

Chemistry of Carbohydrates

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Topics: Monosaccharides, Glucose, Fructose, Mannose, Galactose

Monosaccharides

Definition

- Simplest carbohydrates; cannot be hydrolyzed further.
- General formula: $C_nH_{2n}O_n$.

Classification by Number of Carbons

- **Trioses** – glyceraldehyde
- **Tetroses** – erythrose
- **Pentoses** – ribose, deoxyribose
- **Hexoses** – glucose, fructose, galactose, mannose

Classification by Functional Group

- **Aldoses** ? contain aldehyde group (CHO)
- **Ketoses** ? contain keto group (CO)

Isomerism in Monosaccharides

- **D and L forms** ? based on penultimate carbon orientation
- **Epimers** ? differ at one carbon
- **Anomers** ? differ at hemiacetal carbon (?, ?)
- **Mutarotation** ? ? ? ? interconversion in solution

Glucose

Structure

- Aldohexose; pyranose ring form in solution.
- Four chiral centers.

Important Reactions

- Oxidation ? gluconic acid / glucuronic acid
- Reduction ? sorbitol
- Glycosidic bond formation ? disaccharides & polysaccharides

Biochemical Importance

- Primary fuel of body.
- Required by RBCs, retina, brain.
- Forms glycogen, lactose, triglycerides, amino acids.

Clinical Points

- Hyperglycemia & hypoglycemia disorders
- Sorbitol accumulation ? cataract, neuropathy

Fructose

Structure

- Ketohexose; furanose ring form.
- Sweetest natural sugar.

Metabolism

- Rapid hepatic metabolism; bypasses PFK-1 ? faster glycolysis
- Fructokinase forms **fructose-1-phosphate**

Clinical Points

- Hereditary fructose intolerance ? aldolase B deficiency
- Essential fructosuria ? benign fructokinase deficiency

Mannose

Structure

- C-2 epimer of glucose; aldohexose.

Functions

- Required for **N-linked glycoprotein synthesis**
- Mannose-6-phosphate ? lysosomal enzyme targeting

Clinical Notes

- Congenital disorders of glycosylation (CDG)
-

Galactose

Structure

- C-4 epimer of glucose; aldohexose.

Metabolism

- Leloir pathway ? glucose
- UDP-galactose ? lactose synthesis

Clinical Points

- Classic galactosemia (GALT deficiency)
 - Galactokinase deficiency ? cataracts
 - Galactitol accumulation in lens
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Comparative Summary (Exam-Oriented)

- **Glucose** ? major fuel, sorbitol pathway
- **Fructose** ? rapid metabolism, HFI
- **Mannose** ? glycoproteins, mannose-6-phosphate
- **Galactose** ? lactose synthesis, galactosemia

Reducing vs Nonreducing Sugars

Reducing Sugars

- Contain a **free aldehyde or keto group** (free anomeric carbon).
- Can **reduce** Cu^{2+} to Cu^+ or Ag^+ to Ag .
- All **monosaccharides** are reducing sugars.
- **Examples:** glucose, fructose, galactose, lactose, maltose.

Nonreducing Sugars

- Do NOT have a free anomeric carbon (both anomeric carbons involved in glycosidic bond).
- Cannot reduce Benedict's or Fehling's reagent.
- **Examples:** sucrose, trehalose.

Clinical Note

- Reducing sugar detection in urine ? diabetes mellitus, galactosemia, hereditary fructose intolerance.

Reactions of Monosaccharides

1. Oxidation

- Aldehyde ? acid
- Examples:
 - Glucose ? gluconic acid
 - Glucose ? glucuronic acid (detoxification)
 - Diabetic complications via oxidative stress

2. Reduction

- Aldoses & ketoses ? **sugar alcohols**
- Examples:
 - Glucose ? sorbitol
 - Galactose ? galactitol
- Excess sorbitol ? cataract, neuropathy.

3. Glycoside Formation

- Hemiacetal reacts with alcohol \rightarrow glycosidic bond.
- Basis of disaccharides (maltose, lactose) & polysaccharides (glycogen).

4. Isomerization

- Aldose \leftrightarrow ketose & vice versa.
- Glucose \leftrightarrow fructose \leftrightarrow mannose.

5. Esterification

- OH groups esterified by phosphates.
- Examples: glucose-6-phosphate, fructose-1-phosphate.

