Chapter 21 :- part I

Lipid metabolism

you know that carbohydrate is the main source of energy, But when glucose depleted (ينفذ/يقل) we use (Lipids) as asource of energy

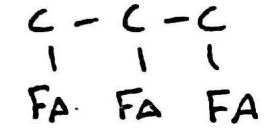
* Lipid consist of diffrent types of compound.

But Fatty Acids are the main type of Lipids used to take energy from

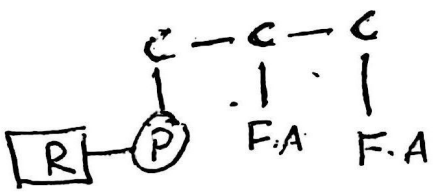
Steroid not asource of energy

Fatty acid could be part of

- TAG (Triacylglycerol)



- phospholipids



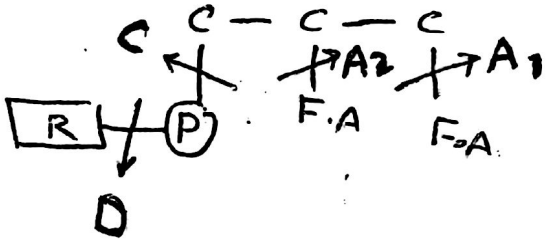
So in order to get Fatty acids out of these Compound we need.

