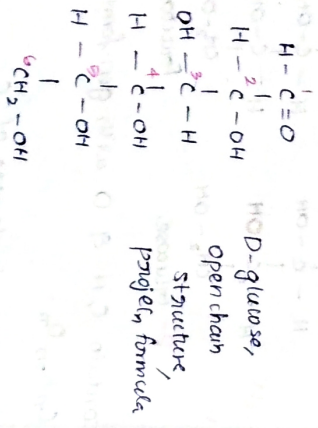
Monosaccharides



- OH - right - D
- OH - left - L
- chiral C → 4 diff. groups are attached.
- AN orientation of C occurs in the penultimate C atom & it is taken as preference.

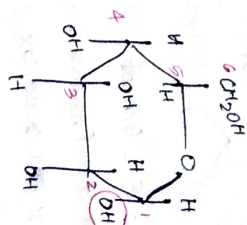
### GLUCOSE

- Most abundant
- Structure rep. in 3 forms
- Open chain formula
- Hemi-acetal ring structure → Fischer's structure
- Pyranose or furanose ring structure → Haworth formula



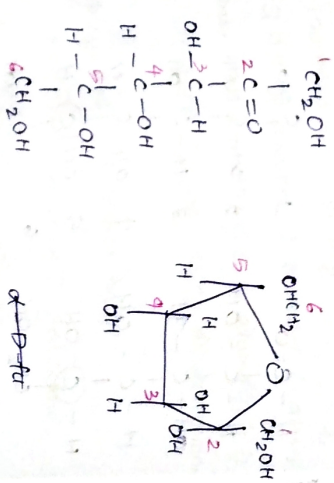
Also to Haworth, glucose exists in 6 membered ring str. (pyranose) in soln.

Five membered ring str. is furanose, 99% is in pyranose structure.

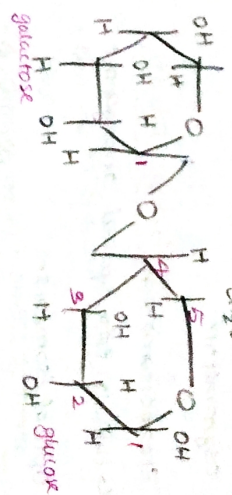


α-D-glucopyranose, Haworth formula.

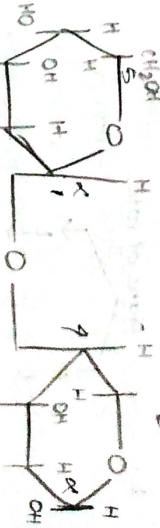
### FRUCTOSE



LACTOSE: Glucose + Galactose

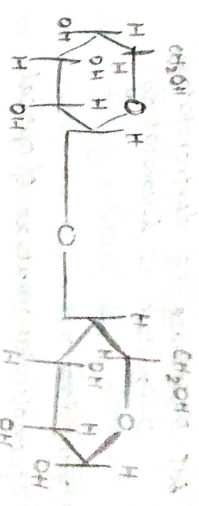


α-D-Glucose (1→4) β-D-Glucose



α-1,4-Glycosidic bond

### ISOMALTOSE



Glucosyl-α-1,6-glucose

### ISOMERISM

Molecules having same molecular formula but diff. structure

- Stereo isomerism
- Optical isomerism
- Presence of asymmetric carbon atoms.

No. of isomers possible is  $2^n$  n is the no. of asymmetric C-atoms.

### DISACCHARIDES

composed of 2 monos. linked together through a glycosidic linkage

Biological imp. → disaccharides

- Sucrose: Glucose + Fructose
- Lactose: Glucose + Galactose
- Maltose: Glucose + Glucose
- Isomaltose: Glucose + Glucose



## Glucose

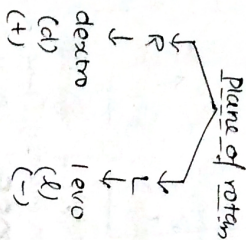
C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> carbon atoms are asymmetric.

Stereoisomerism

↳ diff. in ~~the~~ spatial arrangement

Optical isomerism

• when a plane polarised light is passed through a soln of carbohydrate it rotates the light either to R or L.



Att D-glucose is dextrorotatory  
D-fructose is levorotatory

- Equimolar mixture of optical isomers has no net rotation of polarised light → Racemic mixture.

$$\Rightarrow \text{net rotation} = 0$$

Stereo isomers

Diff. spatial configuration of H & OH gp. around chiral C

- D & L isomerism.
- Anomerism
- Epimerism

## D & L isomerism

Diff. in orientation of H & OH gp around penultimate C-atom resulting in probn of mirror images.