Mutarotation

Definition

Interconversion of α and β anomers through an open-chain form when dissolved in water.

Feature

- Leads to change in optical rotation until equilibrium is reached.
- Occurs in **reducing sugars** only.

Examples

- α -D-glucose \leftrightarrow β -D-glucose
- Lactose mutarotates; sucrose does NOT.

Stereoisomers of Monosaccharides

Definition

Compounds with the same molecular formula but **different spatial orientation**.

D and L Forms

- Determined by configuration at **penultimate carbon**.
- Most human sugars are **D-isomers**.

Number of Stereoisomers

For a sugar with n chiral centers ? **2ⁿ stereoisomers**.

Epimers

Definition

Monosaccharides that differ only at **one specific carbon atom**.

Important Human Examples

- **Glucose & Mannose** ? epimers at **C-2**
- **Glucose & Galactose** ? epimers at **C-4**

Clinical Insight

- Epimerization is used in metabolism (UDP-glucose ? UDP-galactose).

Benedict's Reaction

Principle

- Reducing sugars convert **cupric ions (Cu²⁺)** to **cuprous oxide (Cu₂O)** forming a **red/orange precipitate**.

Indicates

- Presence of **reducing sugar** in sample (urine, blood, CSF).

Clinical Uses

- Diabetes mellitus (glucosuria)
- Galactosemia (galactose in urine)
- Fructosuria
- Inborn errors of carbohydrate metabolism

Colors (Approximate Correlation)

- Green ? trace
- Yellow ? moderate
- Orange/brick red ? strong positive

Osazone Formation

Principle

Reducing sugars react with **phenylhydrazine** to form **crystalline osazones**.

Utility

Differentiates sugars based on **shape & rate** of crystal formation.

Characteristic Osazones

- **Glucose, fructose, mannose** ? *needle-shaped* “broomstick” osazones
- **Maltose** ? *sunflower-like* crystals
- **Lactose** ? *puff-ball* crystals

Mechanism

Reaction occurs at **C-1 and C-2**, so sugars identical at these carbons produce identical osazones.

Clinical Note

Helpful in older lab setups for carbohydrate identification.

Exam-Oriented Summary

- All **monosaccharides** = reducing sugars.
- Sucrose = **nonreducing**, no mutarotation.
- Mutarotation ? ? ? ? anomers interconversion.
- Epimers differ at **one carbon** (C-2, C-4 important).
- Benedict’s test detects reducing sugars in urine.

- Osazone crystals differentiate common sugars.

Structural vs Storage Carbohydrates

Storage Carbohydrates

- Serve as **energy reserves**.
- Easily mobilized.
- Examples:
 - **Glycogen** (animals)
 - **Starch** (plants: amylose + amylopectin)

Structural Carbohydrates

- Provide **rigidity and support**.
- Not easily digested.
- Examples:
 - **Cellulose** (plant cell wall; β -1,4 link ? non-digestible)
 - **Chitin** (exoskeleton; N-acetylglucosamine polymer)
 - **Hyaluronic acid** (ECM component)

Glycoproteins

Definition

Proteins covalently linked with carbohydrate chains (**short, branched oligosaccharides**).

Types

- **N-linked** ? attached to **Asn**
- **O-linked** ? attached to **Ser/Thr**

Functions

- Cell recognition
- Hormones (TSH, FSH, LH)
- Antibodies (IgG)

- Receptors
- Enzymes

Clinical Points

- Congenital disorders of glycosylation (CDG) ? neurological symptoms.
- Blood group antigens are glycoproteins.

Glycosaminoglycans (GAGs)

Definition

Long, unbranched polysaccharides containing repeating **acidic disaccharide units**.

General Composition

Amino sugar + uronic acid

- Glucosamine or galactosamine
- Glucuronic or iduronic acid

Functions

- Hydration
- Lubrication (synovial fluid)
- ECM structure
- Shock absorption

Important GAGs

- Hyaluronic acid
- Chondroitin sulfate
- Dermatan sulfate
- Heparin
- Heparan sulfate
- Keratan sulfate

Clinical Notes

- Defective degradation ? **mucopolysaccharidoses (MPS)**
 - Hurler syndrome (?-L-iduronidase deficiency)
 - Hunter syndrome (iduronate sulfatase deficiency)
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Glycosides

Definition

Carbohydrate linked to a **non-sugar moiety (aglycone)** through a **glycosidic bond**.

