BIOCHEMISTY

Course No.-DTC-111, Credit Hours – 2 (1+1)

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FATTY ACID OXIDATION

- **Fatty acids** => 9000 calories / gram.
- carbohydrates & proteins => 4000 calories / gram
- **Fatty acids are** > **reduced** than carbohydrates and proteins.
- Fatty acids => because of **non-polar character** (not soluble in water) => stored in water free form => so 1 gram contains six times > energy than 1 gram glycogen bound to water .
- Fatty acids => degraded by **sequential removal of two-carbon fragments** from carboxyl end => **β-oxidation**
- Bond b/w **α- and β-carbon atoms** => broken => acetyl-CoA
- β-Oxidation => because the **β-carbon of fatty acids is oxidized** => **mitochondria**.

Hydrolysis of Triglycerides (Lipolysis)

- **Triglycerides** ——(**lipases**)——> **glycerol** and **fatty acids** .

- Activity of **lipase** => regulated by hormones => **epinephrine and glucagon =>** activate **adenylate cyclase** => produce **cAMP (**from ATP) => protein kinase A => phosphorylates **lipase** => **activated**.

- **Glycerol** ——(glycerol kinase)——>phosphorylated => then oxidised ——(glycerol phosphate dehydrogenase)——➔ dihydroxyacetone phosphate => **glycolysis**.

- **Insulin inhibits the hydrolysis of triglycerids**.

