



carbohydrates
isomers
ketone
starch
lipid
protein
amine

Biochemistry

Doctor 2017 | Medicine | JU

● Sheet

○ Slides

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DOCTOR

Faisal

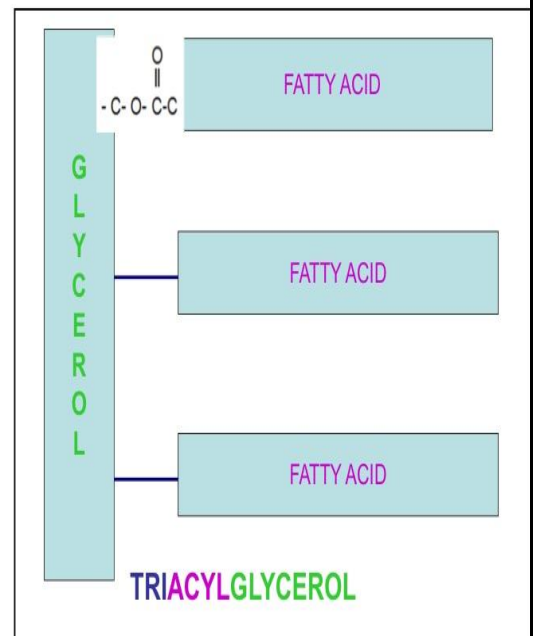
Fatty Acid and Triacylglycerol metabolism

Triacylglycerol

What are the components of triacylglycerol?

Triacylglycerol ; **Tri**= three, **Acyl**= when fatty acid connected to another structure it is called (Acyl), **Glycerol**= alcohol

Triacylglycerol is formed of glycerol (which is an alcohol with 3 carbons, each of them is connected with hydroxyl group) that connected to 3 fatty acids through 3 ester bounds.



Ester bound forms by joining the hydroxyl group of glycerol with carbonate carbon of fatty acid (its functional group). It can be easily hydrolyzed (broken down by adding water to it), in order to get back fatty acid and alcohol.

Fatty Acid

Fatty acid this is a long hydrocarbon chain (formed just from carbons and hydrogen atoms) with terminal carboxyl group (either -COO- or -COOH). The pka of fatty acid nearly = 4.8.

At physiological PH (approximately 7) that is higher than pKa, carboxyl group will not exist as (COOH), it will be in anionic form (the proton will be already lost) and this means that fatty acid in our body will be in ionized/salt form(COO-).

The carboxylic acid (**has a carboxyl group**) is a proton donor as any acid when it dissolves in water.

Because of the long chain structure of the fatty acid that composed of 16 or 18 or other big numbers of carbon atoms, we can write it in a short form like: $\text{CH}_3 (\text{CH}_2)_n \text{COO-}$, the (n) refers to number of carbons.

Due to this long chain we have to number the carbons in the chain, how we do number the carbons?

There are 2 ways:

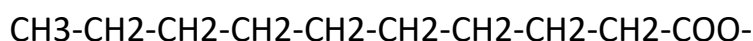
- 1- We start numbering the carbons from the carboxyl group so it is considered as (C1), then the following carbon C2 and the next one is C3 until we reach the end of that chain C16 or C20 and so on.

NOTE: Most of the time the chain has EVEN number of carbons, however there should be exceptions.

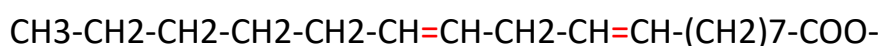
- 2- The other way is numbering the 1st Carbon after the carboxyl group (the 2nd C) carbon by **Alpha** carbon, the following carbon is **beta** (C3), then **gamma** (C4), until we reach the last one we named the last by **Omega**, regardless of the length of the chain.

The fatty acid chains may contain no double bounds (saturated), **OR** they may contain one or more double bounds, examples:

Saturated fatty acid (no double bounds):



Unsaturated (has 2 double bonds) fatty acid:



In the unsaturated fatty acid chain we should determine the location of the double bounds in the chain. The 1st double bounds in C9 and the 2nd double bounds in C12 (remember we should start counting from the carboxyl group). **This fatty acid Called linoleic acid**

Instead of that long chain we can write it in variety shorter forms with these double bounds position.

