

Triglycerides (TG) should actually be called triacylglycerols (TAG). TG or TAG are molecules with a glycerol (a carbohydrate) backbone to which are attached three acyl groups. They represent a concentrated source of metabolic energy contributing 9 kcal/gm. Phospholipids (PL) are also derived from glycerol. If glycerol is not used to synthesize TG or PL it enters gluconeogenesis or glycolysis pathways. It does that by being converted into glycerol-3-phosphate using an enzyme called glycerol kinase.

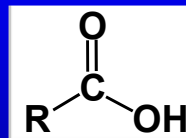
Acyl groups are derived from hydrolyzed fatty acids (which are carboxylic acids or -COOH). When an acyl group is attached to an -OH on a glycerol, the process is called esterification. Esterification of glycerol will produce TG or PL. Glycerol with one acyl group is a monoacylglycerol (MAG), those with 2 acyl groups a diacylglycerol (DAG) and of course those with 3 a triacylglycerol or triglyceride molecule. There are very specific enzymes involved in each of the three esterification steps. The most well known is the enzyme that converts DAG to TAG and it is called diacyl-glycerol transferase (DGAT). Drugs that inhibit DGAT would reduce TG assembly (fibrates, niacin, N-3 fatty acids). Three FA acyl groups supply considerable energy and thus TG serve as an energy supplier for muscle or energy storage molecules in adipocytes. TGs consist of multiple different fatty acids, most with 16, 18 or 20 carbons. The most common saturated fats in TG are lauric and myristic acids (the tropical oils) and palmitic and stearic (from meats). These are also the most atherogenic FA.

Enzymes capable of de-esterifying glycerol esters (TAG, DAG) are called lipases. The most potent triglyceridases (a lipase that hydrolyzes TG) that humans have are lipoprotein lipase (LPL) primarily expressed in adipocyte and muscular vascular beds and hormone sensitive lipase (now called triglyceride lipase) expressed in adipocytes. The lipases ultimately convert TG or TAG to FA and MAG. This de-esterification of the molecule is required as TG as a whole molecule cannot be absorbed into the enterocyte cell membranes or those of other cells throughout the body: of course FA can pass through membranes using fatty acid binding proteins. TG present in food are hydrolyzed almost immediately by salivary, gastric and ultimately pancreatic lipases. In the plasma LPL hydrolyzes the TG carried in the TG-rich lipoproteins (chylomicra and VLDLs). Please refer to the figure below showing TG structure. Each of the carbons in the glycerol molecule are numbered using the "stereospecific numbering (sn) system." Thus one FA acyl group is attached to the -sn1 position, the second (middle carbon) to the -sn2 position and the third to the -sn3 position. Believe it or not the positioning of the acyl groups to the various sn positions has great biologic importance but that is beyond this discussion. Providers are not taught to consider which FA acyl groups are in a given patient's TG. Do your TG carry 3 saturated fats (hope not), monounsaturated?, polyunsaturated? N-3FA? or combinations of all. As one might imagine there are thus multiple types of possible TG molecules. A TAG mixture with just five different fatty acids can therefore exist as 105 different TAG molecular species (TAG-MS) according to differences in positional composition. What would you call a TG that consists of a saturated fat (say palmitic acid: an 16 carbon fat with no double bonds), a monounsaturated fat (say oleic acid: an 18 carbon fat with one double bond at the n9 position) and a polyunsaturated fat (say linolenic acid: an 18 carbon fat with three double bonds, the first of which is at the 3 position)? That mouthful would be: 1-palmitoyl 2-oleoyl 3-linolenoylglycerol or in short-hand POL (where P is palmitic acid, O is oleic acid and L is linolenic acid). (Nutrition Research Reviews 2009;22:3-17).

Conventionally when describing at which carbon the first double bond exists we count backwards from the terminal methyl group (end) of the FA acyl chain - so if the first double bond is at the third carbon from the end it is called an omega-3 FA (omega being the last letter in the Greek alphabet) or as is now more correct an n3 FA . Omega-3 does not mean the FA has three double bonds (although it might - it means the first double bond is at the 3rd carbon). Oleic acid has its first double bond at the 9th carbon and is an omega-9 or N9 FA. Linoleic acid (not to be confused with the n3 FA linolenic acid mentioned above) is an omega-6 or n6 FA.

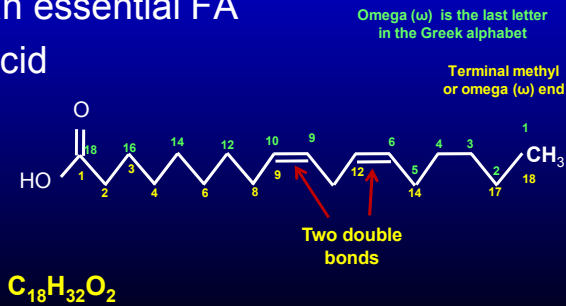
Fatty Acids

- ★ Fatty acids are **carboxylic acids** with mostly long hydrocarbon unbranched aliphatic (non-aromatic) chains ranging from 4 to 36 carbons.
 - ★ Carboxylic acids are organic acids characterized by the presence of a carboxyl group, which has the formula $C(=O)OH$, usually written $-COOH$ or $-CO_2H$.
 - ★ The chain can be **saturated** meaning a saturated compound has no double or triple bonds. In saturated linear hydrocarbons, every carbon atom is attached to two hydrogen atoms, except those at the ends of the chain, which bear three hydrogen atoms.
 - ★ The chain can be **unsaturated** meaning a carbon structure contains double or occasionally triple bonds. Many vegetable oils contain fatty acids with one (*monounsaturated*) or more (*polyunsaturated*) double bonds in them.



