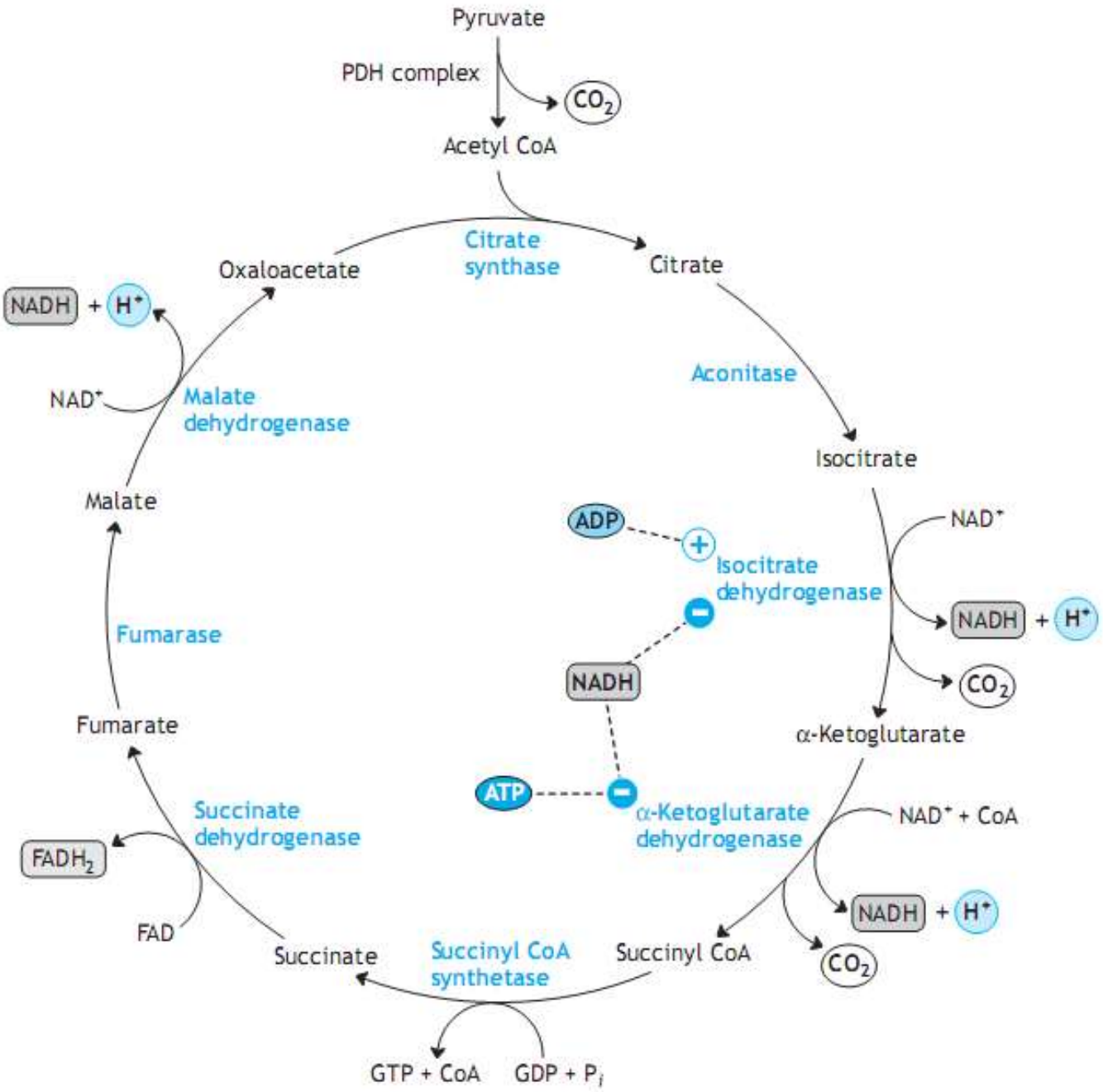
CITRIC ACID CYCLE

-Ms. Rupal Mishra

Introduction

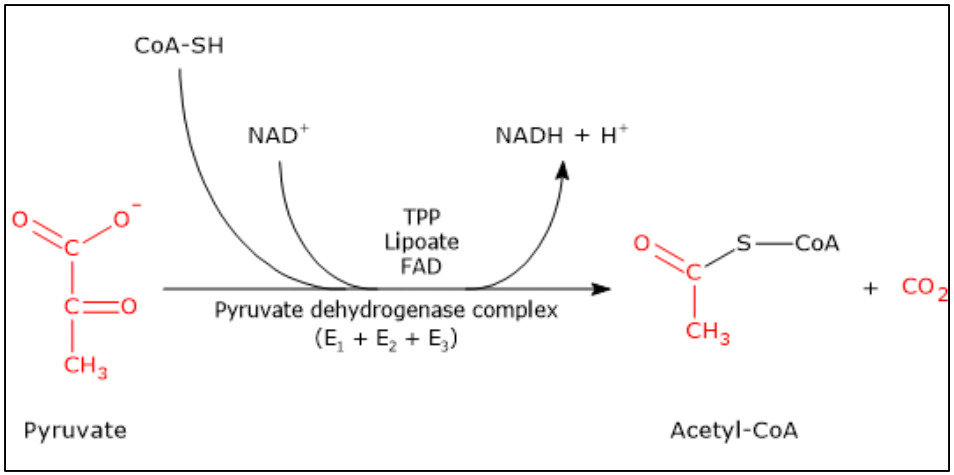
- It is called the Krebs cycle or the tri-carboxylic cycle (TCA).
- TCA cycle is the most important central pathway connecting almost all the individual metabolic pathways.
- Citric acid cycle or TCA cycle or tricarboxylic acid cycle essentially involves the oxidation of acetyl CoA to CO_2 & H_2O.
- Location of the TCA cycle: Reactions of occur in mitochondrial matrix, in close proximity to the ETC.