Formation

- Hemiacetal OH of sugar reacts with alcohol/phenol.

Examples

- Cardiac glycosides ? **Digitalis, digoxin**
- Anthocyanins (plant pigments)

Importance

- Drug metabolism
 - Stability of plant toxins
 - Formation of glycolipids, nucleosides (adenosine, guanosine)
-

Amino Sugars

Definition

Sugars where an OH group is replaced by an **NH₂ group**.

Examples

- **Glucosamine**
- **Galactosamine**
- **N-acetylglucosamine (NAG)** ? chitin
- Present in GAGs, glycoproteins.

Clinical Importance

- Building blocks of cartilage and connective tissue.

Deoxy Sugars

Definition

Sugars in which an OH group is replaced by H.

Examples

- **Deoxyribose** ? DNA
- **L-fucose** ? blood group antigens
- **Rhamnose** ? plant products

Disaccharides

Disaccharides = two monosaccharides joined by a **glycosidic bond**.

General Concepts

- Reducing or nonreducing depends on availability of free anomeric carbon.
- Important in diet and digestion.

Sucrose

Composition

- Glucose + Fructose
- Linkage: **α-1,β-2** glycosidic bond
- **Nonreducing sugar**

Sources

- Cane sugar, beet sugar

Notes

- Does not show mutarotation
 - No reaction with Benedict's reagent
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Lactose

Composition

- Galactose + Glucose
- Linkage: β -1,4

Nature

- Reducing sugar

Clinical

- Lactose intolerance ? lactase deficiency ? bloating, diarrhea
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Maltose

Composition

- Glucose + Glucose
- Linkage: α -1,4

Nature

- Reducing sugar

Importance

- Product of starch digestion (amylase activity)
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Exam-Oriented Summary

- Storage carbs = glycogen, starch; structural = cellulose, chitin.
- Glycoproteins = short, branched sugars; GAGs = long, unbranched, acidic.
- Amino sugars = glucosamine, galactosamine; deoxy sugars = deoxyribose.

- Sucrose = nonreducing; lactose & maltose = reducing.
- Lactose ? α -1,4; Maltose ? α -1,4; Sucrose ? α -1, β -2.

Polysaccharides

Definition

Large polymers of monosaccharides linked by **glycosidic bonds**.

Types

- **Storage polysaccharides** – starch, glycogen
- **Structural polysaccharides** – cellulose, chitin
- **Mucopolysaccharides (GAGs)** – hyaluronic acid, chondroitin sulfate, etc.

Starch

Composition

- Plant storage carbohydrate
- Mixture of:
 - **Amylose** ? linear α -1,4 link
 - **Amylopectin** ? branched α -1,4 and α -1,6 links

Features

- Digested by **salivary and pancreatic amylase**
- Major dietary carbohydrate

Clinical Notes

- Lack of amylase ? poor starch digestion
- Resistant starch ? improves gut flora (prebiotic)

Glycogen

Composition

- Major **animal storage polysaccharide**
- Highly branched polymer of glucose
- Linkages: α -1,4 (chains) and α -1,6 (branches)

Location

- Liver α maintains blood glucose
- Muscle α for contraction energy

Clinical Correlation

- **Glycogen storage diseases (GSD)**
 - Type I: von Gierke (G6Pase deficiency)
 - Type V: McArdle (muscle phosphorylase deficiency)
 - Type II: Pompe (lysosomal acid maltase deficiency)

Cellulose

Composition

- Linear chains of glucose linked by β -1,4 bonds.

Characteristics

- Humans cannot digest (lack cellulase)
- Provides **dietary fiber** α gut motility, reduced cholesterol

Mucopolysaccharides (GAGs)

Definition

Long, negatively charged polysaccharides composed of **repeating disaccharide units** containing an **amino sugar + uronic acid**.