- **18: (9,12)** → (18) refers to the total number of carbons, (9) location of the 1st double bound, (12) location of the 2nd double bound.
- **18:2 Δ ^{9,12}** → (18) number of carbons, (2) number of double bounds, (9,12) the location of the double bounds.
- **Omega 6** → which means we start from carbon Omega (the last carbon) until we reach to the first double bounds which was C6 above. **NOTE: we don't pay attention to the other double bounds only the nearest one to the Omega carbon.** By using this way, it would help us the know the type of that acid either omega 3,6 etc..

In the following table, there are some fatty acids of physiological importance:

	COMMON NAME	STRUCTURE
	Formic acid	1
	Acetic acid	2:0
	Propionic acid	3:0
→	Butyric acid	4:0
	Capric acid	10:0
→	Palmitic acid	16:0
	Palmitoleic acid	16:1(9)
	Stearic acid	18:0
→	Oleic acid	18:1(9)
→	Linoleic acid	18:2(9,12)
	Linolenic acid	18:3(9,12,15)
→	Arachidonic acid	20:4(5, 8, 11,14)
	Lignoceric acid	24:0
	Nervonic acid	24:1(15)

NOTE: Formic acid, acetic acid and propionic acid are not considered fatty acids, they are grouped under the carboxylic acids.

- The shortest fatty acid is called **Butyric acid (4 carbons)** because it extracted from the butter.
- **Capric acid (10 carbons)** is fatty acid that isolated from goats milk (**NOTE: this is not for memorization**).
- **Palmitic acid (16 carbons), Palmitoleic acid (16 carbons)** are isolated from the palms tree oil.
- **stearic acid (18 carbons)** isolated from the wax (الشمع).
- **Oleic acid (18 carbons)** isolated from the olive oil.
- **Linoleic and linolenic (18 carbons- they are very similar to each other)** isolated from linen (الكتان).
- **Arachidonic acid (20 carbons)** isolated from peanut butter(فستق).

The table is for memorization, you have to know the common names with their structures very well. (The last 2 names are not for memorization as well).

FAT (or Triacylglycerol) is the major energy reserve in the body. It is more efficient to store energy in the form of Triacylglycerol (TAG) rather than in form of carbohydrates.

Why we store energy in the form of FAT not in Carbohydrates?

- 1- FAT is more reduced, it has higher level of reduction (less oxidized) and the percentage of Oxygen is less. For example 18 carbons atom have 2 Oxygen atoms

in FAT, however in carbohydrates 6 carbon atoms have 6 oxygen atoms. So, we obtain our energy by oxidation and FAT is more reduced so can be oxidize more and we get energy more from it.

If we burned 1 gram of FAT we get 9 kcal, whereas, if we burned 1 gram of carbohydrate we get 4 kcal. So we can store little amount of fat to get more energy.

- 2- FAT is hydrophobic (non-polar) can be stored without water, whereas carbohydrates are hydrophilic stored with water (each 1 gram of carbohydrates binds to 2 grams of water).

Some calculation to prove what was mentioned above:

1- Average adult has 10Kg of FAT, how many calories?

1 gram = 9 Kcal.

10 Kg = 10,000 g

$9 \times 10,000 = 90,000$ Kcal.

*this is a huge amount of energy that can provide the body with its need of energy for 1.5 month (because average person require 2000 Kcal per day)

2- What is the mass of carbohydrates that produces 90,000Kcal?

1 gram = 4 Kcal

$90,000 / 4 = 22,500$ g

We need to convert the (g) into (Kg):

$22,500 / 1000 = 22.5$ Kg

-How much water with it?

1 gram carbohydrates = 2 grams of water

$22,500 \times 2 = 45,000$ g of water

= 45 Kg of water

As you can see we can store 90,000 kcal in 10 Kg of FAT, however in carbohydrates we store 90,000 kcal in 22.5 Kg.

Fatty acids are used as continuous fuel for the body and major fuel for the tissues. It is also preferred fuel for the muscles (e.g. Cardiac muscles).Whereas; the glucose is the major fuel in the extracellular fluids.

Fuel type	Amount in fluids (Gram)	Amount used/ 12 hours gram
FA	0.5g	60g (540 Kcal)
Glucose	20g	70g (280 Kcal)

In the previous table, it shows each type of fuel that is in the plasma and they are used continuously (continuously turned over with in 12 h) to get certain amount of energy (Kcal) while they are used.

We can come out from this table that even though glucose is more available (20 g), the preferred fuel is FA (0.5 g).

