

Chemistry of Lipids

Chemistry of Lipids

Topics covered: **Classification of lipids, Classification of fatty acids, Saturated fatty acids**

Classification of Lipids

Definition

Lipids are **hydrophobic or amphipathic** organic molecules, insoluble in water but soluble in non-polar solvents.

Major Classes

1. Simple Lipids

- **Fats (Triacylglycerols)** ? glycerol + 3 fatty acids
- **Waxes** ? long-chain fatty acids + long-chain alcohols

2. Compound Lipids

Contain additional non-lipid groups

- **Phospholipids** ? fatty acids + alcohol + phosphate
 - Glycerophospholipids (lecithin, cephalin)
 - Sphingophospholipids (sphingomyelin)
- **Glycolipids** ? fatty acids + carbohydrate
 - Cerebrosides
 - Gangliosides
- **Lipoproteins** ? lipid + protein (transport forms)

3. Derived Lipids

Formed during hydrolysis of other lipids

- Fatty acids
- Steroids (cholesterol)
- Fat-soluble vitamins (A, D, E, K)
- Eicosanoids

4. Miscellaneous Lipids

- Carotenoids
- Squalene
- Prostaglandins

Classification of Fatty Acids

Fatty acids are long-chain hydrocarbons ending in a **carboxyl group (-COOH)**.

A. Based on Saturation

- **Saturated fatty acids**
- **Unsaturated fatty acids**
 - Monounsaturated (one double bond)
 - Polyunsaturated (multiple double bonds)

B. Based on Chain Length

- **Short-chain** (<6 carbons)
- **Medium-chain** (6–12 carbons)
- **Long-chain** (13–20 carbons)
- **Very-long chain** (>20 carbons)

C. Based on Nutrition

- **Essential fatty acids (EFAs)** ? linoleic, linolenic (cannot be synthesized)
- **Non-essential fatty acids** ? synthesized by the body

D. Based on Configuration

- **Cis fatty acids** ? naturally occurring
 - **Trans fatty acids** ? industrial hydrogenation, associated with heart disease
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Saturated Fatty Acids

Definition

Fatty acids containing **no double bonds**; all carbon atoms are “saturated” with hydrogen.

Common Saturated Fatty Acids

- **Acetic acid** (2C)
- **Butyric acid** (4C)
- **Caproic acid** (6C)
- **Caprylic acid** (8C)
- **Capric acid** (10C)
- **Lauric acid** (12C)
- **Myristic acid** (14C)
- **Palmitic acid** (16C)
- **Stearic acid** (18C)
- **Arachidic acid** (20C)

Sources

- Animal fats (ghee, butter)
- Coconut oil
- Palm oil
- Dairy products
- Meat

Properties

- Solid at room temperature
- High melting point
- No susceptibility to oxidation (unlike PUFA)

Clinical Importance

- Excess intake ? increased **LDL cholesterol**
- Risk of **atherosclerosis** & cardiovascular disease
- Butyric acid supports colonic mucosal health
- Medium-chain triglycerides (MCTs) used in malabsorption disorders

Unsaturated Fatty Acids

Definition

Fatty acids containing **one or more double bonds** in their carbon chain.

Types

- **Monounsaturated fatty acids (MUFA)** ? 1 double bond
- **Polyunsaturated fatty acids (PUFA)** ? ? 2 double bonds

Common Examples

- **MUFA:** Oleic acid (18:1)
- **PUFA:** Linoleic (18:2), Linolenic (18:3), Arachidonic acid (20:4)

Properties

- Liquid at room temperature
- Lower melting point than saturated fats
- Refined oils rich in unsaturated fatty acids

Polyunsaturated Fatty Acids (PUFA)

Common PUFA

- **Linoleic acid (18:2)**
- **Alpha-linolenic acid (18:3)**
- **Arachidonic acid (20:4)**
- **EPA (20:5)**

- **DHA (22:6)**

Functions

- Fluidity of membranes
- Precursor of eicosanoids (prostaglandins, leukotrienes)

Essential Fatty Acids (EFAs)

Definition

Fatty acids **not synthesized by humans**; must be supplied by diet.

Essential FAs

- **Linoleic acid (?-6)**
- **Alpha-linolenic acid (?-3)**

Conditionally Essential

- **Arachidonic acid** (essential if linoleic acid deficient)

Deficiency Features

- Dry scaly skin
- Hair loss
- Poor wound healing
- Growth retardation

Omega-3 and Omega-6 Fatty Acids

Omega-3 Fatty Acids (?-3)

- Alpha-linolenic acid (ALA)
- EPA, DHA (fish oils)

Benefits

- Anti-inflammatory
- Improves heart health

- Essential for brain/retina
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Omega-6 Fatty Acids (?-6)

- Linoleic acid
- Arachidonic acid

Functions

- Growth, reproduction
 - Pro-inflammatory eicosanoid precursor
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Omega-3 : Omega-6 Balance

Ideal ratio: **1:4**

Modern diet: **1:20** (excess inflammation)