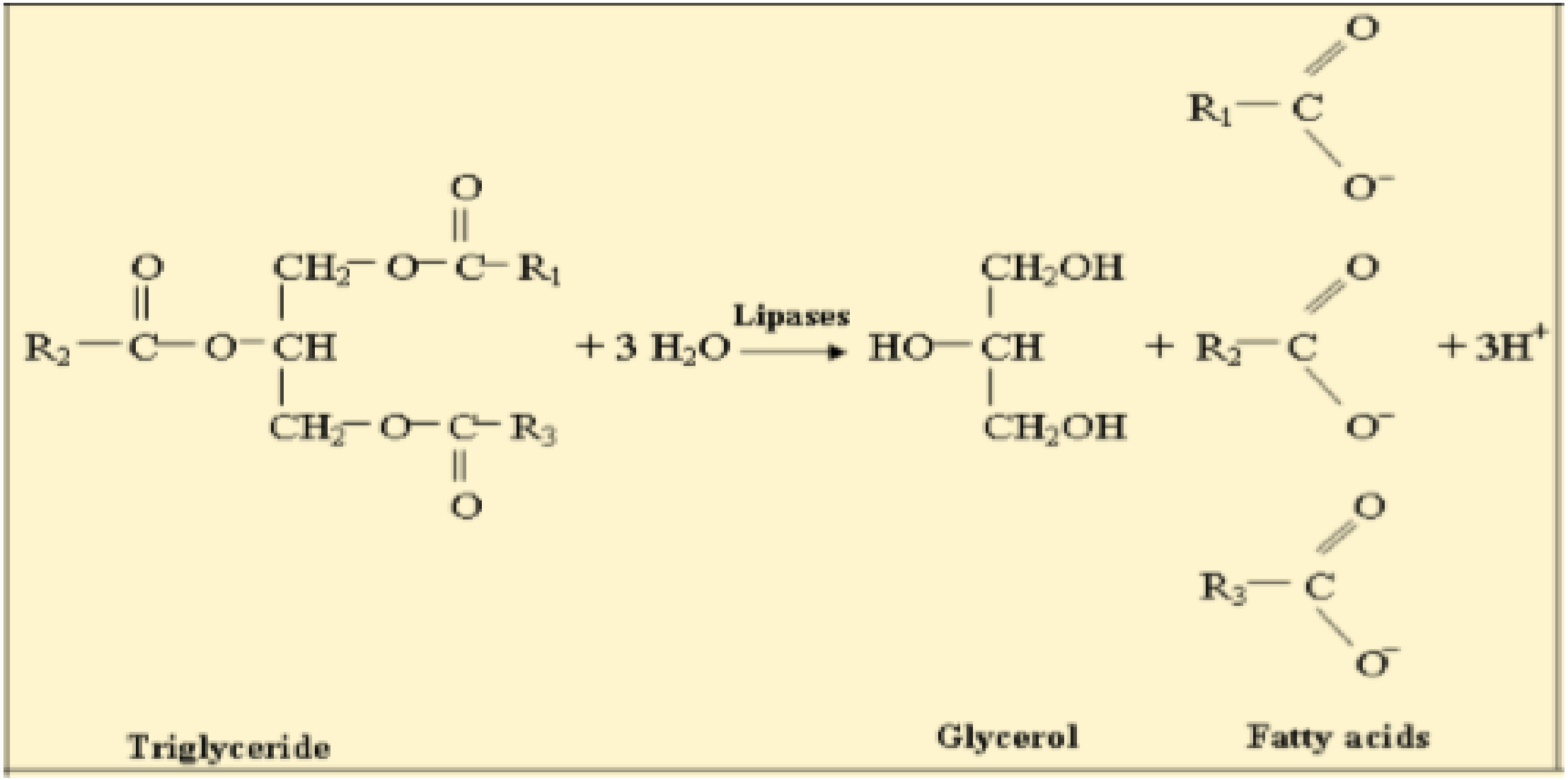


Fig 20.1 Hydrolysis by lipases of triglycerol in glycerol and fatty acids.

Fatty Acid Activation

- Fatty acid => activated => with ATP and CoA ==========(acyl CoA synthetase, in the cytosol)==========> **fatty acyl-CoA**

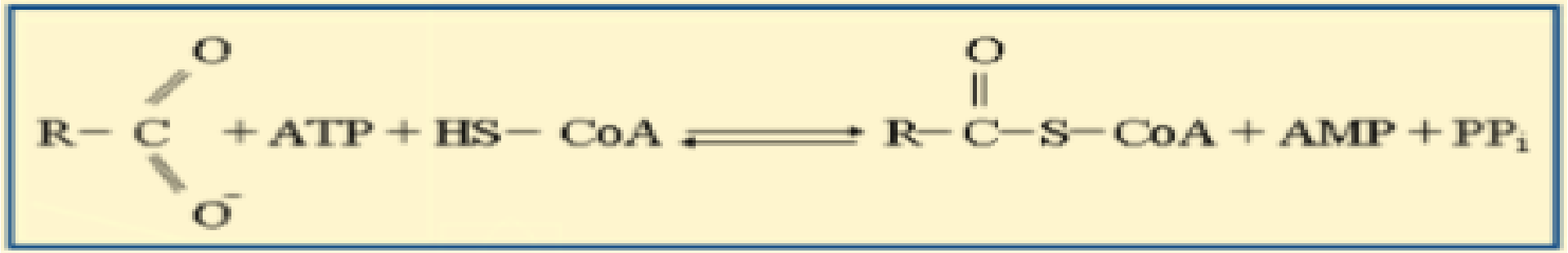


Fig. 20.2 Activation of Fatty acid

- **Acyl CoA synthetase** =>bound => at **outer membrane of the mitochondria**
- Hydrolysis of **pyrophosphate** moves the reaction => in forward direction**.**