Functions

- Lubrication (synovial fluid)
- Shock absorption

- Structural ECM support
- Hydration due to negative charge

Main Types

- **Hyaluronic acid** – synovial fluid, ECM
- **Chondroitin sulfate** – cartilage
- **Dermatan sulfate** – skin, vessels
- **Heparin** – anticoagulant
- **Heparan sulfate** – basement membranes
- **Keratan sulfate** – cornea, cartilage

GAG Disorders (Mucopolysaccharidoses – MPS)

General Features

- Lysosomal storage disorders
 - Due to failure to degrade GAGs
 - Accumulation ? coarse facies, hepatosplenomegaly, joint stiffness, developmental delay
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Important MPS Disorders

1. Hurler Syndrome (MPS I – severe)

- **Enzyme:** α -L-iduronidase deficiency
 - **Accumulated GAGs:** dermatan sulfate, heparan sulfate
 - **Features:**
 - Coarse facies
 - Corneal clouding
 - Hepatosplenomegaly
 - Developmental delay
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2. Hunter Syndrome (MPS II – milder, X-linked)

- **Enzyme:** iduronate sulfatase deficiency
 - **Accumulated GAGs:** dermatan sulfate, heparan sulfate
 - **Features:**
 - Coarse facies
 - **No corneal clouding**
 - Behavioral issues
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3. Sanfilippo Syndrome (MPS III)

- **Defects in heparan sulfate degradation**
 - **Predominantly neurological deterioration**
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4. Morquio Syndrome (MPS IV)

- **Enzyme:** galactose-6-sulfatase deficiency
 - **Accumulated GAG: keratan sulfate**
 - **Features:**
 - Skeletal abnormalities
 - Short stature
 - Normal intelligence
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5. Maroteaux–Lamy Syndrome (MPS VI)

- **Enzyme:** arylsulfatase B deficiency
 - **Accumulated GAG:** dermatan sulfate
 - **Features:**
 - Similar to Hurler
 - Normal intelligence
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Clinical Correlations (Carbohydrate Chemistry)

1. Cataracts in diabetes

- Excess glucose ? sorbitol (aldose reductase) ? osmotic swelling ? lens opacity.

2. Lactose intolerance

- Lactase deficiency ? bloating, diarrhea.

3. Galactosemia

- GALT deficiency ? galactose ? ? galactitol in lens ? cataracts.

4. Hereditary fructose intolerance

- Aldolase B deficiency ? vomiting, hypoglycemia, jaundice.

5. Mucopolysaccharidoses

- Accumulation of GAGs ? coarse facies, organ enlargement, joint deformity.

6. Glycogen storage diseases

- Impaired glycogen metabolism ? hypoglycemia, muscle weakness.

7. Dietary fiber (cellulose)

- Prevents constipation, lowers cholesterol.

Exam-Oriented Quick Summary

- Starch ? amylose (?-1,4) + amylopectin (?-1,4 & ?-1,6).
- Glycogen ? highly branched (?-1,4 & ?-1,6).
- Cellulose ? ?-1,4; non-digestible.
- GAGs ? long, acidic, structural polysaccharides.
- MPS disorders ? failure to degrade GAGs.
- Hurler = corneal clouding; Hunter = no clouding.
- Morquio = skeletal deformity, keratan sulfate accumulation.

Pentoses: Ribose, Deoxyribose, Clinical Points

Pentoses

Definition

Pentoses are **5-carbon monosaccharides** important in nucleic acid structure and metabolic pathways.

General Properties

- Formula: **C₅H₁₀O₅** (ribose)
- Exist mainly in **furanose (5-membered) ring** form
- All pentoses are **reducing sugars**

Ribose

Structure

- Aldopentose
- Component of **RNA**, ATP, NAD⁺, FAD, CoA

Biochemical Roles

- Part of **ribose-5-phosphate** in the HMP shunt
- Required for synthesis of:
 - RNA nucleotides
 - ATP, GTP
 - Coenzymes (NAD⁺, NADP⁺, FAD, CoA)

Formation

- Generated from **glucose-6-phosphate** via:
 - **HMP shunt (oxidative)**
 - **Transketolase reactions (non-oxidative)**

Deoxyribose

Structure

- Aldopentose
- Differs from ribose by **absence of OH at C-2** ? replaced by **H**
- Component of **DNA**

Importance

- Gives DNA chemical stability (less reactive than RNA).
- Essential for genome replication and repair.

Formation

- Produced from ribose via **ribonucleotide reductase** (requires NADPH).

Clinical Points

1. HMP Shunt Disorders

- Defects in enzymes like **transketolase** decrease ribose-5-phosphate production.
- Thiamine deficiency reduces transketolase function ? neurological symptoms.