• Mirror images = enantiomers

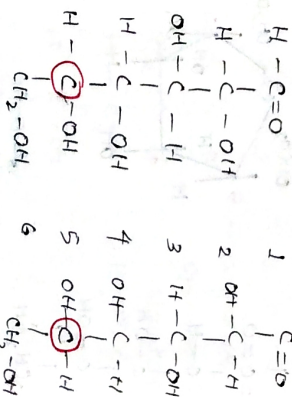


eg: D-glucose & L-glucose

D-fructose & L-fructose

D-lactose & L-lactose

- Naturally occurring sugars are D-sugars & body can metabolise only D-sugars.



D-glucose (natural)      L-glucose

Epimerism

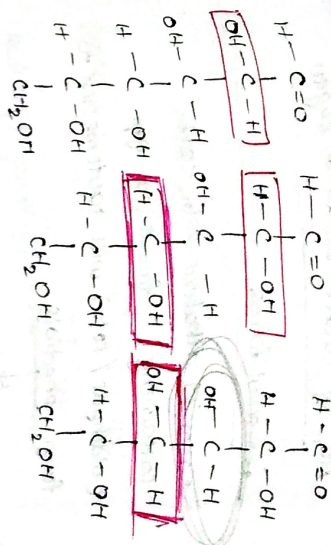
Diff. in orientation of H & OH gp. around a single asymmetric C-atom other than the ref. C atom.

eg: Glucose & Mannose

- C<sub>2</sub> 2nd epimer of glucose

- Glucose & Galactose

- C<sub>4</sub> 4th epimer of glucose



D-mannose

D-glucose

D-galactose

Mannose & Galactose are not epimers. ∵ 2 assy. C atoms

orientation is diff. ∴ diastereoisomers.

Diastereoisomerism

- Isomers with change in orientation of H & OH gp around 1 or more C-atoms other than penultimate C-atom (C<sub>5</sub>, C<sub>3</sub> & C<sub>4</sub> in glucose) are called diastereoisomers.

• They are not mirror images.

eg: D-mannose & D-galactose

Anomerism

- Diff. in orientation of H & OH gp. around the anomeric C-atom.

• Anomeric C-atom is the one with that gp which is converted to asymmetric C when ring shr. is formed.

• C<sub>1</sub> in glucose & C<sub>5</sub> in fructose

• The isomers are known as α & β

• β anomeric form of D-glucose is predominant in soln.

## Mutarotation

- Change in optical rotation with time
- A change in sp. rotation of plane polarised light due to the interconversion of α & β anomers in soln.
- The optical rotation of α D-glucose is +11.2°
- The optical rotation of β D-glucose is +19°
- In soln, when eq. attained, the specific rotation becomes +52.5° [around 63% are β-form]
- In a freshly prepared soln, α form are more. When the soln is kept for sometime, mutarotation takes place and at eqm, 63% is in the β form, rotation changes to +52.5°.

\* Clinically significant.

↳ sugar level → β-form is what we check → if kept for long → α-form get reduced (β ↑)

Aldose-ketose isomerism

• Glucose & Fructose have same mol. formula but they differ in that gp. Glucose has an aldehyde gp & fructose a keto gp. (anomerism, isomerism)  
Glucose → normally → 2° → 32 isomers  
→ 2° → 32 isomers



## Reactions of Monosaccharides

### Aln of dilute alkali on sugar

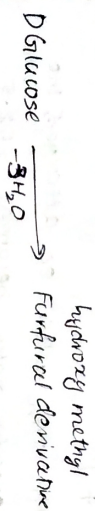
#### • functional form

- When treated with conc.  $\alpha$  mono-saccharides undergo dehydration with removal of 3 molecules of water.

- Hexoses gives hydroxymethyl functional  $\&$  pentoses give functional.

- Functional derivatives can be condensed with phenolic comp. to give coloured ppts which forms the basis of

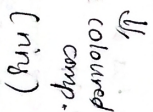
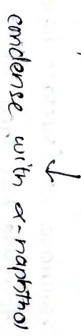
Molisch test - General test for carbonyl groups.



### MOLISCH TEST

- General  $\&$  of carbohydrates/Toit for identification of carbohydrates.

carb + conc.  $H_2SO_4 \rightarrow$  functional derivative



#### • enediol form

- In mild alkaline soln, carb. containing a free sugar gp (aldehyde / keto) will tautomerise to form enediols.

highly reactive, unstable  $\&$  powerful R.A  $\rightarrow$  basis of

Benedict's test  $\&$

Test presence of reducing sugar

- Glucose is converted into fructose  $\&$  mannose. The intercon. of sugar through a common enediol form is called Lobry de Bruyn-Van Ekenstein transform.