CAC

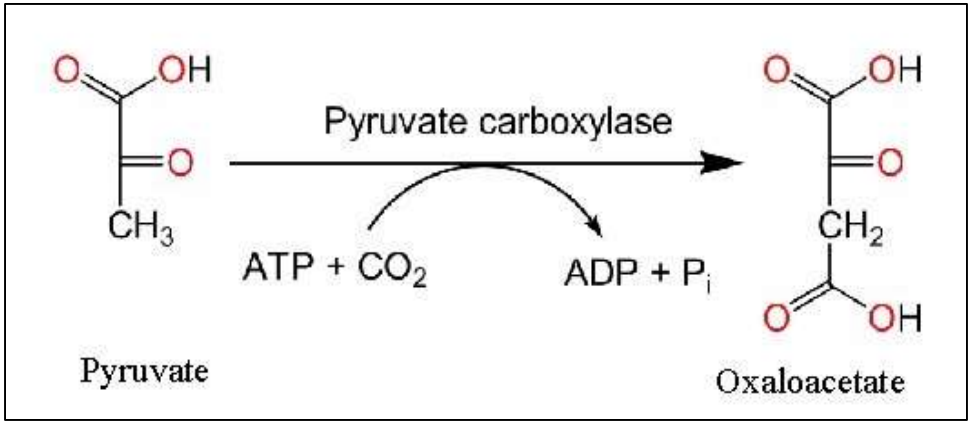

Pyruvate
PDH complex
CO_2
Acetyl CoA
Citrate synthase
Oxaloacetate
Citrate
Aconitase
Isocitrate
NADH + H^+
NAD^+
Malate dehydrogenase
Malate
ADP
Isocitrate dehydrogenase
NAD^+
NADH + H^+
CO_2
NADH
Fumarase
Fumarate
α-Ketoglutarate
ATP
α-Ketoglutarate dehydrogenase
NAD^+ + CoA
Succinate dehydrogenase
$FADH_2$
FAD
NADH + H^+
CO_2
Succinate
Succinyl CoA synthetase
Succinyl CoA
GTP + CoA
GDP + P_i