2. DNA Repair Disorders

- Deoxyribose deficiency affects DNA stability and repair mechanisms.
- Seen in some inherited nucleotide metabolism disorders.

3. Oxidative Stress

- Ribose is needed for NADPH production (via pentose phosphate pathway).
- NADPH deficiency ? increased oxidative damage (RBC hemolysis in G6PD deficiency).

4. Rapid Cell Division

- Cancer cells require **high ribose** for accelerated nucleotide synthesis.
- Basis for targeting nucleotide metabolism in chemotherapy.

5. Genetic Diseases of Purine/Pyrimidine Metabolism

- Overproduction or underutilization of ribose-based nucleotides causes:
 - Gout (excess purines)
 - SCID (adenosine deaminase deficiency)
 - Orotic aciduria (pyrimidine synthesis defect)

Exam-Oriented Summary

- Ribose ? RNA, ATP, NAD?, FAD, CoA
- Deoxyribose ? DNA
- Ribose made from HMP shunt; deoxyribose from ribose via ribonucleotide reductase
- Pentoses are reducing sugars
- Clinically relevant in G6PD deficiency, cancer metabolism, nucleotide disorders

FAQs

1. What are pentoses?

Pentoses are **5-carbon monosaccharides** important for nucleic acid structure and cellular metabolism.

2. What is the main difference between ribose and deoxyribose?

Deoxyribose lacks the **OH group at carbon-2**, making DNA more stable than RNA.

3. Where is ribose found in the body?

In **RNA**, ATP, GTP, NAD?, FAD, and CoA.

4. Where is deoxyribose found?

In **DNA** only.

5. How is ribose produced in the cell?

From **glucose-6-phosphate** via the **HMP shunt**.

6. How is deoxyribose formed?

By reduction of ribonucleotides via **ribonucleotide reductase**, using **NADPH**.

7. Are pentoses reducing sugars?

Yes, all pentoses are **reducing sugars**.

8. What is the clinical relevance of the HMP shunt in RBCs?

It generates **NADPH**, protecting RBCs from oxidative damage.

Defect ? **G6PD deficiency** ? hemolysis.

9. Why does DNA use deoxyribose instead of ribose?

Deoxyribose is **less reactive** and provides long-term **chemical stability** to DNA.

10. How does ribose relate to cancer cell metabolism?

Cancer cells require **large amounts of ribose** for rapid nucleotide synthesis.

11. What happens if ribose-5-phosphate levels fall?

Nucleotide synthesis decreases ? impaired cell proliferation and DNA repair.

12. Which enzyme defect reduces ribose formation?

Transketolase deficiency (exacerbated by thiamine deficiency).

13. Which metabolic disorder affects deoxyribose in DNA?

Defects in nucleotide metabolism (e.g., **adenosine deaminase deficiency**) impair DNA synthesis.

14. Is ribose involved in oxidative stress defense?

Yes. Ribose ? NADPH ? antioxidant protection via glutathione.

15. Why does fructose enter glycolysis faster than glucose?

Because fructose bypasses the **PFK-1** step and enters at the triose phosphate level (side concept linking monosaccharides).

Important Points to Remember

- **Ribose = RNA sugar, Deoxyribose = DNA sugar**
- Deoxyribose has **no OH at C-2** ? increases DNA stability
- Ribose is essential for **ATP, NAD⁺, FAD, CoA, RNA**
- Ribose-5-phosphate is formed via the **HMP shunt**
- Deoxyribose is formed by **ribonucleotide reductase** (needs NADPH)
- All pentoses are **reducing sugars**
- NADPH generated by ribose pathway protects RBCs (G6PD deficiency ? hemolysis)
- Deoxyribose defects affect **DNA replication and repair**
- Pentose metabolism is tightly linked to **cell division, cancer metabolism, oxidative balance**
- Ribose and deoxyribose form the **backbone of nucleic acids**

Clinical Importance of Carbohydrates

Carbohydrates are essential for **energy metabolism, structural integrity, cellular communication, and detoxification**. Their clinical importance becomes clear when examining genetic diseases, acquired metabolic disorders, nutritional issues, and diagnostic applications.

