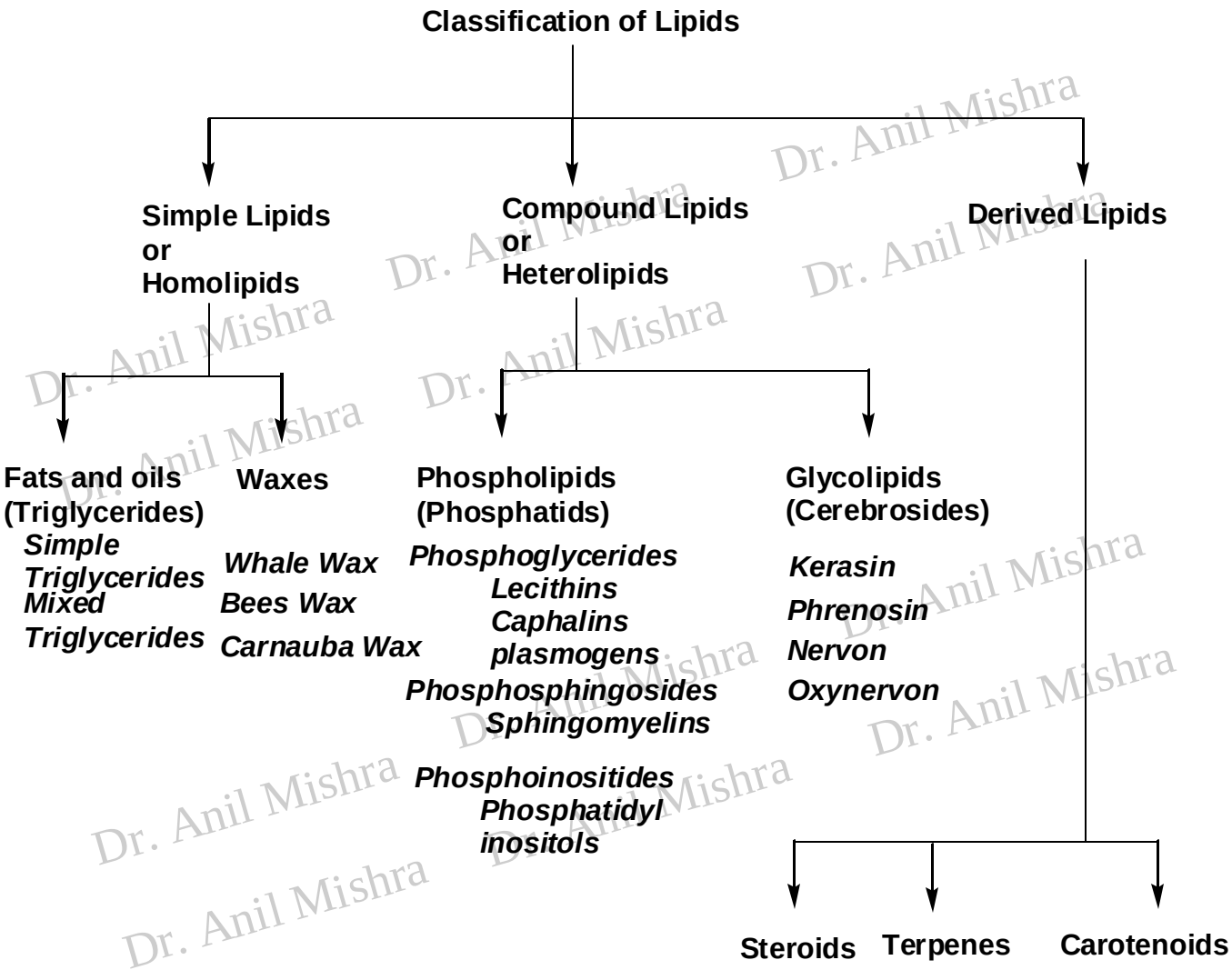
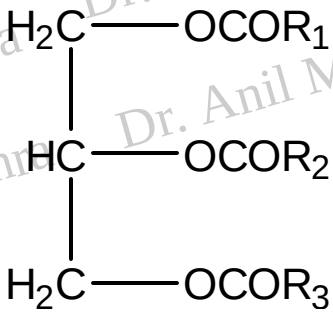