Cis-Trans Isomerism

Cis Configuration

- Natural form
- Creates a **bend** in chain
- ? membrane fluidity
- Healthier

Trans Configuration

- Formed by hydrogenation of oils
 - Straight-chain, behaves like saturated fat
 - ? LDL, ? HDL
 - Associated with **atherosclerosis & heart disease**
-

Properties of Lipids

Physical Properties

- Insoluble in water
- Soluble in ether, chloroform
- Hydrophobic (some amphipathic)

Chemical Properties

- Hydrolysis ? fatty acids + glycerol
- Hydrogenation ? solid fat formation
- Oxidation ? rancidity
- Saponification ? soap formation

Triglycerides (Triacylglycerols)

Definition

Glycerol + **3 fatty acids**

Types

- **Simple TAG** ? same FA
- **Mixed TAG** ? different FAs

Functions

- Major **energy reserve**
- Stored in adipose tissue
- Provides insulation, protection

Clinical Importance

- High TAG ? risk of pancreatitis
- Low TAG ? malnutrition, fat malabsorption

Lipid Peroxidation

Definition

Oxidative damage to **PUFA** in cell membranes by free radicals.

Steps

- Initiation ? free radical attack
- Propagation ? chain reaction
- Termination ? antioxidants stop cycle

Consequences

- Membrane damage
- Cell injury, aging
- Seen in liver diseases, CCl₄ toxicity

Protection

- **Vitamin E**, vitamin C, glutathione, superoxide dismutase

Classification of Compound Lipids

Compound lipids are lipids containing **additional non-lipid components** (phosphate, carbohydrate, proteins).

Main Types

1. Phospholipids

Contain:

- Fatty acids
- Alcohol (glycerol or sphingosine)
- **Phosphate**
- Nitrogenous base (choline, ethanolamine)

Includes:

- Glycerophospholipids
 - Sphingophospholipids
-

2. Glycolipids

Contain:

- Fatty acids
- **Carbohydrate** (galactose, sialic acid)
- Sphingosine

Includes:

- Cerebrosides
 - Gangliosides
-

3. Lipoproteins

- Lipid + **protein**
 - Transport vehicles for TAG, cholesterol, phospholipids
 - Types: chylomicrons, VLDL, LDL, HDL
-

4. Sulfolipids

- Fatty acids + carbohydrate + **sulfonic acid**
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5. Aminolipids

- Fatty acids + **amino alcohols**
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Phospholipids

Definition

Lipids containing **phosphate**, essential part of **cell membranes** and lipoproteins.

Classification

1. Glycerophospholipids

Alcohol = **glycerol**

Examples:

- **Lecithin (phosphatidylcholine)**
 - **Cephalin (phosphatidylethanolamine)**
-

- Phosphatidylserine
- Phosphatidylinositol
- Cardiolipin

Cardiolipin

Definition

Cardiolipin is a **unique diphosphatidylglycerol phospholipid** found almost exclusively in the **inner mitochondrial membrane**.

It contains:

- **Glycerol + 2 phosphatidic acid units**
- Total of **4 fatty acids**
- Highly acidic (two phosphate groups)

Structure (Text Description)

Cardiolipin is formed by linking **two phosphatidylglycerol molecules** through an additional glycerol unit.

This produces a **twin phospholipid** structure with:

- Central glycerol
- Two phosphatidic acids
- Four long-chain fatty acids in total

This unique architecture makes it essential for mitochondrial membrane stability.

Location

Cardiolipin is concentrated in:

- **Inner mitochondrial membrane (IMM)**
- Particularly abundant in tissues with high energy demand:
 - Heart
 - Skeletal muscle

- Liver
- Kidney

Functions

1. Stabilizes Mitochondrial Membrane & ETC Complexes

Cardiolipin binds tightly to:

- Complex I
- Complex III
- Complex IV
- ATP synthase

Maintains the structure and function of the **electron transport chain (ETC)**.

2. Essential for ATP Production

Helps maintain proton gradient and optimal function of oxidative phosphorylation.

3. Involved in Apoptosis

Cardiolipin undergoes oxidation during apoptosis ? facilitates release of **cytochrome c**, triggering programmed cell death.

4. Component of Bacterial Membranes

Because bacteria contain cardiolipin, antibodies to cardiolipin are clinically significant (see below).

Clinical Importance

1. Barth Syndrome (X-linked cardiomyopathy)

- Defect: **TAZ gene mutation** (encodes tafazzin).
- Impairs cardiolipin remodeling.
- Leads to:
 - Dilated cardiomyopathy
 - Skeletal muscle weakness
 - Neutropenia
 - Growth delay

This is the **classic disorder** linked to cardiolipin.

2. Anticardiolipin Antibodies (Autoimmune)

Seen in:

- **Antiphospholipid syndrome (APS)**
- **Systemic lupus erythematosus (SLE)**

Effects:

- Hypercoagulability
- Recurrent miscarriages
- Thrombosis (venous & arterial)

Anticardiolipin antibodies are used in **diagnosis of APS**.

3. Mitochondrial Diseases

Abnormal cardiolipin ? impaired ETC ?

