Department of biology

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((Microbial Physiology))

Stage (-3-)

LEC- ((7))

Krebs cycle

By

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Krebs cycle (also known as citric acid cycle or tricarboxylic acid cycle) is a step wise cyclic process which is used to oxidize the pyruvate formed during the glycolytic break down of glucose into carbon dioxide (CO_2) and water (H_2O) . It also oxidizes acetyl Co-A which arises from break down of carbohydrate , lipid, and protein . The actual Krebs cycle begins when acetyl –Co-A enters into a reaction to form citric acid.

Location of Krebs cycle

In Eukaryotes Krebs cycle operates in matrix of mitochondria. It is absent in prokaryotes. Its substrate Acetyl Co-A is entrant or connecting link between glycolysis and Krebs cycle. The oxalacetate acts as acceptor molecule.

Steps of Krebs cycle

Krebs cycle is a stepwise cyclic oxidation process in which four dehydrogenation steps and two decarboxylations steps of active acetate group takes place to produce reduced co-enzymes and carbon dioxide. The following nine steps occur in overall Krebs cycle (figure 1) :

1. Condensation 2- Isomerisation

3-Dehydrogenation 4-Decarboxylation

5- Oxidative Decarboxylation 6- Substrate level ATP/GTP synthesis

7-Dehydrogenation (oxidation) of Succinate

8- Hydration and 9- Dehydrogenation (Oxidation) of Malate

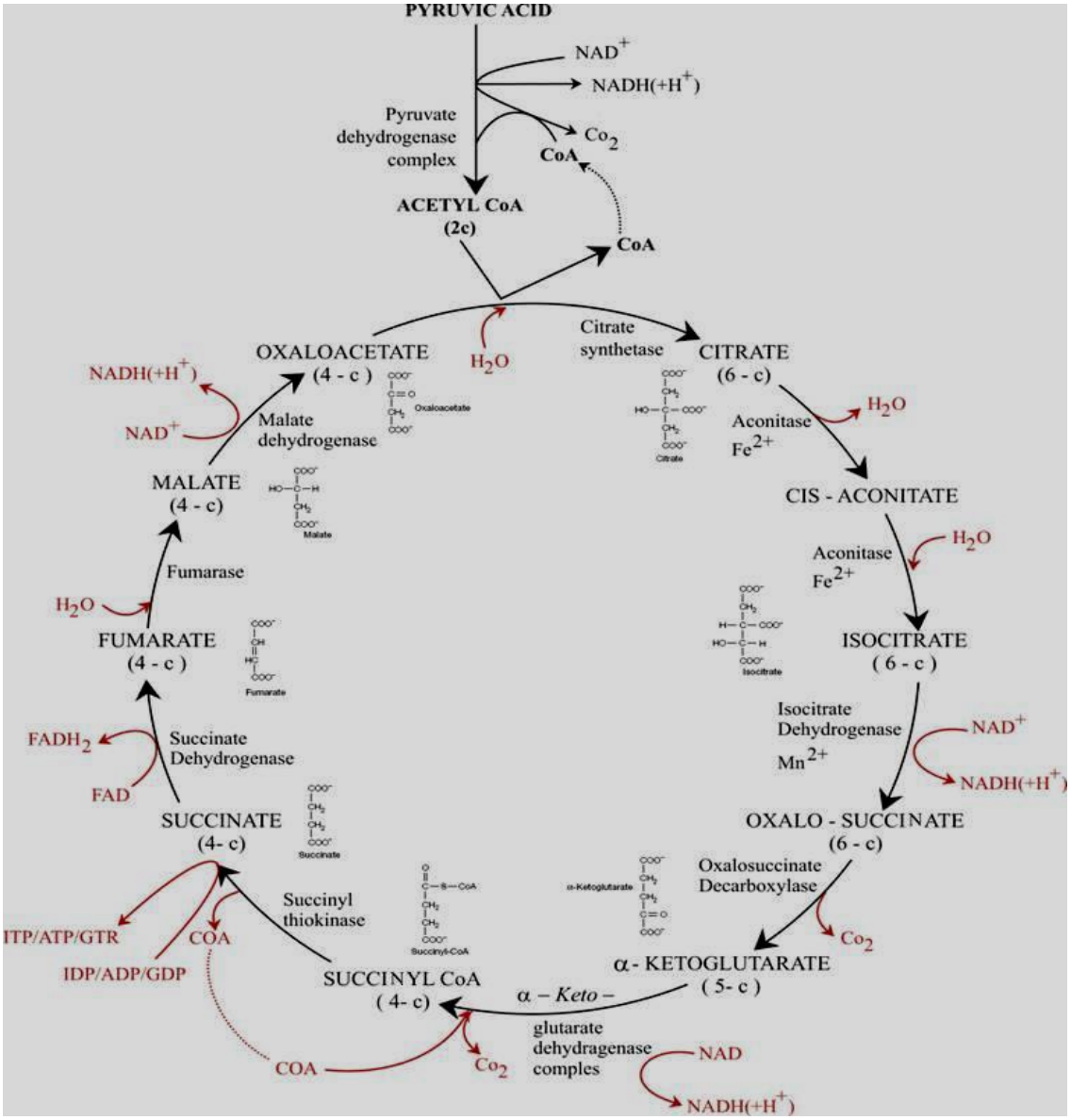


Figure (1) : Citric Acid or Krebs cycle completed in Nine steps

Step 1: Condensation

In first step of Krebs cycle, Acetyl CoA combines with oxaloacetate in the presence of condensing enzymes **citrate synthetase**. Co-A is released out. The product of condensation is citrate which is a tricarboxylic 6-carbon compound.

$$\text{Acetyl Co-A} + \text{Oxaloacetate} + H_2O \xrightarrow{\text{citrate synthetase}} \text{Citrate} + \text{CoA}$$

Step 2: Isomerisation

Citrate formed in first step is converted into its isomer isocitrate in a two – step reaction in the presence of iron containing enzyme **Aconitase**.

