LIPIDS OVERVIEW

FROM CHATTERJEA

- Chemically, lipids are all esters of glycerol with higher fatty acids.
- **Phospholipids examples**:
  1. Phosphatidyl choline (Lecithin)
  2. Phosphatidyl ethanolamine (Cephalin)
  3. Phosphatidyl inositols (Lipositols)
  4. Phosphatidyl serine
  5. Plasmalogens
  6. Sphingomyelins
- Glycolipids contain a special alcohol called sphingosine or sphingol and nitrogenous base in addition to fatty acids but does not contain phosphoric acid or glycerol.
- General Formula of saturated fatty acids: $C_nH_{2n+1}COOH$
- Saturated Fatty acids: Palmitic acid, Stearic acid
- Oleic acid (mono unsaturated fatty acids) is found in nearly all fats
- **Poly-unsaturated fatty acids**:
  1. Linoleic acid (two double bonds)
  2. Linolenic acid (three double bonds)
  3. Arachidonic acid (four double bonds)
     These three are essential fatty acids (have to be provided in diet, as they cannot be synthesized in body)
- Sebum (from sebaceous glands) contain branched chain fatty acid
- **Substituted fatty acids**:
  1. Hydroxy fatty acid
     - Carbonic acid of brain glycolipids
     - Ricinoleic acid in castor oil
  2. Methyl fatty acid
- Saturated acids end in “anoic” e.g. octanoic acid
- Unsaturated acids end in “enoic” e.g. octadecenoic acid (oleic acid)
- Expressing fatty acid by formula
  e.g. oleic acid ($C_{17}H_3COOH$) expressed as 18:1:9
  18 indicates number of carbon atoms
  1 indicates number of double bond
  9 indicates position of double bond
- Oleic acid could have 15 different positional isomers
- Arachidonic acid is precursor from which prostaglandins and leukotrienes are synthesized inn the body
  Prostaglandins are synthesized from arachidonic acid by cyclo oxygenase enzyme system

- Leucotrienes are conjugated trienes formed from arachidonic acid in leucocytes by the Lipoxygenase pathway
- Fats with high content of polyunsaturated fatty acids tends to lower serum level of cholesterol
- **Docosahexanoic acid (DHA)**
    - Poly unsaturated fatty acid synthesized from α-linolenic or obtained directly from dietary fish oil
    - DHA is present in high concentration in retina, cerebral cortex, testes and sperms
    - DHA is particularly needed in development of brain and retina and is supplied via the placenta and milk
- Triene/Tetratriene ratio in plasma lipids can be used to diagnose the extent of essential fatty acid deficiency
- **Glycerol:**
    - Commonly called as glycerin
    - Simplest trihydric alcohol (3 –OH groups)
    - Presence of glycerol detected by acrolein test
    - Nitroglycerine is used as a vasodilator. Glycerol therapy in cerebrovascular diseases reduce cerebral oedema
- **Unsaturated alcohols**

  Many of them are pigments
    1. Phytol (Phytyl alcohol) – constituent of chlorophyll
    2. Lycophyll – A polyunsaturated dihydroxy alcohol which occurs in tomatoes as purple pigment
    3. Carotene – split to give two molecules of Vitamin A
    4. Sphingosine or Sphingol – constituent of phospholipid, sphingomyelin and various glycolipids
- Diet rich in cholesterol are butter, cream, milk, egg yolk, meat etc.
- Endogenously, cholesterol is synthesized in body from Acetyl CoA
- **Cholesterol in body**

  Adult brain and nervous tissue – 2%
  Liver – 0.3%
  Skin – 0.3%
  Intestinal mucosa – 0.2%
  Endocrine glands (adrenal cortex) – 10% or more
  Also present in blood and bile
- **Esterification of cholesterol in plasma**

  Lecithin + Cholesterol $\xrightarrow{\text{LCAT}}$ Lysolecithin + Cholesterol ester

  LCAT: Lecithin Cholesterol Acyl Transferase
- **Norum's Disease:**

  A genetic deficiency of LCAT produces Norum's disease due to failure of esterification of cholesterol at the cost of lecithin. This disease is characterized by
    - Rise in free cholesterol

- Rise in lecithin in plasma
- Fall in cholesterol ester, lysolecithin and α-lipoproteins in plasma

- Other **Sterols** of Biological Importance
    1. 7-Dehydrocholesterol (pre-cholecalciferol) also called pro Vitamin-D_3
    2. Ergosterol – plant sterol, also called provitamin-D_2
    3. Stigmasterol or Sitosterol – plant sterols having no nutritional value for human beings. Sitosterol appears to decrease the intestinal absorption of both exogenous and endogenous cholesterol, thus lowering blood cholesterol level
    4. Coprosterol (Coprostanol) – occurs in faeces
    5. Others
        - Bile acids
        - Adrenocortical hormones
        - Gonadal hormones
        - D vitamins
        - Cardiac glycosides
        - Some alkaloids
- Simple Lipids : Neutral fats (Triglycerides or Triglycerol)
  Compound Lipids : Phospholipids
- The fats may be hydrolyzed with:
    - Super heated steam
    - By acids or alkalies
    - By the specific fat splitting enzymes lipase
- Lipases are enzymes which hydrolyze a triglyceride yielding fatty acids and glycerol
    1. Lingual lipase
    2. Gastric lipase
    3. Pancreatic lipase
    4. Intestinal lipase
    5. Adipolytic lipase
    6. Serum lipase