- Muscle weakness
- Lactic acidosis
- Exercise intolerance

Seen in:

- Mitochondrial myopathies

- Multiple acyl-CoA dehydrogenase deficiency
 - Aging-related mitochondrial dysfunction
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4. Heart Failure & Ischemia

Ischemic damage alters cardiolipin composition ? reduces ETC activity ? worsens cardiac dysfunction.

Cardiolipin & Surfactant Link

Cardiolipin is synthesized from **phosphatidylglycerol**, which is also a surfactant component.

Thus mitochondrial defects affecting cardiolipin synthesis may also affect phosphatidylglycerol turnover.

Exam-Oriented Points to Remember

- Cardiolipin = **diphosphatidylglycerol** with 4 fatty acids
- Located in **inner mitochondrial membrane**
- Stabilizes **ETC complexes & ATP synthase**
- Required for **oxidative phosphorylation**
- Mutated in **Barth syndrome** (dilated cardiomyopathy)
- **Anticardiolipin antibodies** ? antiphospholipid syndrome
- Reduced in **mitochondrial myopathies & ischemic heart disease**
- Formed from **phosphatidylglycerol**

Functions:

- Membrane structure
 - Surfactant
 - Second messengers (IP?, DAG)
-

2. Sphingophospholipids

Alcohol = **sphingosine**

Example:

- **Sphingomyelin**

Functions:

- Myelin sheath structure
- Nerve conduction

Liposomes

Definition

Artificial spherical vesicles composed of **phospholipid bilayers**.

Functions

- Drug delivery systems
- Gene delivery (DNA/RNA transport)
- Model membranes for research
- Stabilize and transport hydrophobic drugs

Structure

- Aqueous core surrounded by one or more phospholipid bilayers
- Amphipathic nature allows hydrophilic and hydrophobic drug entrapment

Lecithin (Phosphatidylcholine)

Definition

Most abundant glycerophospholipid in human tissues.

Composition

- Glycerol
- 2 fatty acids
- Phosphate
- **Choline**

Functions

- Important membrane component
- Major pulmonary **surfactant** (Lecithin : Sphingomyelin ratio used for fetal lung maturity)
- Lipoprotein structure (VLDL export from liver)

Clinical Notes

- **Respiratory Distress Syndrome (RDS)** ? low lecithin in premature infants
- Lecithin: Sphingomyelin ratio > **2:1** indicates mature fetal lungs

Phospholipases

Enzymes that hydrolyze specific bonds of phospholipids.

Types & Actions

Phospholipase A1

- Removes **fatty acid at C-1** of glycerol

Phospholipase A2

- Removes **fatty acid at C-2**
- Releases **arachidonic acid** ? prostaglandins & leukotrienes
- Found in venom, pancreas

Phospholipase B

- Removes **both C-1 and C-2 fatty acids**

Phospholipase C

- Splits **phosphate-containing head group**
- Cleaves **PIP? ? DAG + IP?** (second messengers)

Phospholipase D

- Removes **alcohol (choline/ethanolamine)**
- Converts PC → phosphatidic acid

Clinical Importance

- Snake venom contains potent phospholipase A2 → membrane destruction
- Excess activation → inflammation
- Defects in phospholipid metabolism → neurological disorders

Lung Surfactants

Definition

Mixture of phospholipids & proteins that **reduces surface tension** inside alveoli.

Major Component

- **Dipalmityl phosphatidylcholine (DPPC)** → the key surfactant.
- Also contains phosphatidylglycerol & surfactant proteins (SP-A, SP-B, SP-C, SP-D).

Function

- Prevents alveolar collapse at end-expiration
- Improves lung compliance

Clinical Points

- **Respiratory Distress Syndrome (RDS)**
 - Due to **low surfactant** in premature infants
 - Lecithin : Sphingomyelin ratio > **2:1** = lung maturity
- Maternal steroids enhance fetal surfactant synthesis.

Phosphatidylglycerol

Definition

A **glycerophospholipid** composed of:

- Glycerol backbone
- Two fatty acids
- Phosphate group
- **Glycerol as the head group**

It is one of the **major phospholipids** in cell membranes and plays a key role in **lung surfactant**.

Structure

- Glycerol + fatty acid at C-1 and C-2
- Phosphate at C-3
- Another glycerol molecule attached to phosphate

This forms a **phosphatidyl-glycerol-phosphate unit**, later dephosphorylated to phosphatidylglycerol.

Biosynthesis

Phosphatidylglycerol is synthesized from:

1. **Phosphatidic acid**
2. Converted to **CDP-diacylglycerol**
3. Reacts with **glycerol-3-phosphate**
4. Final dephosphorylation yields **phosphatidylglycerol**

This is the pathway used in lung cells (type II pneumocytes) for surfactant synthesis.

Functions

1. Lung Surfactant Component

Phosphatidylglycerol is the **second most abundant surfactant phospholipid** after DPPC (dipalmitoyl phosphatidylcholine).