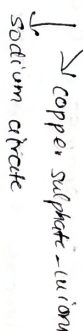
### Benedict's test

- common test to detect the presence of glucose in urine (glucosuria)  $\&$  is a test to diagnose diabetes mellitus.

- Glucose is a reducing sugar due to free aldehyde gp.

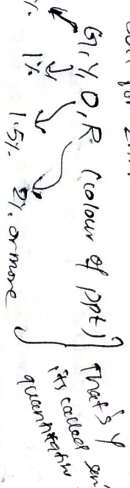
- B.T  $\rightarrow$  semiquantitative test

- B. Reagent  $\rightarrow$  sodium carbonate

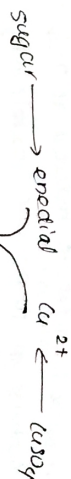


- 5ml B. R + 0.5ml of urine sample.

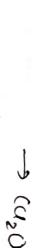
Boil for 2hr.



### B. in



oxidised Reduced



- Reducing property is seen in mild acidic med.  $\rightarrow$  Benedict's test  $\star$

### OSAZONE FORM

- All reducing sugars will form osazones with excess of phenylhydrazine when kept at boiling temp.

Osazones are insoluble

Each sugar will have characteristic crystal form of osazone

- Osazone of glucose, fructose  $\&$  mannose: needle shaped crystals arranged like a broom.

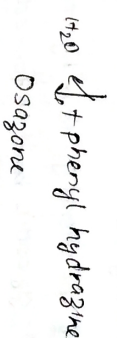
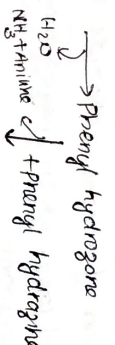
- Dif. in glucose, fructose  $\&$  mannose are dependent on the 1st  $\&$  2nd c atoms.

Needle  $\rightarrow$  Glucosazone (Glucose)

petal  $\rightarrow$  Maltosazone (Maltose)

pinusion  $\rightarrow$  Lactosazone (Lactose)

Hydroxy  $\rightarrow$  Glucosazone (Glucose)



### Action of strong alkali on sugar

- Sugars + strong alkali  $\rightarrow$  enolised  $\&$  double bond

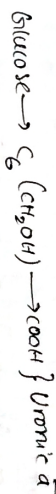
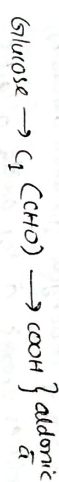
shift from 1:2 to 2:3, 3:4 to 4:5 to form the corresponding enediols  $\&$  get fragmented.

The fragmented molecules will polymerise to form a yellow resinous material called caramel.

Alkali dotting test

dif. b/w monosaccharide  $\&$  disaccharide

### Oxidn of sugars



- Mild oxidn, condn

$\rightarrow$  aldehyde gp  $\xrightarrow{oxidn}$  carboxyl gp

$\rightarrow$  to produce  $\alpha$  (aldonic  $\alpha$ )

eg: Glucose to gluconic  $\alpha$

Mannose to mannonic  $\alpha$

Galactose to galactonic  $\alpha$

### Gluconic $\alpha$

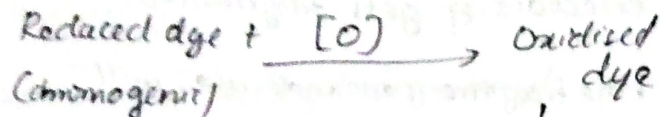
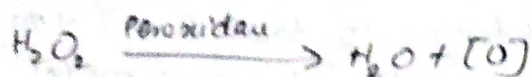
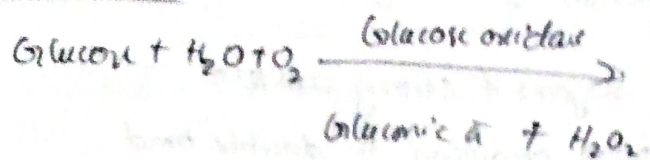
- Enzymatic oxidn of glucose:  $\star$

Glucose oxidase enzyme is specific for glucose, converts glucose to gluconic  $\alpha$

This  $\&$  is used to estimate glucose in lab.



## Principle



↓  
Diff. shades of color depending on degree of oxidation.