1. Energy Supply & Metabolic Needs

Primary Fuel in Humans

- Glucose is the **universal fuel** for most tissues.
- Brain, RBCs, renal medulla, retina ? highly glucose-dependent.
- Hypoglycemia ? confusion, seizures, coma.

Clinical Point

- Any condition causing **low blood glucose** (insulin overdose, sepsis, adrenal insufficiency) becomes a medical emergency.

2. Genetic Disorders of Carbohydrate Metabolism

A. Glycogen Storage Diseases (GSD)

Type I – von Gierke Disease

- Glucose-6-phosphatase deficiency
- Severe fasting hypoglycemia, lactic acidosis, hepatomegaly.

Type II – Pompe Disease

- Lysosomal acid maltase deficiency
- Cardiomegaly, hypotonia.

Type V – McArdle Disease

- Muscle phosphorylase deficiency
 - Exercise intolerance, muscle cramps, myoglobinuria.
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B. Disorders of Monosaccharide Metabolism

1. Galactosemia

- GALT deficiency
- Jaundice, vomiting, cataracts, hepatomegaly.
- Galactitol accumulation ? lens opacity.

2. Hereditary Fructose Intolerance

- Aldolase B deficiency
- Hypoglycemia, liver failure after consuming fruits/sucrose.

3. Essential Fructosuria

- Benign fructokinase deficiency
 - Fructose spills into urine.
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C. Pentose Pathway Defects

G6PD Deficiency

- Low NADPH ? oxidative stress ? hemolysis.
 - Triggers: fava beans, infections, sulfa drugs, antimalarials.
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3. Disorders of Disaccharide Digestion (Acquired/Genetic)

Lactose Intolerance

- Lactase deficiency (genetic or post-infectious).
- Bloating, diarrhea, gas.

Sucrase-Isomaltase Deficiency

- Intolerance to sucrose and starch digestion.
 - Watery diarrhea in infants.
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4. Acid-Base Homeostasis & Carbohydrates

- Anaerobic glycolysis ? **lactate production**.
 - Excess lactate ? **lactic acidosis** in:
 - Shock
 - Sepsis
 - Liver failure
 - Thiamine deficiency
 - Metformin toxicity
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5. Carbohydrates in Diet & Nutrition

Role in Balanced Diet

- 50–60% of daily calories.
- Complex carbs preferred over simple sugars.

High Carbohydrate Intake

- Hyperinsulinemia ? weight gain
- Increased triglycerides
- Increased risk of fatty liver

Low-Carb Diets (Keto, Atkins)

- Used for weight loss and type 2 diabetes control.
- Risk: ketoacidosis in type 1 diabetics if insulin is absent.

6. Dietary Fiber (Cellulose, Pectins, Gums)

Benefits

- Prevents constipation
- Reduces postprandial glucose spikes
- Lowers LDL cholesterol
- Improves gut microbiota
- Reduces colon cancer risk

Clinical Use

- Recommended in diabetes, obesity, hyperlipidemia.

7. Carbohydrates in Cell Structure & Immunity

Glycoproteins & Glycolipids

- Blood group antigens
- Immunoglobulins
- Cell adhesion molecules
- Receptor recognition (viral attachment)

Clinical Point

- Carbohydrate defects contribute to congenital disorders of glycosylation (CDG).

8. Carbohydrates in Connective Tissue

Glycosaminoglycans (GAGs)

- Important in joints, cartilage, ECM.

Defects ? Mucopolysaccharidoses (MPS)

- Hurler (cloudy cornea)
- Hunter (no corneal clouding)
- Morquio (skeletal deformity)
- Sanfilippo (CNS degenerative)

9. Carbohydrate Toxicity & Complications

A. Advanced Glycation End Products (AGEs)

- Chronic hyperglycemia ? nonenzymatic glycation of proteins.
- Complications:
 - Retinopathy
 - Nephropathy
 - Neuropathy

– Atherosclerosis

B. Sorbitol Accumulation

- In lens, nerves, kidney ? osmotic damage.
- Seen in uncontrolled diabetes.

10. Carbohydrates in Cancer Biology

Warburg Effect

- Cancer cells rely on **aerobic glycolysis**, converting glucose to lactate even with oxygen.
- High glucose uptake ? basis of **FDG-PET scans**.

Clinical Use

- PET scan detects tumors based on glucose uptake.