***we can say that glucose is the main energy fuel in the blood, but fats are the major fuel used in the blood.**

So fatty acids in adipose tissue is not only stored and whenever we need it we used it, instead is dynamic tissue and used continuously used for the body.

Mobilization of stored fats

Mobilizations of the stored fats need hormonal signals. The fatty acids that are used in our body are stored in the adipose tissue (adipose cells). If you have a look on these cells, you will find out that nearly 85-90% of the cells are filled of TAG. TAG is not used by adipose tissue itself; however, they stored to be transported to other tissues (such as muscles) in our body.

- Hormonal signals → adipose tissue → TAG transported to other tissues need energy.

The 1st step in the utilization of the TAG is hydrolysis of TAG by (3 H₂O), so the ester bound is broken.

- TAG + 3 H₂O -----→ 3 FA + glycerol (the catalyze enzyme used is **LIPASE**)
Lipase: Hormone sensitive lipase. They are activated by hormones.

The hormones that activate the LIPASE enzyme to stimulate the hydrolysis of TAG:

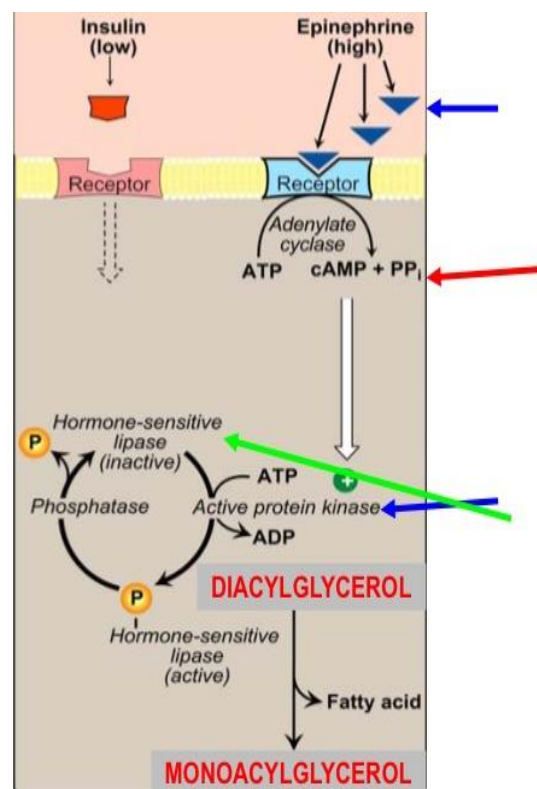
- Glucagon: it is secreted when the blood sugar level is low, so it secreted from the pancreas.
- Epinephrine & Norepinephrin: are secreted during stress(fight or flight).
- ACTH : stimulates adrenal-cortex gland.

Let's see how these are working

Will take the epinephrine as example:

- 1- High levels of epinephrine are presented in the cytoplasm .
- 2- The epinephrine binds to specific receptors on the cell membrane which stimulates the Adenylate cyclase, therefore it converts the ATP to the cyclic AMP (cAMP).
- 3- 2 phosphates are released as PP_i and the 1st phosphate form the cAMP. The cAMP has nothing to do except to tell the cell there are hormonal signals outside.
- 4- Then, cAMP diffuses and binds to the enzyme called Protein kinaseA. It converts it into active protein kinase A (Kinase: means an enzyme that transfer phosphate group from ATP to its substrate).
- 5- Then the active form of the protein kinase will add a phosphate group to the hormone sensitive lipase to make it in active form.
- 6- The active LIPASE is then catalysis to hydrolysis the TAG to Diacylglycerol then to monoacylglycerol.
- 7- Then the LIPASE hydrolysis the monoacylglycerol into glycerol and fatty acid.

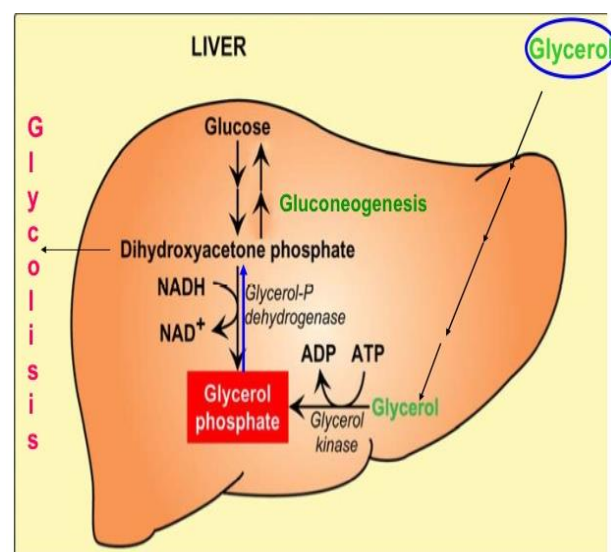
*fatty acid that are released bound to albumin because they are poorly soluble in water, whereas glycerol is soluble in water.