Dyes used - Osmotoluidine  
- orthodiansidine

• Protection of aldehyde group while oxidising, produces uronic acid by oxidation of last C-atom.

eg: Glucose to glucuronic acid  
Galactose to galacturonic acid

## Glucuronic acid

- conjugated agent
- constituent of glycosaminoglycans

Under strong oxidation conditions simultaneous oxidation of both 1st & last C atoms occur forming saccharic acid.

• Glucose → glucose saccharic acid

Galactose → mucic acid

↑  
Identification of galactose

- Mucic acid forms insoluble crystals  
→ basis for mucic acid test for identification of galactose

## Reduction to form alcohols

• Monosaccharides are reduced at their carbonyl group to produce corresponding alcohols

• Glucose → sorbitol

Mannose → mannitol

Fructose → sorbitol & mannitol

Galactose → dulcitol

• sorbitol, mannitol & dulcitol are used to identify bacterial colonies

• Mannitol is also used to reduce intracranial tension by forced diuresis

• The osmotic effect of sorbitol & dulcitol produces changes in tissues when they accumulate in abnormal amounts,

eg: - cataract of lens.

→ Diabetic patient more prone

## Derived sugars

• Monosaccharides whose structure cannot be represented by the general formula  $(\text{CH}_2\text{O})_n$  or which have some unusual features.

## Glycosides

• Glycosides are formed by condensation between the hydroxyl group of the anomeric carbon of a monosaccharide & a second compound which may or may not be a carbohydrate.

• If the second group is a hydroxyl group O-glycosidic bond is formed & if the second group is an amine an N-glycosidic bond is formed.



• Hydroxyl gp of 1 monosaccharide reacts with hydroxy gp or amino gp of another molecule

- Sugar position = glycone
- Non-sugar " = aglycone  
[glycerone, methanol, phenol, adenine]

### \* Importance of glycosides.

- Cardiac glycosides  
eg: Digitalis  
Ouabain
- Antibiotics eg: - Streptomycin  
Purpurosamine

### Deoxy Sugars

- Lack an oxygen atom - hydroxyl gp is replaced by hydrogen.
- Deoxy ribose is the most imp deoxy sugar - DNA

- L-Fructose  
(6-deoxy-L-Galactose)  
- present in glycoproteins

- L-Rhamnose  
(6-deoxy-L-Mannose)

- Deoxy ribose: Feulgen staining is specific for deoxy sugars.

L-fucose - 6 Deoxy L Galactose



occurs in glycoproteins & in blood gp substances.

### Amino Sugars

- Amino gp substituted for hydroxyl gp of sugars to give rise to amino sugars.
- eg: • Glucosamine seen in heparin, hyaluronic a, blood gp substances
- Galactosamine in chondroitin
- Mannosamine constituent of glycoproteins

### Importance of aminosugars

- components of glycoproteins, gangliosides, glycolipids.
- Antibiotics containing aminosugars.  
eg: Erythromycin.

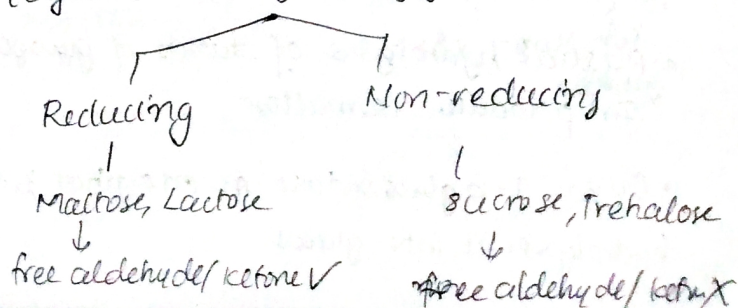
- Amino gp can be further acetylated to produce N-acetylated sugars.
- N-acetyl-galactosamine (GlcNAc)  
: constituent of glycoprotein.

### Esters

- Hydroxyl gp of sugars can be esterified to form acetates, propionates, benzoates, phosphates etc.
- Sugar, phosphates are intermediates of glucose metabolism.

### Disaccharides

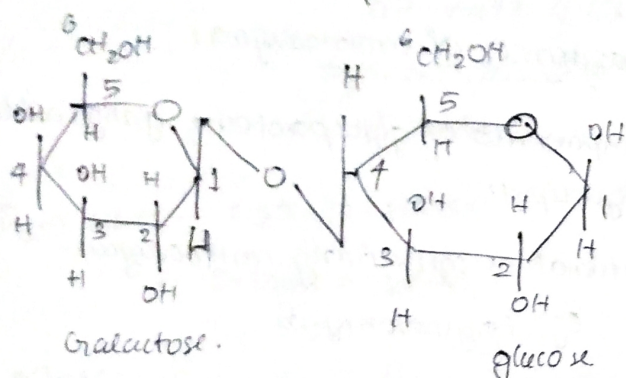
Disaccharides are carbohydrates composed of two monosaccharides linked together through a glycosidic linkage.