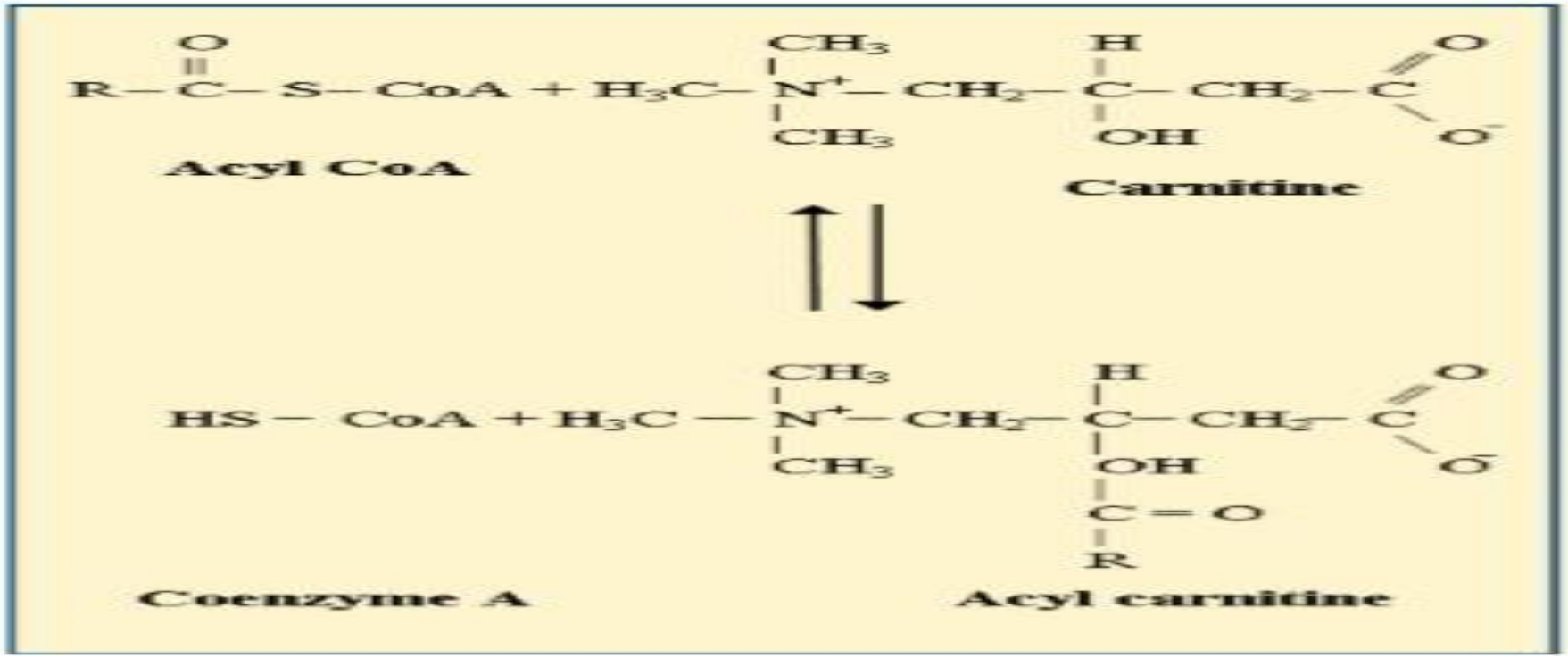
Translocation of activated fatty acids into the mitochondrial matrix