Preparatory Phase

Conversion of Pyruvate to Acetyl-CoA



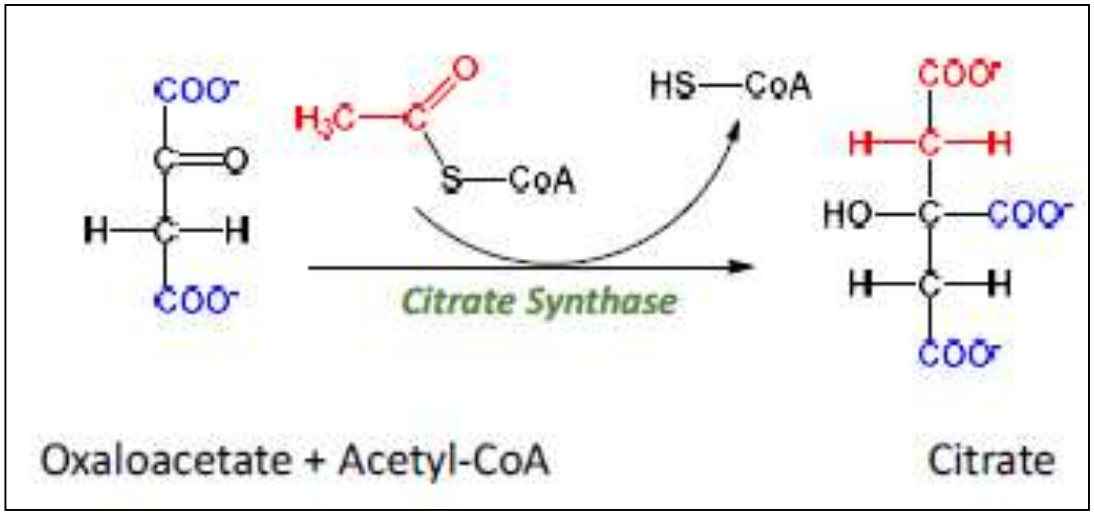
Conversion of Pyruvate to Oxaloacetate



Steps of the Cycle

Step1- Formation of citrate

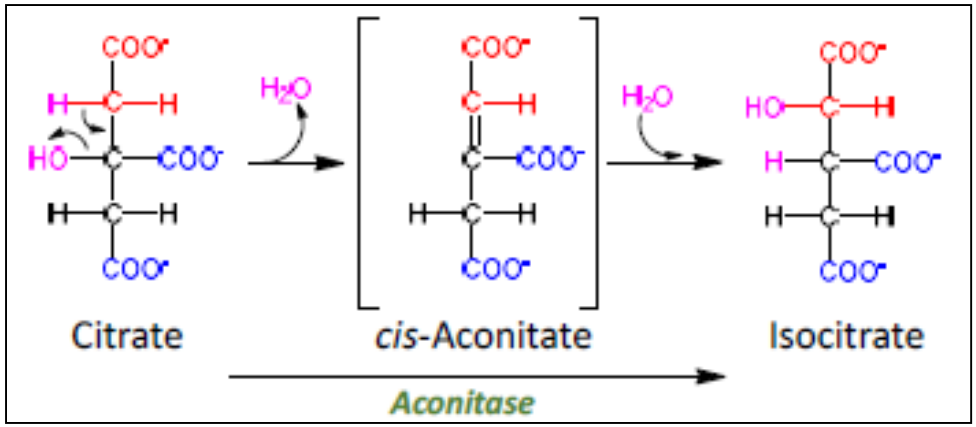
- Oxaloacetate condenses with acetyl CoA to form Citrate, catalysed by the enzyme citrate synthase .



Steps of the Cycle

Step2- Formation of Isocitrate via cis-Aconitate

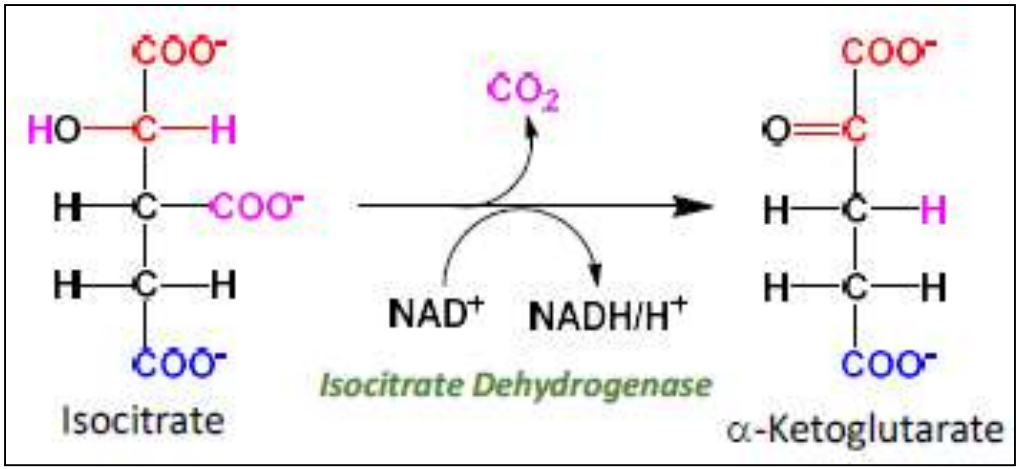
- Reaction is the isomerization of citrate to isocitrate, and it is mediated by an enzyme named Aconitase.
- The enzyme is named for the cis-aconitate intermediate that forms during the reaction.