## Lactose

- Glucose + Galactose
- Milk sugar
- Digested by enzyme Lactase
- Reducing
- Can exist as  $\alpha$  &  $\beta$  anomers
- Osazone: resembles flower of "touch-me-not" plant.



$\beta$ -D-Galactosyl (1 $\rightarrow$ 4)  $\beta$ -D-glucose

Lactose

## Maltose

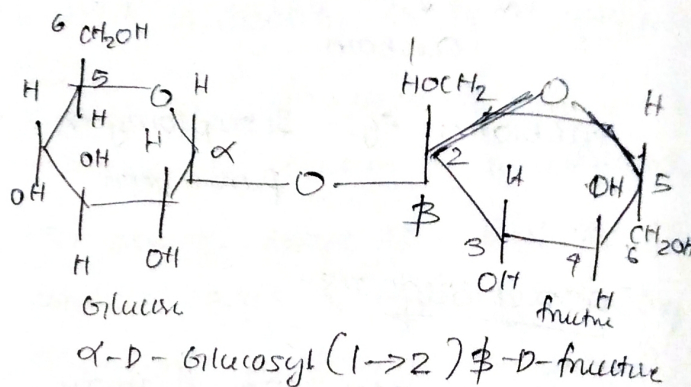
- Malt sugar
- Germinating cereals.
- Glucose + Glucose
- Formed in intestine during digestion of starch & glycogen.
- Reduced sugar
- Can exist as alpha &  $\beta$ -anomers

## Isomaltose

- Reducing sugar
- 2 glucose units in alpha 1-6 linkage
- Partial hydrolysis of starch & glycogen can produce isomaltose
- Oligo 1-6 glucosidase in intestinal juice hydrolyses it into glucose

## Sucrose

- Cane sugar
- Present in sugarcane & fruits
- Glucose + Fructose
- Non-reducing sugar (linkage involves first carbon of glucose & 2nd C of fructose; free sugar groups are not available)
- Will not form osazone
- Hydrolysed by enzyme sucrase/invertase



## INVERT SUGAR.

- Optical rotation of sucrose is  $+66.5^\circ$
- On hydrolysis (by sucrase or invertase) sucrose yields one molecule of glucose ( $+52.5^\circ$ ) & 1 molecule of fructose ( $-92^\circ$ ) so that the plane of rotation is inverted. Fructose is strongly levorotatory.
- Equimolecular mixture of glucose & fructose thus formed is invert sugar.

- Honey contains invert sugar & it is sweeter than sucrose

## Trehalose

- 2 glucose unit.
- $\alpha$ -1-1 linkage
- Not reducing.



## OLIGOSACCHARIDES

- 3 - 10 monosaccharides linked by glycosidic linkages make oligosaccharides

|       |            |                                  |
|-------|------------|----------------------------------|
| Tri   | Raffinose  | Glucose + Fructose + Galactose   |
| Tetra | Stachyose  | 2 Galactose + Glucose + Fructose |
| Penta | Verbascose | 3 Galactose + Glucose + Fructose |

- constituent of glycoproteins, glycolipids.
- Involved in cell to cell recognition.
- Antigenic specificity of blood group substance is due to oligosaccharide units.

## POLYSACCHARIDES

- consist of more than 10 monosaccharides linked by glycosidic bonds (Glycans)
- Homopolysaccharides: only 1 type of monosaccharide unit.

Eg: Starch, cellulose, Glycogen, Inulin, Dextrans, Chitin.

- Heteropolysaccharides: Polysaccharides with different types of monosaccharide units.

Eg: Agar, Agarose, Heparin, Chondroitin, Sulphate, Mucopolysaccharide

### Homopolysaccharide

Branched (same type monomer)      unbranched

### Heteropolysaccharide

Branched      Unbranched

Multiple monomer type

## Homopolysaccharides

### Starch

- Reserve carb. in plant kingdom.
- Major source of carb. in diet

Sources: Potato, tapioca, cereals.  
Glucose units with  $\alpha$ -1,4-glycosidic linkage to form long chain.

$\alpha$ -1,6-linkage: - branching point.

- Starch is non-reducing because the free sugar groups are negligible in no.

\* Starch = amylose + amylopectin.

