CITRIC ACID CYCLE= TCA CYCLE =KREBS CYCLE

(TCA = Tricarboxylic acid cycle)

In 1937, Sir Hans krebs proposed a complete cycle, and in 1953 got nobel prize for it.

Definition:

Acetyl CoA is completely *oxidized* to CO_2 in a cycle of reactions with simultaneous production of energy is termed as the *citric acid cycle.*

Acetyl-CoA, is derived from pyruvate and other metabolites

All enzymes are in the mitochondrial m**atrix**

Functions of TCA cycle

Final common oxidative pathway that oxidises acetyl CoA to CO_2

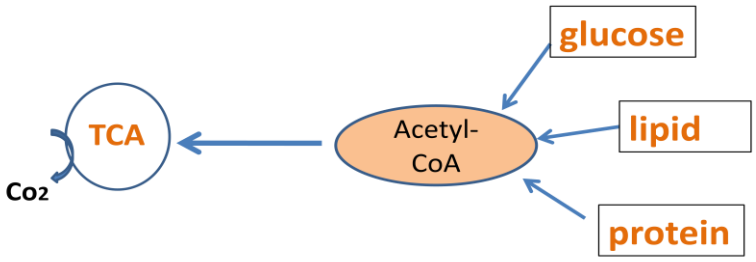
The source of reduced coenzymes that provide the substrate for the respiratory chain

The link between catabolic and anabolic pathways (amphibolic role)

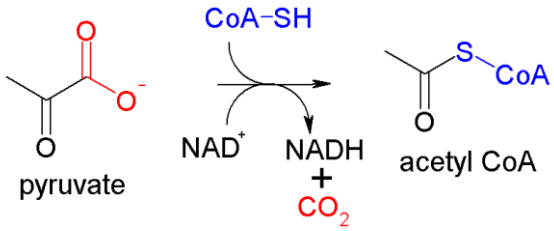
Provides precursors for synthesis of amino acids and nucleotides

Components of the cycle have a direct or indirect controlling effects on key enzymes of the pathways