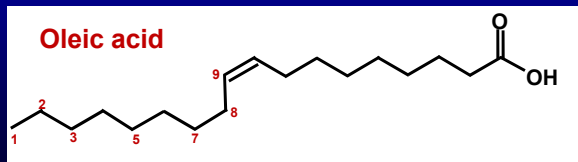
Fatty Acid Nomenclature

- ◆ **Flax Seed Oil** (Greek word for flax is linon)
- ◆ An unsaturated (polyunsaturated) omega-6 FA
 - Is a carboxylic acid with 18 carbons and two cis double bonds, with the first double bond at the 6th carbon from the methyl (omega) end.
 - Linoleic Acid : an essential FA
 - Octadecanoic acid
 - cis,cis Δ^9, Δ^{12}
 - 18:2
 - 18:2 n-6



Fatty Acid Characteristics

- ◆ **Monounsaturated fatty acids:** Examples
 - Palmitoleic acid(16:1 n-7) which has 16 carbon atoms with the first double bond occurring 7 carbon atoms away from the methyl group (and 9 carbons from the carboxyl end).
 - cis-Vaccenic acid (18:1 n-7)
 - **Oleic acid** (18:1 n-9) has 18 carbon atoms with the first double bond occurring 9 carbon atoms away from the methyl group.



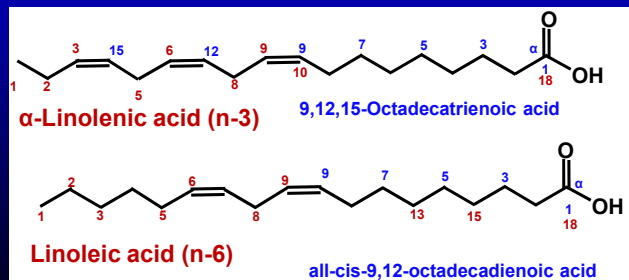
Fatty Acid Characteristics

✦ Polyunsaturated fatty acids (PUFA): examples

- Methylene-Interrupted Polyenes: These fatty acids have 2 or more double bonds that are separated from each other by a single methylene group (a carbon atom is bonded to two hydrogen atoms).



- Examples are certain omega-3 (n-3) like alpha-Linolenic acid
- Or certain Omega-6 (n-6) like Linoleic acid



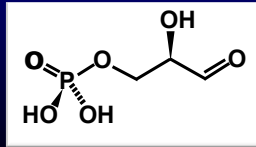
Glycerol

- ✦ **Glycerol** is classified by the FDA among the sugar alcohols as a caloric macronutrient. Glycerol has three hydrophilic **hydroxyl** groups that are responsible for its solubility in water and its hygroscopic nature.
- ✦ The glycerol substructure is a central component of many lipids including TG and phospholipids.
 - Glycerol is currently categorized by the American Dietetic Association as a carbohydrate.



Glycerol

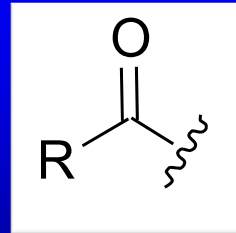
- ♦ Glycerol is a precursor for **synthesis of triacylglycerols and of phospholipids** in the liver and adipose tissue.
- ♦ When the body uses stored fat as a source of energy, glycerol and fatty acids are released into the bloodstream. The glycerol component can be converted to glucose by the liver and provides energy for cellular metabolism.
- ♦ Before glycerol can enter the pathway of glycolysis or gluconeogenesis (depending on physiological conditions), it must be converted to their intermediate **glyceraldehyde 3-phosphate**



<http://en.wikipedia.org/wiki/Glycerol>

Acyl Groups

- ♦ An **acyl group** is a functional group derived by beta oxidation of FA or the removal of one or more hydroxyl groups from an oxoacid (an acid containing oxygen).
- ♦ The acyl group is usually derived from a carboxylic acid of the form $\text{RC}-\text{O}-\text{OH}$. It therefore has the formula $\text{RC}(=\text{O})-$, with a double bond between the carbon and oxygen atoms (i.e. a carbonyl group), and a single bond between R moiety and the carbon.
- ♦ Acyl groups can also be derived from other types of acids such as sulfonic acids and phosphonic acids.
- ♦ **Acyl CoAs are derivatives of fatty acid metabolism**, with acetyl CoA as an example.



<http://en.wikipedia.org/wiki/acyl>

The molecular formula of the depicted TG depicted below is $C_{55}H_{98}O_6$ and consists of a saturated at sn-1, monounsaturated at sn-2 and polyunsaturated fatty acid at sn-3. Its proper name is: 1-palmitoyl 2-oleoyl 3-linolenoylglycerol or in short-hand POL (where P is palmitic acid, O is oleic acid and L is linolenic acid).