Steps of the Cycle

Step3- Oxidation of Isocitrate to alpha-Ketoglutarate & CO_2

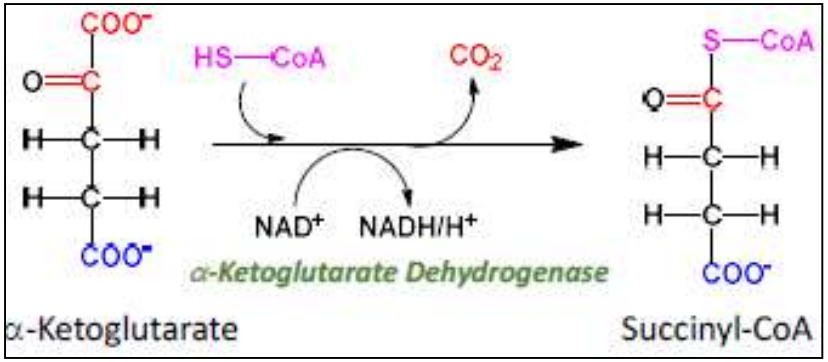
- Isocitrate undergoes both oxidation and decarboxylation to form alpha-Ketoglutarate.
- CO2 is released and a molecule of NADH is formed in the process.



Steps of the Cycle

Step4- Oxidation of alpha-Ketoglutarate to Succinyl-CoA and CO2

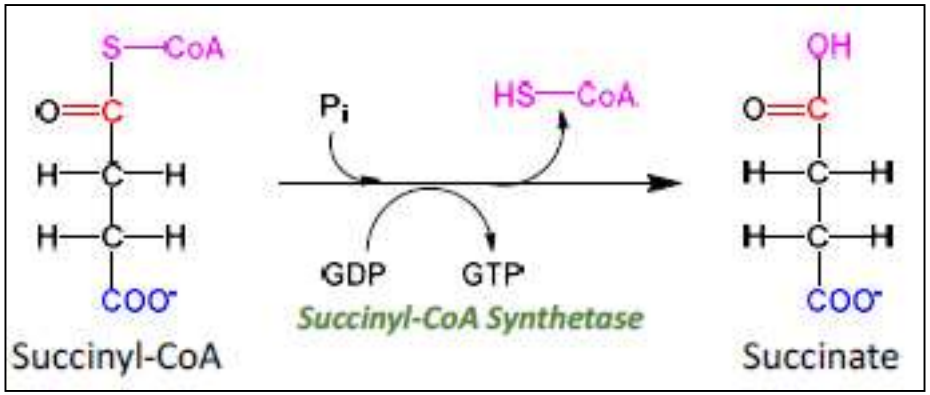
- The alpha-ketoglutarate dehydrogenase (KGDH) has a reaction mechanism that is very similar with pyruvate dehydrogenase (PDH) complex.
- It also liberates CO2 and a molecule of NADH and a proton, in the process of forming Succinyl-CoA.