The citric acid cycle is final common oxidative pathway



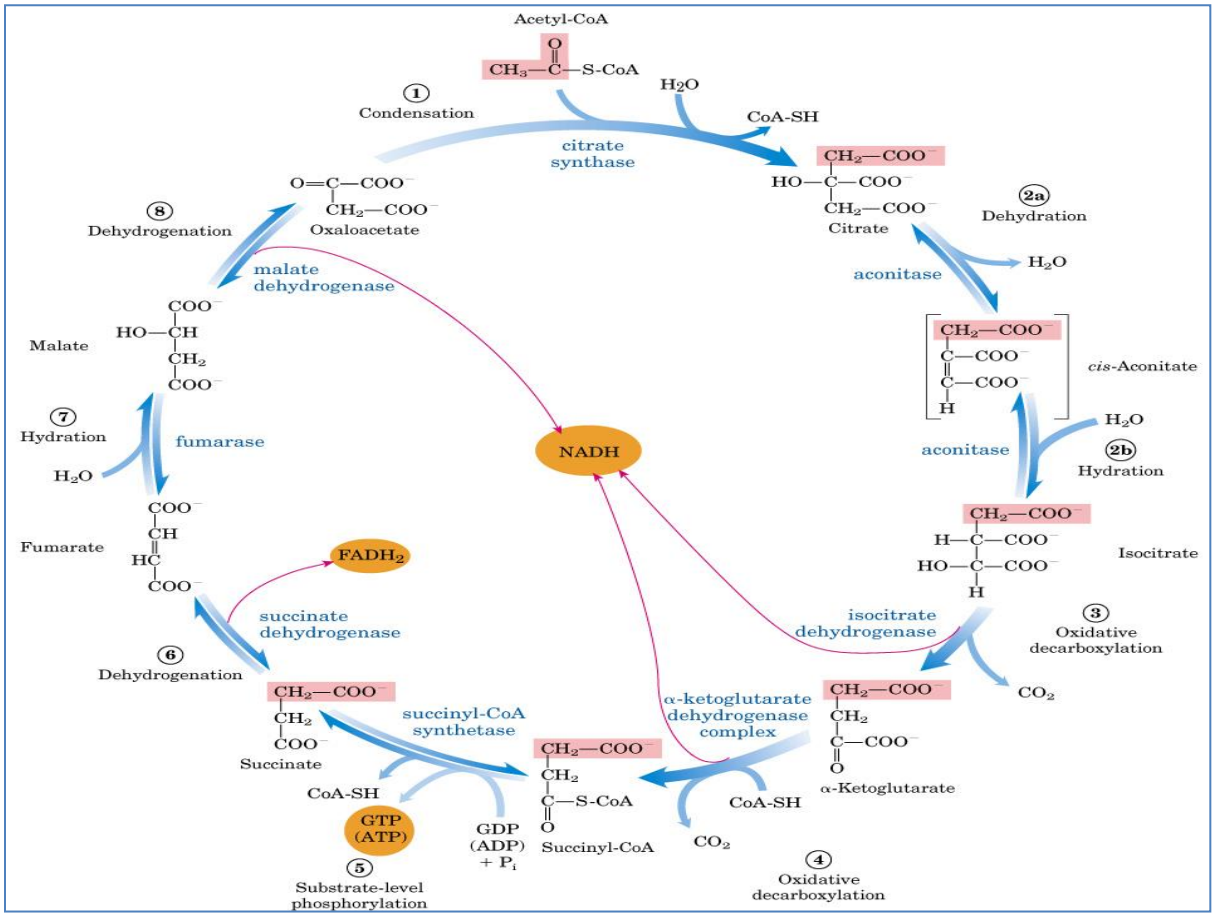
Conversion of pyruvate to acetyl-CoA



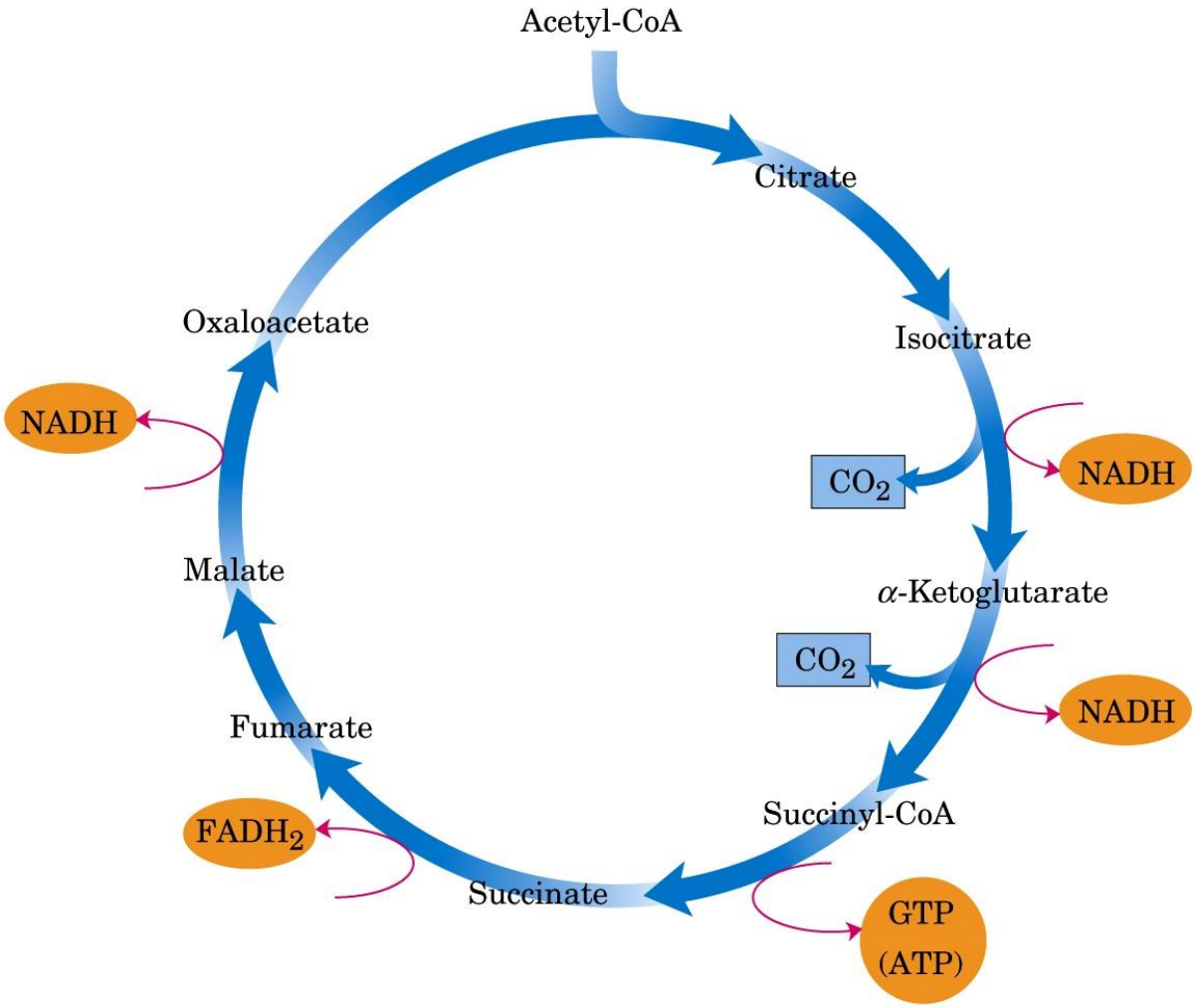
Enzyme = pyruvate dehydrogenase complex and Location = mitochondrial matrix