Its presence is crucial because:

- It enhances **spreading and stability** of DPPC
 - It appears late in gestation (~34–36 weeks), so it is used as a marker of **fetal lung maturity**
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2. Membrane Integrity

- Helps maintain membrane curvature
 - Important for mitochondrial membranes
 - Serves as a precursor for **cardiolipin**
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Clinical Importance

1. Fetal Lung Maturity Marker

- Used in amniotic fluid analysis
- Presence of phosphatidylglycerol indicates **low risk of Respiratory Distress Syndrome (RDS)**
- Appears after L:S (lecithin:sphingomyelin) ratio becomes > 2:1

2. Surfactant Deficiency ? RDS

In premature infants:

- Low DPPC + low phosphatidylglycerol
- ? alveolar collapse
- ? severe respiratory distress

Maternal steroids increase surfactant production and **increase phosphatidylglycerol levels**.

3. Cardiolipin Precursor

- Phosphatidylglycerol is required for **cardiolipin synthesis**
 - Cardiolipin maintains mitochondrial membrane function
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- Abnormal cardiolipin is seen in **Barth syndrome** and mitochondrial disorders

Exam-Oriented Points to Remember

- Phosphatidylglycerol = **glycerol + phosphate + glycerol**
- Essential for **lung surfactant** ? appears late in gestation
- Marker of **fetal lung maturity** in amniotic fluid
- Precursor to **cardiolipin**
- Deficiency ? higher risk of **RDS in preterm infants**
- Located in **mitochondria and lung** tissue prominently

Cephalin (Phosphatidylethanolamine)

Definition

A glycerophospholipid containing **ethanolamine**.

Functions

- Structural component of cell membranes
- Important in **blood coagulation**
- Precursor for formation of phosphatidylcholine

Sources

- Brain and nervous tissue

Plasmalogens

Definition

Ether phospholipids where fatty acid at C-1 is replaced by **unsaturated ether linkage**.

Types

- **Phosphatidylethanolamine plasmalogen** ? abundant in **nerve tissue**
- **Phosphatidylcholine plasmalogen** ? present in **heart muscle**

Functions

- Membrane stabilizers
- Antioxidant properties

Clinical Note

- Reduced in **Zellweger syndrome** (peroxisomal disorder)

Sphingolipids

Definition

Lipids containing **sphingosine** instead of glycerol.

Types

1. **Sphingomyelin** (phospholipid)
2. **Glycosphingolipids**
 - Cerebrosides
 - Sulfatides
 - Globosides
 - Gangliosides

Functions

- Myelin sheath integrity
- Cell recognition, adhesion
- Signal transduction

Non-phosphorylated Lipids (Glycolipids)

Contain **carbohydrate + ceramide** with no phosphate.

Types

- Cerebrosides
- Sulfatides
- Globosides
- Gangliosides

Functions

- Found in nerve & muscle membranes
- Brain white matter
- Cell signaling & recognition

Cerebrosides

Definition

- Ceramide + **one sugar** (glucose or galactose)

Types

- Glucocerebroside
- Galactocerebroside (major myelin component)

Clinical Disorder

- **Gaucher Disease**
 - Glucocerebrosidase deficiency
 - Hepatosplenomegaly, bone pain, “crumpled tissue paper” macrophages

Gangliosides

Definition

- Ceramide + **oligosaccharide containing sialic acid (NANA)**

Functions

- Cell surface receptors
- Neurotransmission
- Brain development

Clinical Disorder

- **Tay-Sachs Disease**
 - Hexosaminidase A deficiency
 - Accumulation of GM2 ganglioside
 - Cherry-red spot on macula, neurodegeneration
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Cholesterol Chemistry

Structure

- Steroid nucleus = **cyclopentanoperhydrophenanthrene ring**
- 27-carbon molecule
- Hydroxyl at C-3, double bond between C-5 and C-6

Functions

- Membrane fluidity regulator
- Precursor of:
 - Bile acids
 - Steroid hormones
 - Vitamin D
 - Lipoproteins

Clinical Correlations

- High LDL ? atherosclerosis
 - Gallstones ? excess cholesterol precipitation
 - Smith-Lemli-Opitz syndrome ? cholesterol biosynthesis defect
-

Eicosanoids

Definition

Bioactive lipids derived from **arachidonic acid (20:4)**.

Types

- **Prostaglandins (PG)**
- **Thromboxanes (TX)**
- **Leukotrienes (LT)**
- **Lipoxins**

Functions

- Inflammation
- Platelet aggregation
- Bronchial tone regulation
- Renal blood flow

Clinical Correlations

- NSAIDs block **COX** ? ? prostaglandins
- Asthma ? leukotrienes cause bronchoconstriction
- Low-dose aspirin ? inhibits TXA? ? antiplatelet effect

Lipid Storage Disorders (Sphingolipidoses)

1. Tay-Sachs Disease

- Enzyme: **Hexosaminidase A**
 - Accumulation: GM? ganglioside
 - Features: neurodegeneration, cherry-red macula
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2. Gaucher Disease

- Enzyme: **Glucocerebrosidase**
 - Accumulation: Glucocerebroside
 - Features: hepatosplenomegaly, bone crises, “crumpled tissue paper” cells
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3. Niemann–Pick Disease