Fate of Glycerol

Glycerol released from the TAG is transported to the plasma (very small molecule) and taken up from the blood to the liver:

- 1-Glycerol is taken up from the blood to the liver and phosphorylated by hepatic glycerol kinase to produce **glycerol phosphate** by converting ATP to ADP by taking one phosphate.



2-Then, the glycerol phosphate is oxidized by Glycerol-P dehydrogenase and converting NAD^+ to NADH TO form **Dihydroxyacetone phosphate** (this structure is used in Glycolysis or in Gluconeogenesis).

What is more beneficial?

Gluconeogenesis is more preferred to go through, because in low blood glucose we need more glucose synthesis.

*ONLY GLYCEROL CAN BE CONVERTED TO GLUCOSE ,whereas fatty acid cannot do that(only 3 carbon out of 50/52/54...).

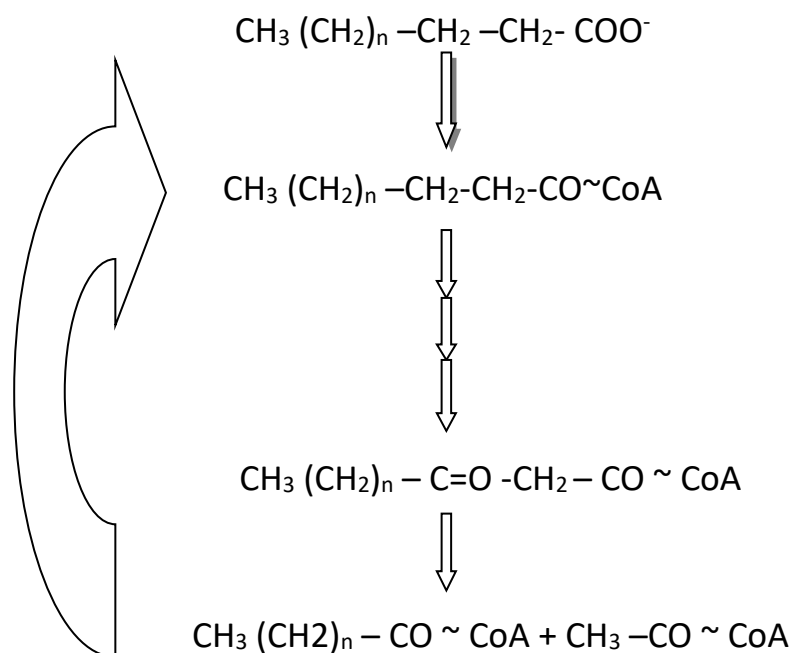
Beta Oxidation of Fatty Acids

This type of oxidation happens in carbon Beta (C_3) in fatty acid chain. The CH_2 is oxidized by loss there 2 Hydrogen atoms, then oxidized again by adding Oxygen atom.

- Degraded by oxidation at β carbon followed by cleavage of two carbon units.



Overview of the Beta Oxidation of Fatty Acids:



- 1- Firstly, the molecule CoA join with the fatty acid to get acylCoA then this compound get to the mitochondria.
- 2- The Carbon Beta went through 3 steps (has lost 2 hydrogen atoms and gained one oxygen) to be oxidized (the product is called β -keto/3-ketofatty acid) .
- 3- The following step is that compound is cleaved to get acetyl-CoA and Acyl-CoA. (Acetyl-CoA is Acyl- CoA, however Acyl-CoA is not necessary to be Acetyl-CoA. Acyl is the general term).
- 4- The end product (Acyl-CoA) will oxidized again and again until the fatty acid is completely degraded into acetyl-CoA.

The structure of CoA is not for memorization just to own information, BUT you have to know its components.

- The green structure (adenine +Ribose+ 2 Phosphate) is ADP
- The blue structure (pantothenic acid) is Vitamin.
- The purple structure (Beta-Mercapto ethylamine) is ethylamine.

