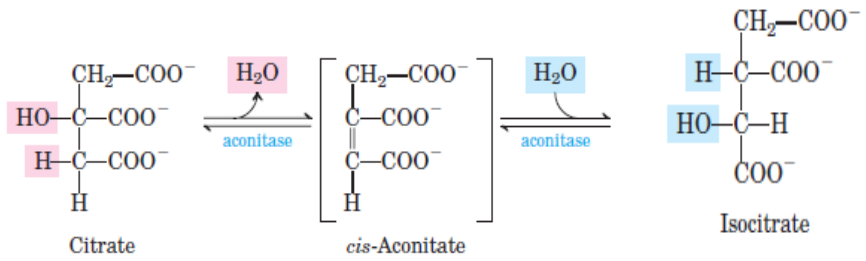
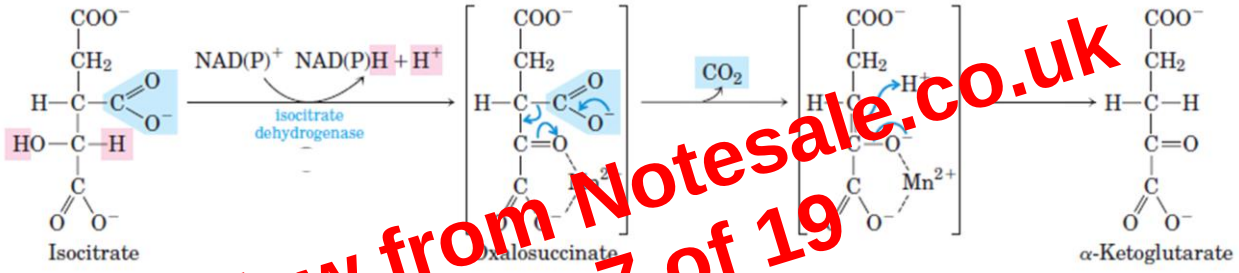


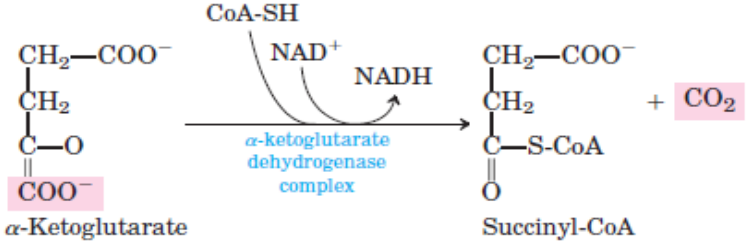
Fluoroacetate often used as a rodenticide inhibits the aconitase enzyme activity. Naturally it is non-toxic, but in the body, it is metabolized to fluoroacetyl-CoA, which gives rise to fluorocitrate after condensing with oxaloacetate. The aconitase is strongly inhibited by fluorocitrate. This is a form of metabolic lethal synthesis.