- Test: - Iodine test. (Blue color, disappears on heating; reappears when cooled)

\* Amylose consists of glucose units linked through  $\alpha$ -1,4-glycosidic linkage  $\rightarrow$  long unbranched chain & water soluble

### \* Amylopectin

- insoluble
- branched
- branching @  $\alpha$ -1,6-gly. ln.

### Hydrolysis of starch

Amylodextrin - Violet color with  $I_2$

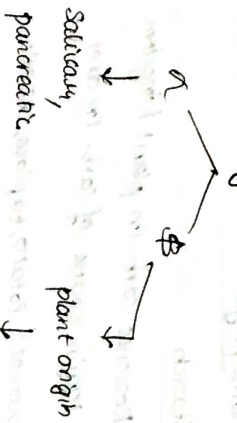
Erythro-dextrin - Red color

Achro-dextrin - No color, reducing

Maltose - No color, powerful reducing



## Amylase



Salivary, pancreatic  
↓  
at random on  $\alpha$ -1,4-glycosidic bonds  
↓  
split starts to dextrins of finally to  $\alpha$ -maltose.  
↓  
Amylase stops @ branching pt.  
↓  
limit dextrin / residual dextrin (cleaves behind)

## Glycogen

- \* Reserve carbohydrate in animals. stored in liver & muscle
- \* 7% of wt of liver
- \* More branched & compact than starch
- \* Glucose units
- \*  $\alpha$ -1,4-linkage (stiff chain)
- \*  $\alpha$ -1,6-linkage (branching pt.)
- \* highly branched [every 11-18 residues]
- \* Glycogenin is the primer protein found in innermost core of glycogen mol.
- \* Liver glycogen: source of glucose during fasting.

## Muscle glycogen: provides energy during muscle contraction

### Cellulose

- \* Chief const. of plant cell walls.
- \* Support tissue of plants.

## Cellulose

- \* Most abundant organic material in nature
- \* Glucose unit -  $\beta$ -1,4 glycosidic linkage
- \* Unbranched linear polymer
- \* Hydrolysed by enzyme cellulase
- \* Cellulose cannot be digested by humans as enzyme is absent
- \* Herbivorous animals, e.g., - present

- \* It is the major component of dietary fibre (assists in normal bowel movement & the risk of constipation)
- \* Repeating disaccharide unit in cellulose is cellobiose
- \*  $\beta$ -D-glucose units linked through  $\beta$ -1,4 bonds to form long straight chains

## INULIN

- \* Polymer of  $\beta$ -D fructose
- \* Linkage  $\beta$ -1 $\rightarrow$ 2 glycosidic
- \* Tensens of dahlia, onions, garlic
- \* Readily soluble in water
- \* Used to assess GFR - Inulin clearance test - it is not digested by enzymes of intestine & does not

## undergo metabolic change in the body

↳ Inulin can't be digested in our body

- \* Neither absorbed or secreted by renal tubules.

## Dextran

- \* highly branched homopolymer of glucose unit with 1-6, 1-4 & 1-3 link.
- \* Produced by microorganisms
- \* Used intravenously to treat hypovolemic shock as plasma expander since it will not go out of vascular compartment

## Chitin

- \* Present in exoskeleton of crustacean & insects
- \* composed of repeated units of N-acetylglucosamine with  $\beta$ -1,4 glycosidic link
- \* It is extremely hard & functions as protective external cover

## Hetero polysaccharide

- \* Diff types of monosaccharide units
- \* Agar
- \* Agarose
- \* Mucopolysaccharide (only osamine glycan)

## Agar

- \* Prepared from sea weeds
- \* Contains glucose, galactose & other sugar

- \* Used as in electrophoresis of immunodiffusion. [Supporting media]
- \* Boils  $\rightarrow$  dissolve  $\rightarrow$  cool  $\rightarrow$  gel like
- \* Used to prepare culture media for bacteria.

## Agarose

- \* Galactose & 3,6 anhydro galactose
- \* Used for electrophoresis.

## Mucopolysaccharides

### [Glycosaminoglycan]

- \* Unbranched h.t. poly. chains composed of repeated disaccharide units
- \* Repeated units consists of amino sugar & uronic acid
- \* Amino sugars - glucosamine & galactosamine
- \* Uronic acid - glucuronic acid or iduronic acid

- \* Acetylated amino groups, sulfate & carbonyl group can also be present

## Forms ground substance

- \* Located more H<sub>2</sub>O mol.
- \* Because of polyanionic polyanionic groups, they attract water mol. & produce viscous sol.
- \* Major component in ECM
- \* Synthesis of GAG occur in ER & Golgi apparatus



## Biologically imp - GAGs

- Hyaluronic  $\bar{\alpha}$
- Heparin & Heparan sulfate
- Chondroitin sulfate
- Keratan sulfate
- Dermatan sulfate

## Hyaluronic $\bar{\alpha}$

- Repeating units of N-Acetyl glucosamine & glucuronic  $\bar{\alpha}$
- Present in C.T., tendons, synovial fluid, vitreous humor & serves as a lubricant in jt. cavities
- Role in permitting cell migration during morphogenesis & wound repair.