- **Carnitine mediated specialized mechanism**

carnitine acyltransferase I

- **Acyl CoA** & **carnitine** ==========at==========> **acyl carnitine**

outer face of inner membrane of mitochondria



Activated long-chain fatty acids are combined with carnitine

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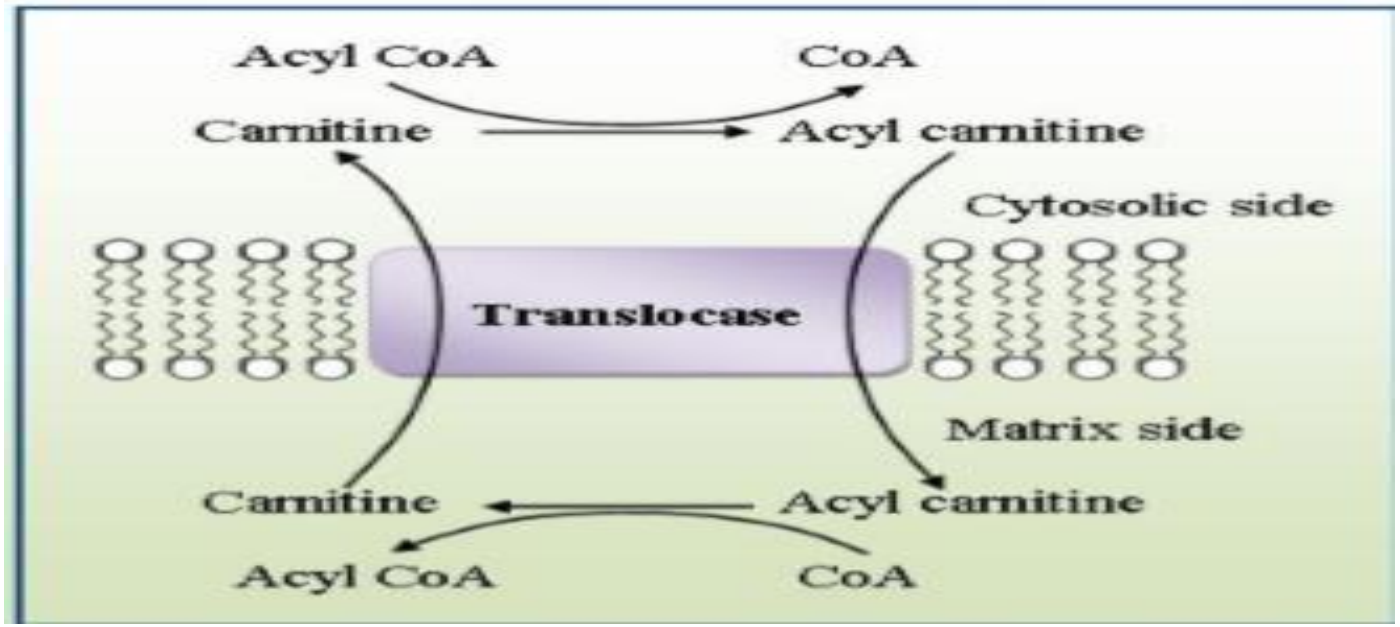


translocase enzyme (membrane protein)