## Triglycerides

- **Triglycerides** are glycerides in which the glycerol is esterified with three fatty acids. They are the main constituents of vegetable oil and animal fats.
- General structure is




Where $R_1$, $R_2$, and $R_3$ are **fatty acids**; the three fatty acids can be all different, all the same, or only two the same.

$R_1 = R_2 = R_3 = C_{17}H_{35}$ Tristearin (*tristearoylglycerol*)

$R_1 = R_2 = R_3 = C_{17}H_{33}$ Triolein (*trioelylglycerol*)

$R_1 = R_3 = C_{17}H_{33}$, $R_2 = C_{15}H_{31}$ Oleopalmitin (*a-oleo-b,a'-dipalmitin*)

$R_1 = C_{17}H_{33}$, $R_2 = C_{15}H_{31}$, $R_3 = C_{17}H_{35}$ Oleopalmitostearin (*a-oleo-b,-dipalmitin-a'-stearin*)

- Chain lengths of the fatty acids in triglycerides can be from 4 to 22 C atoms, but 16 and 18 are most common.

## Metabolism

- Triglycerides play an important role in metabolism as energy sources.
- They contain twice as much energy (8000 Kcal/kg) as carbohydrates.
- In the intestine, triglycerides are split into glycerol and fatty acids (with the help of lipases and bile secretions), which can then move into blood vessels.
- The triglycerides are rebuilt in the blood from their fragments and become constituents of lipoproteins.
- Various tissues can release the free fatty acids and take them up as a source of energy. Fat cells can synthesize and store triglycerides.
- When the body requires fatty acids as an energy source, the hormone glucagon signals the breakdown of the triglycerides by hormone-sensitive lipase to release free fatty acids.

## Role in disease

- In the human body, high levels of triglycerides in the bloodstream have been linked to atherosclerosis, and, by extension, to the risk of heart disease and stroke.
- The negative impact of raised levels of triglycerides is lower than that of LDL-cholesterol.
- The risk can be partly accounted for a strong inverse relationship between triglyceride level and HDL-cholesterol level.
- Other diseases caused by high triglycerides include pancreatitis

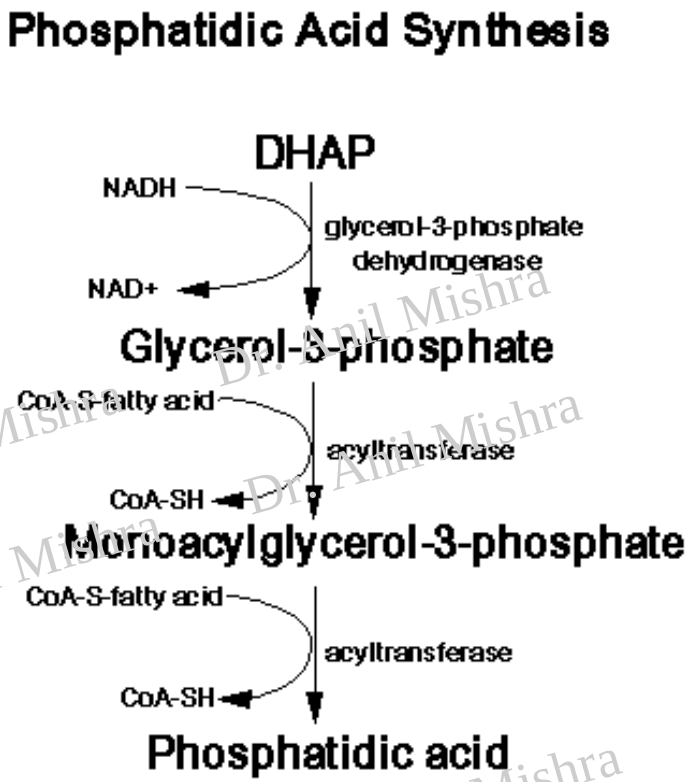
## Guidelines

The American Heart Association has set guidelines for triglyceride levels:

| **Level mg/dl** | **Level mmol/L** | **Interpretation** |
|---|---|---|
| <150 | <1.69 | Normal range, lowest risk |
| 150-199 | 1.70-2.25 | Borderline high |
| 200-499 | 2.25-5.63 | High |
| >500 | >5.65 | Very high, increased risk |

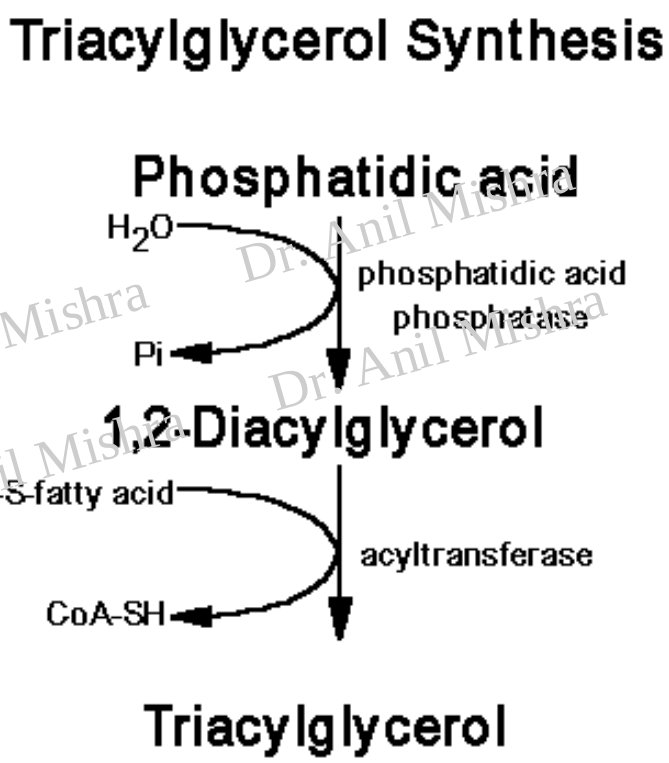
## Biosynthesis of Triglycerides

- Fatty acids are stored for future use as triacylglycerols in all cells, but primarily in adipocytes of adipose tissue. Triacylglycerols constitute molecules of glycerol to which three fatty acids have been esterified. The fatty acids present in triacylglycerols are predominantly saturated.
- The major building block for the synthesis of triacylglycerols, in tissues other than adipose tissue, is glycerol.
- Adipocytes lack glycerol kinase, therefore, **dihydroxyacetone phosphate (DHAP),** produced during glycolysis, is the precursor for triacylglycerol synthesis in adipose tissue.




- This means that adipoctes must have glucose to oxidize in order to store fatty acids in the form of triacylglycerols. DHAP can also serve as a backbone precursor for triacylglycerol synthesis in tissues other than adipose, but does so to a much lesser extent than glycerol.

- The glycerol backbone of triacylglycerols is activated by phosphorylation at the C-3 position by glycerol kinase.
- The utilization of DHAP for the backbone is carried out through the action of glycerol-3-phosphate dehydrogenase, a reaction that requires NADH.
- The fatty acids incorporated into triacylglycerols are activated to acyl-CoAs through the action of acyl-CoA synthetases.
- Two molecules of acyl-CoA are esterified to glycerol-3-phosphate to yield 1,2-diacylglycerol phosphate (commonly identified as phosphatidic acid).