## Chondroitin sulfate

- Glucuronic  $\bar{\alpha}$  & galactosamine sulfate.
- Present in ground subs. of C.T. widely distributed in cartilage, bone, tendons, cornea & skin
- Most abundant GAG in body

## Heparin

- Potent anticoagulant helps to prevent clotting of circulating blood
- Heparin is present in granules of mast cells & in liver, lungs & skin.
- Anticoagulant for taking blood for blood & urine.

- Repeating disaccharide unit contains glucosamine & either of uronic  $\bar{\alpha}$  90% are iduronic  $\bar{\alpha}$

- Most - sulfated
- Some - acetylated

## Heparan sulfate

- Some units
- Glucosamine with few sulfated
- Predominant uronic  $\bar{\alpha}$  is glucuronic  $\bar{\alpha}$
- Present on cell surface & extracellular

## Keratan sulfate

- Repeating units are galactose & N-acetyl glucosamine in  $\beta$ -linkage
- Do not contain any uronic  $\bar{\alpha}$
- Found in cornea & C.T. (cartilage)

## Dermatan sulfate

- L-Iduronic  $\bar{\alpha}$  & N-acetyl galactosamine in  $\beta$ -1,3 linkage
- Found in skin, blood vessel & heart valves.

|                          | Hyaluronic $\bar{\alpha}$ | Glicuronic $\bar{\alpha}$ | $\beta$ 1 $\rightarrow$ 3  |
|--------------------------|---------------------------|---------------------------|----------------------------|
| Heparin                  | Iduronic                  | Glicuronic                | $\alpha$ 1 $\rightarrow$ 4 |
| Heparan sulfate          |                           |                           | $\alpha$ 1 $\rightarrow$ 4 |
| Chondroitin sulfate      |                           |                           | $\beta$ 1 $\rightarrow$ 3  |
| Keratan sulfate          |                           |                           | $\beta$ 1 $\rightarrow$ 4  |
| Dermatan                 |                           |                           | $\beta$ 1 $\rightarrow$ 3  |
| no uronic $\bar{\alpha}$ |                           |                           |                            |

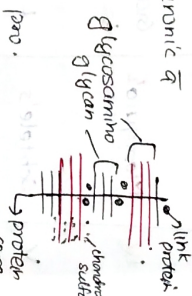
## Proteoglycans

- Proteins that contain covalently linked glycosaminoglycans
- GAG molecules are attached to a core protein forming a protein monomer

- Structure resembling a bottle brush
- Several proteoglycan monomers associate to form proteoglycan aggregates.

- Proteoglycan - GAG + Protein
- Proteoglycan monomer associate with a mol. of hyaluronic  $\bar{\alpha}$

- Association is stabilised by additional small proteins called link proteins.



## Functions of GAGs of proteoglycan.

- As structural components of extracellular matrix
- Role in cell migration, lubricating agent.

- Contribute to the characteristic turgor of vascular tissue

↳ due to GAGs

- Role in compressibility of cartilage in weight bearing

- Role in connective transparency.

- Act as anticoagulant

- Components of PM, act as receptors in the form of proteoglycans.

## Clinical importance.

### Role in disease and Aging

- Tumour cells induce fibroblasts to synthesise large amount of hyaluronic  $\bar{\alpha}$

- Hyaluronic  $\bar{\alpha}$  permits tumour cells to migrate through ECM and facilitate metastasis

- Role in development of arthritis. Proteoglycans act as auto-antigens & contribute to pathogenesis

- Chondroitin sulfate in cartilage ↓ with age whereas keratan sulfate & hyaluronic  $\bar{\alpha}$  ↑. These changes contribute to osteoarthritis

- High amount of Dermatan sulfate is present in arterial smooth muscle cells. They get bound to LDL & play a role in development of atherosclerosis.

- Changes in conc. of GAGs in skin are seen with ageing which accounts for the changes in skin of the elderly

### Degradation of GAGs.

- GAGs are degraded by specific hydrolytic enzymes in lysosomes. They include exo & endo glycosidases & sulfatases acting in seq. to degrade various GAGs.