Steps of the Cycle

Step5- Conversion of Succinyl-CoA to Succinate

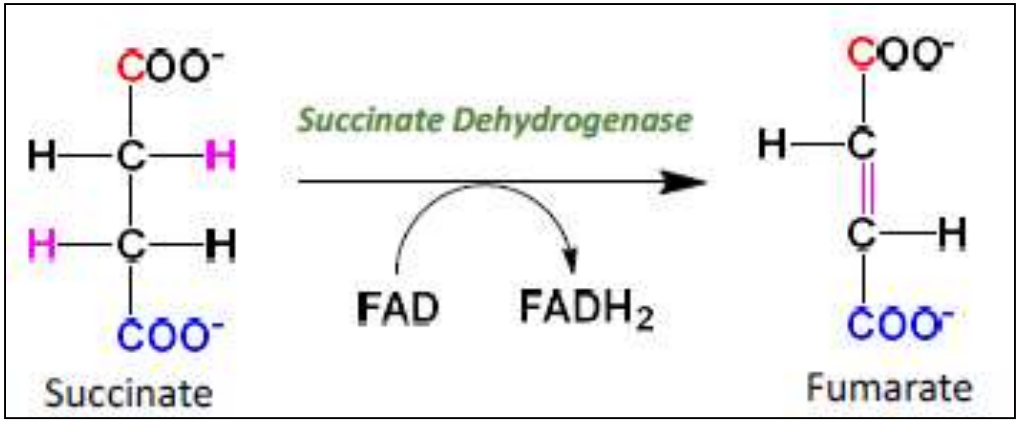
- The Succinyl-CoA synthetase is an enzyme that creates a molecule of GTP (ATP equivalent) through the phosphorylation of GDP.
- This process releases the Coenzyme A and forms a molecule of succinate.



Steps of the Cycle

Step6- Oxidation of Succinate to Fumarate

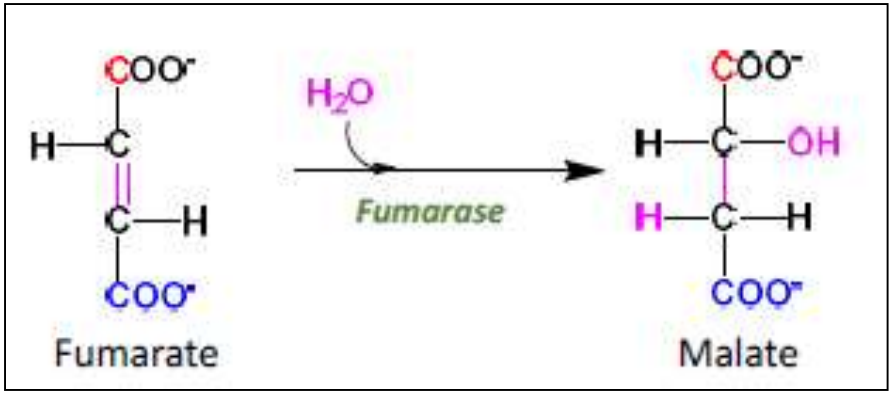
- The succinate formed from succinyl-CoA is oxidized to fumarate by the flavoprotein succinate dehydrogenase.



Steps of the Cycle

Step7- Hydration of Fumarate to Malate

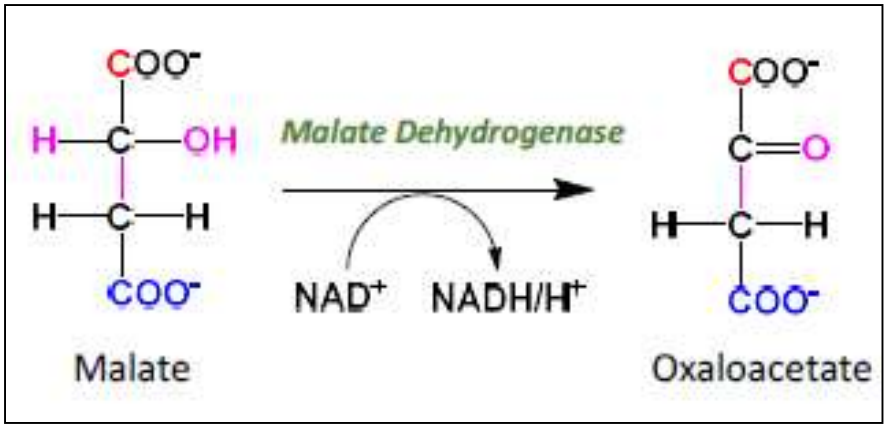
- In this reaction, the lyase, known as fumarase, converts fumarate to malate.
- This enzyme is also a hydrolase, as water is incorporated into the final structure.