Irreversible

Irreversible means acetyl-CoA cannot flow backward to pyruvate; hence “fat cannot be converted to carbohydrate”



Each turn of the citric acid cycle produces 3 NADH, 1 $FADH_2$, 1 GTP (or ATP), and 2 CO_2



What is the maximum yield of high energy ATP in the aerobic catabolism of glucose?

Glycolysis:

glucose →2pyruvate + 2NADH+2ATP 7 ATPs

Pyruvate Dehydrogenase:

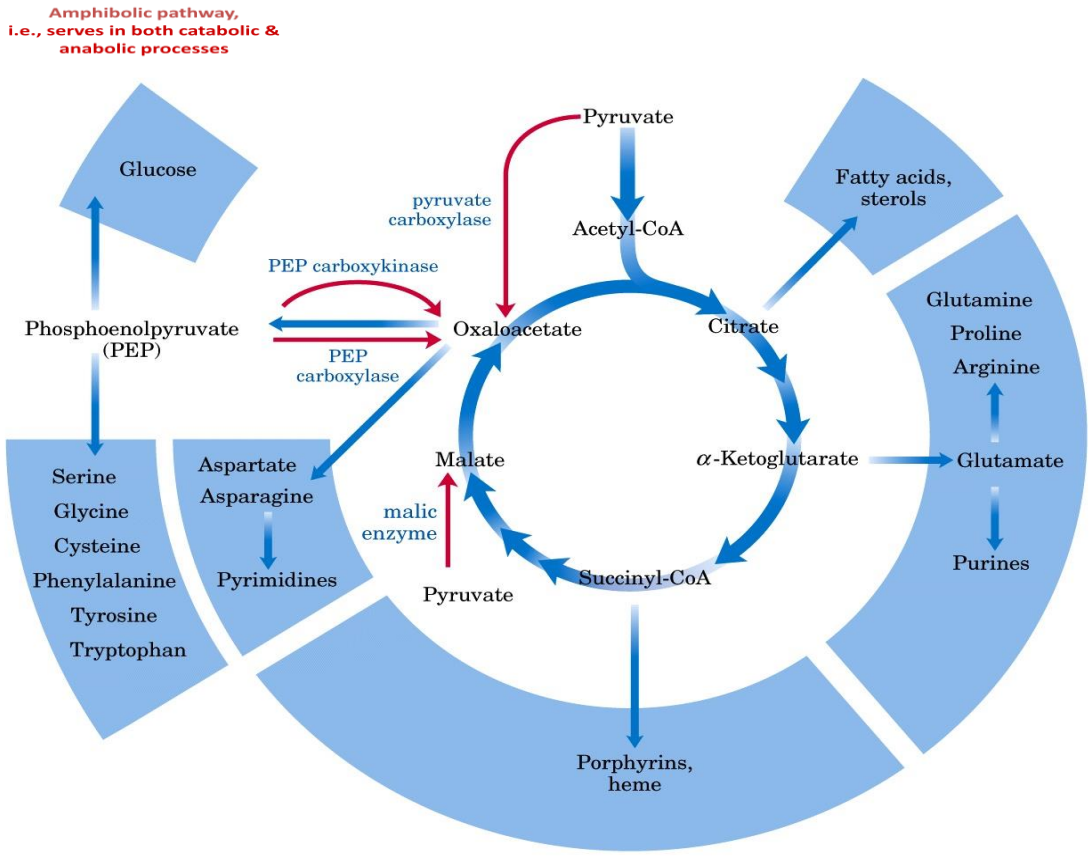
2pyruvate → 2acetyl CoA + 2NADH 5 ATPs

TCA cycle:

acetyl CoA→$2CO_2$+3NADH+$FADH_2$+GTP 20ATPs

OVERALL yield from glucose 32 ATPs

Citric acid cycle components are important biosynthetic intermediates



REGULATION OF CITRIC ACID CYCLE

The citric acid cycle is regulated at its three exergonic steps

Citrate and Citrate synthase- ATP is an allosteric inhibitor.