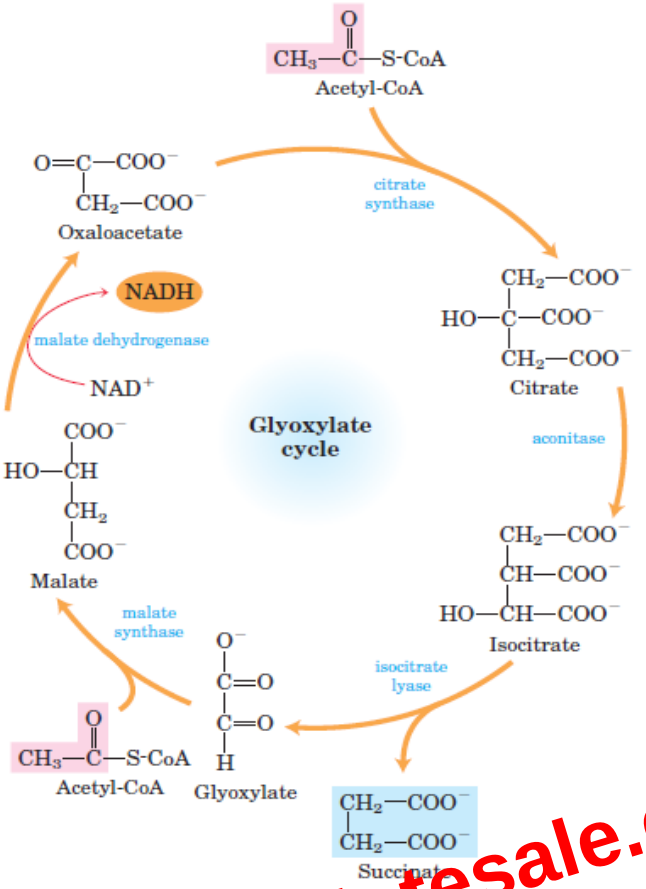
STEP3: Oxidation of Isocitrate to α-ketoglutarate and CO_2: at this stage, the enzyme "isocitrate dehydrogenase" catalyzes the oxidative decarboxylation of isocitrate to α-ketoglutarate . This reaction involves a carbonyl intermediate (oxalosuccinate). Also , manganese ion is a required cofactor, while either NAD+ or NADP function as a coenzyme in the reaction(depending on the form of isocitrate dehydrogenase present); reducing C2 –OH group to a keto group



STEP4: Oxidation of α-ketoglutarate to succinylCoA and CO_2: this step is another oxidative decarboxylation in which α-ketoglutarate is converted to succcinylCoA and CO_2 by the enzyme "α-ketoglutarate dehydrogenase complex".in this reaction, NAD+ is the electron acceptor and CoA-SH functions as the carrier of the succinyl group.

It is worthy of note that the enzyme involved; α-ketoglutarate dehydrogenase closely resembles the PDH complex in structure and function, having three domain homologous to the E1, E2, & E3 of PDH complex, as well as enzyme bound TPP, lipoate, NAD and CoA-SH, the main difference between the two homologous enzyme is their substrate specificities at their E1 domain





In conclusion, it is imperative that we learn the co-ordinate regulation between the glyoxylate cycle and the citric acid cycle.

Between the glyoxylate cycle and the citric acid cycle, four distinct pathways participate in the conversion:

a. **Fatty acid catabolism into acetylCoA (in the glyoxysome)**

b. **The glyoxylate cycle (in the glyoxysome)**

c. **The citric acid cycle (in the mitochondria)**

d. **Gluconeogenesis (in the cytosol)**

Isocitrate is a crucial intermediate at the branch point between glyoxylate and the citric acid cycle. Isocitrate dehydrogenase is regulated by covalent modification: through a specific Protein kinase which phosphorylates and inactivates the dehydrogenase and shunts isocitrate (the substrate) into the glyoxylate cycle.

Another enzyme Phosphoprotein-phosphatase removes the phosphoryl group from the isocitrate dehydrogenase; activating it and signaling the proceeding of the citric acid cycle.

References

This study guide is a simplified and compressive presentation of the topic compiled from Success biochemistry academy lecture note and some other trusted biochemistry authority and classical textbook. All pieced together in a simplified easily digestible form for all and sundry.

Classical textbooks whose phrases and picture reflect in this writeup are:

1. **Lehningher principles of biochemistry, 6th edition, David Nelson & Micheal Cox**
2. **Medical Biochemistry by N. Mallikarjuna Rao**
3. **Harper's illustrated biochemistry, 26th edition. Murray, Granner, Mayer, Rodwell**
4. **Textbook of medical biochemistry. MN Chatterjea, Rana shinde**
5. **Biochemistry: the chemical reactions of living cell . David Metzler**
6. **Fundamentals of biochemistry, life at molecular level. Donald & Judith Voet, Charlotte Pratt**