VIVEKANANDA COLLEGE
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NAAC ACCREDITED 'A' GRADE

Topic:	RESPIRATION
Course Title:	PLANT PHYSIOLOGY AND METABOLISM
Paper:	BOT-G-CC-4-4-TH
Unit:	5.1
Semester:	IV
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Name of the Department:	Botany (Morning)

KREBS CYCLE (TCA cycle)

The **tricarboxylic acid (TCA) cycle,** also known as the **Krebs or citric acid cycle (CAC)**, is the **main source of energy for cells** and an important part of aerobic respiration. The cycle harnesses the available chemical energy of **acetyl coenzyme A** (acetyl CoA) **into** the reducing power of nicotinamide adenine dinucleotide (**NADH**).

The cycle was first elucidated by scientist Sir Hans Adolf Krebs (1900 to 1981). He shared the Nobel Prize for physiology and Medicine in 1953 with Fritz Albert Lipmann, the father of ATP cycle.

The TCA cycle is part of the larger glucose metabolism whereby glucose is oxidized to form pyruvate, which is then oxidized and enters the TCA cycle as acetyl-CoA.

The process oxidises **glucose derivatives, fatty acids and amino acids** to carbon dioxide (CO2) 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 FADH2 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).

Half of the intermediates on which the cycle depends are also the origin of pathways leading to important compounds such as fatty acids, amino acids, or porphyrins. If any of these intermediates are thus diverted, the integrity of the cycle is broken and the cycle no longer functions. Production of essential energy can only be resumed if the diverted intermediate or a subsequent intermediate that leads to oxaloacetate can be replenished by *anaplerotic* (refilling) reactions.

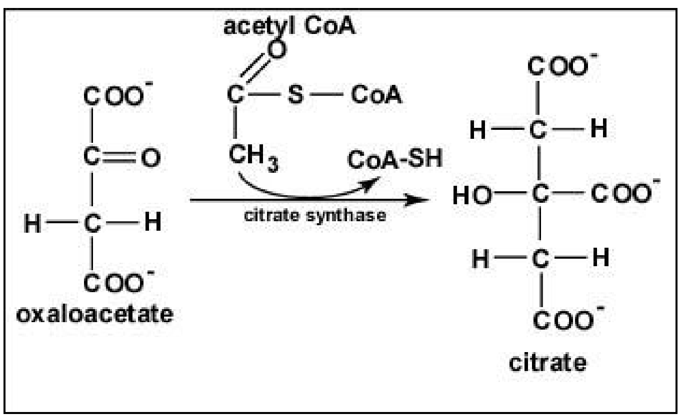
- ***Location*** **:** In prokaryotic cells, the citric acid cycle occurs in the cytoplasm; in eukaryotic cells, the citric acid cycle takes place in the matrix of the mitochondria.

- ***Krebs cycle consists of eight reactions which are as follows:***

Reaction 1: Formation of Citrate (condensation reaction)

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.

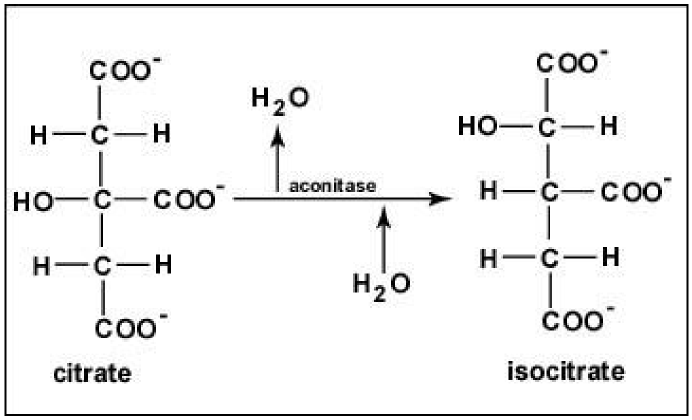


Reaction 2: Formation of Isocitrate (hydration reaction)

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

In this reaction, **a water molecule is removed** from the citric acid (resulting cis- aconitic 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 (oxidative decarboxylation)

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**.