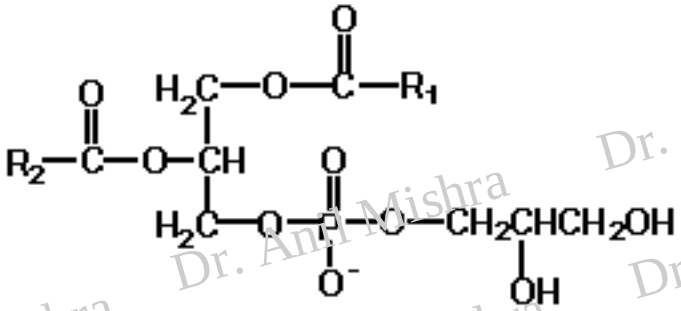

- The phosphate is then removed, by phosphatidic acid phosphatase, to yield 1,2-diacylglycerol, the substrate for addition of the third fatty acid. Intestinal monoacylglycerols, derived from the hydrolysis of dietary fats, can also serve as substrates for the synthesis of 1,2-diacylglycerols.

## PHOSPHOLIPIDS

- Phospholipids are comprised of two fatty acids and a phosphorus containing region joined by ester linkages to a glycerol backbone.
- Since phosphate groups can ionize, phospholipids have both a polar (charged) region and a nonpolar (uncharged) region. Hence, when phospholipids are used to construct membranes in cells, the fatty acids are directed toward the core of the membrane whereas the polar phosphate containing group is directed away from the core.
- These are most abundant in the membrane lipids.
- Differ from triglycerides in posessing usually one hydrophillic polar head group and usually two hydrophobic nonpolar tails.
- There are three types of phospholipids
  - Phosphoglycerides
  - Phosphoinositides
  - Phosphosphingosides

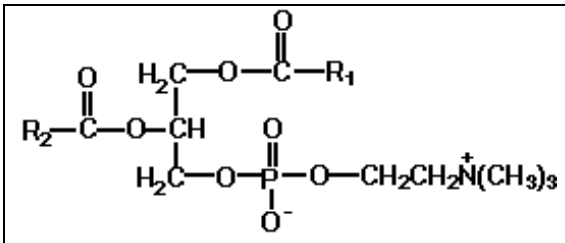
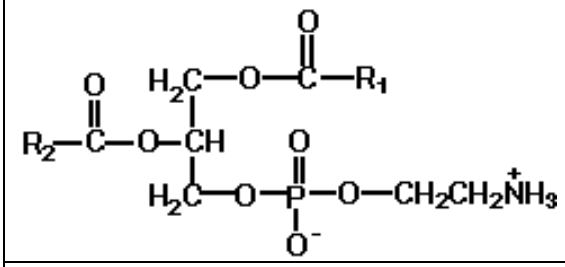
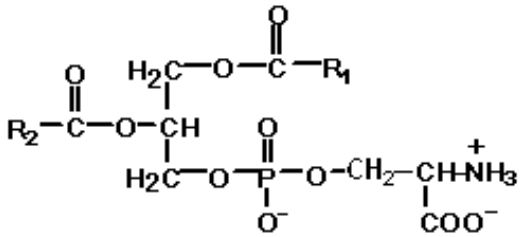
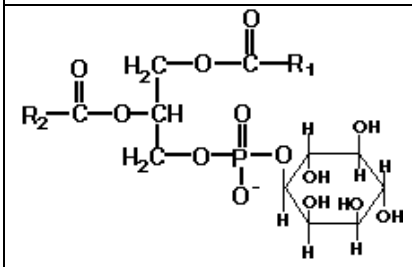
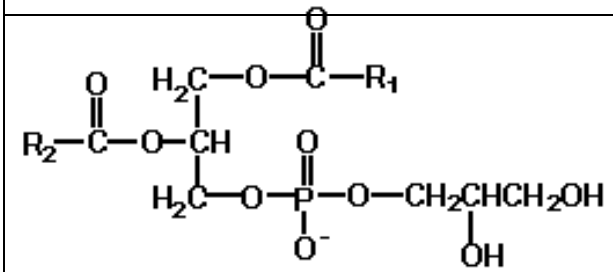
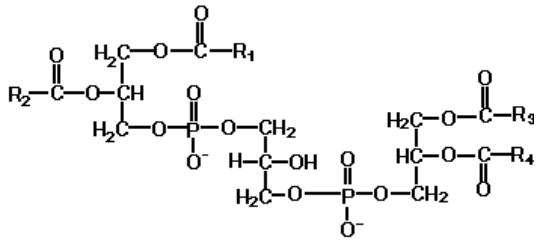
## PHOSPHOGLYCERIDES