- Enzyme: **Sphingomyelinase**
 - Accumulation: Sphingomyelin
 - Features: hepatosplenomegaly, neurodegeneration, cherry-red spot
-

4. Krabbe Disease

- Enzyme: **Galactocerebrosidase**
 - Accumulation: Galactocerebroside
 - Features: optic atrophy, severe demyelination
-

5. Metachromatic Leukodystrophy

- Enzyme: **Arylsulfatase A**
 - Accumulation: Sulfatides
 - Features: progressive demyelination
-

6. Fabry Disease (X-linked)

- Enzyme: **α-galactosidase A**
 - Accumulation: Ceramide trihexoside
 - Features: angiokeratomas, renal failure, neuropathy
-

7. Zellweger Syndrome

- Not a sphingolipidosis, but **peroxisomal disorder**
- ? plasmalogens
- Features: hypotonia, seizures, craniofacial abnormalities

Compound Lipids

Definition

Lipids that contain **additional non-lipid components** such as phosphate, carbohydrate, nitrogen base, or protein.

Main Groups

- **Phospholipids** (contain phosphate)
- **Glycolipids** (contain carbohydrate)
- **Lipoproteins** (contain proteins)
- **Sulfolipids** (contain sulfate)
- **Aminolipids** (contain amino groups)

Glycerophosphatides (Glycerophospholipids)

Definition

Phospholipids containing **glycerol** as the backbone.

General Structure

- Glycerol
- Two fatty acids
- Phosphate
- Nitrogenous base (choline, ethanolamine, serine, inositol)

Important Types

- **Phosphatidylcholine (Lecithin)**
- **Phosphatidylethanolamine (Cephalin)**
- **Phosphatidylserine**
- **Phosphatidylinositol (PI)**
- **Cardiolipin**

Functions

- Major part of cell membranes
- Surfactant (DPPC)
- Signal transduction (PIP? ? IP? & DAG)
- Lipoprotein assembly (VLDL formation in liver)

Sphingolipids

Definition

Lipids containing **sphingosine** as the backbone instead of glycerol.

Components

- Sphingosine
- Fatty acid (forms ceramide)
- Carbohydrate OR phosphate group
- Head group (varies by type)

Classification

1. **Sphingomyelin** – contains phosphate
2. **Cerebrosides** – contain one sugar
3. **Globosides** – multiple sugars
4. **Gangliosides** – sugars + sialic acid
5. **Sulfatides** – sulfate group

Functions

- Cell membrane stability
- Neuronal insulation (myelin)
- Cell recognition and adhesion
- Signal transduction

Sphingomyelin

Definition

A **sphingophospholipid**: sphingosine + fatty acid (ceramide) + **phosphate + choline**.

Location

- **Myelin sheath**
- Cell membranes (especially nerve tissue)

Functions

- Electrical insulation
- Cell signaling
- Membrane stability

Clinical Correlation

- **Niemann–Pick disease** ? sphingomyelinase deficiency
 - Hepatosplenomegaly, neurodegeneration, cherry-red macula

Cerebrosides

Definition

Glycolipids with **ceramide + a single sugar** (glucose or galactose).

Types

- **Glucocerebroside**
- **Galactocerebroside** (abundant in myelin)

Functions

- Important in **white matter**
- Role in nerve conduction and myelin stability

Clinical Correlation

- **Gaucher disease**
 - Glucocerebrosidase deficiency
 - “Crumpled tissue paper” macrophages
 - Hepatosplenomegaly, bone pain

Gangliosides

Definition

Glycosphingolipids with **ceramide + oligosaccharide + sialic acid (NANA)**.

Location

- Neuronal membranes
- Synaptic junctions
- Gray matter

Functions

- Cell recognition
- Neurodevelopment
- Modulation of synaptic transmission

Clinical Correlation

- **Tay–Sachs disease**
 - Hexosaminidase A deficiency
 - Accumulation of GM2 ganglioside
 - Neurodegeneration, cherry-red macula, no hepatosplenomegaly

Exam-Oriented Summary

- **Compound lipids** contain phosphate or carbohydrate.
- **Glycerophosphatides** are glycerol-based phospholipids (lecithin, cephalin).
- **Sphingolipids** are sphingosine-based lipids.
- **Sphingomyelin** = ceramide + phosphate + choline.
- **Cerebrosides** = ceramide + single sugar.
- **Gangliosides** = ceramide + oligosaccharide + sialic acid.
- Clinical disorders: **Niemann–Pick, Gaucher, Tay–Sachs**.

Extra Note :

Sulfatides

Definition

Sulfatides are **sulfated glycolipids** belonging to the **glycosphingolipid** family.

They consist of:

- **Ceramide** (sphingosine + fatty acid)
- **Galactose**
- **Sulfate group** added to the galactose

They are also called **sulfogalactocerebrosides**.

Structure (text description)

A ceramide backbone is attached to a **galactose molecule**, which is further esterified with **sulfuric acid**, producing a negatively charged lipid.

This structure gives sulfatides strong **acidic properties** and allows interaction with proteins in nerve tissue.

