Krebs (Citric Acid) Cycle Steps by Steps Explanation

It is also known as TriCarboxylic Acid (TCA) cycle. In prokaryotic cells, the citric acid cycle occurs in the cytoplasm; in eukaryotic cells, the citric acid cycle takes place in the matrix of the mitochondria.

The process oxidises glucose derivatives, fatty acids and amino acids to carbon dioxide (CO_2) through a series of enzyme controlled steps. The purpose of the Krebs Cycle is to collect (eight) high-energy electrons from these fuels by oxidising them, which are transported by activated carriers NADH and $FADH_2$ to the electron transport chain. The Krebs Cycle is also the source for the precursors of many other molecules, and is therefore an amphibolic pathway (meaning it is both anabolic and catabolic).

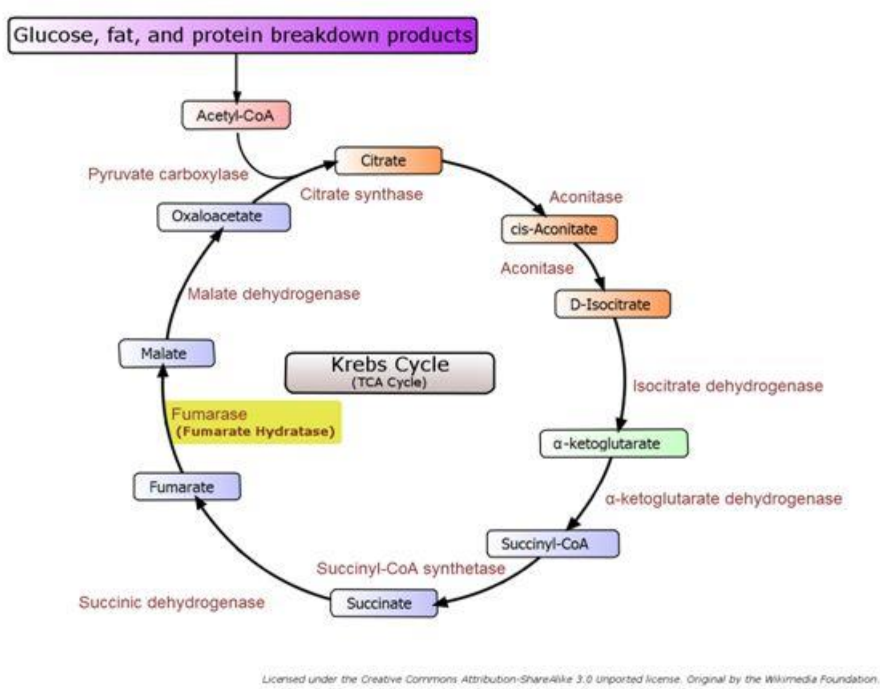
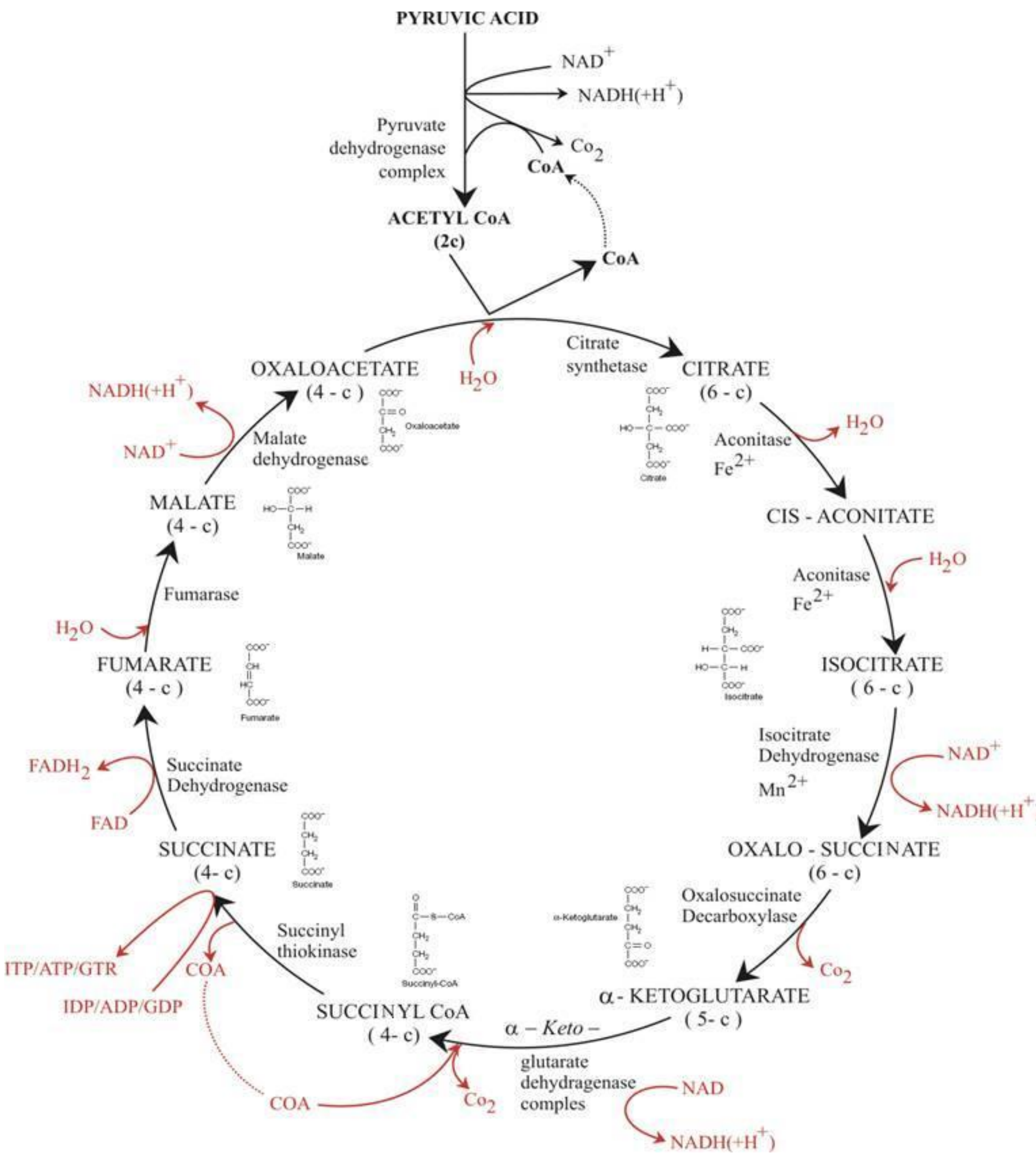