       Pancreatic lipase is peculiar in that it can hydrolyze ester bonds in positions 1 and 3 preferentially, than in position 2 of triglyceride molecule
- Hydrolysis of fat by an alkali (e.g. NaOH) is called **saponification**. The resultant products are glycerol and the alkali salts of fatty acids, which are called soaps
- **Na-ricinoleate** (a soap) has detoxifying activity against diphtheria and tetanus toxins
- Fats very rich in unsaturated fatty acids such as linseed oil undergo spontaneous oxidation at the double bond forming aldehydes, ketones and resins which form transparent coating on the surfaces to which the oil is applied. These are called **drying oils** and are used in the manufacture of paints and varnishes.
- **Causes of rancidity**
    1. Hydrolysis
    2. Oxidation

- Vegetable fats contain certain substances like vitamin E, phenols, hydroquinones, tannins and others which are antioxidants and prevents development of rancidity.
  Hence vegetable fats preserve for longer periods than animal fats.
- **IDENTIFICATION OF FATS AND OILS**
  1. **Saponification Number:**
     The fats containing short chain fatty acids will have more –COOH groups per gram than long chain fatty acids and this will take up more alkali and hence will have higher saponification number
     Butter – 220 to 230
     Oleomargarine – 195 or less
  2. **Acid Number:**
     It indicates the degree of rancidity of given fat
  3. **Reichert-Meissl Number**:
     It measures the amount of volatile soluble fatty acids.
     Butter fat is the only common fat with a high Reichert-Meissl number and this determination, therefore, is of interest in that it aids the food chemist in detecting butter sunstitutes in food products
  4. **Iodine Number**:
     It is a measure of the degree of unsaturation of a fat. The determination of iodine number is useful to the chemist in determining the quality of oil and its freedom from adulteration.
  5. **Acetyl Number**:
     It is a measure of the number of –OH group present. It can be used to detect adulteration.
- **Phospholipds**:
  Fatty acids + Glycerol/ Other alcohol + Phosphoric acid residue + Nitrogen containing base
- **Classification of phospholipids**
  1. **Glycerophosphatides**
     Alcohol present – Glycerol
     Examples:
     - Phosphatidyl ethanolamine (cephalin)
     - Phosphatidyl choline (Lecithin)
     - Phosphatidyl serine
     - Plasmalogens
     - Phosphatidic acid
     - Cardiolipins
     - Phosphatides
  2. **Phosphoinositides**
     Alcohol present – Inositol
     Examples:
     - Phosphatidyl inositol (Lipositol)

3. **Phosphosphingosides**
   Alcohol present – Sphingosine (Sphingol)
   Examples:
   - Sphingomyelin

- Phosphatidyl choline (Lecithin)
  Animal Sources – liver, brain, nervous tissues, sperm, egg yolk
  Plant Sources – seeds, sprouts
- When aqueous solution of lecithins are shaken with H_2SO_4, choline is split off, forming phosphatidic acid.
- When lecithins are boiled with alkalies or mineral acids, not only choline is split off, phosphatidic acid is further hydrolysed to glycerophosphoric acid and two molecules of fatty acids.
- **Plasmalogens** make up about 10% of total phospholipids of brain and nervous tissue, muscle and mitochondria
- **Sphingosine** molecule in which a fatty acyl group is substituted on the –NH2 group is called ceramide and when a phosphate group is attached to ceramide, it is called ceramide phosphate. When choline is split off from sphingomyelin, ceramide phosphate is left.
- **Niemann-Pick Disease** is an autosomal recessive lipid-storage disease in which large accumulations of sphingomyelins may occur in brain, liver and spleen due to deficiency of enzyme sphingomyelinase.
- **Cardiolipin** found in mitochondria (inner membrane) and bacterial wall.
  Chemically, it is diphosphatidyl glycerol. This is the only phosphoglyceride that possess antigenic properties.
- **Dipalmityl lecithin (DPL)** acts as a surfactant and lowers the surface tension in lung alveoli.
  If DPL is absent, the alveolar radius becomes smaller with expirations, the wall tension rises and the alveoli collapse. Absence of DPL, in premature foetus, produces collapse of lung alveoli, which produces respiratory distress syndrome (hyaline-membrane disease).
- **Lecithin-Sphingomyelin Ratio (L/S Ratio):**
  L/S Ratio in amniotic fluid has been used for evaluation of fetal lung maturity.
- L/S Ratio prior to 34 weeks gestation = 1
  After this time, there is a marked increase in L/S ratio upto greater than 5 at term.
  L/S ratio of >2 or >5 indicate fetal lung maturity.
  L/S ratio approximately 1 or <1 indicate that the infant will probably develop respiratory distress or hyaline membrane disease.
- **Glycolipids**
  1. Cerebrosides (Glycosphingosides)
  2. Gangliosides
  3. Sulpholipids
- **Cerebrosides (Glycosphingosides)**
  - occur in large amounts in the white matter of brain and in myelin sheaths of nerve
  - they are not found in embryonic brain but develops as medullation progresses