Citrate inhibits PFK, fruc 1,6 bis phosphatase,, activates acetyl coA carboxylase

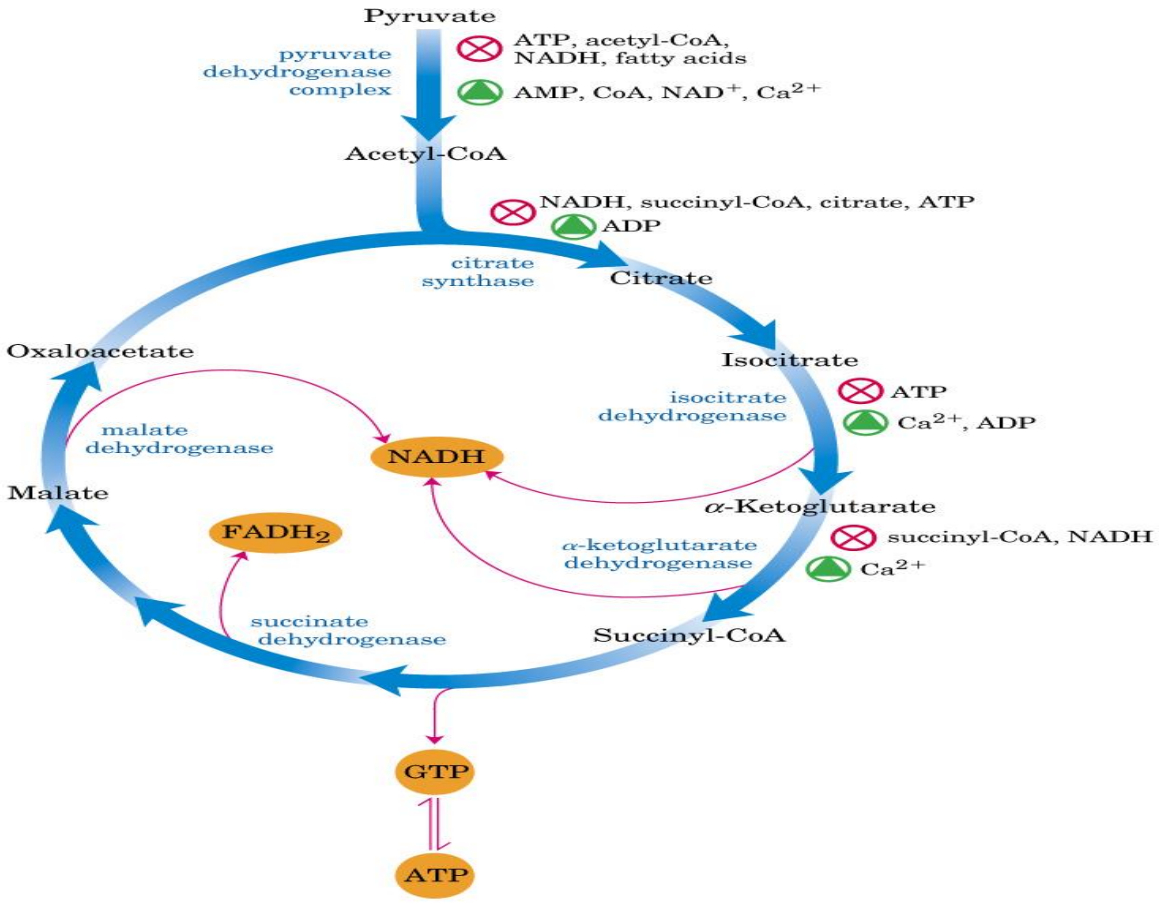
Isocitrate dehydrogenase – ADP acts a Positive modifier ehancing the binding of substrate

α –Ketoglutarate Dehydrogenase- inhibited by NADH and succinyl CoA

Availability of ADP- When energy charge of the cell is low the cycle operates at faster rate

Anaerobiasis inhibit ETC, when NADH, FADH are accumulated

In turn inhibits TCA cycle



ENERGETICS OF TCA CYCLE/ ATP GENERATION

Step No	Reactions	Co-enzymes	No. of ATP' s generated
3	Isocitrate ⟶ Alpha Ketoglutarate	NADH	2.5
4	Alpha Ketoglutarate ⟶ Succinyl-CoA	NADH	2.5
5	Succinyl-CoA ⟶ Succinate	GTP	1
6	Succinate ⟶ Fumarate	FADH2	1.5
8	Malate ⟶ Oxalo acetate	NADH	2.5
		TOTAL	10 per Acetate For 2 acetate 20 ATP