Figure 10 The Krebs Cycle


PYRUVIC ACID
NAD+
NADH(+H+)
Pyruvate dehydrogenase complex
Co2
CoA
ACETYL CoA (2c)
CoA
OXALOACETATE (4 - c)
H2O
Citrate synthetase
CITRATE (6 - c)
NADH(+H+)
NAD+
Malate dehydrogenase
Oxaloacetate
Citrate
H2O
Aconitase Fe2+
MALATE (4 - c)
Malate
CIS - ACONITATE
H2O
Aconitase Fe2+
Fumarase
H2O
FUMARATE (4 - c)
Fumarate
Isocitrate
ISOCITRATE (6 - c)
Isocitrate Dehydrogenase Mn2+
NAD+
NADH(+H+)
FADH2
Succinate Dehydrogenase
FAD
SUCCINATE (4- c)
Succinate
OXALO - SUCCINATE (6 - c)
Oxalosuccinate Decarboxylase
Co2
α-Ketoglutarate
Succinyl thiokinase
Succinyl-CoA
ITP/ATP/GTR
COA
IDP/ADP/GDP
SUCCINYL CoA (4- c)
α - KETOGLUTARATE (5- c)
α – Keto – glutarate dehydragenase comples
COA
Co2
NAD
NADH(+H+)