* TAG ⟹ Lipase

* phospholipid ⟹ phospholipase

we have many types> A_1, A_2, C, D

according to the site of action

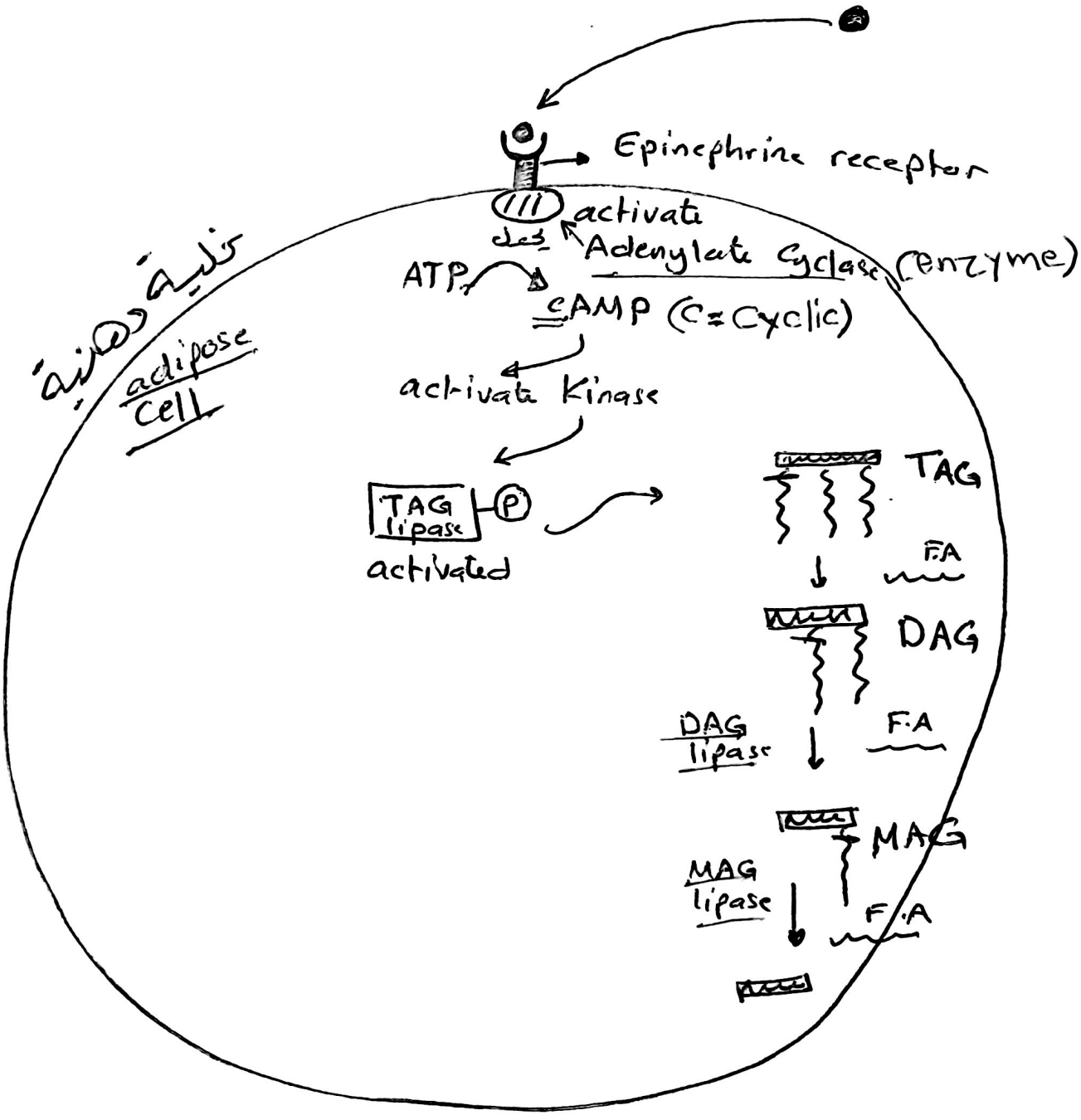


A_2 → most important in nature (widly distributed)

D → in spider Venom
snake Venom
} ⟹ tissue damage.

How we get Fatty acids from TAG?

↓ Glucose → Body release Epinephrine Hormon



Note :- Caffiene has the same effect of Epinephrine

Runners often drink Coffee before the race.

* Fatty acid catabolism :- (all reaction occure in mitochondrial matrix) Except activation step. (1st step).

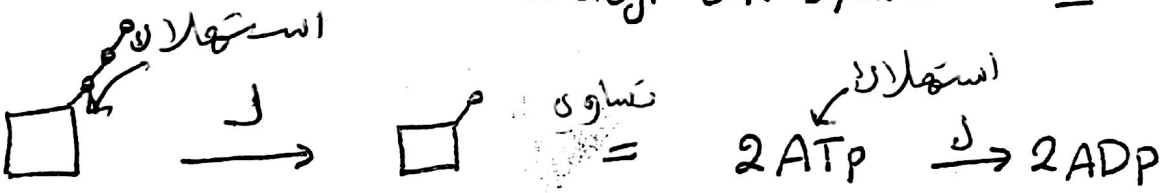
1) activation step in cytosol

Fatty acid + Co-A → acyl-CoA (→ thioester bond)

$-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-\overset{O}{\overset{\|}{C}}-CO-A$

ATP → AMP

« acyl-CoA synthetas » E



So this step need (2ATP)

there is intermediate « acyl-adenylate »

acyl-CoA :-

general name to any FA Bind with Co-A

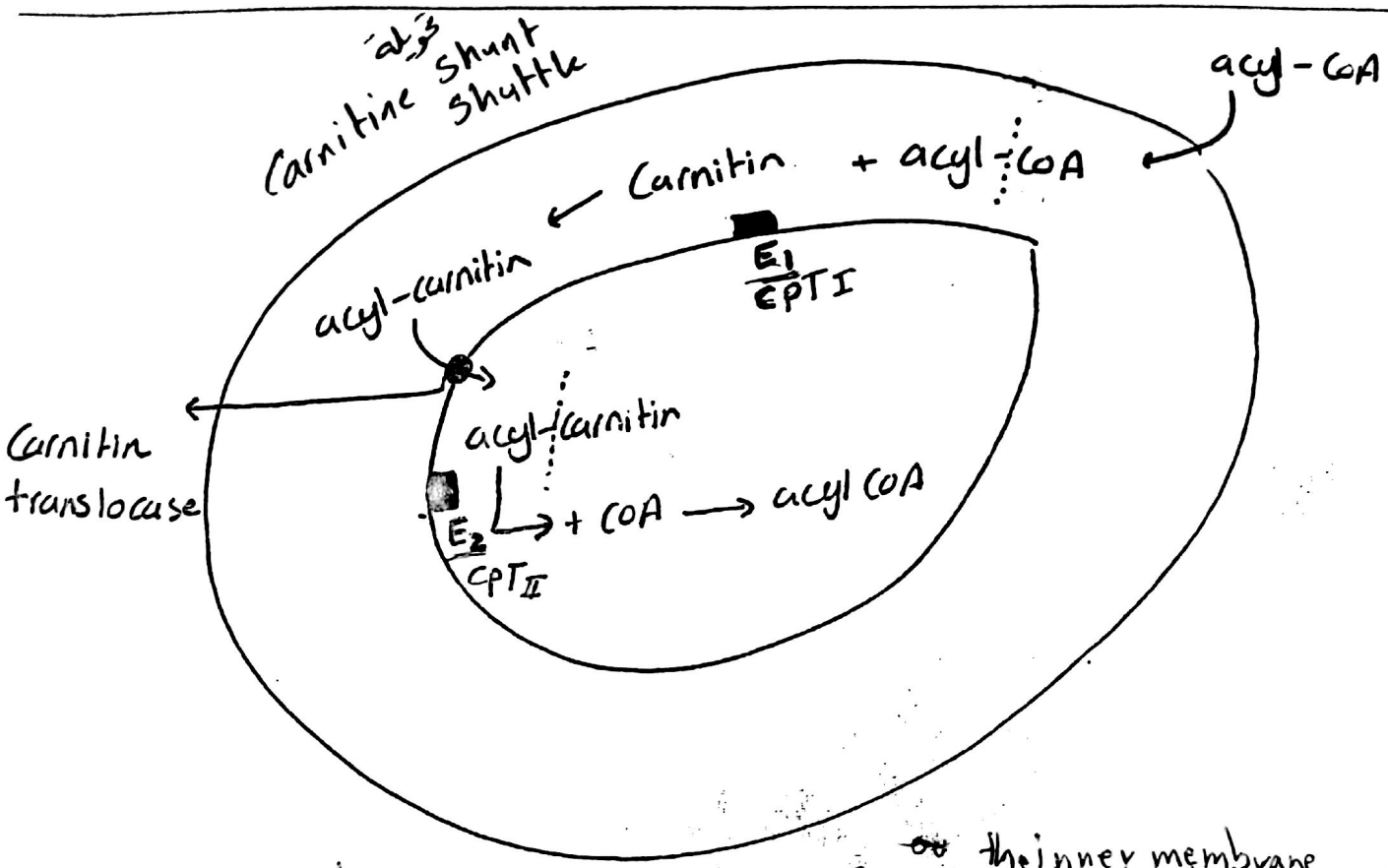
if the Fatty acid was palmitic (16C) then it is called palmityl-CoA,