(i) **Dehydration** : A molecule of water is released and citric acid is changed into cis -aconitate.

$$\text{Citric acid} \xrightarrow{\text{Aconitase, Fe}} \text{Cis} - \text{Aconitate} + H_2O$$

(ii) **Rehydration** : Cis – aconitate combines with a molecule of water and form isocitrate.

$$\text{Cis} - \text{Aconitate} + H_2O \xrightarrow{\text{Aconitase, Fe}} \text{Isocitrate}$$

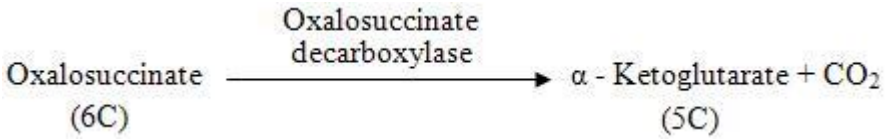
Step 3: Dehydrogenation

Now isocitrate undergoes dehydrogenation in the presence of an enzyme **isocitrate dehydrogenase**. Mn_2^+ ion is required for the functioning of enzyme. Hydrogen given out by isocitrate is picked up by NAD^+ (Nicotinamide adenine dinucleotide) to form $NADH_2$. After losing hydrogen, isocitrate is changed into oxalosuccinate (6C).

$$\text{Isocitrate} + NAD^+ \xrightarrow{\text{Isocitrate dehydrogenase}} \text{Oxalosuccinate} + NADH_2$$

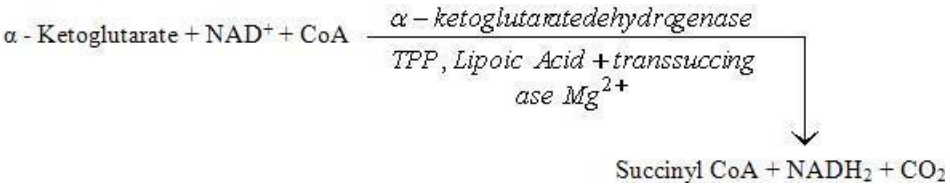
Step 4: Decarboxylation

Oxalosuccinate in step 4 undergoes decarboxylation . In the presence of **oxalosuccinate decarboxylase** enzyme, oxalosuccinate is changed into α-ketoglutarate.



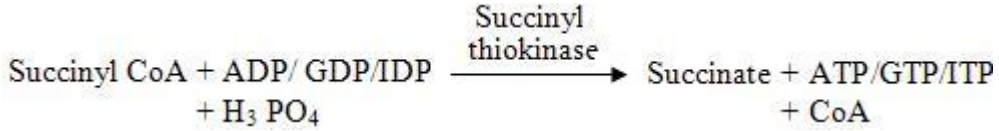
Step 5: Oxidative Decarboxylation

In this step 5-carbon compound, α – Ketoglutarate undergoes simultaneous dehydrogenation and decarboxylation in the presence of enzyme **α – ketoglutarate dehydrogenase** complex . This enzyme complex contain TPP, Lipoic Acid , Mg_2^+ and trans – succinylase. NAD^+ and CoA are required. The products formed are 4 – carbon compound succinyl CoA, $NADH_2$ and CO_2.



Step 6: Substrate level ATP/GTP Synthesis

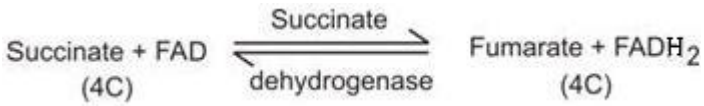
In the presence of enzyme **succinyl thiokinase**, succinyl CoA is hydrolyzed. CoA and Succinate are formed. The energy liberated during the process is used in synthesis of ATP in plants and GTP (Guanosine triphosphate) or ITP (Inosine triphosphate) in animals. CoA is released out.



Step 7: Dehydrogenation (Oxidation)

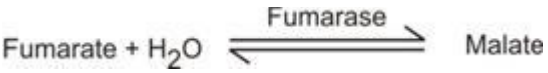
In step 7 of Krebs cycle 4 – Carbon compound Succinate is oxidized to another 4-carbon compound fumarate with the help of enzyme

succinate dehydrogenase and hydrogen acceptor FAD (Flavin Adenine Dinucleotide) . The enzyme is attached to inner mitochondrial membrane . It contains or non haem iron (Fe–S) protein. This enables the enzyme to get directly linked to electron transport chain.



Step 8: Hydration

In step 8, Fumarate reacts with a molecule of water, in the presence of an enzyme **fumarase** forming another 4-carbon dicarboxylic acid called Malate.



Step 9: Dehydrogenation (Oxidation)

With the help of enzyme **malate dehydrogenase** , Malate formed in step 8 is oxidized to oxaloacetate. NAD^+ reduced to $NADH_2$.

An oxaloacetate formed in this reaction becomes available to combine with acetyl CoA to start a new cycle all over again.