- Acyl carnitine ==========> inner membrane =>

carnitine acyltransferase II

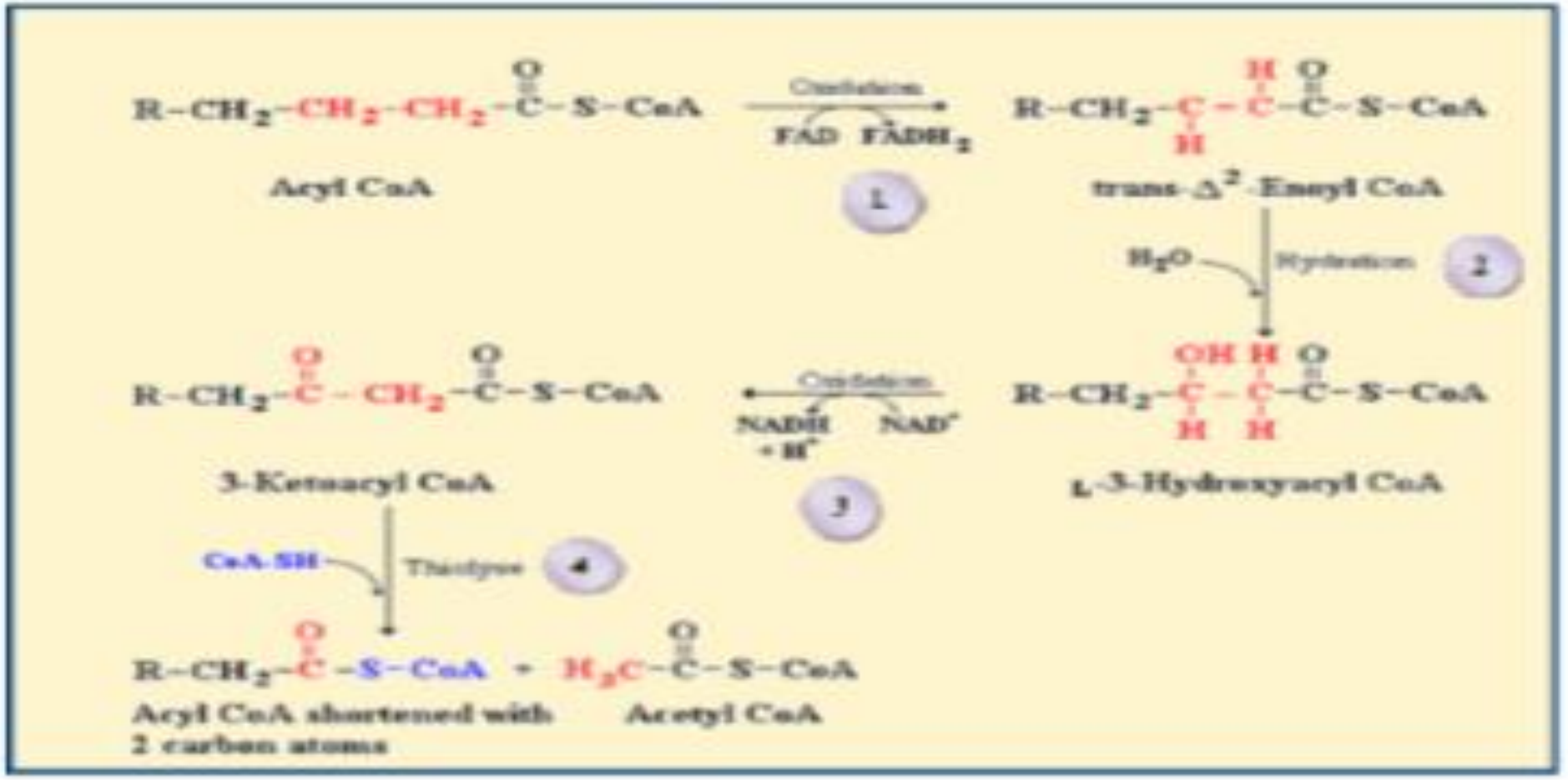
==>Acyl group ==========> coenzyme A at the matrix side

translocase

- **Carnitine** ========➔inter membrane space in exchange for a coming in of acyl carnitine.

Fatty Acid Oxidation

- **Fatty Acids are Broken by Splitting Off Always Two Carbon Atoms.**
- **Reaction order for the breakdown of fatty acids: Oxidation, hydration, oxidation and thiolyse .**