- Defect of enzyme that degrade GAGs result in Mucopolysaccharidoses → group of disorders
- Inborn errors of metabolism usually inherited in autosomal recessive manner



- Mutation of gene coding for the lysosomal enzyme involved in the degradation of GAGs.

- Def. of eng. results in accumulation of various GAG in tissue.

## Mucopolysaccharidoses

- Lysosomal storage disorders due to defective degradation of GAGs.
- Progressive disorder
  - ↳ slow progression
- Affect multiple organs.
- Enlargement of organs.
- Abnormalities in the development of cartilage & bone
  - ↳ skeletal deformities
- Mental retardation,
  - ↳ accumulation in CNS
- Abnormal facies
  - ↳ accumulation in skin
- Abnormalities of hearing, vision, cardiovascular system.
  - ↳ heart valve affected

## Clinical manifestations of accumulation

- Coarse facial features, flat nasal bridge.
- Enlarged mouth & tongue
- Thick skin & corneal opacity due to acc. of GAGs.
- Cloudy cornea, retinal degeneration.
- Mental retardation, growth def.

- Skeletal dysplasia due to defective formation of ground substance.

- Developmental delay, behavioural prob.

- Hearing loss, dwarfism, hepatosplenomegaly

| Type | Enzyme           | Deficient enzyme                                 |
|------|------------------|--------------------------------------------------|
| I    | Hurler's         | L-Iduronidase<br>Heparan sulf.<br>dermatan sulf. |
| II   | Hunter's         | Iduronate sulfatase                              |
| III  | Sanfilippo's     | N-Acetyl glucosaminidase<br>Heparan sulfatase    |
| IV   | Morquio's        | Galactosaminase sulfatase<br>b-D-galactosidase   |
| V    | Scheie's         | L-Iduronidase                                    |
| VI   | Maroteaux-Lamy's | N-Acetyl-b-D-Galactosaminase-4-sulfatase         |
| VII  | Sly's            | b-Galactosaminase                                |

\* All except Hunter's are autosomal recessive.

X-linked

## Diagnosis

- Excessive excretion of GAGs in urine can be detected through urine test

↳ **Cetyl Pyridinium Chloride (CPC) test**

↳ screening test

- Analysis of GAGs in tissue biopsy samples

- Enzyme assay on cells (w/o fibroblast) or serum

- Prenatal diagnosis by amniocentesis

## Glycoproteins

- Proteins containing branched or unbranched oligosaccharide chain.
- Carbohydrate residues are attached to polypeptide chains covalently by N or O glycosidic bonds.

- Present in most organism, plants, bacteria, virus

- Most of the membrane proteins & secretory proteins are glycoproteins.

- Eg. glycopherin - RBC, Blood gp antigens.

• **Carbohydrates commonly seen in glycopro.**

- Mannose
- Glucose
- Galactose
- GlcNAc
- Gal Nac
- Arabinose
- Fucose
- Sialic acid

- Sialic acids are N-OH, O-acyl derivatives of neuraminic acid

- Neuraminic acid: nine C sugar

Fn of glycoprotein.

- Structural mol. of cell wall
- Eg: collagen, elastin, fibron.

- Glycophorin is a major membrane glycoprotein in RBCs

- Acts as lubricant & protective agent
- Eg: mucus & mucous serum

- All plasma pro. except albumin are glycoproteins

- Receptors - involved in hormonal ad.

- Transporters of vit., minerals, hormones, drugs etc. Eg: ceruloplasmin - Cu, transferrin - Fe

- Immunity:

- ↳ constituent of Ig, complement etc.

- Many of hormones & enzymes are glycoproteins.
- Eg: Chorionic gonadotropin, TSH, Ribonuclease

Blood group Antigens.

- ABO, Rh (Rhesus), & MN system of blood grp.

- Genes present in 9th chrom.

- H-antigen. [Basic str.]

- ↳ Fucose - Gal - GalNAc - Protein

- A-antigen

- ↳ Fucose - Gal - GalNAc - Protein

- **GalNAc**

- B-antigen

- ↳ Fucose - Gal - GalNAc - Protein

- **Gal**



- H locus - codes for fucosyl transferase
- A gene - encodes GalNAc transferase that adds the terminal GalNAc to H substance.
- B gene - encodes Gal transferase that adds the Gal residue to H substance
- Lack of both: blood gp O.
- Presence of both: blood gp AB.

protein, carb, lipid

Feb 20 - Phy

Feb 25 - Bio

March - 1st (13th)

Nov 6 -