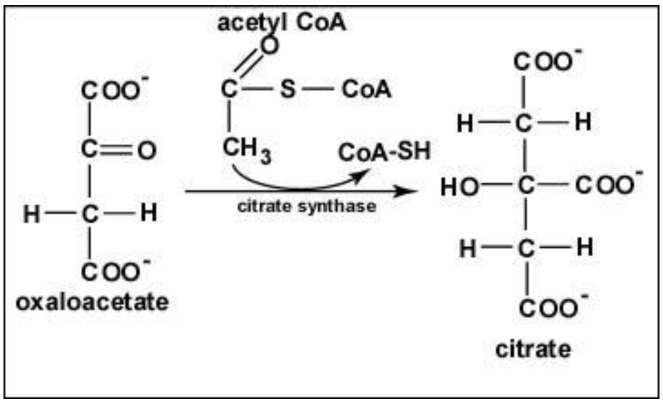
The Net Equation

acetyl CoA + 3NAD + FAD + ADP + HPO_4^{-2} ------> $2CO_2$ + CoA + $3NADH^+$ + $FADH^+$ + ATP

Reaction 1: Formation of Citrate

The first reaction of the cycle is the condensation of **acetyl-CoA** with **oxaloacetate** to form **citrate**, catalyzed by **citrate synthase**.

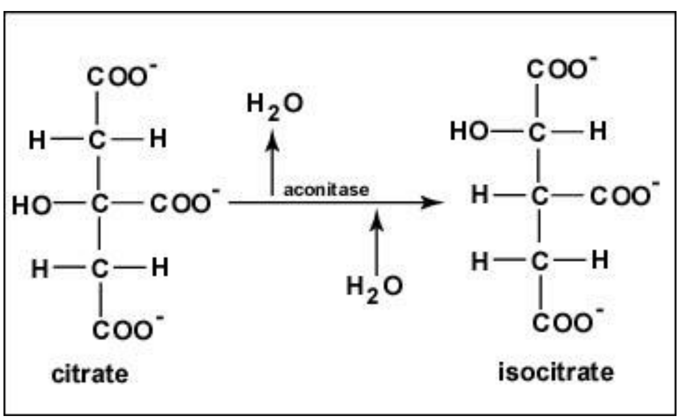
Once oxaloacetate is joined with acetyl-CoA, a water molecule attacks the acetyl leading to the release of coenzyme A from the complex.



Reaction 2: Formation of Isocitrate

The **citrate** is rearranged to form an isomeric form, **isocitrate** by an enzyme **acontinase.**

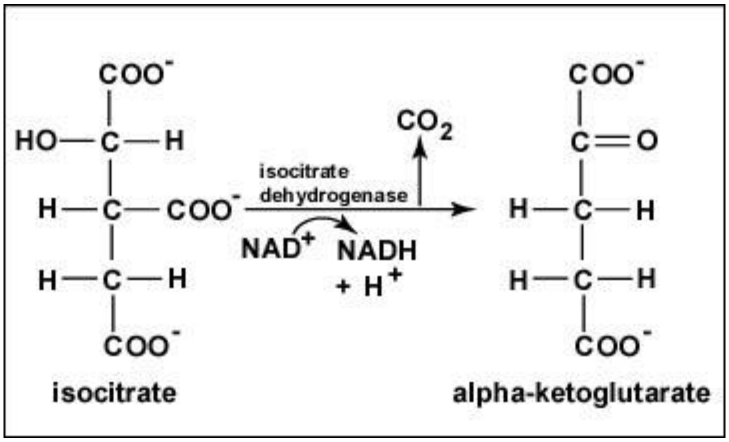
In this reaction, **a water molecule is removed** from the citric acid and then put back on in another location. The overall effect of this conversion is that the –OH group is moved from the 3′ to the 4′ position on the molecule. This transformation yields the molecule **isocitrate.**



Reaction 3: Oxidation of Isocitrate to α-Ketoglutarate

In this step, isocitrate dehydrogenase catalyzes oxidative decarboxylation of **isocitrate** to form **α-ketoglutarate.**