if it is (2C) we call it acetyl-CoA

- the rest of steps of fatty acid catabolism, occure in mitochondria, so acyl-CoA should be transported to mitochondria.

- acyl CoA can pass through outer membran easily But cannot pass through inner membran.

So what happened ?!



E_1 = acyl to Carnitin ترنسفر
Carnitin acyl transferase I OR Carnitin palmityl transferase I (found in ~~the~~ inner membrane surface ~~outer membrane~~ outside)
(CPT I)

E_2 = acyl ل Carnitin تحول
Carnitin acyl transferase II OR Carnitine Palmityl transferase II (found in the inner membrane surface)
(CPT II)

Because this enzyme has specificity for acyl group Between (14 – 18)

E_1 and E_2 found in the inner membrane of mitochondria

in matrix (B-oxidation) of acyl-CoA

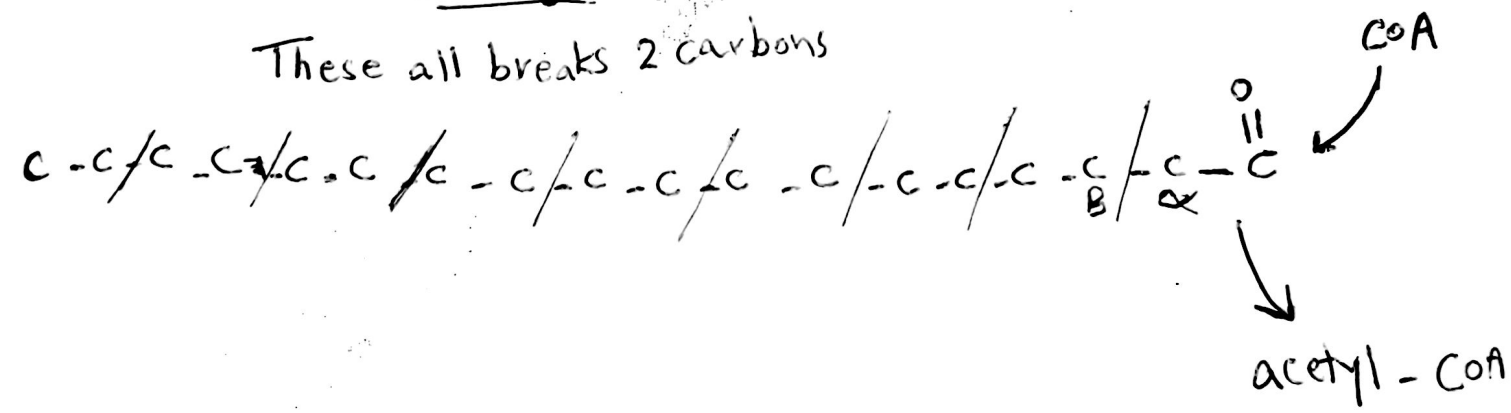
↳ repeated sequance of reactions

cleaves two carbon units from Fatty acids. starting from carboxyl group.

it is 4 step, each turn remove 2 carbon unit (acetyl-CoA) ⟹ citric acid cycle.