- These contain two fatty acid molecules esterified to the first and second hydroxyl group of glycerol. The third hydroxyl group of glycerol forms an ester linkage with phosphoric acid.



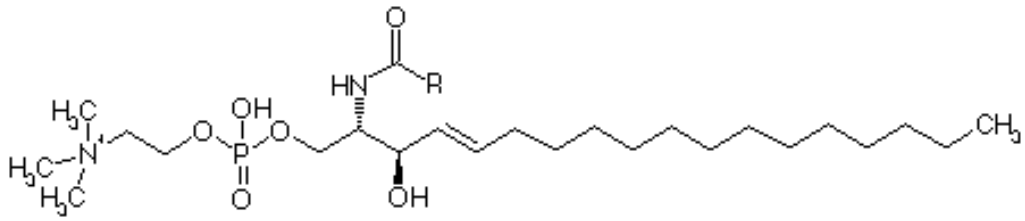
**Phosphatidylglycerol (PG)**

- These also contain a second alcohol, which is esterified to the phosphoric acid (refered to as ***head alcohol group***) and is present at one end of the long phosphoglyceride molecule.
- Various phosphoglycerides differ in their head alcohol group.
- They contain two non polar tails, each containing long chain fatty acids, usually one saturated and one unsaturated. The latter being attached to the middle hydroxyl group.
- All phosphoglycerides have negative charge on the phosphoric group at *p*H 7 and have the L configuration.

| | |
|---|---|
|  | **Phosphatidylcholine (PC)**<br>***(Lecithins)***<br>**a-Lecithin**<br>Phosphoglyceride |
|  | **Phosphatidylethanolamine (PE)**<br>***(Cephalins)*** |
|  | **Phosphatidylserine (PS)**<br>***(Cephalins)*** |
|  | **Phosphatidylinositol (PI)** |
|  | **Phosphatidylglycerol (PG)** |
|  | **Diphosphatidylglycerol (DPG)** |

## PHOSPHOSPHINGOSIDES

- The sphingolipids, like the phospholipids, are composed of a polar head group and two nonpolar tails. The core of sphingolipids is the long-chain amino alcohol, sphingosine. Amino acylation, with a long chain fatty acid, at carbon 2 of sphingosine yields a ceramide.
- The sphingolipids include the
  - **Sphingomyelins**
    Sphingomyelins are sphingolipids that are also phospholipids. These are important structural lipid components of nerve cell membranes. The predominant sphingomyelins contain palmitic or stearic acid N-acylated at carbon 2 of sphingosine.

