

Osaro Evelyn princess

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Fatty acids are oxidized mainly by a process called  $\beta$ -oxidation, in which two carbon units sequentially removed beginning from the carboxyl end of the fatty acid in the form of acetyl-CoA. It is called  $\beta$ -oxidation because oxidation of fatty acids occurs at the  $\beta$ -carbon atom.  $\beta$ -oxidation pathway occurs in mitochondria. It involves following three steps:

1. Activation of fatty acid to acyl-CoA
2. Transfer of acyl CoA into mitochondria by carnitine transport system
3. Reactions of  $\beta$ -oxidation in mitochondria.

#### Activation of Fatty Acid

- Before being catabolized, free fatty acids are converted to an active form called acyl-CoA. It

occurs in the cytosol in the presence of ATP, coenzyme-A (CoA-SH) and the enzyme acyl-CoA

synthetase also called thiokinase. Subsequent steps of  $\beta$ -oxidation occur in the mitochondria of the liver and other tissue cells.

#### Transport of Acyl-CoA into Mitochondria by Carnitine Transport System

Activation of fatty acids occur in the cytosol, whereas

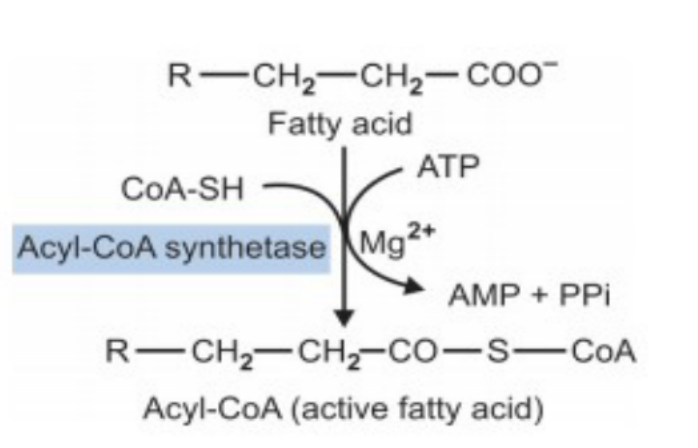
they are oxidized in the mitochondrial matrix. The mitochondrial inner membrane is impermeable to fatty acids. So a special transport mechanism is needed. Activated long chain fatty acids are carried across the inner mitochondrial membrane by carnitine, ( $\beta$ -hydroxy  $\gamma$ -trimethyl ammonium butyrate), formed from lysine and methionine in liver and kidney. This occurs in four steps

1. The acyl group of acyl-CoA is transferred to the carnitine to form acyl-carnitine. This reaction is catalyzed by carnitine acyltransferase-I (CAT-I). which is located on the cytosolic face of the inner mitochondrial membrane.
2. Acyl-carnitine is then transported across the inner mitochondrial membrane by an

enzyme translocase.

3. The acyl group is transferred back to CoA in the mitochondrial matrix by the enzyme carnitine acyl transferase-II (CAT-II), located on the inside of the inner mitochondrial membrane.

4. Acyl-CoA is reformed in the mitochondrial matrix with liberation of carnitine which is returned to the cytosolic side by the translocase in exchange for an incoming acyl-carnitine.



### Reactions of $\beta$ -oxidation of Fatty Acid

After the penetration of the acyl-CoA into mitochondria, it undergoes  $\beta$ -oxidation.

Sequence of Reactions of  $\beta$ -oxidation

A saturated acyl-CoA is degraded by a repeated sequence of four reactions

1. Oxidation by FAD
2. Hydration
3. Oxidation by NAD
4. Cleavage.

1. Oxidation by FAD: The first reaction is the oxidation of acyl-CoA by an acyl-CoA dehydrogenase to give an  $\Delta^2$ -trans enoyl-CoA (a trans double bond between C2 and C3). The coenzyme for the dehydrogenase is FAD which is converted to FADH<sub>2</sub>.

2. Hydration: The next step is the hydration (addition of water) of the double bond between C2 and C3 by  $\Delta^2$ -enoyl-CoA hydratase to form  $\beta$ -hydroxy acyl-CoA. 3. Oxidation

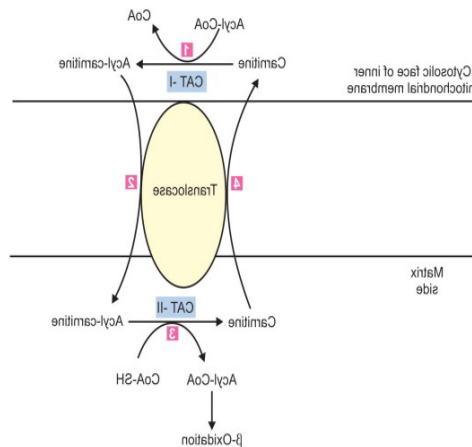
by NAD: The  $\beta$ -hydroxy derivative undergoes second oxidation reaction catalyzed by  $\beta$ -hydroxyacyl-CoA dehydrogenase to form  $\beta$ -ketoacyl CoA and generates NADH.

4. Cleavage: Finally  $\beta$ -ketoacyl-CoA is split at the  $\beta$ -carbon by thiolase to yield acetyl-CoA and an acyl CoA which is shorter by two carbon atoms than the original acyl-CoA that underwent oxidation.

The new acyl-CoA, containing two carbons less than the original, re-enters the  $\beta$ -oxidation pathway at reaction catalyzed by acyl-CoA dehydrogenase. The process continues till the fatty acid degraded completely to acetyl-CoA.

Acetyl-CoA can be oxidized to CO<sub>2</sub> and H<sub>2</sub>O via citric acid cycle in mitochondria and thus oxidation of fatty acids is completed.

Carnitine transport system where, CAT I: Carnitine acyl transferase-I; CAT II: Carnitine acyl transferase-II



And also,