- oxidation $FAD \longrightarrow FADH_2 \times 1.5$
- Hydration (H_2O ساب اضافة)
- oxidation $NAD^+ \longrightarrow NADH \times 2.5$
- cleavage ✂

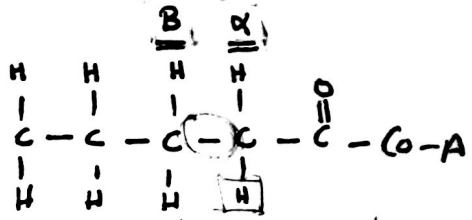
These all breaks 2 carbons



(β Oxidation)

e.g acyl-CoA with 18 C

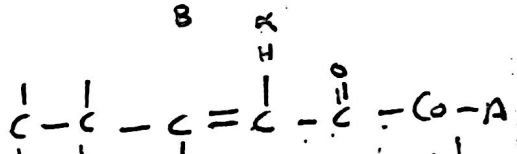
1) acyl CoA → (FAD → $FADH_2$) acyl CoA dehydrogenase



Double bond تنشأ بين α و β بعد إزالة H

Oxidation Step

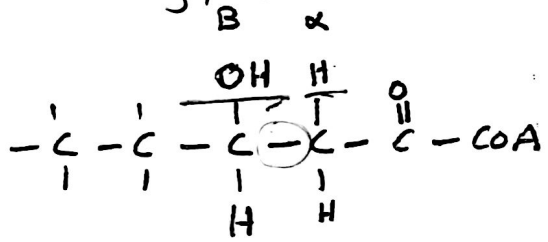
trans-enoyl-CoA → (H_2O +) enoyl CoA Hydratase



Double bond يكسر إضافة ماء وفيها إضافة H و OH

Hydration Step

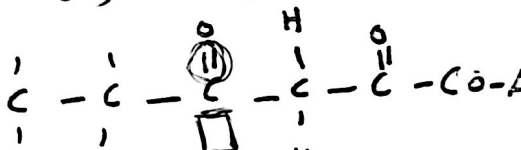
L-β-hydroxyacyl-CoA → (NAD^+ → NADH) L-β-hydroxyacyl CoA dehydrogenase.



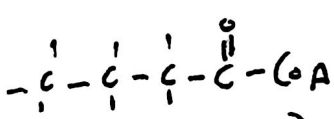
Oxidation Step

Double bond تنشأ بين α و β بعد إزالة HB

β-Keto acyl-CoA → (CoA + ✂) Thiolase

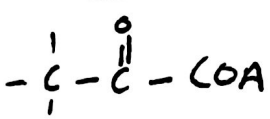


Cleavage Step



acyl-CoA + acyl CoA (16 C)

↳ repeat the cycle again.



↳ Citric acid cycle.

Now:-

if we start with acyl CoA (18c)

- How many acetyl CoA

$\frac{18}{2} = 9$ acetyl CoA

- How many turn in β-oxidation

$\frac{18}{2} - 1 = 8$ turn

* How many ATP produced from Catabolism of FA 18 C

β oxidation:
1 $FADH_2 \rightarrow 1.5$
1 $NADH_2 \rightarrow 2.5$
4

$8 \times 4 = 32$

citric cycle:
3 NADH $\rightarrow 7.5$
1 $FADH_2 \rightarrow 1.5$
1 GTP $\rightarrow 1$
10

$10 \times 9 = 90$

$90 + 32 = 122 - 2$ ATP (used in activation) $= 120$

which give more energy glucose OR Lipid.

1 glucose (6C) ⟹ 32

3 glucose (18C) ⟹ 96 ATP / FA (18C) ⟹ 120 ATP

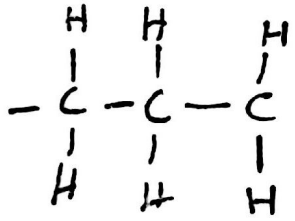
So FA give me more energy than glucose why?!

- you know that each oxidation step will give you NADH / $FADH_2$

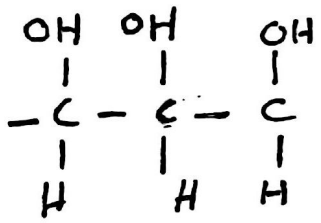
↑oxidation → ↑NADH/$FADH_2$ (ATP) ↑ATP

Fatty acid more reduced.