11. Carbohydrates in Liver Disease

- Liver stores glycogen ? fasting glucose maintenance.
- Liver failure ? hypoglycemia + lactic acidosis.
- High carbohydrate diet can worsen **fatty liver disease**.

12. Diagnostic Use of Carbohydrates

Glucose Tolerance Test (GTT)

- Diagnosis of diabetes mellitus and reactive hypoglycemia.

HbA1c

- Measures long-term glycemic control (AGE formation).

Urinary Reducing Sugar Tests

- Screens for galactosemia, fructosuria, glucosuria.

Important Points to Remember

- Glucose is the primary metabolic fuel; brain & RBCs depend on it.
- GSDs, galactosemia, and fructose intolerance are important genetic carbohydrate disorders.
- G6PD deficiency ? oxidative hemolysis; linked to pentose pathway.
- Lactase deficiency ? common cause of carbohydrate malabsorption.
- Sorbitol accumulation ? diabetic cataract and neuropathy.
- Chronic hyperglycemia leads to **glycation**, causing microvascular complications.
- Fiber improves digestion, lowers cholesterol, and helps control diabetes.
- GAG defects ? mucopolysaccharidoses (Hurler, Hunter, Morquio).
- Carbohydrates are essential for nucleic acids (ribose, deoxyribose), immunity, and ECM.
- Excess carbohydrates ? fatty liver, obesity, hypertriglyceridemia.
- PET scans use glucose analogs to detect tumors.
- Hypoglycemia is more dangerous acutely; hyperglycemia dangerous chronically.

MCQs

1. Which tissue is MOST dependent on glucose for its energy supply?

- A. Liver
- B. Kidney cortex
- C. Brain
- D. Skeletal muscle

Answer: C

2. Sorbitol accumulation is responsible for which diabetic complication?

- A. Retinopathy
- B. Cataract

- C. Hypoglycemia
- D. Ketoacidosis

Answer: B

3. Hereditary fructose intolerance is caused by deficiency of:

- A. Fructokinase
- B. Aldolase B
- C. Galactokinase
- D. Pyruvate kinase

Answer: B

4. Classical galactosemia is due to deficiency of:

- A. Galactokinase
- B. Aldose reductase
- C. GALT
- D. Hexokinase

Answer: C

5. Which pathway produces ribose-5-phosphate for nucleotide synthesis?

- A. Glycolysis
- B. TCA cycle
- C. Pentose phosphate pathway
- D. Beta-oxidation

Answer: C

6. A 5-year-old child develops cataracts after starting milk feeding. Most likely enzyme deficiency?

- A. Galactokinase
- B. Aldolase B

- C. G6PD
- D. Transketolase

Answer: A

7. Which disorder shows “coarse facial features, corneal clouding, hepatosplenomegaly”?

- A. McArdle disease
- B. Hurler syndrome
- C. Hunter syndrome
- D. Pompe disease

Answer: B

8. Corneal clouding is absent in:

- A. Hurler syndrome
- B. Maroteaux–Lamy syndrome
- C. Hunter syndrome
- D. Morquio syndrome

Answer: C

9. Which enzyme is deficient in McArdle disease?

- A. Liver phosphorylase
- B. Muscle phosphorylase
- C. G6Pase
- D. Acid maltase

Answer: B

10. Severe fasting hypoglycemia is characteristic of:

- A. Pompe disease
- B. von Gierke disease

- C. McArdle disease
- D. Cori disease

Answer: B

11. Which molecule protects RBCs from oxidative damage?

- A. NADH
- B. NADPH
- C. ATP
- D. FADH?

Answer: B

12. G6PD deficiency leads to hemolysis because of accumulation of:

- A. Glutathione
- B. NAD?
- C. Peroxide
- D. Sorbitol

Answer: C

13. Dietary fiber helps prevent all EXCEPT:

- A. Constipation
- B. Colon cancer
- C. LDL elevation
- D. Hypoglycemia

Answer: D

14. Which carbohydrate test is positive in fructosuria?

- A. Benedict's test
- B. Seliwanoff test
- C. Barfoed test

D. Rapid urease test

Answer: A

15. Which sugar shows the fastest entry into glycolysis?

- A. Glucose
- B. Fructose
- C. Galactose
- D. Ribose

Answer: B

16. The “flipped LDH pattern” (LDH-1 > LDH-2) indicates:

- A. Hemolytic anemia
- B. Liver disease
- C. Myocardial infarction
- D. Muscle injury