Location

Sulfatides are abundant in:

- **Myelin sheath** (white matter)
- Oligodendrocytes
- Schwann cells
- Renal tubular cells
- Gastrointestinal mucosa

Functions

1. Myelin Stability & Nerve Conduction

Sulfatides help maintain:

- Compact structure of myelin
- Saltatory conduction

- Adhesion between myelin lamellae
-

2. Cell–Cell Interaction & Signaling

Important for:

- Immune cell adhesion
 - Axonal–glial communication
 - Trafficking of membrane proteins
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3. Membrane Organization

Contribute to formation of **lipid rafts**, influencing signal transduction.

Clinical Importance

1. Metachromatic Leukodystrophy (MLD)

Key disorder involving sulfatides

- Enzyme deficiency: **Arylsulfatase A**
- Result: Accumulation of **sulfatides** in CNS & PNS
- Pathology: Myelin destruction ? “metachromatic staining” of deposits
- Features:
 - Progressive motor loss
 - Hypotonia
 - Developmental delay
 - Vision & hearing loss
 - Peripheral neuropathy

This is the classic sulfatide storage disease.

2. Multiple Sclerosis (MS)

- Myelin breakdown alters sulfatide composition
 - Used as potential biomarker for demyelinating activity
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3. Diabetic Kidney Disease

- Changes in renal sulfatides observed in early diabetic nephropathy
-

4. Cancer Biology

- Altered sulfatide levels seen in gastric and colon cancers
 - May modulate immune evasion
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Metabolism (text description)

Sulfatides are degraded in lysosomes.

Steps:

1. **Arylsulfatase A** removes the sulfate group
 2. Remaining galactocerebroside is further broken down by galactosidases
Failure of the first step ? Metachromatic leukodystrophy.
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Exam-Oriented Points to Remember

- Sulfatides = **sulfated galactocerebrosides**
 - Major lipids of **myelin**
 - Synthesized in **Golgi apparatus**
 - Degraded by **arylsulfatase A**
 - Deficiency ? **Metachromatic leukodystrophy**
-

- Important in **nerve conduction, membrane adhesion, lipid rafts**
- Excess sulfatides ? demyelination disorders

Important Points to Remember (Whole Lipid Chapter)

- Lipids are **hydrophobic or amphipathic** molecules essential for energy storage, membranes, signaling, and insulation.
- Simple lipids ? fats (TAGs) and waxes; compound lipids ? phospholipids, glycolipids, lipoproteins; derived lipids ? fatty acids, steroids, eicosanoids.
- **Fatty acids** may be saturated, unsaturated, essential, cis/trans, short- or long-chain.
- Essential fatty acids ? **linoleic (?-6)** and **?-linolenic (?-3)**; deficiency causes dry skin, poor wound healing, growth failure.
- Unsaturated fatty acids increase membrane fluidity; **trans fats** behave like saturated fats and increase cardiovascular risk.
- **Triglycerides** are the main storage lipids; high levels can trigger pancreatitis.
- Phospholipids are major membrane components; **lecithin** is key surfactant; **cephalin** is found in brain; **plasmalogens** are reduced in peroxisomal disorders.
- **Phosphatidylglycerol** and **DPPC** form the backbone of **lung surfactant**; absence ? neonatal RDS.
- **Cardiolipin** is unique to the inner mitochondrial membrane and stabilizes ETC complexes; altered in Barth syndrome and mitochondrial diseases.
- Sphingolipids contain **sphingosine**; important for myelin and signal transduction.
- Cerebrosides = ceramide + one sugar; gangliosides = ceramide + oligosaccharide + sialic acid; sulfatides = sulfated cerebrosides.
- Cholesterol is a steroid alcohol with 27 carbons and rigid ring structure; precursor of **bile acids, vitamin D, steroid hormones**.

- Eicosanoids (prostaglandins, thromboxanes, leukotrienes) derive from **arachidonic acid** and regulate inflammation, vasoconstriction, bronchial tone, platelet function.
- Lipid peroxidation damages membranes; prevented by **vitamin E, vitamin C, glutathione**.
- Lipid storage disorders = enzyme defects in sphingolipid degradation ? Gaucher, Tay-Sachs, Niemann–Pick, Krabbe, MLD, Fabry.
- High LDL increases atherosclerosis risk; HDL is protective; trans fats increase LDL and decrease HDL.
- Omega-3 fatty acids (EPA, DHA) reduce inflammation and improve cardiovascular health.
- Myelin lipids (cerebrosides, sulfatides, sphingomyelin) are essential for nerve conduction; defects cause progressive neurological disease.

FAQs (Whole Lipid Chapter)

1. What is the simplest definition of a lipid?

A water-insoluble, hydrophobic or amphipathic organic molecule.

2. What is the major function of triglycerides?

Long-term **energy storage** and metabolic fuel.

3. Which fatty acids are essential and why?

Linoleic and α -linolenic acids ? humans lack enzymes to introduce double bonds beyond C-9.

4. What makes omega-3 and omega-6 fatty acids different?

The position of the **first double bond** from the methyl end (C-3 for omega-3, C-6 for omega-6).