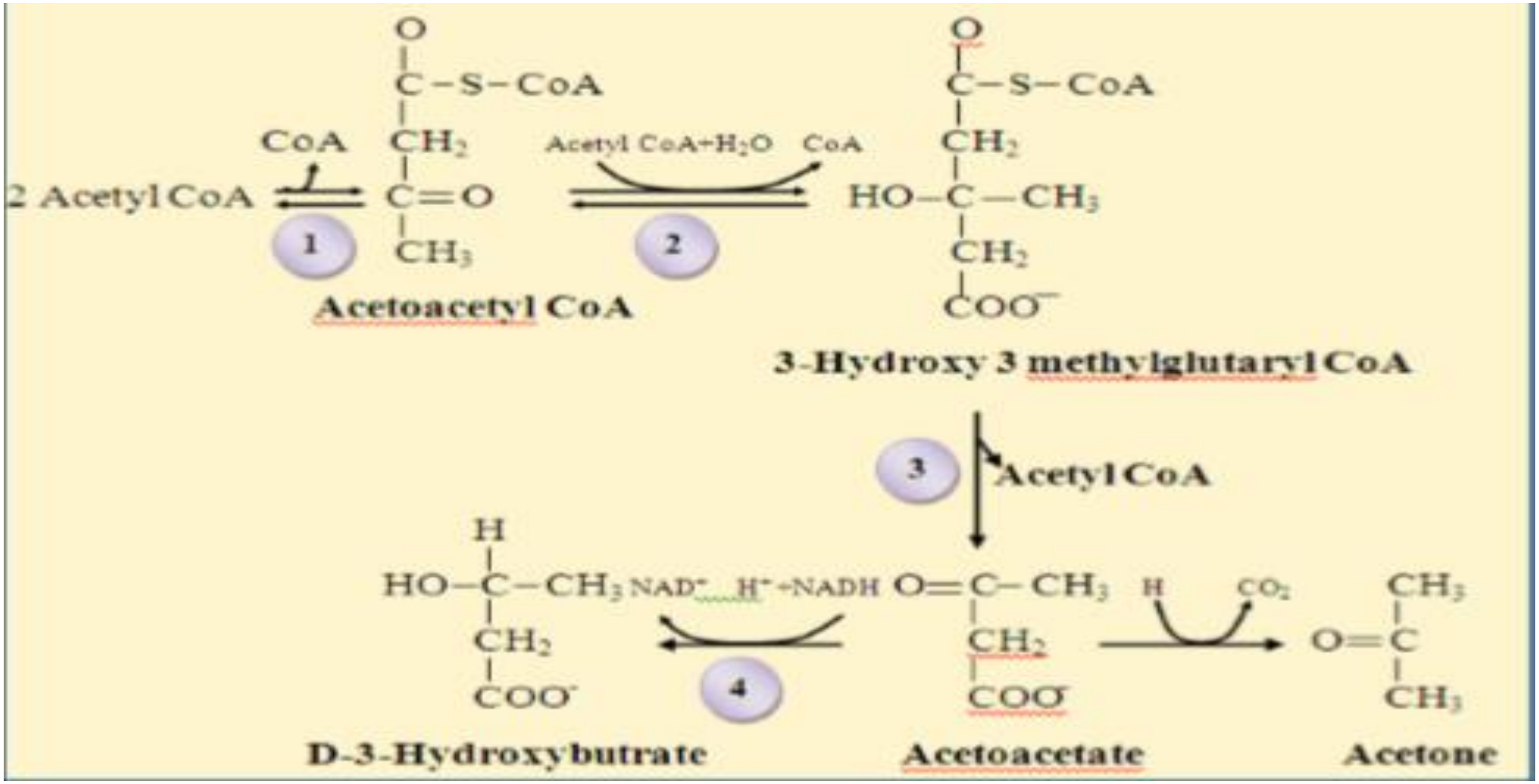


Excess Acetyl CoA are Converted into Ketone Bodies

- Fatty acid => active **acetyl CoA => citric acid cycle** (when sufficient oxaloacetate is present).

- Fasting /diabetes => oxaloacetate => used for the **gluconeogenesis =>** insufficient oxaloacetate available => to react with acetyl CoA.

- Then 2 molecules of acetyl CoA => one molecule of **aceto acetyl CoA => ketone bodies** : **aceto acetate, D-3-hydroxybutyrate and acetone**.



Two molecules acetyl CoA form one acetoacetyl CoA and from this the ketone bodies are formed

Enzymes that accelerate these reactions in liver are:

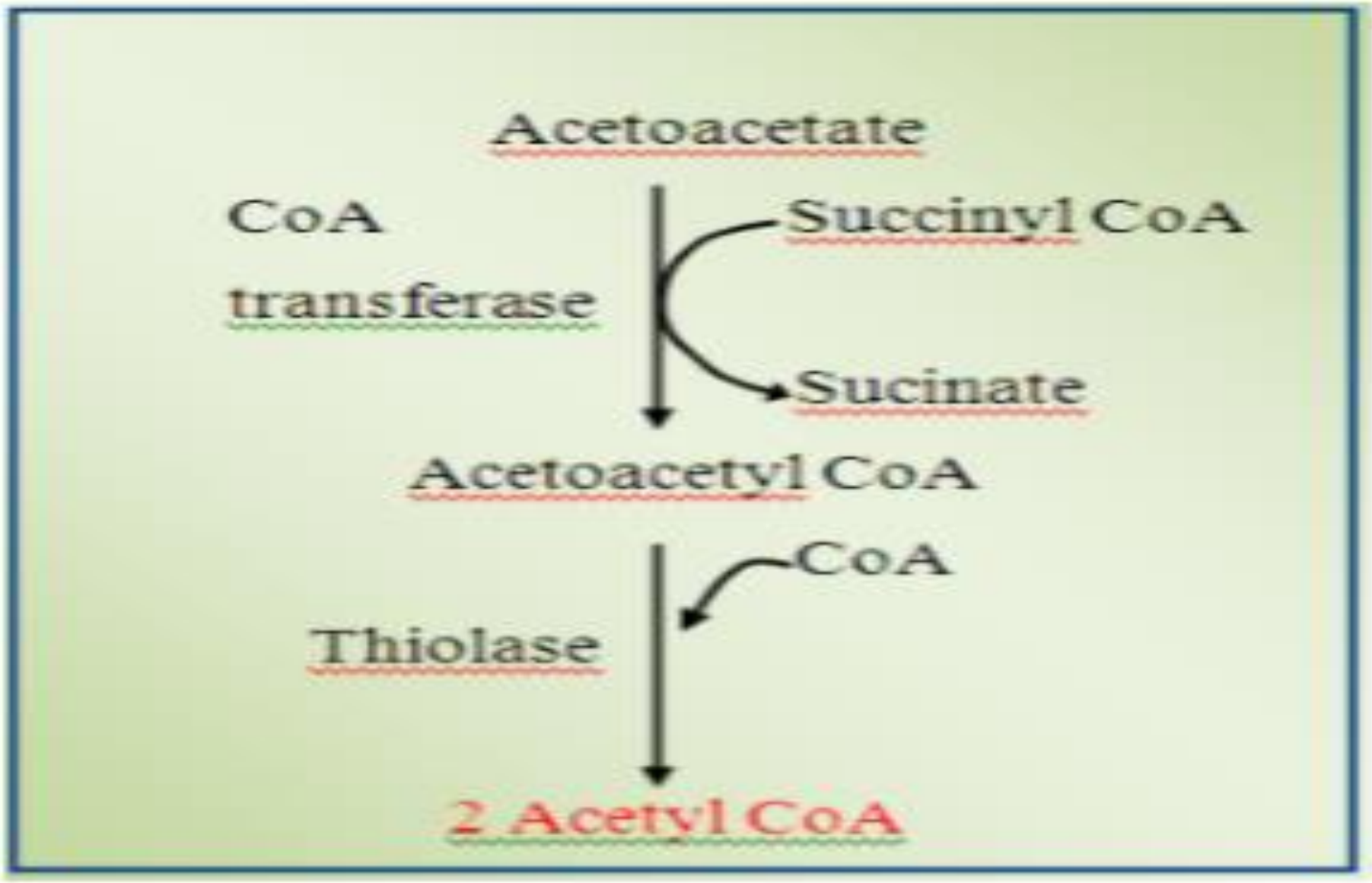
(1) 3- keto thiolase,
(2) Hydroxymethyl glutaryl CoA synthetase,
(3) hydroxy methylglutaryl CoA lyase and
(4) the mitochondrial enzyme D-3hydroxy butyrate dehydrogenase.

- **Acetoacetate** decarboxylates => to **acetone(** a volatile compound) => smell is observed in the breath of diabetic / fasting people .

- **Ketone bodies** => energy sources => primary fuels for **heart muscle** & **kidney**.

- In fasting / diabetics => **brains =>** use **acetoacetate** as fuel.

- **Acetoacetate** reacts with succinyl CoA => **Acetoacetyl CoA** => thiolysed to 2 molecules of **acetyl CoA** => **citric acid cycle**.



The use of acetoacetate as a fuel by TCA cycle after conversion in acetyl CoA

- **Humans and animals** => can't convert **fatty acids** => into **glucose** because they can't use the **acetyl CoA =>** make **pyruvate or oxaloacetate =>** taken up => **citric acid cycle** => converted to CO_2

- acetyl CoA does not provide **oxaloacetate** => needed for **gluconeogenesis**.

- acetyl CoA is converted to **ketone bodies**