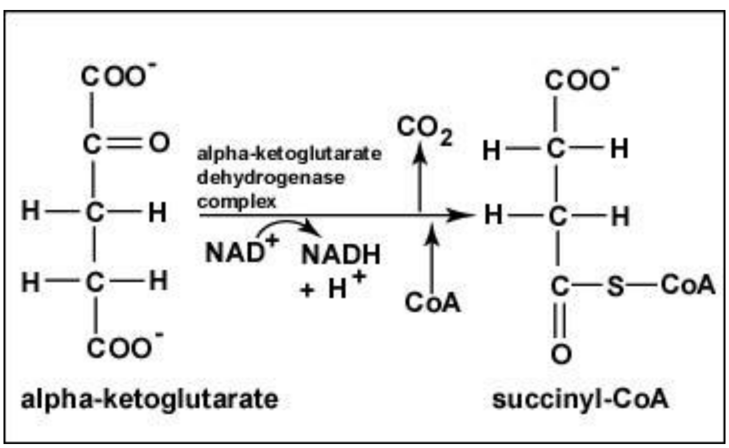
In the reaction, generation of NADH from NAD is seen. The enzyme **isocitrate dehydrogenase** catalyzes the oxidation of the –OH group at the 4′ position of isocitrate to yield an intermediate which then has a carbon dioxide molecule removed from it to yield **alpha-ketoglutarate**.



Reaction 4: Oxidation of α-Ketoglutarate to Succinyl-CoA

Alpha-ketoglutarate is oxidized, carbon dioxide is removed, and coenzyme A is added to form the 4-carbon compound **succinyl-CoA**.

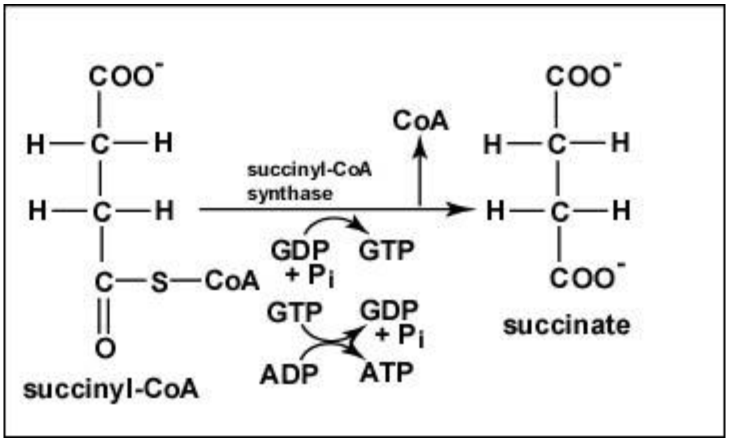
During this oxidation, NAD+ is reduced to NADH + H+. The enzyme that catalyzes this reaction is **alpha-ketoglutarate dehydrogenase.**



Reaction 5: Conversion of Succinyl-CoA to Succinate

CoA is removed from **succinyl-CoA** to produce **succinate.**

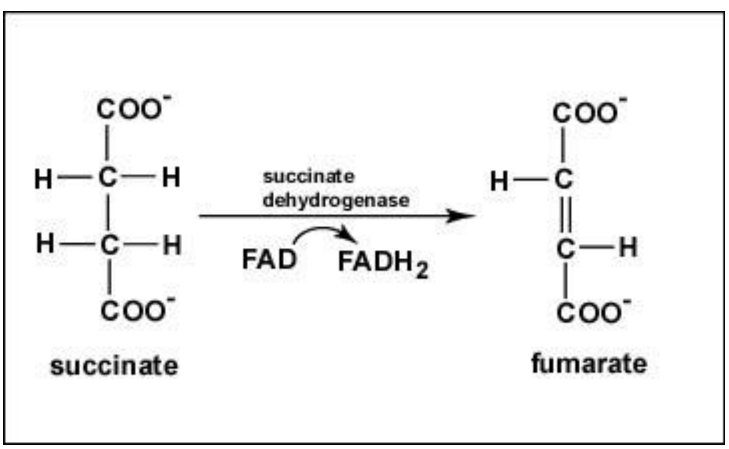
The energy released is used to make guanosine triphosphate (GTP) from guanosine diphosphate (GDP) and Pi by substrate-level phosphorylation. GTP can then be used to make ATP. The enzyme **succinyl-CoA synthase** catalyzes this reaction of the citric acid cycle.