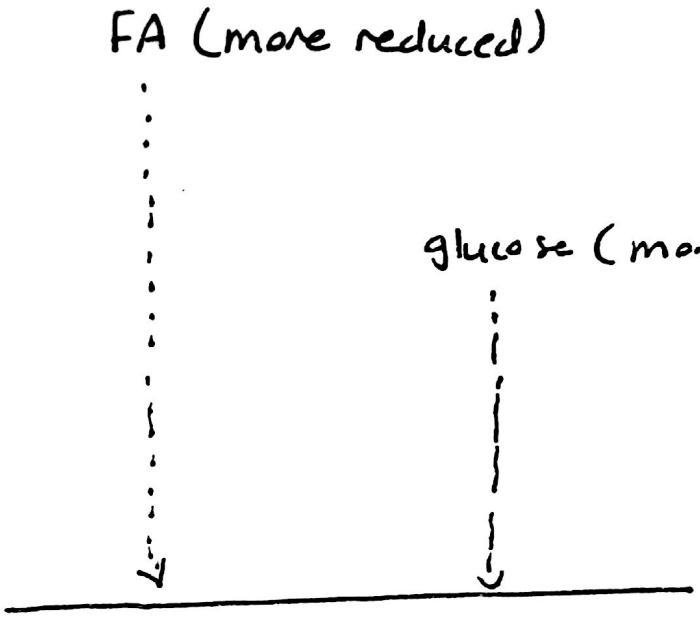
which mean it under go more oxidation steps, more NADH/ $FADH_2$, more ATP.



FA



gluclox



All $NADH/FADH_2$ produced from Fatty acid catabolism, will go to E.T.C, then to O_2

And Form H_2O (water)

This water called **metabolic water**

نكون هادين بسبب نقل الالكترون

يتحملوا العطش أكثر Camel

Kangoro rat

Both Lipid → catabolism → metabolic water.

you know By now, That B-oxidation occure in Mitochondria

But it also happened in perioxisome / glyoxysomes ← في النبات

« hypolipidemic drugs (الأدوية المخفضة) (to control obesity) work By ↑ B-oxidation in peroxisomes.

End of part I

How many ATP from acyl-CoA with 18c ?!

wish you all the best ☺

odd number FA: (أعداد الفردية)

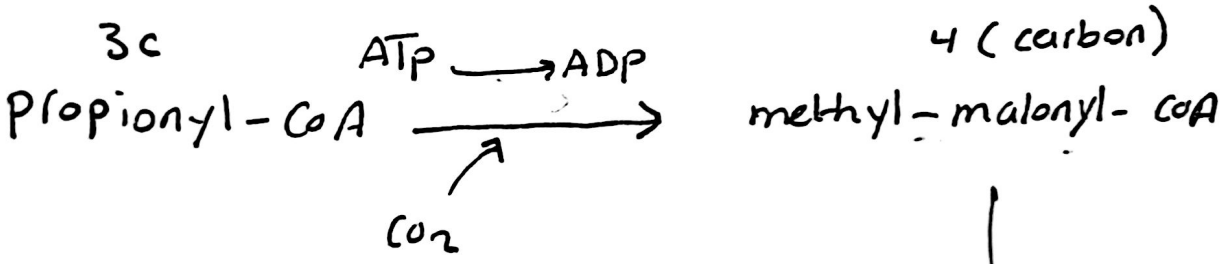
e.g 15 Carbon FA

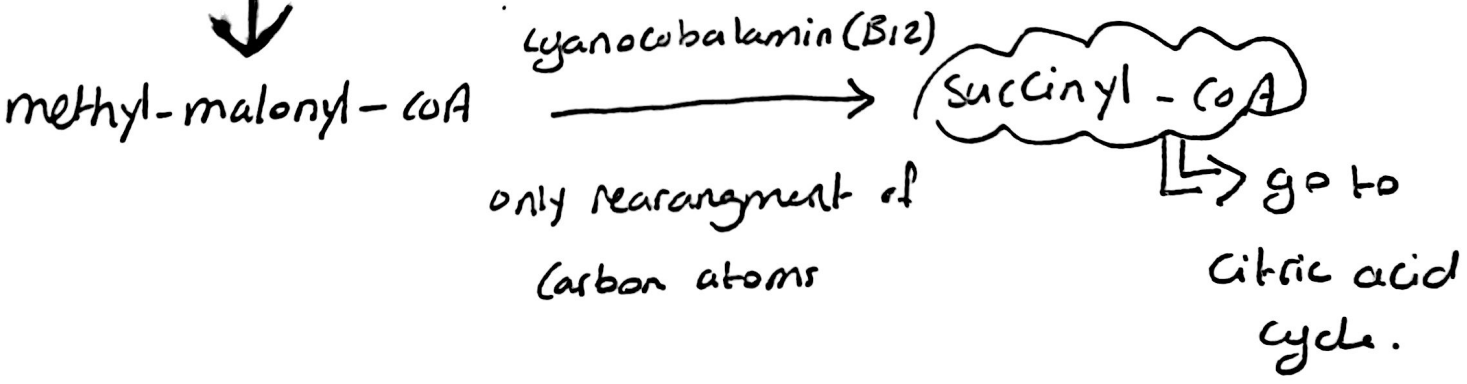
we enter B-oxidation, and succissivly remove 2 carbon unit each turn, till we reach 5 carbon unit