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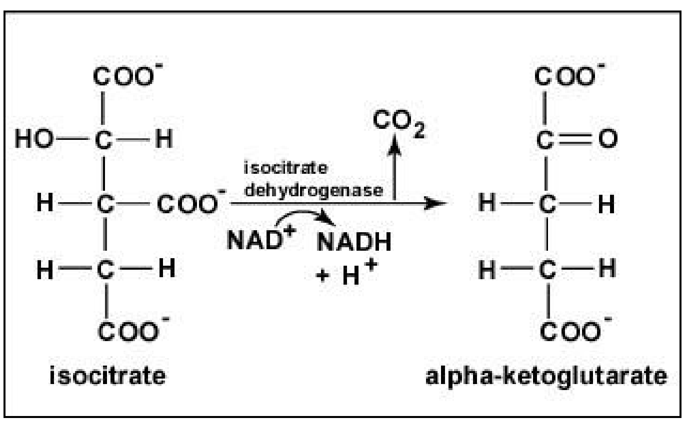
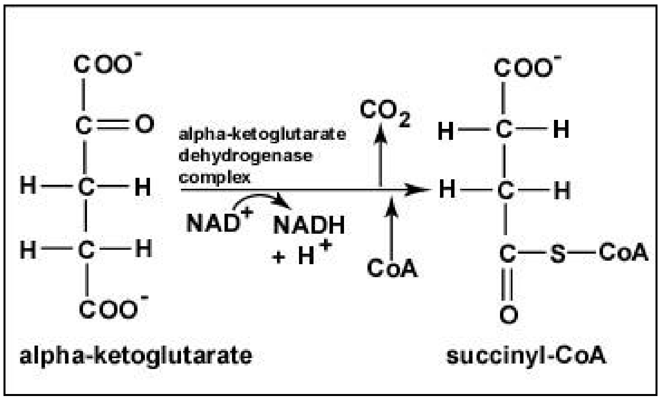


Reaction 4: Oxidation of α-Ketoglutarate to Succinyl-CoA (oxidative decarboxylation)

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

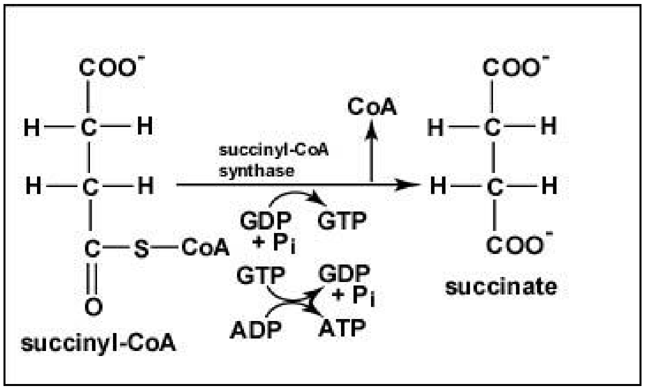
During this oxidation, NAD+ is reduced to NADH + H+. The enzyme that catalyzes this reaction is **alpha-ketoglutarate dehydrogenase.**



Reaction 5: Conversion of Succinyl-CoA to Succinate (substrate level phosphorylation)