Reaction 6: Oxidation of Succinate to Fumarate

Succinate is oxidized to **fumarate**.

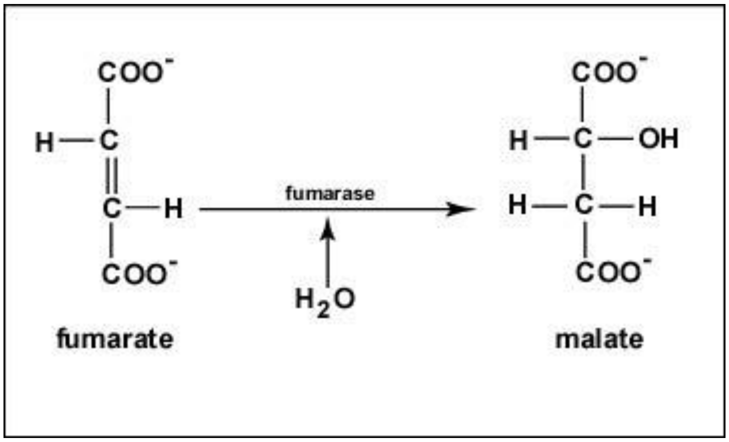
During this oxidation, FAD is reduced to FADH2. The enzyme **succinate dehydrogenase** catalyzes the removal of two hydrogens from succinate.



Reaction 7: Hydration of Fumarate to Malate

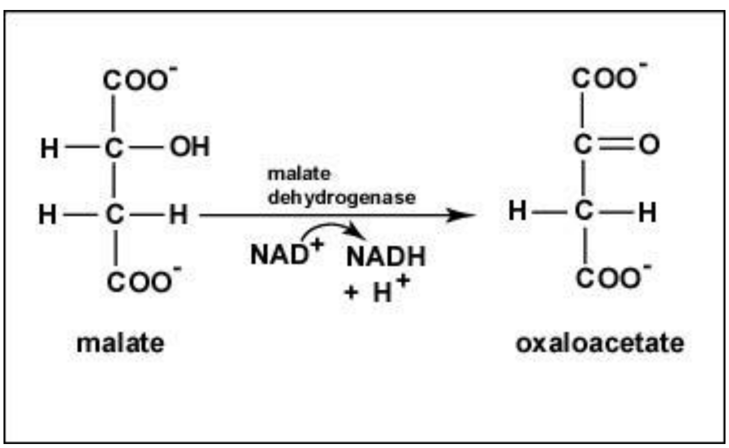
The reversible hydration of **fumarate** to **L-malate** is catalyzed by **fumarase (fumarate hydratase).**

Fumarase continues the rearrangement process by adding **Hydrogen** and **Oxygen** back into the substrate that had been previously removed.



Reaction 8: Oxidation of Malate to Oxaloacetate

Malate is oxidized to produce **oxaloacetate**, the starting compound of the citric acid cycle by **malate dehydrogenase**. During this oxidation, NAD+ is reduced to NADH + H+.



ATP Generation

Total ATP = 12 ATP

- 3 NAD+ = 9 ATP
- 1 FAD = 2 ATP
- 1 ATP = 1 ATP

Reviewing the whole process, the Krebs cycle primarily transforms the acetyl group and water, into carbon dioxide and energized forms of the other reactants.

Significance of Krebs Cycle

1. Intermediate compounds formed during Krebs cycle are used for the synthesis of biomolecules like amino acids, nucleotides, chlorophyll, cytochromes and fats etc.
2. Intermediate like succinyl CoA takes part in the formation of chlorophyll.
3. Amino Acids are formed from α- Ketoglutaric acid, pyruvic acids and oxaloacetic acid.
4. Krebs cycle (citric Acid cycle) releases plenty of energy (ATP) required for various metabolic activities of cell.
5. By this cycle, carbon skeleton are got, which are used in process of growth and for maintaining the cells.