Then B-oxidation of this will give me

① acetyl CoA (2C) (من تكسير أون 12 كربون)

② propionyl-CoA (3C) (وتبقى آخر 3 كربونات)





15 carbon :- How many acetyl CoA

* $\frac{15-3}{2} = \frac{12}{2} = 6$ acyl CoA

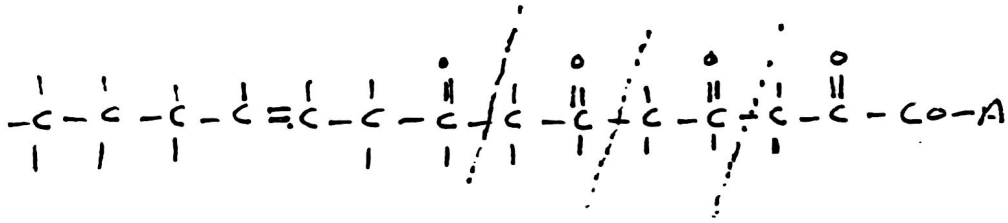
* How many turn (B-oxidation)

Same 6 turn. (12 carbons)

* Fatty acid (unsaturated)

* mono unsaturated

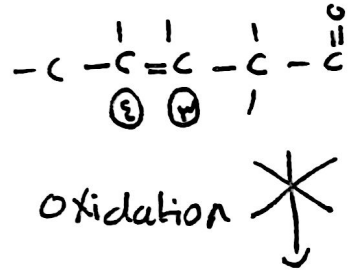
- FA ($18:1\Delta^9$)

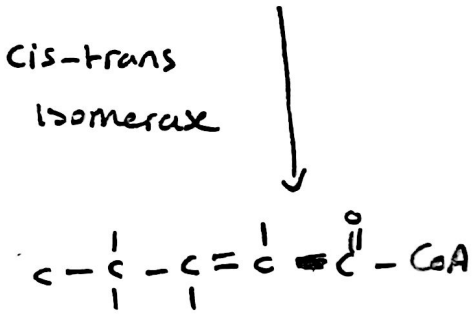


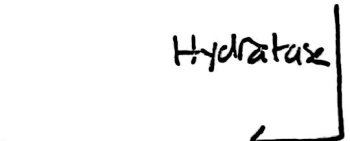
First step in B-oxidation will not occure [oxidation]

(because there can't be 2 Double bond next to each other)

instead, There is Enzyme cis-trans isomerase will transport the double Bond from (3,4) to (2,3)

