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

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

Omega-6 Fatty Acids (?-6)

• Linoleic acid
• Arachidonic acid

Functions

• Growth, reproduction
• Pro-inflammatory eicosanoid precursor

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, CCl? 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

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2. Glycolipids

Contain:

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

Includes:

• Cerebrosides
• Gangliosides

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3. Lipoproteins

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

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4. Sulfolipids

• Fatty acids + carbohydrate + **sulfonic acid**

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5. Aminolipids

• Fatty acids + **amino alcohols**

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.

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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**.

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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)

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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

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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**

Clinical Importance

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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**.

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3. Cardiolipin Precursor

• Phosphatidylglycerol is required for **cardiolipin synthesis**
• Cardiolipin maintains mitochondrial membrane function

• 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 GM? ganglioside
– Cherry-red spot on macula, neurodegeneration

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)

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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

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4. Krabbe Disease

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

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5. Metachromatic Leukodystrophy

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

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6. Fabry Disease (X-linked)

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

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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

Notes downloaded from **Medmentoredu** | Page 25

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 GM? 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

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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

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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.

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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

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4. Cancer Biology

• Altered sulfatide levels seen in gastric and colon cancers
• May modulate immune evasion

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.

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)

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1. What is the simplest definition of a lipid?

A water-insoluble, hydrophobic or amphipathic organic molecule.

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2. What is the major function of triglycerides?

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

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3. Which fatty acids are essential and why?

Linoleic and ?-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 (?-6) and ?-linolenic acid (?-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?

DPPC — 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 galactocerebrosides.

---

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.