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

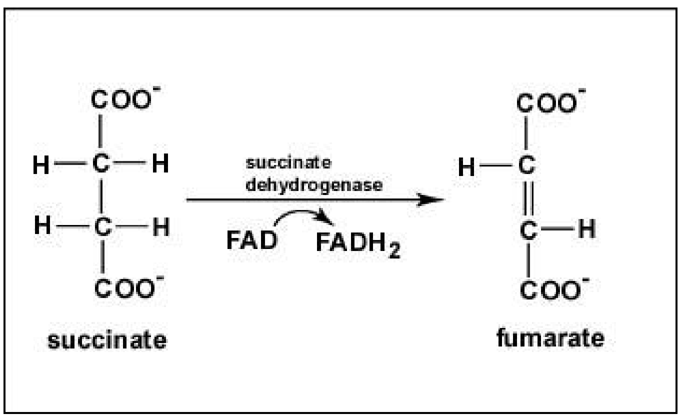
The energy released is used to make guanosine triphosphate (GTP) from guanosine diphosphate (GDP) and Pi by substrate-level phosphorylation. GTP can then be used to make ATP. The enzyme **succinyl-CoA synthase** catalyzes this reaction of the citric acid cycle.



Reaction 6: Conversion of Succinate to Fumarate (oxidation reaction)

Succinate is oxidized to **fumarate**.

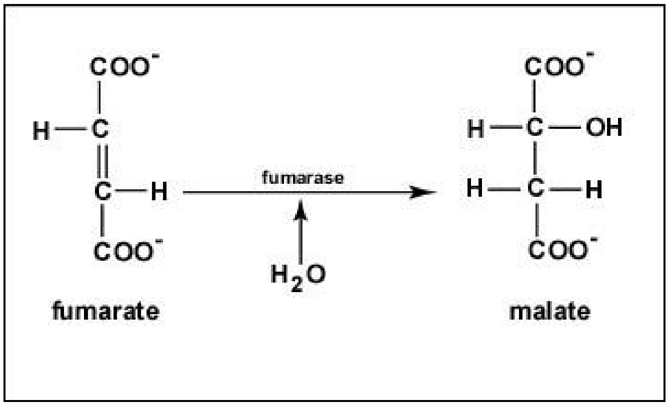
During this oxidation, FAD is reduced to FADH2. The enzyme **succinate dehydrogenase** catalyzes the removal of two hydrogens from succinate.



Reaction 7: Conversion of Fumarate to Malate (hydration reaction)

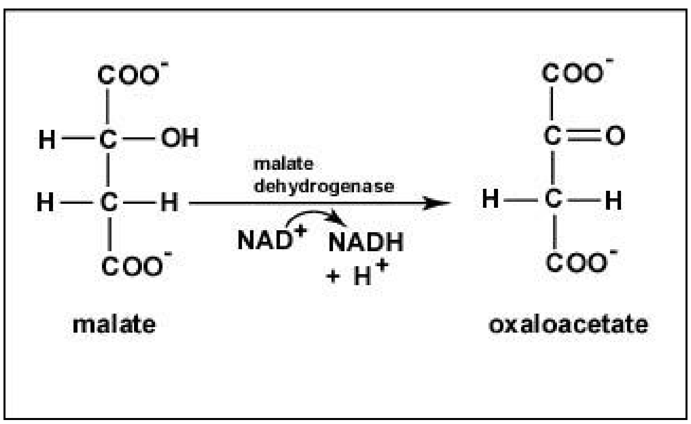
The reversible hydration of **fumarate** to **L-malate** is catalyzed by **fumarase (fumarate hydratase).**

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



Reaction 8: Conversion of Malate to Oxaloacetate (oxidation reaction)

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+.



The Net Equation:

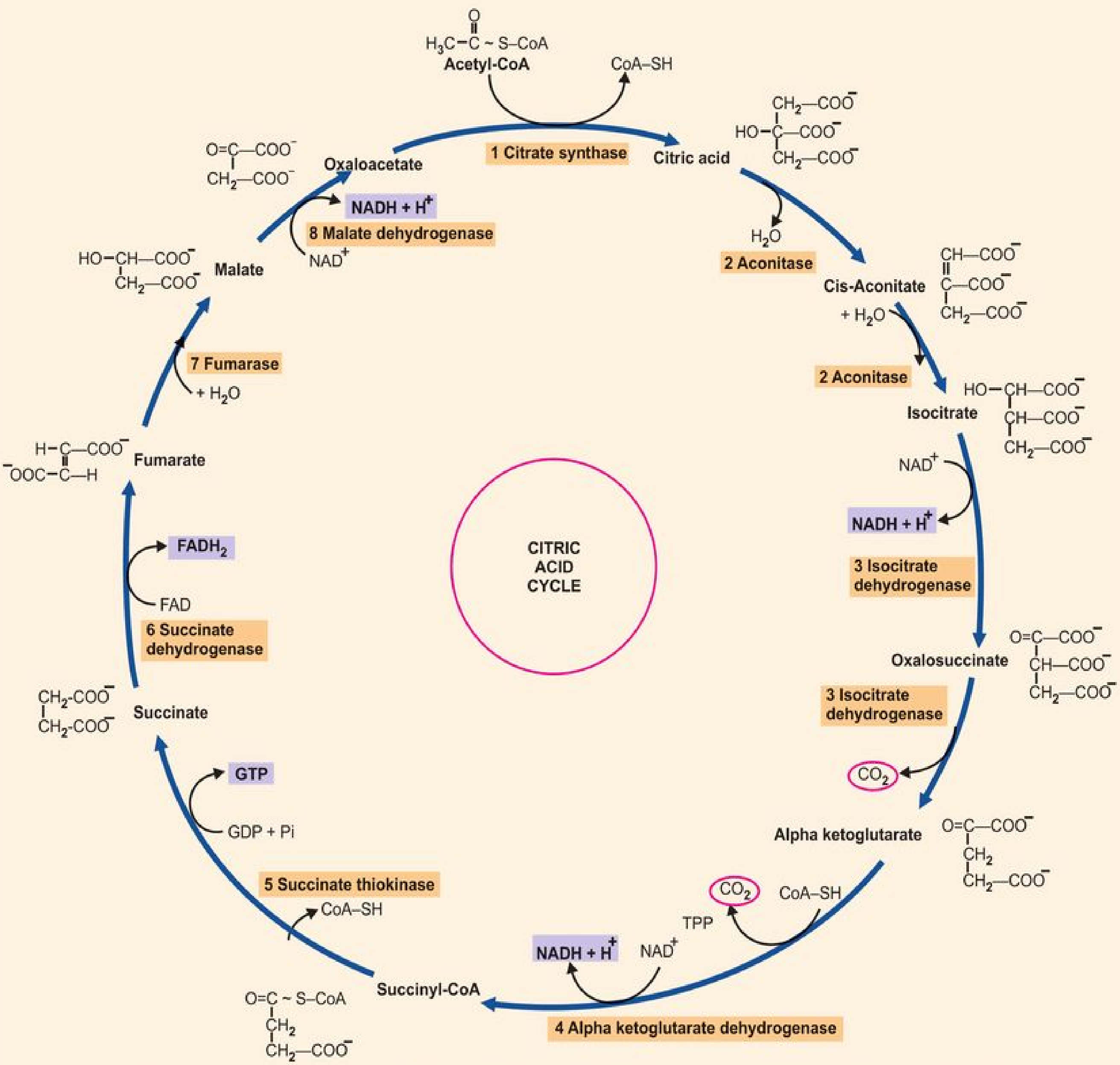
Acetyl CoA + 3 NAD + FAD + ADP + Pi ————> 2 CO_2 + CoA + 3 $NADH^+$ + $FADH^+$ + ATP

ATP Generation *(from 1 molecule of acetyl CoA entering TCA cycle):*

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.



Acetyl CoA (2 carbon), enters the cycle. These are released as CO_2 in steps 3 and 4. So Acetyl CoA is completely oxidized by the time cycle reaches alpha ketoglutarate.

All reactions are reversible; except 1st and 4th steps

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. The Krebs cycle (citric Acid cycle) releases plenty of energy (ATP) required for various metabolic activities of cells.
5. By this cycle, carbon skeletons are obtained, which are used in the process of growth and for maintaining the cells.