- Cerebroside = Sugar (Galactose or Glucose) + Fatty acid + Alcohol (Sphingosine or Dihydrosphingosine)
- There is no glycerol, no phosphoric acid and no nitrogenous base
- Cerebrosides contain nitrogens through there is no nitrogenous base
- **Types of Cerebrosides (based on fatty acids)**
    1. Kerasin (contain Lignoceric acid)
    2. Cerebron/ Phrenosin (contain cerebronic acid)
    3. Nervon (contain Nervonic acid)
    4. Oxynervon (contain hydroxyl derivative of nervonic acid)

- **Gaucher's Disease**
    - An autosomal recessive disorder of cerebrosides metabolism (lipidosis) due to deficiency of a lysosomal enzyme (β-Glucocerebrosidase)
    - Normally this enzyme hydrolyses glucocerebrosides to form ceramide and glucose.
      In absence of the enzyme, the cerebrosides cannot be degraded in the body, as a result large amounts of glucocerebrosides, usually kerasin accumulate in RE viz. liver, spleen, bone marrow and also brain.
    - Biochemically, there is characteristically elevation in serum acid phosphatase level.
- **Gangliosides**
    - Gangliosides are most complex of glycosphingolipids.
    - Isolated from ganglion cells, neuronal bodies and dendrites, spleen and RBC stroma.
    - The highest concentrations are found in gray matter of brain
    - Ganglioside = Fatty acid + Alcohol sphingosine + Carbohydrate
    - The carbohydrate moiety usually contains:
        - Glucose or Galactose
        - One molecule of N-acetyl galactosamine, and
        - At least one molecule of N-acetyl neuraminic acid (NANA) – also called sialic acid
    - Over 30 types of gangliosides have been isolated from brain tissue.
    - Four important types of gangliosides are: GM-1, GM-2, GM-3, GD-4
    - GM-3 is simplest and common ganglioside found in tissues.
      GM-3 = Ceramide + Glucose + Galactose + Neuraminic acid (NeuAc)
    - GM-1 is a more complex ganglioside derived from GM-3 and is now known to be the receptor in human intestine for cholera toxin.
    - Gangliosides are mainly components of membranes.
      Water soluble (hydrophilic) portions – sugar units and sialic acid
      Lipid soluble (hydrophilic) portions – ceramide
      Hydrophobic portions embedded in membrane lipids.
      Hydrophilic portions protrudes externally towards the medium.
      The gangliosides, therefore, can serve as specific membrane binding sites (receptor sites) for circulating hormones and thereby influence various biochemical processes in the cell.
- Tay Sach's Disease (GM-2 Gangliosidosis)

- An autosomal recessive disease in which accumulation of gangliosides in brain and nervous tissue takes place due to deficiency of enzyme hexosaminidase A.
- This rare inherited disorder is associated with progressive development of idiocy and blindness in infants soon after birth. This is due to widespread injury to ganglion cells in brain (cerebral cortex) and retina
- There may be seizures and association of microcephaly. Prognosis is bad, usually death follows.

- **GM-1 Gangliosidosis**
  - Accumulation of GM-1 gangliosides, glycoproteins and mucopolysaccharide karatan sulphate due to deficiency of enzyme β-galactosidase.
- **Sulpholipids**
  - Found in liver, kidney, testes, brains and certain tumors
  - Most abundant in white matter of brain
- **Amphipathic lipids**
  - Hydrophilic or polar parts – fatty acids, phospholipids, bile salts, to a lesser extent cholesterol
  - Amphipathic lipids get oriented at oil-water interfaces with the polar groups in the water phase and non-polar groups in the oil phase.
  - **Micelles**: When critical concentrations of these amphipathic lipids is present in aqueous medium, they form micelles. Micelles formation, facilitated by bile salts, is prerequisite of fat digestion and absorption from the intestine.
  - **Liposomes**: formed by sonicating an amphipathic lipid in aqueous medium
    - they consist of spheres of lipid bilayers that enclose part of aqueous medium
    - liposomes when combined with tissue-specific antibodies, as carriers of drugs in circulation, targeted to specific organs e.g. in cancer therapy
    - Liposomes used for gene transfer into vascular cells
- **Emulsions**
  - They are larger in size formed usually when non-polar lipids (e.g. triglycerides) are mixed with water.
  - They are stabilized by emulsifying agents such as amphipathic lipids (e.g. phosphatidyl choline) which form a surface layer separating the main bulk of non-polar material from the water.

Disease	Enzyme deficiency
1. Niemann-Pick Disease	Sphingomyelinase
2. Gaucher's disease	β-glucosidase
3. Tay-Sach's Disease	Hexosaminidase B
4. Metachromatic Leukodystrophy	Arylsulphatase A
5. Fabry's Disease	α-Galactosidase
6. Krabbe's Disease	β-Galactosidase