5. Why is trans fat harmful?

It raises LDL, lowers HDL, and increases atherosclerosis risk.

6. What is lecithin clinically important for?

It is the key **surfactant lipid**; used in L:S ratio to assess fetal lung maturity.

7. What is cardiolipin and where is it found?

A diphosphatidylglycerol found in the **inner mitochondrial membrane**; essential for ETC stability.

8. What are cerebrosides and where are they found?

Ceramide + one sugar; abundant in **white matter** and myelin.

9. What are gangliosides used for?

Cell recognition, neurodevelopment, and synaptic function.

10. What causes the cherry-red spot in Tay-Sachs disease?

GM? ganglioside accumulation in retinal ganglion cells.

11. What is the key enzyme deficient in Gaucher disease?

Glucocerebrosidase.

12. Why is sphingomyelin important?

It forms part of the **myelin sheath** and contributes to nerve conduction.

13. What is lipid peroxidation?

Free radical–driven oxidation of polyunsaturated fatty acids ? membrane damage.

14. How do eicosanoids affect inflammation?

Prostaglandins ? inflammation

Thromboxanes ? platelet aggregation

Leukotrienes ? bronchoconstriction

15. What is the function of cholesterol in the membrane?

Controls **fluidity**, stabilizes lipid bilayer, reduces permeability.

16. What causes RDS in premature infants?

Low surfactant (mainly **DPPC & phosphatidylglycerol**).

17. What is the role of bile acids derived from cholesterol?

Emulsification of fats and aiding lipid digestion.

18. Which disease involves arylsulfatase A deficiency?

Metachromatic leukodystrophy.

19. Why are omega-3 fatty acids cardioprotective?

They reduce triglycerides, inflammation, and platelet aggregation.

20. What makes phospholipids amphipathic?

Hydrophilic head + hydrophobic fatty acid tails.

MCQs — Chemistry of Lipids

1. Essential fatty acids include:

- A. Oleic acid
- B. Palmitic acid
- C. Linoleic acid

D. Stearic acid

2. Trans-fatty acids behave physiologically like:

- A. Omega-3 fatty acids
 - B. Saturated fatty acids
 - C. Polyunsaturated fatty acids
 - D. Short-chain fatty acids
-

3. The major component of lung surfactant is:

- A. Phosphatidylserine
 - B. Dipalmitoyl phosphatidylcholine
 - C. Cardiolipin
 - D. Sphingomyelin
-

4. Cardiolipin is located mainly in:

- A. Outer mitochondrial membrane
 - B. Inner mitochondrial membrane
 - C. Golgi apparatus
 - D. Lysosomal membrane
-

5. Plasmalogens are characteristically low in:

- A. Gaucher disease
 - B. Zellweger syndrome
 - C. Tay-Sachs disease
 - D. Fabry disease
-

6. Glycolipids differ from phospholipids because they contain:

- A. Phosphate
- B. Nitrogen base
- C. Carbohydrate

D. Glycerol

7. A ganglioside always contains:

- A. Sulfate
 - B. Sialic acid (NANA)
 - C. Phosphate
 - D. Ceramide + one sugar
-

8. The lipid that stabilizes the electron transport chain is:

- A. Lecithin
 - B. Ceramide
 - C. Cardiolipin
 - D. Phosphatidylglycerol
-

9. Niemann–Pick disease is due to accumulation of:

- A. GM2 ganglioside
 - B. Glucocerebroside
 - C. Ceramide trihexoside
 - D. Sphingomyelin
-

10. The enzyme deficient in Tay–Sachs disease is:

- A. Arylsulfatase A
 - B. Hexosaminidase A
 - C. Glucocerebrosidase
 - D. Sphingomyelinase
-

11. Arachidonic acid is a precursor for:

- A. Prostaglandins
- B. Steroid hormones
- C. TAGs

D. Bile acids

12. Omega-3 fatty acids are beneficial because they:

- A. Increase platelet aggregation
 - B. Increase LDL
 - C. Reduce inflammation
 - D. Raise trans-fat levels
-

13. Sulfatides accumulate in deficiency of:

- A. Arylsulfatase A
 - B. Hexokinase
 - C. Lipoprotein lipase
 - D. Ceramidase
-

14. The main storage form of lipids in humans is:

- A. Phospholipid
 - B. Triglyceride
 - C. Cholesterol ester
 - D. Free cholesterol
-

15. Which lipid is essential for myelin insulation?

- A. Sphingomyelin
 - B. Phosphatidylinositol
 - C. Lecithin
 - D. Cardiolipin
-

16. The major dietary source of trans fats is:

- A. Butter
 - B. Coconut oil
 - C. Hydrogenated vegetable oils
-

D. Olive oil

17. Which test uses lecithin–sphingomyelin ratio?

- A. Renal function test
 - B. Fetal lung maturity test
 - C. Liver function test
 - D. Lipid profile
-

18. Lipid peroxidation affects mainly:

- A. Cholesterol
 - B. PUFA in membranes
 - C. Short-chain fatty acids
 - D. Triglycerides in adipose tissue
-