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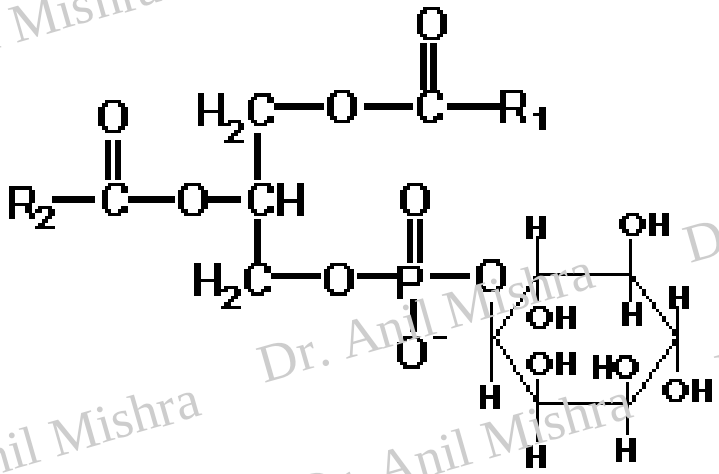
  - **Glycosphingolipids**
    Glycosphingolipids, or glycolipids, are composed of a ceramide backbone with a wide variety of carbohydrate groups (mono- or oligosaccharides) attached to carbon 1 of sphingosine. The four principal classes of glycosphingolipids are the
    - Cerebrosides
    - Sulfatides
    - Globosides
    - Gangliosides

- **CEREBROSIDES** ***have a single sugar group linked to ceramide***. The most common of these is galactose (galactocerebrosides), with a minor level of glucose (glucocerebrosides). Galactocerebrosides are synthesized from ceramide and UDP-galactose. Excess accumulation of glucocerebrosides is observed in **Gaucher's disease**.
- **SULFATIDES** ***The sulfuric acid esters of galactocerebrosides*** are the sulfatides. Sulfatides are synthesized from galactocerebrosides and activated sulfate, 3'-phosphoadenosine 5'-phosphosulfate (PAPS). Excess accumulation of sulfatides is observed in **Sulfatide lipidosis** (metachromatic leukodystrophy).
- **GLOBOSIDES** ***Globosides represent cerebrosides that contain additional carbohydrates***, predominantly galactose, glucose or GalNAc. Lactosyl ceramide is a globoside found in erythrocyte plasma membranes. Globotriaosylceramide (also called ceramide trihexoside) contains glucose and two moles of galactose and accumulates, primarily in the kidneys, of patients suffering from **Fabry's disease**.
- **GANGLIOSIDES** ***Gangliosides are very similar to globosides except that they also contain N-acetyl nuraminic acid (NANA) in varying amounts***. The specific names for gangliosides are a key to their structure. The letter G refers to ganglioside, and the subscripts M, D, T and Q indicate that the molecule contains mono-, di-, tri and quatra(tetra)-sialic acid. The numerical subscripts 1, 2 and 3 refer to the carbohydrate sequence that is attached to ceramide; 1 stands for GalGalNAcGalGlc-ceramide, 2 for GalNAcGalGlc-ceramide and 3 for GalGlc-ceramide

## PHOSPHOINOSITIDES

- These are phospholipids where a cyclic hexahydroxy alcohol called inositol replaces the base.
- These are found in the phospholipids of the brain tissues.
- They play an important role in the transport processes of the cell.
- Upon hydrolysis, phosphoinositides yield 1 mole of glycerol, two moles of fatty acid, one mole of inositol and 1, 2 or 3 moles of phosphoric acid, accordingly mono, di or tri phosphoinositides are found.