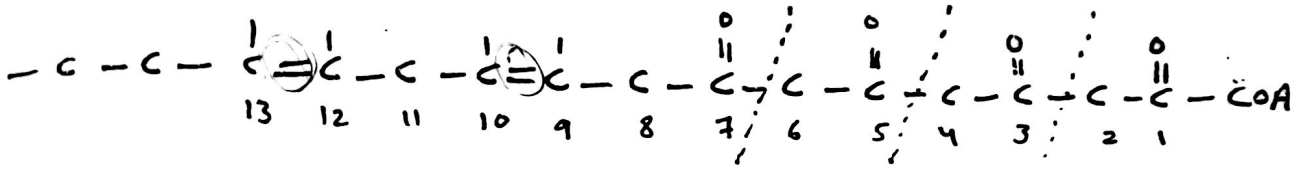


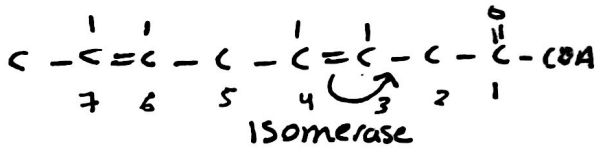


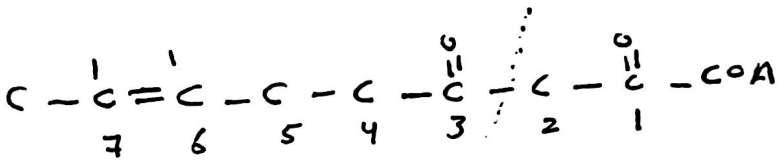


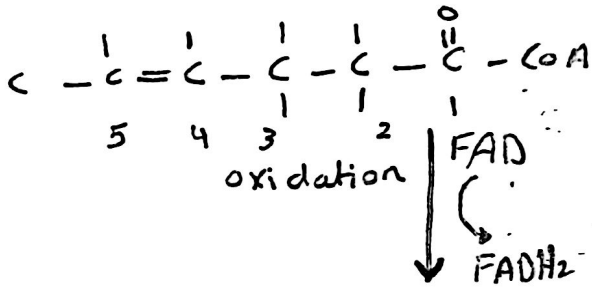
Continue as Befor

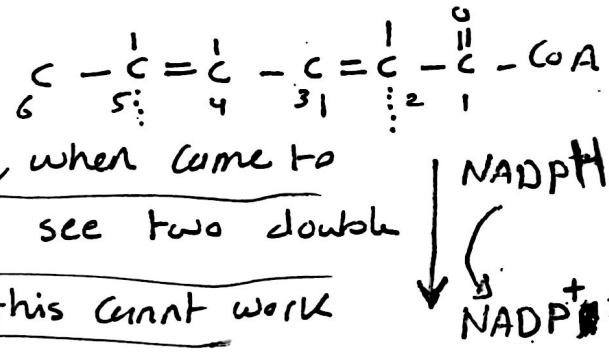
Polyunsaturated :- (FA 18:2 $\Delta^{9,12}$)









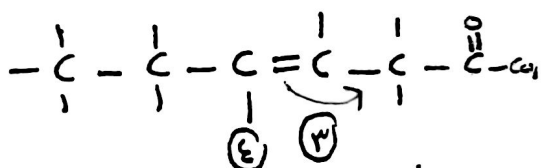


C = C — C = C

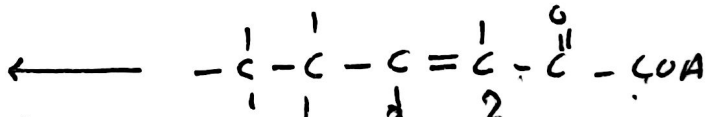
Not a substrate for the enzyme Hydratase

Hydratase, when came to work and see two double bond like this cannt work instead (~~reductase~~) << Dienoyl-CoA reductase >>

H كسب



Enoyl CoA isomerase



Hydratase

Continue

Note :-

* when double bond on odd # , like 9
  you need [cis/trans isomerase] to solve the problem

* when double bond on even # , like 12
  you need two enzyme to solve the problem
  [reductase + enoyl-CoA isomerase]

which give me more energy , saturated FA OR unsaturated FA ?!

Answer :- saturated why

if you notic , we didn't perform 1st oxidation step « when double bond on 9 » and this step will give me $FADH_2$

So less oxidation step.
less $FADH_2$
less ATP.
} in unsaturated F.A

Best wishes
Dr. Tariq . Jibril
07909791 88

1. Phospholipases break down fats by
   a. adding a phosphate group to them.
   b. reducing the double bonds to single bonds.
   c. hydrolyzing them.
   d. removing acetyl-CoA units.

   ANS: C

2. Which of the following is true concerning phospholipases?
   a. Many snake venoms contain phospholipases
   b. Phospholipase D is a component in some spider venoms
   c. Phospholipases in snake venoms can lead to the lysing of blood cells
   d. All of these

   ANS: D

3. Which of the following statements below about the activation of fatty acids is false?
   a. Activation involves the formation of a high energy thioester bond.
   b. Activation is accompanied by hydrolysis of ATP to ADP and P_i.
   c. Activation includes the formation of an acyl-adenylate intermediate.
   d. Activation includes hydrolysis of ATP to produce AMP and PP_i, with the further hydrolysis of PP_i to drive the reaction to completion.