Steps of the Cycle

Step8- Oxidation of Malate to Oxaloacetate

- In the last reaction of the citric acid cycle, NAD-linked L-malate dehydrogenase catalyzes the oxidation of L-malate to oxaloacetate



Energy Yield in Kreb Cycle

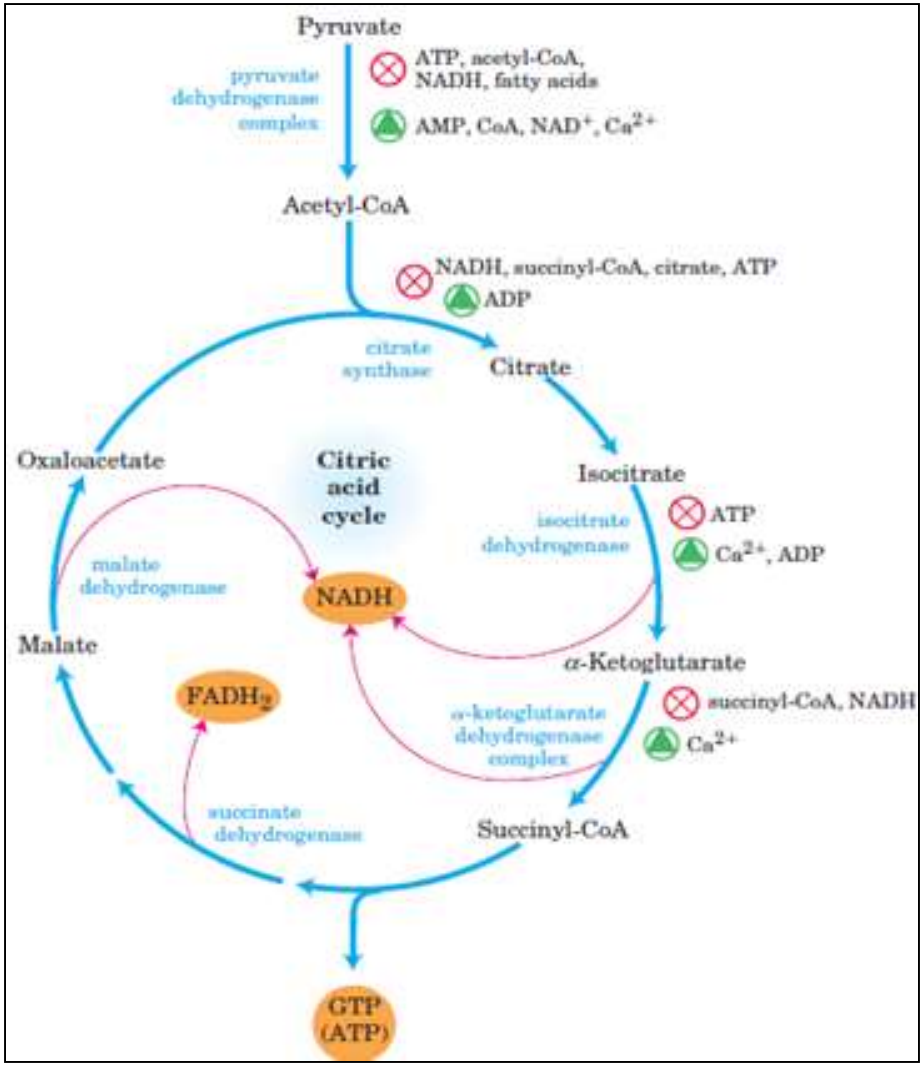
- Per Cycle
  - 3 NADH/H+
  - 1 FADH2
  - 1 GTP (ATP equivalents)

- Per Glucose = 2 Cycles (2 Acetyl-CoA molecules)
  - 6 NADH/H+
  - 2 FADH2
  - 2 GTP (ATP equivalents)

Regulation of the Kreb Cycle

Each of the Four strongly exergonic steps in the cycle those catalyzed by –

1. Pyruvate Dehydrogenase Complex
2. Citrate synthase
3. Isocitrate dehydrogenase
4. Alpha-ketoglutarate dehydrogenase



Regulation of the Kreb Cycle

- The **First step** is the conversion of Pyruvate into Acetyl Coenzyme A i.e., where Pyruvate Dehydrogenase Complex is involved.
- The **Second step** is conversion of oxaloacetate into citrate with the help of enzymes Citrate Synthase.
- The **Third step** is the conversion of Isocitrate into α-Ketoglutarate is also one of the regulating steps.
- The **Forth step** is the conversion of α-Ketoglutarate into Succinyl Coenzyme A.

THANK YOU