| **Disorder** | **Enzyme Deficiency** | **Accumulating Substance** | **Symptoms** |
|---|---|---|---|
| Tay-Sachs Disease | Hexosaminidase A (HEXA) | $G_{M2}$ ganglioside | rapidly progressing mental retardation, blindness, early mortality |
| Sandhoff-Jatzkewitz disease | Hexosaminidase B (HEXB) | Globoside, $G_{M2}$ ganglioside | same symptoms as Tay-Sachs, progresses more rapidly |
| Tay-Sachs Ab variant | $G_{M2}$ activator (GM2A) | $G_{M2}$ ganglioside | same symptoms as Tay-Sachs |
| Gaucher's Disease | Glucocerebrosidase | Gluco cerebroside | hepatosplenomegaly, mental retardation in infantile form, long bone degeneration |
| Fabry's Disease | $\alpha$-Galactosidase A | Globotriaosylceramide; ceramide trihexoside CTH) | kidney failure, skin rashes |
| Niemann-Pick disease, | Sphingomyelinase | Sphingomyelin LDL-derived cholesterol | mental retardation, hepatosplenomegaly, early fatality potential |
| Krabbe's Disease: Globoid Leukodystrophy | Galacto cerebrosidase | Galacto cerebroside | mental retardation, myelin deficiency |
| $G_{M1}$ Gangliosidosis | $G_{M1}$ ganglioside: $\beta$ -galactosidase | $G_{M1}$ ganglioside | mental retardation, skeletal abnormalities, hepatomegaly |
| Sulfatide Lipodosis; Metachromatic leukodystrophy | Arylsulfatase A | Sulfatide | mental retardation, metachromasia of nerves |
| Fucosidosis | $\alpha$-L-Fucosidase | Pentahexo sylfucoglycolipid | cerebral degeneration, thickened skin, muscle spasticity |
| Farber's Lipogranulo matosis | Acid ceramidase | Ceramide | hepatosplenomegaly, painful swollen joints |

- Lipids are heterogeneous group of compounds related to fatty acids, fats, oils, waxes and other related substances.

- Nearly all of the energy needed by the human body is provided by the oxidation of carbohydrates and lipids. Carbohydrates provide a readily available source of energy, lipids function primarily as an energy reserve.

- Lipids as compared with carbohydrates, are much more reduced (i.e., there are many more C-H bonds and far fewer C-OH or C=O bonds).

- Because of this greater degree of reduction, lipids store more energy per gram than do carbohydrates (nine vs. four, respectively).

- Lipids or fats are stored in cells throughout the body principle in special kinds of connective tissue called adipose tissue or depot fat. Many cells contain phospholipids in the bilayer cell membranes, adipose tissue cells consist of fat globules of triglycerides which may occupy as much as 90% of the cell volume.

- Lipids ingested as food are digested in the small intestine where bile salts are used to emulsify them and pancreatic lipase hydrolyzes them into fatty acids, glycerol, soaps, or mono- and diglycerides.

- Since lipids are not soluble in blood, they are transported as lipoproteins after reaction with water-soluble proteins in the blood.

- Lipids in the blood are absorbed by liver cells to provide energy for cellular functions. The liver is responsible for providing the proper concentrations of lipids in the blood. Some lipids are utilized by brain cells to synthesize brain and nerve tissue. Excess lipids in the blood are eventually converted into adipose tissue. If lipid levels in the blood become too low, the body synthesizes lipids from other foods, such as carbohydrates, or removes lipids from storage.

- **Acid Number:**
  - It is the number of milligrams of KOH required to neutralize the free fatty acid present in 1g of fat. The acid number thus tells us of the quantity of free fatty acid present in fat.

- **Saponification number:**
  - It is the number of milligrams of KOH required to saponify 1 g of fat. The saponification number thus provides information on the average chain length of the fatty acid in the fat. It varies inversely with the chain length of the fatty acid. The shorter the chain length of the fatty acid, the higher the saponification number.

- **Iodine Number:**
  - It is the number of grams of iodine absorbed by 100 g of the fat. The iodine number is thus a measure of the degree of unsaturation. However the iodine number does not give any indication about the number of double bonds present in the fatty acid molecule.

- **Polenske Number:**
  - It is the number if milliliters of 0.1N KOH required to neutralize the insoluble fatty acid obtained from 5 g of fat.

- **Reichert-Meissl Number**
  - It is the number if milliliters of 0.1N KOH required to neutralize the soluble, volatile fatty acid obtained from 5 g of fat.

- **Acetyl Number**
  - It is the number of milligrams of KOH required to neutralize the acetic acid obtained by the saponification of 1g of fat after it has been acetylated. This is therefore the measure of number of hydroxyl groups in the fat.