   ANS: B

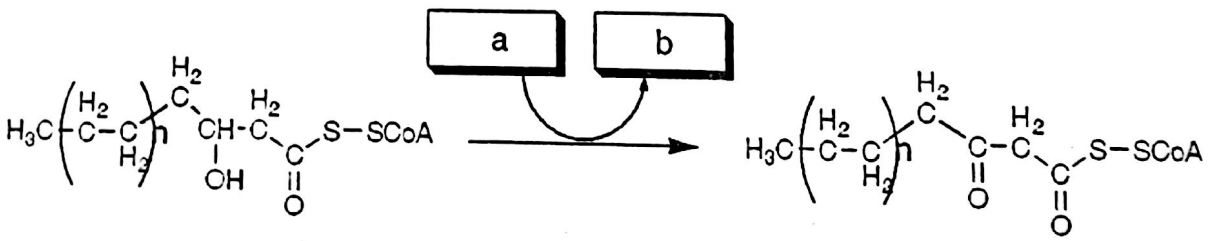
4. Which of the following is not true regarding catabolism of triacylglycerols?
   a. Control of release of fatty acids from triacylglycerols in adipocytes involves cyclic AMP as a second messenger.
   b. When cAMP is a second messenger in the catabolsim of triacylglycerols, it activates a protein kinase
   c. The protein kinase, once activated, cleaves fatty acids from the triacylglycerol
   d. The phosphorylated form of triacylglycerol lipase is the active form
   e. All of these are true

   ANS: C

5. The use of cyclic AMP to mobilize fatty acids from adipose tissue is analogous to cyclic AMPs role in mobilization of sugars from glycogen in the liver.
   a. True
   b. False

   ANS: A

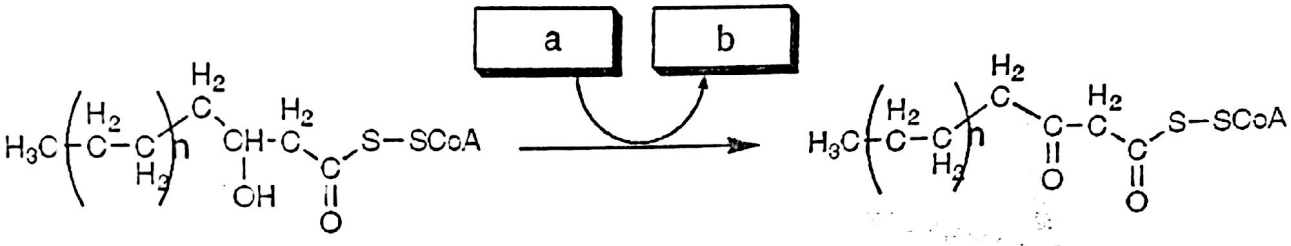
6. The enzyme activity catalyzing the reaction shown is best termed a



a. reductase
b. hydratase
c. dehydratase
d. dehydrogenase

ANS: D

7. Which group of small molecules best fit the boxes associated with the reaction shown?



	a	b
I.	ATP	ADP
II.	NAD^+	NADH
III.	$NADP^+$	NADPH
IV.	FAD	$FADH_2$

a. I
b. II
c. III
d. IV

ANS: B

8. Which of the following is not a product of the activation of fatty acids?
a. A thioester
b. ADP
c. Pyrophosphate
d. Phosphate
e. All of these are products of the activation of a fatty acid.

ANS: B

9. Fatty acid catabolism is called β-oxidation, since the second or β carbon from the carboxyl group is the site of oxidation.
a. True
b. False

ANS: A

10. The reactions involved in β-oxidation of fatty acids include the following:

1. Cleavage of acetyl-CoA from the fatty acid.
2. Hydration of a double bond.

3. Formation of a C–C double bond.
4. Oxidation of an alcohol.

The correct order of these reactions is:

a. $1 \rightarrow 2 \rightarrow 3 \rightarrow 4$
b. $4 \rightarrow 3 \rightarrow 2 \rightarrow 1$
c. $3 \rightarrow 2 \rightarrow 4 \rightarrow 1$
d. $2 \rightarrow 4 \rightarrow 3 \rightarrow 1$
e. $1 \rightarrow 4 \rightarrow 3 \rightarrow 2$

ANS: C

11. Which of the following vitamins and cofactors is not used in β-oxidation?
    a. Biotin
    b. Niacin
    c. Pantothenic acid
    d. Riboflavin
    e. All of these are important in the β-oxidation of fatty acids.

    ANS: A

12. How many NAD^+ are reduced in the degradation of palmitoyl-CoA to form eight molecules of acetyl-CoA?
    a. 1
    b. 7
    c. 8
    d. 14
    e. 16

    ANS: B

13. Lipids yield more ATP than sugars because
    a. they have more carbon atoms than sugars.
    b. their carbon atoms are more highly reduced.
    c. both of these
    d. neither of these

    ANS: C

14. A key intermediate in the catabolism of fatty acids with uneven numbers of carbon atoms is
    a. malonyl-CoA
    b. propionyl-CoA
    c. oxaloacetate
    d. phosphoenolpyruvate

    ANS: B

15. The *cis* double bonds of naturally-occurring fatty acids react well with the hydratase enzyme.
    a. True
    b. False

ANS: B