19. Which lipid is a precursor of bile acids?

- A. Phosphatidylserine
 - B. Cholesterol
 - C. Arachidonic acid
 - D. Ceramide
-

20. In Gaucher disease, which cell type is characteristic?

- A. Auer rods
 - B. “Crumpled tissue paper” macrophages
 - C. Onion skin macrophages
 - D. Foamy macrophages
-

21. A newborn with respiratory distress likely lacks:

- A. Omega-3 FA
 - B. Phosphatidylglycerol
 - C. Cholesterol
-

D. Ceramide

22. Which lipid carries a net negative charge due to sulfate?

- A. Ceramide
 - B. Sulfatide
 - C. Sphingomyelin
 - D. Phosphatidylcholine
-

23. The most abundant sterol in human tissues is:

- A. Ergosterol
 - B. Sitosterol
 - C. Cholesterol
 - D. Lanosterol
-

24. Which lipid is a major component of LDL?

- A. Triglyceride
 - B. Cholesterol ester
 - C. Lecithin
 - D. Ganglioside
-

25. Phospholipase A2 releases a fatty acid that is a precursor of:

- A. Steroid hormones
 - B. Eicosanoids
 - C. Amino acids
 - D. Ketone bodies
-

Answers

- 1-C
- 2-B
- 3-B

4-B
5-B
6-C
7-B
8-C
9-D
10-B
11-A
12-C
13-A
14-B
15-A
16-C
17-B
18-B
19-B
20-B
21-B
22-B
23-C
24-B
25-B

Viva Voce — Chemistry of Lipids

1. What is the simplest definition of a lipid?

A hydrophobic or amphipathic molecule insoluble in water.

2. What makes a lipid amphipathic?

It contains both a **hydrophilic head** and **hydrophobic tail**.

3. Name the major storage form of lipids.

Triglycerides (triacylglycerols).

4. Which fatty acids are essential?

Linoleic acid (ω -6) and ω -linolenic acid (ω -3).

5. Why are essential fatty acids needed?

Humans cannot introduce double bonds beyond carbon 9.

6. What is the difference between saturated and unsaturated fatty acids?

Saturated have **no double bonds**; unsaturated have **one or more** double bonds.

7. What is a trans-fat?

An unsaturated fatty acid with **trans configuration**, acting like saturated fat.

8. What type of lipid is the main membrane component?

Phospholipids.

9. What is the principal surfactant in lungs?

DPPE — dipalmitoyl phosphatidylcholine.

10. What is the importance of phosphatidylglycerol?

A key surfactant lipid; appears late in fetal development.

11. Cardiolipin is located where?

Inner mitochondrial membrane.

12. What is the function of cardiolipin?

Stabilizes ETC complexes and ATP synthesis.

13. Which disease results from cardiolipin abnormality?

Barth syndrome.

14. What is a glycerophospholipid?

A phospholipid with **glycerol** backbone.

15. Give two examples of glycerophospholipids.

Lecithin and cephalin.

16. What is a plasmalogen?

A phospholipid with an **ether linkage** at carbon-1.

17. What is a sphingolipid?

A lipid containing **sphingosine** backbone.

18. What is the basic building block of all sphingolipids?

Ceramide.

19. What is sphingomyelin?

A sphingophospholipid containing **phosphate + choline**.

20. Which disorder results from sphingomyelinase deficiency?

Niemann–Pick disease.

21. What are cerebrosides?

Ceramide + **one sugar** (glucose or galactose).

22. Which disease shows accumulation of glucocerebroside?

Gaucher disease.

23. What are gangliosides?

Ceramide + **oligosaccharide** + **sialic acid (NANA)**.

24. Which enzyme deficiency causes Tay–Sachs disease?

Hexosaminidase A.

25. What are sulfatides?

Sulfated galactocerebroside.

26. Which enzyme is defective in metachromatic leukodystrophy?

Arylsulfatase A.

27. What is the structure of cholesterol?

A 27-carbon steroid with four fused rings.

28. Name important products derived from cholesterol.

Bile acids, steroid hormones, vitamin D.

29. What is the main function of cholesterol in membranes?

Regulates fluidity and stability.

30. What are eicosanoids derived from?

Arachidonic acid.

31. Name three types of eicosanoids.

Prostaglandins, thromboxanes, leukotrienes.

32. Which enzyme releases arachidonic acid from membranes?

Phospholipase A2.

33. What is lipid peroxidation?

Free-radical oxidation of polyunsaturated fatty acids causing membrane damage.

34. Which vitamin protects against lipid peroxidation?

Vitamin E.

35. Why are omega-3 fatty acids beneficial?

Reduce inflammation, improve cardiac health.

36. Which lipids dominate the myelin sheath?

Cerebrosides, sulfatides, sphingomyelin.

37. What is the L:S ratio used for?

Assessment of fetal lung maturity.

38. What is the biological role of bile acids?

Emulsification and absorption of dietary lipids.

39. What is the precursor of prostaglandins?

Arachidonic acid.

40. Why do trans fats increase atherosclerosis risk?

Increase LDL and decrease HDL.