Answer: C

17. Which polysaccharide contains α -1,4 linkages and is indigestible?

- A. Glycogen
- B. Amylose
- C. Amylopectin
- D. Cellulose

Answer: D

18. The Warburg effect refers to:

- A. Glycogen breakdown in liver
- B. Aerobic glycolysis in cancer cells
- C. Lactose intolerance
- D. Ketone body formation in diabetes

Answer: B

19. Which of the following is a nonreducing disaccharide?

- A. Maltose
- B. Lactose
- C. Sucrose
- D. Cellobiose

Answer: C

20. Which MPS results primarily in neurological symptoms with heparan sulfate accumulation?

- A. Hurler
- B. Hunter
- C. Sanfilippo
- D. Morquio

Answer: C

Viva Voce

1. What is the primary function of carbohydrates?

To provide **immediate energy**, mainly in the form of glucose.

2. Which tissues are absolutely dependent on glucose?

Brain, RBCs, retina, renal medulla.

3. What is the carbohydrate requirement of the brain per day?

Approximately 120 grams of glucose.

4. Why do RBCs use only glucose?

RBCs **lack mitochondria**, so they depend entirely on glycolysis.

5. What is the most dangerous acute complication of carbohydrate imbalance?

Hypoglycemia, because it affects the brain quickly.

6. What causes fasting hypoglycemia in von Gierke disease?

Deficiency of **glucose-6-phosphatase** prevents glucose release from liver.

7. Which enzyme deficiency causes cataracts in infants fed with milk?

Galactokinase deficiency.

8. What causes severe symptoms immediately after fructose intake in infants?

Aldolase B deficiency ? hereditary fructose intolerance.

9. What is the biochemical basis of hemolysis in G6PD deficiency?

Low NADPH ? inability to neutralize oxidants ? **oxidative damage to RBCs**.

10. What triggers hemolysis in G6PD deficiency?

Fava beans, infections, antimalarials, sulfa drugs.

11. What is the main role of the HMP shunt in RBCs?

To generate **NADPH** for glutathione regeneration.

12. Which monosaccharide accumulates in diabetics leading to cataract?

Sorbitol, due to aldose reductase activity.

13. In which tissues does sorbitol accumulation cause complications?

Lens, retina, kidney, peripheral nerves.

14. What causes lactic acidosis in shock?

Tissue hypoxia ? anaerobic glycolysis ? **lactate accumulation.**

15. What is the hallmark of lactose intolerance?

Bloating and diarrhea due to undigested lactose fermenting in colon.

16. Which mucopolysaccharidosis presents with corneal clouding?

Hurler syndrome (?-L-iduronidase deficiency).

17. Which mucopolysaccharidosis is X-linked and spares the cornea?

Hunter syndrome.

18. What is the defect in Morquio syndrome?

Defective degradation of **keratan sulfate.**

19. Why is cellulose indigestible in humans?

Lack of **?-1,4 glucanase** (cellulase).

20. What is the dietary role of cellulose?

Acts as **fiber**, improving bowel movement and lowering cholesterol.

21. What is the Warburg effect?

Cancer cells preferentially perform **aerobic glycolysis**, producing lactate even with oxygen.

22. What diagnostic tool uses glucose analog uptake?

FDG-PET scan for tumor detection.

23. What causes the “flipped pattern” in LDH during myocardial infarction?

LDH-1 exceeds LDH-2 due to cardiac muscle damage.

24. Why is sucrose a nonreducing sugar?

Both anomeric carbons are involved in the **α-1,β-2 glycosidic bond**.

25. What is the biochemical reason for postprandial hyperglycemia after high-carb meals?

Rapid digestion and absorption of **simple carbohydrates** → glucose spike → insulin release.

26. How does dietary fiber help in diabetes?

Slows glucose absorption → **reduces postprandial spikes**.

27. What is the function of glucuronic acid in the body?

Helps in **detoxification (conjugation reactions)**.

28. Which enzyme converts ribonucleotides to deoxyribonucleotides?

Ribonucleotide reductase.

29. What is the significance of ribose?

Component of **ATP, NAD⁺, RNA**.

30. Which test detects reducing sugars in urine?

Benedict's test.
